Bone Tumor

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- Primary bone tumors are considerably less common than bone metastases from other primary sites.
- Primary bone tumors exhibit great morphologic diversity and clinical behaviors—from benign to aggressively malignant.
- Most are classified according to the normal cell counterpart and line of differentiation.
- Most bone tumors arise without any previous known cause.
- Nevertheless, genetic syndromes (e.g., Li-Fraumeni and retinoblastoma syndromes) are associated with osteosarcomas, as are (rarely) bone infarcts, chronic osteomyelitis, Paget disease, irradiation, and use of metal orthopedic devices.

Tumor Type	Common Locations	Age (yr)
Bone-Forming		
Benign		
Osteoma	Facial bones, skull	40–50
Osteoid osteoma	Metaphysis of femur and tibia	10–20
Osteoblastoma	Vertebral column	10–20
Malignant		
Primary osteosarcoma	Metaphysis of distal femur, proximal tibia, and humerus	10–20
Secondary osteosarcoma	Femur, humerus, pelvis	>40
Cartilaginous		
Benign		
Osteochondroma	Metaphysis of long tubular bones	10–30
Enchondroma	Small bones of hands and feet	30–50
Malignant		
Chondrosarcoma	Bones of shoulder, pelvis, proximal femur, and ribs	40–60
Miscellaneous		
Giant cell tumor (usually benign)	Epiphysis of long bone	20–40
Ewing sarcoma	Diaphysis and metaphysis	10–20

Clinical Presentation

Benign lesions frequently are asymptomatic and are detected as incidental findings. Others produce pain or a slowly growing mass.

Occasionally, a pathologic fracture is the first manifestation.

Radiologic imaging is critical in the evaluation of bone tumors; however, biopsy and histologic study and, in some cases, molecular tests are necessary for diagnosis.

Bone-Forming Tumors

Osteoma

- Osteomas are benign lesions most commonly encountered in the head and neck, including the paranasal sinuses, but which can occur elsewhere as well.
- They typically present in middle age as solitary, slowly growing, hard, exophytic masses on a bone surface.
- Multiple lesions are a feature of Gardner syndrome.
- On histologic examination, osteomas recapitulate cortical type bone and are composed of a mixture of woven and lamellar bone.
- They are not locally aggressive and do not undergo malignant transformation.

Osteoid Osteoma and Osteoblastoma

- Both are benign neoplasms with very similar histologic features, typically appear during the teenage years and 20s, with a male predilection (2 : 1 for osteoid osteomas).

- They are distinguished from each other primarily by their size and clinical presentation.

- Osteoid osteomas arise most often beneath the periosteum or within the cortex in the proximal femur and tibia are by definition less than 2 cm in diameter, whereas osteoblastomas are larger.

- Localized pain, most severe at night, is an almost universal complaint with osteoid osteomas, and usually is relieved by aspirin.

- Osteoblastomas arise most often in the vertebral column; they also cause pain, although it often is more difficult to localize and is not responsive to aspirin.

