Osteoblastoma

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Osteoblastoma is a rare benign bone tumor. Although the histologic features in most cases are distinctive, there are various permutations that make the diagnosis challenging. It can mimic a variety of other benign bone tumors, but more importantly, distinguishing it from osteoblastoma-like osteosarcoma can be difficult. In this case report, I describe the clinicopathologic findings for a 13-year-old adolescent boy with T7 spinal osteoblastoma and review salient clinical, radiographic, and pathologic features of osteoblastoma, as well as the differential diagnoses.

(REport of a case)

A 13-year-old adolescent boy presented with painful scoliosis. He had reported relapsing/remitting back pain during the previous 2 years, and progressive scoliosis was detected on serial physical examinations. Computed tomography (CT) scan of the spine revealed a 2.2-cm, expansile, osteolytic and osteosclerotic bone tumor centered within the pedicle of T7 (Figure 1). After core biopsy it was excised. Grossly, the tumor was gritty to hard, expansile but well-marginated, and had a central sclerotic nidus surrounded by trabecular bone and by a peripheral rind of sclerotic bone. Microscopically, it had typical features of osteoblastoma (Figure 2). At last follow-up, 18 months postoperatively, the patient continues to have intermittent back pain. However, there is no evidence of recurrent tumor by imaging.

(comment)

Osteoblastoma is rare, accounting for only 1% of primary bone tumors. It has a wide age range (6–75 years). However, it most commonly affects adolescents and young adults (mean age, 20 years).1 Virtually any bone can be involved, with spine and sacrum accounting for one-third of cases (Figure 3). Progressive pain is the most common symptom. However, it usually does not have the intense pain pattern that awakens one at night, as does osteoid osteoma. Spinal osteoblastoma presents with neurologic findings and often with progressive scoliosis, as in this case. In general, osteoblastoma has a good prognosis with a local recurrence rate of about 15% to 20%,1 and most recurrent tumors can be successfully treated by reexcision. Tumors located near the central neural axis tend to have a worse prognosis probably owing to difficulty in achieving complete excision. Only very rare examples of osteoblastoma progressing to osteosarcoma have been reported.1

Radiographic Features

The radiographic appearance of osteoblastoma is variable, often nonspecific, and can mimic other tumors, including malignant ones.2 Most often, however, the appearance is benign and the diagnosis can at least be suggested from the radiographs. For example, many tumors show intratumoral ossification, including some with a central nidus of sclerotic bone surrounded by a radiolucent halo similar to osteoid osteoma (Figure 1). Most osteoblastomas are sharply marginated and have a peripheral rind of sclerotic bone (Figure 4). Some tumors are very expansile, similar to aneurysmal bone cyst (Figure 5). Most tumors remain confined to bone and do not destroy or penetrate cortex. However, up to 25% have features that can mimic a malignant bone tumor,2 such as large size or destructive growth (Figure 6). Spinal osteoblastoma has a high tendency to affect the dorsal elements (lamina, pedicle, or spinous process) as opposed to the vertebral body. For example, 55% are limited to dorsal elements and 42% involve dorsal elements and body, while only 3% involve the body alone.1

Pathology

Because most osteoblastomas are treated by curettage, the gross specimen usually consists of fragments of red gritty tissue. Within an intact specimen, osteoblastoma is usually sharply demarcated from adjacent bone, often with a scalloped edge, and is often surrounded by a rim of sclerotic host bone. Expansile tumors may be encased by a thin shell of cortical bone. Some tumors have a central sclerotic nidus similar to osteoid osteoma (Figure 7). Some are very hemorrhagic with cystic areas of hemorrhage or loculated secondary aneurysmal bone cyst changes. The average size is 3 to 3.5 cm, but osteoblastoma can be quite sizeable, up to 15 cm.1

Microscopically, osteoblastoma is composed of interanastomosing trabeculae of woven bone, set within loose edematous fibrovascular stroma (Figure 2). It may or may not have a central sclerotic nidus (Figure 8). Most tumors show a spectrum of bony maturational changes ranging from cords and clusters of activated osteoblasts associated with minimal osteoid (Figure 9, A) to lacelike wispy osteoid (Figure 9, B) to broad anastomosing trabeculae of woven bone (Figure 9, C) to sclerotic sheets of woven bone (Figure 9, D). As a rule, the osseous trabeculae are lined by

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a single layer of osteoblasts. Because osteoblastoma undergoes continuous remodeling, osteoclastic giant cells are usually in abundance. Howship lacunae and pagetoid remodeling changes with numerous reversal lines (Figure 9, D) attest to ongoing remodeling. The bony trabeculae connect with the peripheral bony edge of the tumor (Figure 10). Osteoblastoma does not permeate adjacent bone or invade soft tissue.

