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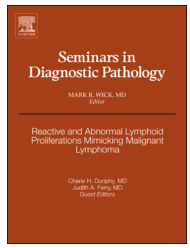

Osteogenic tumors of bone

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ABSTRACT

In this paper we provide an overview of benign and malignant osteogenic bone tumors. We describe the diagnostic features, radiographic findings, and pertinent ancillary studies needed to diagnose these bone-forming lesions. We begin with osteoid osteoma and osteoblastoma, which are histologically bland and eminently benign with rare possible exceptions. On the other end of the behavioral spectrum is osteosarcoma, which encompasses many subtypes ranging from high-grade osteogenic osteosarcoma to less overtly osteogenic lesions such as telangiectatic and small cell osteosarcoma. While classic osteogenic osteosarcoma can be easily recognized by its high grade morphology and formation of extracellular lace-like osteoid, its variants may pose diagnostic dilemmas as their differential diagnoses can include benign, fibrous, and vascular lesions, among others. Recognition of these variants is essential to avoid diagnostic pitfalls. In equivocal cases, some forms of osteosarcoma have shown molecular alterations that may prove diagnostically useful.

Osteogenic tumors of the bone encompass a spectrum of entities, ranging from benign lesions to frankly malignant, with many histologic variations. In this group of neoplasms, one also encounters lesions of uncertain malignant potential such as aggressive osteoblastomas, as well as overt biological malignancies that may closely mimic benign and reactive processes. For instance, telangiectatic osteosarcoma can be easily mistaken for an aneurysmal bone cyst and fibroblastic osteosarcoma can closely resemble a proliferating fracture callus. Indeed, distinguishing between reparative processes and sarcoma is one of the most critical tasks for the practicing pathologist in analyzing an osteogenic lesion.

This brief review will consider benign bone tumors such as osteoid osteoma and osteoblastoma as well as the array of osteosarcoma subtypes and the diagnostic pitfalls they evoke. Although the recognition of rare sarcoma morphotypes—such as small-cell osteosarcoma—is unlikely to be necessary in the day-to-day practice of surgical pathologists, it is paramount that one cultivates basic familiarity with those entities to ensure that they are not missed or confused with other lesions.

In this article, the gross and histologic features of each tumor are discussed, as well as their radiographic attributes. The last of those data is a critical inclusion for any pathologist who is attempting to interpret an osseous lesion because bone tumors and their mimics cannot, and should not, be diagnosed confidently using only their histologic features. Correlation with imaging characteristics has utmost importance and should *never* be omitted, and any discordance between the microscopic and radiographic findings warrants a careful discussion with colleagues in radiology and orthopedic surgery. Furthermore, pathologists who see bone lesions with any frequency must themselves become comfortable with the interpretation of skeletal imaging studies.

Finally, the molecular findings in this group of lesions are considered, with an emphasis on those with the potential to inform targeted treatments. The therapeutic arsenal for osteosarcoma has been limited for some time, but advances in molecular pathology may provide for a more directed approach to that malignancy.

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Benign osteogenic tumors

Osteoid osteoma

Osteoid osteoma is a relatively common osteogenic tumor with a classic presentation that features dull pain that is worse at night and relieved with aspirin. These tumors tend to arise in adolescent males, usually in the metaphysis or diaphysis of long bones. By definition, osteoid osteomas measure <1.5 cm in greatest dimension; lesions with the same microscopic image but larger than that are, by convention, classified as osteoblastomas. Those tumors will be discussed in further detail in the next section.

Radiographs of osteoid osteomas reproducibly demonstrate a lucent "nidus" surrounded by a sclerotic peripheral zone. On cut gross sections of the lesion, the nidus has a red granular appearance. It is important that the nidus be clearly demonstrated in histologic sections for the correct diagnosis to be rendered. If the clinical information and radiologic impressions are consistent with an interpretation of osteoid osteoma but the microscopic appearance is not typical of that entity, one should reassess and resample the gross specimen to ensure that the nidus can be visualized. Histologically, it may be identified as a focus with anastomosing bony trabeculae that are mantled with osteoblasts (Fig. 1). Delicate capillary proliferation is typically present between the trabeculae. Reactive osteoclast-like giant cells may be prominent in some cases of osteoid osteoma, as is true of several other benign and malignant bone lesions. Osteoid osteoma is successfully treated with thorough curettage or *en-bloc* excision.