Osteoid Osteoma and Osteoblastoma

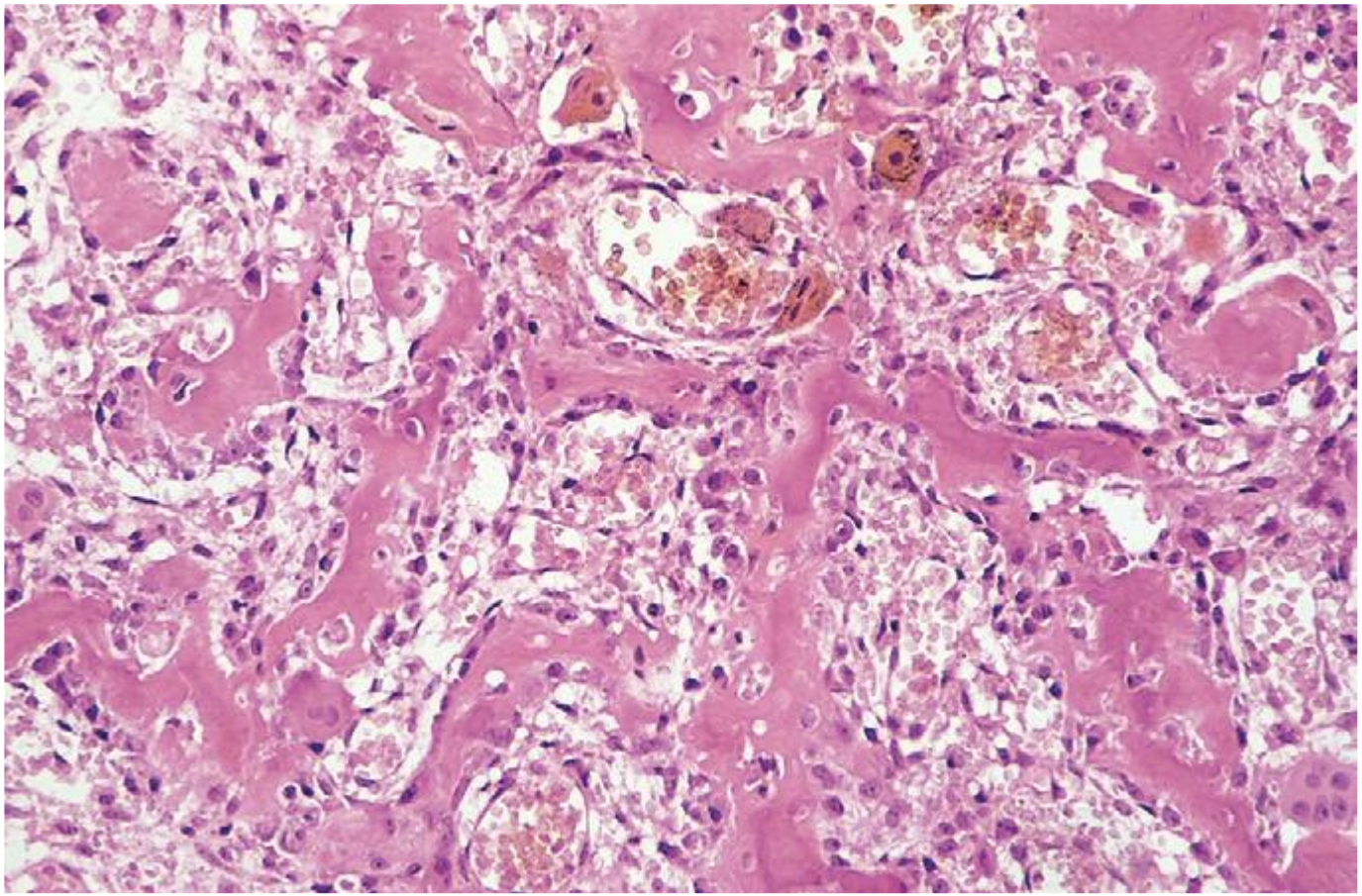
- Local excision is the treatment of choice; incompletely resected lesions can recur.
- Malignant transformation is rare unless the lesion is treated with irradiation

MORPHOLOGY

- On gross inspection, both lesions are round-to-oval masses of hemorrhagic, gritty-appearing tan tissue. A rim of sclerotic bone is present at the edge of both types of tumors.

- On microscopic examination, both neoplasms are composed of interlacing trabeculae of woven bone surrounded by osteoblasts. The intervening stroma is loose, vascular connective tissue containing variable numbers of giant cells.

Osteoid osteoma showing randomly oriented trabeculae of woven bone rimmed by prominent osteoblasts. The intertrabecular spaces are filled by vascular loose connective tissue.