The cytologic features of osteoblasts are variable. Large immature osteoblasts have abundant, eccentric, basophilic, finely granular cytoplasm; perinuclear hof consistent with Golgi apparatus; and large vesicular nucleus with a prominent nucleolus (Figure 11). Mature osteoblasts are smaller with less cytoplasm and smaller nuclei, while mature osteocytes are smaller yet and contained within the bony matrix. Mitotic activity is low and atypical mitotic figures are not seen. Osteoclasts vary from polygonal cells with only a few nuclei to large multinucleated giant cells with dozens of nuclei.

Other microscopic findings present in some osteoblastomas include heavily calcified immature bone or “spiculated blue bone” (Figure 12), prominent spindle cell fibrovascular stroma (Figure 13), and extensive intraläsional hemorrhage (Figure 14), including tumors with secondary aneurysmal bone cyst changes. Rarely, one finds cartilage or chondro-osseous matrix within an osteoblastoma (Figure 15) in the absence of fracture, a finding once believed to be more in keeping with osteosarcoma. Degenerative cytologic atypia is characterized by cells with large degenerated nuclei and smudged chromatin mimicking a malignant tumor (Figure 16). This finding is similar to that seen in ancient schwannoma. Osteoblastomas with extensive degenerative atypia are termed pseudomalignant osteoblastomas. Multifocal (or multinodular) osteoblastoma defines a subset of tumors.

Figure 1. This computed tomography image depicts an osteoblastoma in the pedicle of T7. The tumor is expansile, surrounded by a sclerotic rim, and has a central ossified nidus. Most spinal osteoblastomas occur in the dorsal vertebral elements.

Figure 2. Osteoblastoma comprises interanastomosing trabeculae of woven bone lined by a single layer of osteoblasts within a loosely textured fibrovascular stroma. Osteoclasts are invariably present (hematoxylin-eosin, original magnification X200).

Figure 3. Epidemiology and skeletal localization of osteoblastoma. Data from Lucas et al.,1 with permission from Elsevier, Oxford, United Kingdom.
Osteoblastoma can occasionally present with features suggestive of a malignant tumor, such as large size and cortical destruction. This large ossified rib tumor was considered to be suggestive of osteosarcoma before biopsy.

Grossly, osteoblastomas are well demarcated from adjacent host bone, expansile and hemorrhagic, and often contain a central osseous nidus; all these features are depicted in this tibial tumor.

Radiographically, osteoblastomas are highly variable in appearance. Most have benign features, such as circumscription and sclerotic margination, as depicted in the intramedullary iliac tumor.

Osteoblastomas can be very expansile and mimic aneurysmal bone cyst, such as this intracortical tibial tumor contained by a thin rim of cortical bone (arrow).
Figure 8. The nidus is formed by dense sclerotic woven bone, as illustrated in this low-power photomicrograph (hematoxylin-eosin, original magnification ×200).

Figure 9. Osteoblastomas show a spectrum of bony maturational changes, often present within a single tumor, ranging from cords and clusters of activated osteoblasts associated with minimal osteoid (A) to lacelike wispy osteoid (B) to broad anastomosing trabeculae of woven bone (C) to sclerotic sheets of woven bone (D). Note the irregular or mosaic-like reversal lines indicative of active remodeling similar to that seen in Paget disease (hematoxylin-eosin, original magnifications ×400 [A through C] and ×200 [D]).

