Bone-Forming Tumors

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KEYWORDS

• Bone • Neoplasm • Osteoid osteoma • Osteoblastoma • Fibrous dysplasia • Osteosarcoma

Key points

1. Bone-forming tumors have a broad spectrum of biological behavior and morphology and their accurate diagnosis requires correlation of their clinical, pathologic, and radiological findings.
2. Benign bone-forming tumors are usually slow growing, well demarcated, and composed of cytologically benign cells that deposit neoplastic trabeculae of woven bone. These tumors have the potential to locally recur and are usually ablated or removed surgically by curettage or en bloc resection.
3. Malignant bone-forming tumors (ie, osteosarcomas) are usually rapidly growing, large, destructive neoplasms composed of malignant cells that at least focally deposit recognizable tumor bone. High-grade tumors are aggressive and need to be treated with systemic therapy, wide resection, and radiotherapy when indicated.

ABSTRACT

Bone-forming tumors are defined by neoplastic cells that differentiate along the lines of osteoblasts that deposit woven bone. The morphology and biological spectrum of bone-forming tumors is broad and their accurate diagnosis requires the careful correlation of their clinical, morphologic, and radiological characteristics. Immunohistochemical and molecular analyses have an important role in select instances. At present, the identification of neoplastic bone largely depends on histologic analysis, which can be subjective. The major types of osteosarcoma are defined according to their morphology, origin within or on the surface of the bone, and their histologic grade.

OVERVIEW

Bone-forming tumors are defined as benign or malignant neoplasms in which the proliferating cells have an osteoblastic phenotype and manufacture and secrete the organic components of bone, which may or may not mineralize.[1] These tumors are heterogeneous and have a broad spectrum of biological behavior ranging from indolent to very aggressive with a rapidly fatal outcome. Their accurate diagnosis is critical to patient care and incorporates careful assessment of the clinical, radiological, and pathologic features; an incorrect diagnosis can result in significant mismanagement of the patient. At present, the identification of osteoblastic phenotype in surgical pathology is based on histologic analysis. Important lineage-specific molecules related to osteoblasts such as runt-related transcription factor 2 (RUNX2), Osterix, and special AT-rich sequence-binding protein 2 (SATB2) have been identified. Although these molecules are sensitive markers of osteoblastic differentiation, they are also expressed in nonosteoblastic neoplasms, therefore the immunohistochemical expression of these markers in neoplasms should be carefully assessed in the context of the morphology of the tumor.[2–4] Molecular analysis can be useful in select situations and requires tissue to be fixed and decalcified in a manner that does not degrade nucleic acids.

OSTEOID OSTEOMA

Osteoid osteoma is a benign, usually solitary, bone-forming tumor that by definition is 2 cm or less in diameter (**Table 1**). The neoplastic nature

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Table 1
Key points of osteoid osteoma and osteoblastoma

Osteoid Osteoma	Osteoblastoma
• Incidence: accounts for 13% of all primary benign bone tumors	• Uncommon; accounts for 1% of primary bone tumors
• Small size; <2 cm	• Larger tumor; >2 cm
• Limited growth potential	• Locally aggressive
• Severe localized pain often worse at night, relieved by aspirin or other nonsteroidal antiinflammatory medication	• Constant achy pain
• Imaging: well-defined, round, lucent tumor surrounded by zone of sclerosis	• Expansile, well-defined, oval, mixed lytic and blastic mass
• Radiofrequency ablation is treatment of choice	• Curettage or en bloc excision

of osteoid osteoma has been questioned because of its limited growth potential; however, cytogenetic studies have shown aberration of chromosome 22q, which supports the concept that the lesion is neoplastic.[5]

Osteoid osteoma accounts for approximately 10% to 12% of benign bone tumors and 3% of all primary bone tumors.[6] It most commonly develops in individuals 5 to 25 years of age, has a peak incidence in the second decade of life, and there is a male predominance of 2:1 to 3:1. Osteoid osteoma can arise in any bone in the body, but most commonly develops in the long bones of the lower extremities, with the femoral neck being the single most frequent anatomic site.

Clinically, patients typically complain of severe localized pain that is often worse at night and that is relieved by aspirin or other nonsteroidal antiinflammatory medications. Patients with lesions located close to or within joints can present with joint pain, swelling, and effusions, mimicking a primary intra-articular process. Tumors located in the vertebral column can cause painful scoliosis secondary to paravertebral muscle spasm, whereas lesions of the small bones of the hands and feet may produce soft tissue swelling, mimicking infection.

On roentgenograms the lesion is usually round to oval, 1 to 2 cm in diameter, and has a targetoid appearance. The tumor shows avid uptake of technetium and computed tomography (CT) shows a well-circumscribed, lucent mass with central mineralization that is usually surrounded by a zone of sclerosis (**Fig. 1**). Significant surrounding bone marrow edema can be seen on fluid-sensitive MRI sequences. Technetium bone scan, CT, and MRI studies are very important in localizing intra-articular tumors and those obscured by abundant reactive bone.[7]

Grossly, osteoid osteomas are small, round to oval, sharply demarcated, gritty, and dark red with central tan-white speckled areas (**Fig. 2**). On histology, the well-circumscribed tumor is composed of haphazard, interanastomosing trabeculae and sheetlike aggregates of woven bone that are rimmed prominently by plump, metabolically active osteoblasts (**Fig. 3**). The stroma filling the intertrabecular spaces is composed of richly vascularized loose connective tissue containing fibroblasts and thin-walled, congested blood vessels. Osteoclasts are frequently scattered along the bony surfaces. Juxta-articular or intra-articular osteoid osteomas may be associated with a periosteal reaction and chronic synovitis that contains lymphoid follicles resembling rheumatoid arthritis.[8] The proliferating osteoblasts in osteoid osteoma show strong nuclear staining for Runx2 and Osterix.[2]

In the past, osteoid osteoma was frequently removed by curettage or en bloc resection; however, radiofrequency ablation is now the treatment of choice except for tumors that are in close proximity to crucial structures such as the spinal cord or articular cartilage. Minimally invasive techniques such as CT-guided core drill excision, cryoablation, and laser photocoagulation are other forms of effective therapy. The cure rate for osteoid osteoma varies according to technique but ranges from 80% to 90%.

OSTEOBLASTOMA

Osteoblastoma is histologically similar to osteoid osteoma but has greater growth potential and is more locally aggressive (see **Table 1**). The tumor is larger than 2 cm and commonly originates in the posterior elements of the spine, sacrum, mandible, and the metadiaphyseal region of the long tubular bones. Few cytogenetic abnormalities have been identified but they include a unique 3-way translocation involving