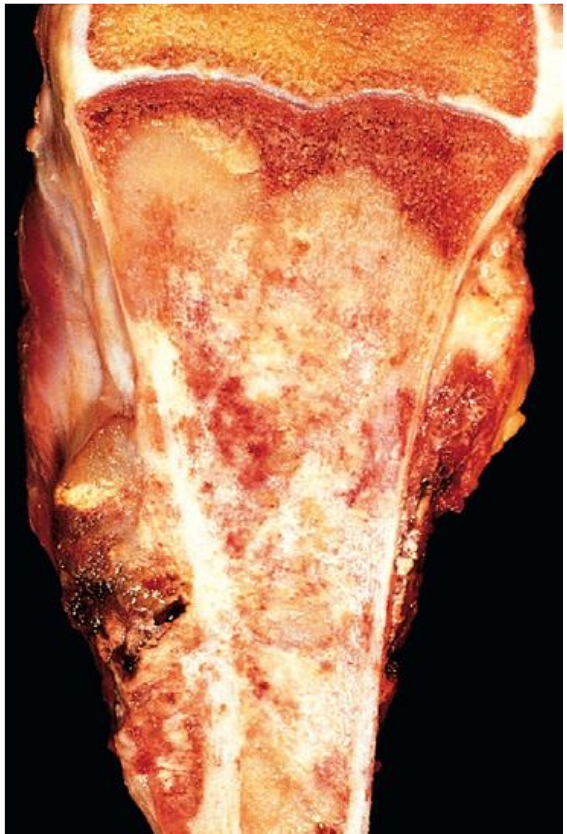


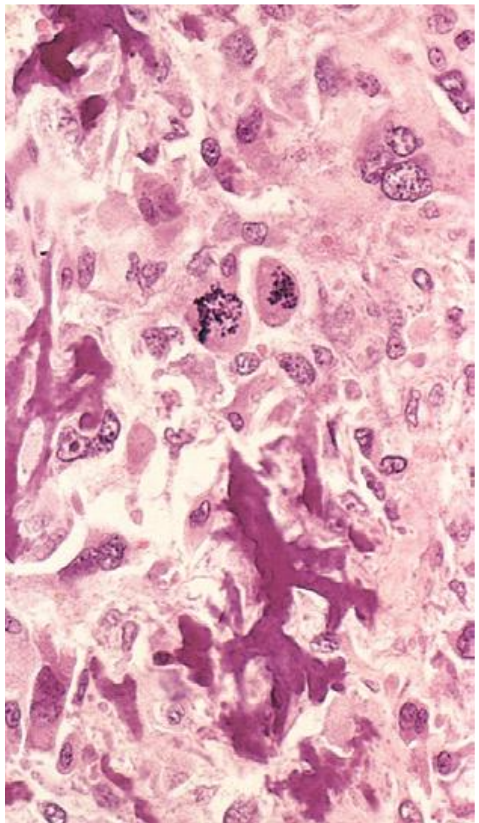
Osteosarcoma

- Osteosarcoma is a bone-producing malignant mesenchymal tumor.
- After myeloma and lymphoma, osteosarcoma is the most common primary malignant tumor of bone.
- Osteosarcomas occur in all age groups, but about 75% of patients are younger than 20 years of age, with a second peak occurring in elderly persons.
- Men are more commonly affected than women (1.6 : 1).
- Most tumors arise in the metaphyseal region of the long bones of the extremities, with almost 60% occurring about the knee.
- Microscopically: Tumor cells vary in size and shape and frequently have large hyperchromatic nuclei; bizarre tumor giant cells are common, as are mitotic figures. **The production of coarse and lacelike mineralized or unmineralized bone (osteoid) by malignant cells is essential for diagnosis of osteosarcoma** .
- Vascular invasion is common, as is spontaneous tumor necrosis.

Macroscopically. Mass involving the upper end of the tibia. The tan-white tumor fills most of the medullary cavity of the metaphysis and proximal diaphysis. It has infiltrated through the cortex, lifted the periosteum, and formed soft tissue masses on both sides of the bone.

Microscopically, with coarse, lacelike pattern of neoplastic bone produced by anaplastic tumor cells. Note the wildly aberrant mitotic figures





Pathogenesis:

Several mutations are closely associated with the development of osteosarcoma. In particular, RB gene mutations.

Clinical Features:

- Osteosarcomas typically manifest as painful enlarging masses, although a pathologic fracture can be the first sign.
- Radiographic imaging usually shows a large, destructive, mixed lytic and blastic mass with indistinct infiltrating margins. A triangular shadow on the x-ray film between the cortex and raised periosteum (*Codman triangle*) is characteristic of osteosarcomas.
- Osteosarcomas typically spread hematogenously.