Figure 10. In general, osteoblastomas are well marginated and do not penetrate cortex or permeate medullary bone. Tumor trabeculae frequently connect with the surrounding bone, as depicted (hematoxylin-eosin, original magnification ×100).
with multiple nidi or growth centers within a single tumor, separated by reactive bone or spindle cell stroma (Figure 17). These tumors frequently contain epithelioid osteoblasts.5

Osteoblastoma frequently occurs in the jaws, mandible more often than maxilla. It is often associated with the root of a tooth where it forms an ossified, well-demarcated tumor (Figure 18). Tooth root tumors are also referred to as cementoblastomas. Microscopically, the bony matrix tends to be abundant in these tumors and to radiate from the tooth root in parallel arrays (Figure 19).

The term aggressive osteoblastoma was introduced in 1984 by Dorfman and Weiss.6 This rare entity is purported to have clinicopathologic features that set it apart from conventional osteoblastoma, although not all investigators have been able to validate this conclusion.7,8 Aggressive osteoblastoma is characterized by locally aggressive but nonmetastasizing behavior and distinctive histologic features. It comprises large epithelioid osteoblasts, defined as cells with abundant eosinophilic cytoplasm twice the size of conventional osteoblasts (Figure 20). They either rim the osteoid as in conventional osteoblastoma or

Figure 11. Cytologically, the neoplastic osteoblasts have abundant basophilic, finely granular cytoplasm with a perinuclear hof of less dense cytoplasm and an eccentric vesicular nucleus with a solitary prominent nucleolus (hematoxylin-eosin, original magnification ×400).

Figure 12. Heavily calcified immature woven bone is sometimes present and is referred to as “spiculated blue bone” (hematoxylin-eosin, original magnification ×400).

Figure 13. In some osteoblastomas, spindle cell stroma dominates (hematoxylin-eosin, original magnification ×200).

Figure 14. Extensive intralesional hemorrhage is common, sometimes obscuring the diagnostic areas (hematoxylin-eosin, original magnification ×40).

Figure 15. Although uncommon, cartilaginous or chondro-osseous matrix can be found in osteoblastoma in the absence of fracture (hematoxylin-eosin, original magnification ×200).

Figure 16. Enlarged, hyperchromatic nuclei with smudged chromatin, indicative of degenerative atypia, can be present. When this feature is prominent, it can be mistaken for a malignant tumor. Such tumors are referred to as pseudomalignant osteoblastomas (hematoxylin-eosin, original magnification ×400).

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Figure 17. Multifocal osteoblastoma defines a subset of tumors with multiple nidi or growth centers within a single tumor, separated by reactive bone or spindle cell stroma, as depicted in this low-power photomicrograph (hematoxylin-eosin, original magnification ×40).

Figure 18. Osteoblastoma of the jaw most often occurs in the mandible and is often associated with a tooth root. This radiograph depicts a well-demarcated, heavily ossified tumor involving a tooth root. Such tumors are also referred to as cementoblastomas.

Figure 19. Parallel arrays of sclerotic bone that radiate away from center (tooth root) are a common pattern in osteoblastoma of the jaw (hematoxylin-eosin, original magnification ×200).

Figure 20. So-called aggressive osteoblastoma is a rare variant of osteoblastoma, believed to be more locally aggressive than conventional osteoblastoma. It is primarily defined by epithelioid osteoblasts, cells with abundant eosinophilic cytoplasm twice the size of conventional osteoblasts. These cells are frequently arranged in sheets with little or no intervening osteoid, as depicted (hematoxylin-eosin, original magnification ×400).
arrange themselves in sheets and clusters devoid of matrix. Differentiating aggressive osteoblastoma from epithelioid osteosarcoma can be challenging. Certainly, aggressive behavior is within the spectrum of osteoblastoma, whether or not it has a prominent epithelioid osteoblastic morphology.\textsuperscript{1,7} For example, tumors near the spinal cord and skull base can cause considerable morbidity and even mortality because of a limitation to surgical extirpation by anatomic constraints.

**Differential Diagnosis**

**Osteoid Osteoma.**—Distinguishing osteoblastoma from osteoid osteoma is somewhat arbitrary. In fact, many authors believe they represent members of a spectrum of neoplasia. For example, many osteoblastomas have the architectural configuration of an osteoid osteoma consisting of a central ossified nidus surrounded by trabecular woven bone. In fact, an early designation for osteoblastoma was “giant osteoid osteoma.”\textsuperscript{11} In general any tumor larger that 1.5 cm is called osteoblastoma, while anything less than that is an osteoid osteoma. Osteoid osteoma, however, differs clinically from osteoblastoma in that it is more painful (worse at night, relieved by analgesics) and less likely to progress.