Osteoblastoma

As cited above, the morphological overlap between osteoid osteoma (OO) and osteoblastoma (OB) is evidenced by the fact that osteoblastoma was once known as "giant osteoid osteoma." Although it could still be argued that those tumors are part of the same continuum, some clinical differences between OO and OB are worth noting. First, although the gender and age distributions of the two neoplasms are roughly parallel, with a distinct predilection for males between 10 and 20 years, OBs have a distinctive anatomic distribution. They tend to involve not only long bones but also the axial skeleton; approximately one-third arise in the spine. Conflicting opinions exist regarding the incidence of nocturnal pain relieved by aspirin in OB cases, but that clinical history is generally less common when compared to examples of OO.

On imaging, OBs also have a radiolucent nidus, with or without peripheral sclerosis. The histologic picture also is comparable to that of OO, with anastomosing bony trabeculae, osteoblastic rimming, capillary proliferation, and variable numbers of osteoclast-like giant cells (Fig. 2). The advancing border of OB should not show evidence of permeative growth, and the finding of definite intraosseous infiltration should instead raise concern over a diagnosis of OB-like osteosarcoma.

The latter lesion is certainly important to consider in the differential diagnosis of OB, but it can usually be excluded on the basis of radiographic findings, gross and microscopic demarcation, and cytological characteristics. Although reports have been made of osteosarcomas "arising" in OB, our opinion is that such tumors were, in all likelihood, OB-like osteosarcomas *ab initio*.[1,2] This topic is further complicated by the controversial entity of "aggressive osteoblastoma" (AOB), as proposed by Dorfman and Weiss.[1] AOBs are said to resemble OB histologically but they show locally aggressive behavior. Microscopically, such lesions contain epithelioid osteoblasts with prominent nucleoli. A study reported a unique balanced translocation in AOB that involves chromosomes 4, 7, and 14.[3] However, debate persists over whether or not AOB is, indeed, a reproducible entity.

Malignant osteogenic tumors

Osteosarcoma is a mesenchymal malignancy that is characterized by production of osteoid matrix variable additional components of chondroid material and fibrous tissue. The World Health Organization has divided osteosarcoma into eight categories, including conventional, secondary,

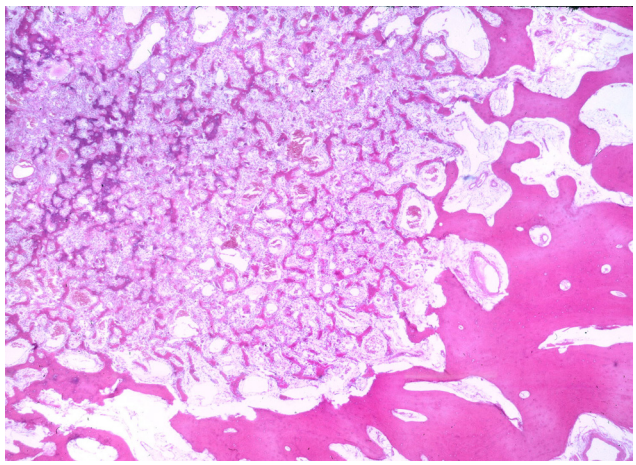

Fig. 1 – Osteoid osteoma nidus (upper left) characterized by anastomosing bony trabeculae in prominent capillaries.

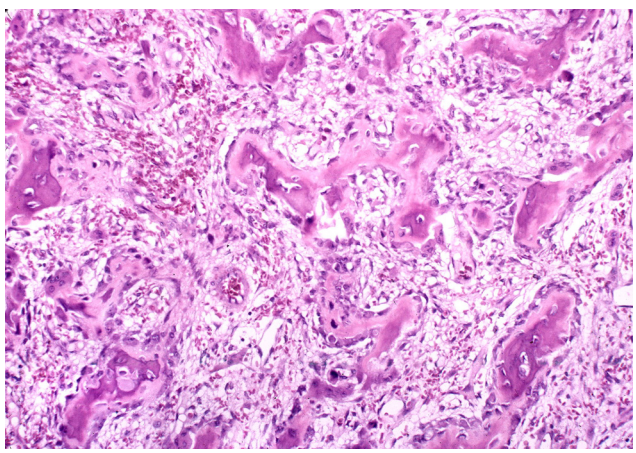

Fig. 2 – Osteoblastoma showing delicate capillaries and trabeculae rimmed by osteoblasts.