Seminars in Diagnostic Pathology (2011) 28, 73-85

ELSEVIER

Seminars in
Diagnostic
Pathology

Benign bone tumors—recent developments

Roberto A. Garcia, MD,[a] Carrie Y. Inwards, MD,[b] Krishnan K. Unni, MD[c]

From the [a]Department of Pathology, Mount Sinai School of Medicine, New York, New York; [b]Department of Pathology, Mayo Clinic College of Medicine, Rochester, Minnesota; and the [c]Department of Pathology, Elmbrook Memorial Hospital, Brookfield, Wisconsin.

KEYWORDS
Benign bone tumors;
Osteoid osteoma;
Osteoblastoma;
Fibrous dysplasia;
Osteochondroma;
Enchondroma;
Chondroblastoma;
Chondromyxoid fibroma;
Giant cell tumor;
Benign notochordal cell tumor

Benign bone tumors frequently pose a diagnostic challenge for general surgical pathologists. Accurate pathologic diagnosis requires careful clinical and radiological correlation. The most significant recent advances in some benign bone tumors have occurred at the molecular and cytogenetic level. The detection of clonal chromosomal aberrations, various specific molecular genetic events, and the description of the bone cell signaling pathways in the field of osteoimmunology have provided a better understanding of the pathophysiology of certain tumors and an important aid in the diagnostic workup and differential diagnosis of some bone lesions demonstrating overlapping clinical and pathologic features. Future directions include prognostic and therapeutic applications of these findings. Newer less invasive therapeutic techniques and medical management have been developed for the treatment of certain benign bone tumors.

Osteoid osteoma

Osteoid osteoma is a solitary, benign bone-forming tumor that commonly arises in the cortex of long bones and is associated with marked cortical thickening and periosteal reaction.[1,2] The lesion causes significant nocturnal pain that usually responds to nonsteroidal anti-inflammatory drugs (NSAIDs). The pain has been ascribed to local production of high levels of prostaglandin E2, which is mediated by cyclooxygenases (COX-1 and COX-2).[3,4] Osteoid osteoma is more common in the second and third decades of life and has limited growth potential. Its incidence is 12.9% of benign bone tumors and 3% of all primary bone tumors.[1,2] The male-to-female ratio is 3:1.[2] Most lesions occur in the lower extremity (most commonly the femur and tibia) or the vertebral posterior elements. They usually involve the diaphysis or metaphysis and may be intracortical, intramedullary or associated with the periosteum. Some cases may be intra-articular.[5,6] By definition, the tumor is less than 2 cm in size. Lesions larger than 2 cm are diagnosed as osteoblastoma. In some cases, regression and spontaneous healing occur.[1] Radiographically, osteoid osteoma classically presents as an area of cortical thickening and sclerosis containing a lucent focus called a "nidus". Sometimes it has a targetoid appearance caused by a central calcified nidus surrounded by a lucent halo and a rim of reactive sclerosis[7] (Figure 1). Additional imaging techniques including radionuclide bone scan, CT scanning, and MRI are helpful in localizing the lesion.[1] The classic bone scan appearance of double density is specific.[1] CT is extremely useful in identifying the nidus within the radiologically dense reactive zone. Histologically, the nidus of an osteoid osteoma consists of an interlacing network of woven bone trabeculae with variable mineralization in a loose fibrovascular stroma (Figure 2). The bone trabeculae are rimmed by osteoblasts, with scattered osteoclastic-type multinucleated giant cells.[4,5] The main

Address reprint requests and correspondence: Roberto A. Garcia, MD, Mount Sinai School of Medicine, One Gustave L Levy Place, Annenberg 15-235, Box 1194, New York, NY 10029.
E-mail address: roberto.garcia@mountsinai.org.

0740-2570/$ -see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1053/j.semdp.2011.02.013

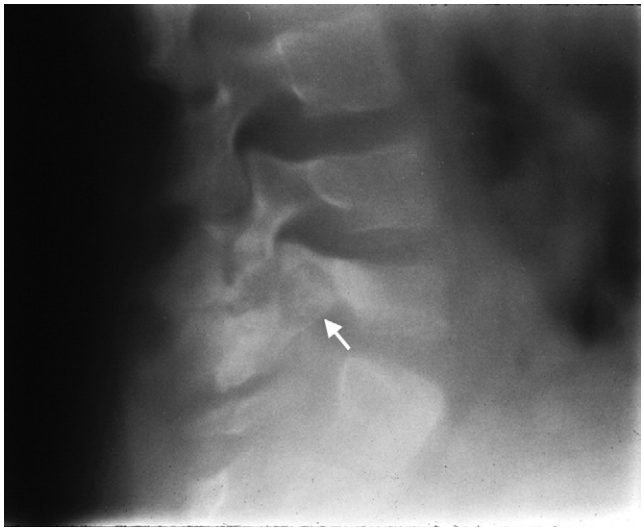

Figure 1 Lateral view of osteoid osteoma of the spine arising in the posterior vertebral elements with a small, central, calcified nidus surrounded by a lucent halo and adjacent bone sclerosis. (Courtesy of Dr. Michael Klein.)

differential diagnosis of osteoid osteoma is with Brodie abscess (chronic osteomyelitis) but the classic clinical presentation, pain pattern, and histologic features are usually diagnostic.