**Aneurysmal Bone Cyst.**—Because osteoblastoma can be very hemorrhagic and show secondary aneurysmal bone cyst changes, and conversely, because primary aneurysmal bone cyst can show extensive reactive new bone production that resembles osteoblastoma, it can be challenging to tell them apart in some cases. In general, however, in osteoblastoma with secondary aneurysmal bone cyst change, one can usually find a sizeable intact focus of tumor seemingly independent of the cystic changes. Distinguishing osteoblastoma from aneurysmal bone cyst can be especially challenging in spinal tumors since both tend to form expansile tumors originating from the dorsal vertebral elements. Fortunately, this distinction has little clinical relevance, since they are treated and behave in a similar manner.

**Giant Cell Tumor of Bone.**—Osteoblastoma and giant cell tumor of bone are usually easy to distinguish. Giant cell tumor is composed of sheets of mononuclear histiocytoid stromal cells admixed with numerous, evenly dispersed osteoclastic giant cells. Clinically, giant cell tumor also differs from osteoblastoma. For example, in long bone it involves the epiphysis and in the spine it involves the vertebral body, both of which are uncommon locations for osteoblastoma, which tends to metaphyseal in long bone and to involve the neural arch of a vertebra. Giant cell tumor, however, can show a variety of secondary histologic changes including osteoid and woven bone formation and secondary aneurysmal bone cyst changes that mimic osteoblastoma. Occasionally, giant cell tumor produces a large amount of collagenous matrix that forms interanastomosing trabeculae of osteoid-like matrix that mimics osteoblastoma.

**Osteoma With Osteoblastoma-like Features.**—Although osteoblastoma occurs in the maxilla and calvarium, it is very rare in the paranasal sinuses, nasal cavity, and orbit. By contrast, osteoma commonly affects these anatomic sites and is the most common tumor of the paranasal sinuses.\textsuperscript{9} Sino-orbital osteoma typically forms a solid bony mass that produces a sessile polypoid growth within a sinonasal cavity space or within the orbit. It is composed primarily of mature compact or trabecular bone. However, nearly 40% have foci of immature woven bone within loose fibrovascular stroma indistinguishable from osteoblastoma.\textsuperscript{10} Although believed by some to have a more aggressive behavior, osteoma with osteoblastoma-like features has the same behavior as conventional sino-orbital osteoma.\textsuperscript{10} Distinguishing this tumor from osteoblastoma often requires clinicopathologic and radiographic correlation.

**Osteoblastoma-like Osteosarcoma.**—Osteosarcoma can have focal areas indistinguishable from osteoblastoma. In addition, there is a subset of osteosarcomas, comprising broad interanastomosing trabeculae of bone, that closely mimics and can be misdiagnosed as osteoblastoma.\textsuperscript{13} Important histologic features that distinguish it from osteoblastoma include presence of a compact solid proliferation of neoplastic cells in between the bony trabeculae (unlike the single row of osteoblasts seen in osteoblastoma), permissive growth or infiltration beyond the confines of the tumor into adjacent bone or soft tissue, and high mitotic rate.\textsuperscript{7}

**CONCLUSIONS**

Although uncommon, osteoblastoma presents with microscopic features that can mimic a variety of other benign as well as malignant entities. Following are important features to be cognizant of: (1) virtually any bone can be affected; (2) it commonly involves the spine, where it has a strong propensity to involve the dorsal vertebral elements as opposed to the body; (3) it can sometimes show locally aggressive growth, which correlates mostly with surgical resectability and possibly with specific histologic features such as prominent epithelioid cell morphology (“aggressive osteoblastoma”); (4) other benign tumors such as osteoid osteoma, aneurysmal bone cyst, giant cell tumor of bone, and sino-orbital osteoma can mimic it histologically; and (5) distinguishing it from osteoblastoma-like osteosarcoma, on the basis of careful evaluation of sometimes subtle cytoarchitectural features, is essential to avoid a misdiagnosis.

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