Structural chromosomal alterations involving 22q13 have been described in osteoid osteoma [del(22)(q13.1)], which may affect critical genes involved in the regulation of cell proliferation.[8]

The most recent development in osteoid osteoma has been in its treatment, which is primarily directed to control pain. Complete removal of the nidus is essential for pain relief.[1] Traditionally, osteoid osteoma is treated with surgical resection (marginal, wide, or curettage). The possibility of spontaneous regression during the course of several years may make medical management feasible for some patients. There is a definitive role for conservative treatment with NSAIDs.[1] Newer minimally invasive techniques that have been recently developed include CT-guided core drill excision, percutaneous radiofrequency ablation (RFA), cryoablation, or laser photocoagulation.[5,9] Radiofrequency ablation has gained great popularity because of its advantages over traditional surgery. It is minimally invasive, safe, and highly effective (pain relief within 24 h to 1 wk after treatment).[10] It is useful in the treatment of lesions in atypical or technically challenging locations (intra-articular, spinal, or short bone lesions).[5,6] Tissue necrosis is induced by thermal coagulation through insertion of an electrode into the lesion. The technique is ideal for small lesions measuring less than 1 cm. The success rate of RFA in the treatment of osteoid osteoma is comparable with that of traditional surgery (87%-100%).[10] The main advantages of the procedure include minimal bone loss and structural weakening, less morbidity (infections), shorter anesthesia, minimal restriction of physical activity, short hospitalization and recovery time (usually a few hours), and lower cost.[5,9,10]

The pathologic evaluation of osteoid osteoma has been affected by the increasing use of RFA or other minimally invasive techniques. Some lesions are treated without prior biopsy and the diagnosis is established only on clinical and radiographic grounds. In other instances, a core biopsy is obtained prior to the procedure. In a third scenario, bone fragments obtained from the drill are submitted for pathologic analysis. These tissues frequently have crush and heat artifacts.[11] Consequently, pathologists may or may not be able to confirm the diagnosis on smaller, usually fragmented, and frequently distorted fragments of tissue.

The recurrence rate for osteoid osteomas treated with RFA is 5%-10%.[11] Currently, traditional surgery is reserved for cases where RFA is contraindicated (eg, lesions that are too close to the spinal cord or nerves). Complications are rare and include skin burns, infection, and damage to neighboring nerves.[10] Other techniques may have similar success rates but CT-guided drilling has a morbidity rate of 24%, cryoablation is limited by its higher cost, and laser therapy precludes histologic confirmation and is more expensive than RFA.[6,9]

Osteoblastoma

Osteoblastoma is a rare, benign bone neoplasm (1% of primary bone tumors) that is histologically and clinically similar to osteoid osteoma but has a potential for progressive growth and local recurrence.[2,12-15] It is characterized by larger size (>2 cm) and dull pain that may not be relieved by NSAIDs. The peak incidence is in the second decade of life and it is more common in males.[2,12] Osteoblastoma has predilection for the axial skeleton (posterior vertebral elements) but also occurs in the appendicular long bones and the mandible.[12,14,15] It may be intracortical, intramedullary or arise on the bone surface, so-called periosteal osteoblas-

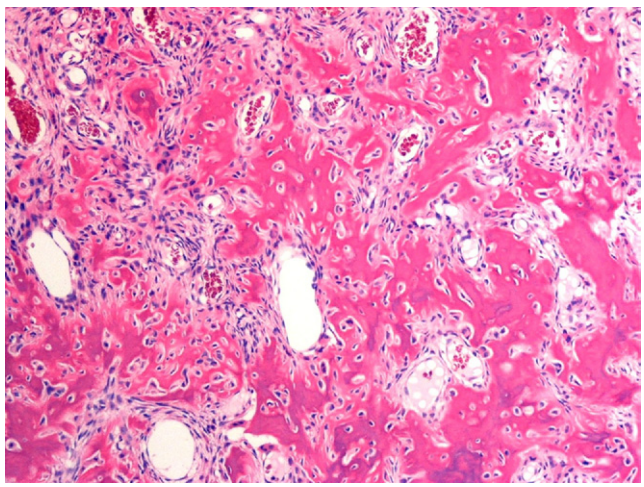

Figure 2 The nidus of an osteoid osteoma has interconnecting trabeculae of woven bone in a moderately cellular fibrovascular stroma with numerous rimming osteoblast and scattered osteoclasts (hematoxylin and eosin stain, original magnification ×10).