- Secondary osteosarcomas occur in older adults most commonly in the setting of Paget disease or previous radiation exposure.

- Despite aggressive behavior, standard treatment with chemotherapy and limb salvage therapy currently yields long-term survivals of 60% to 70%.

Cartilage-Forming Tumors

- Cartilage-forming tumors produce hyaline or myxoid cartilage; fibrocartilage and elastic cartilage are rare components.

- Like the bone-forming tumors, cartilaginous tumors constitute a spectrum from benign, self-limited growths to highly aggressive malignancies.

Chondroma

- Chondromas are benign neoplasms of hyaline cartilage.
- When they arise within the medulla, they are termed enchondromas; when on the bone surface, they are called juxtacortical chondromas.
- Enchondromas usually are diagnosed in persons between the ages of 20 and 50 years; they typically are solitary and located in the metaphyseal region of tubular bones, the favored sites being the short tubular bones of the hands and feet.
- Solitary chondromas rarely undergo malignant transformation, but those associated with enchondromatoses are at increased risk for such change.
- On microscopic examination, they are well circumscribed and composed of hyaline cartilage containing cytologically benign chondrocytes.
- Ollier disease is characterized by multiple chondromas preferentially involving one side of the body.
- Maffucci syndrome is characterized by multiple chondromas associated with soft tissue spindle cell hemangiomas.

Chondrosarcoma

- Chondrosarcoma is a malignant connective tissue tumor (sarcoma) whose cells manufacture and secrete neoplastic cartilage matrix.

- It is subclassified according to site (e.g., intramedullary versus juxtacortical) and histologic variants.

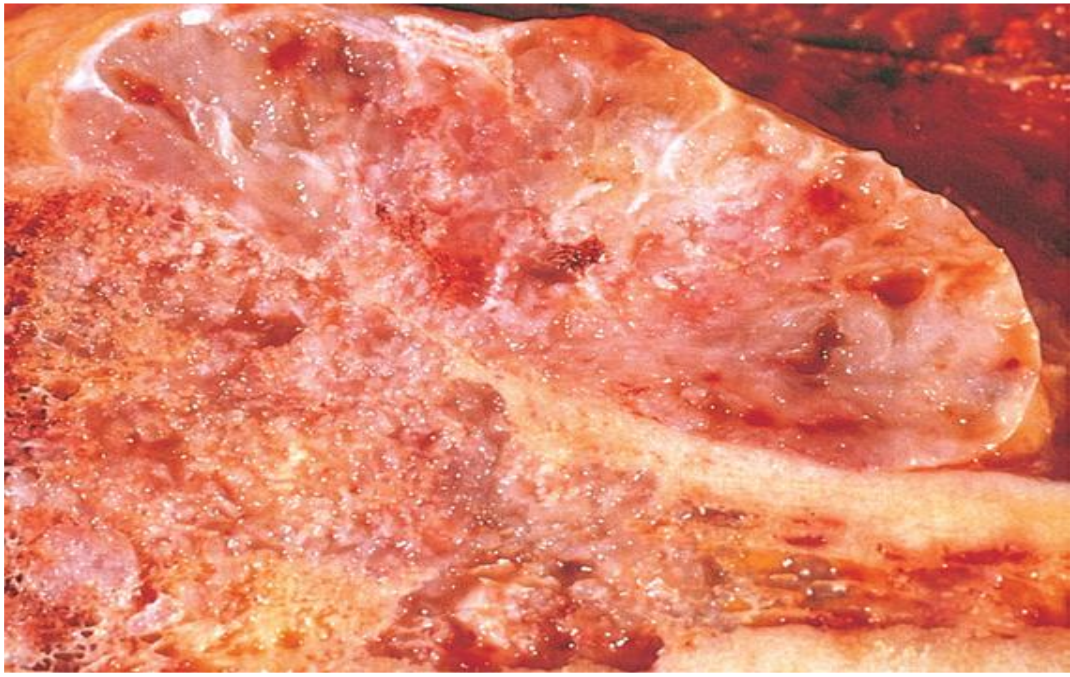
- Chondrosarcomas occur roughly half as frequently as osteosarcomas.

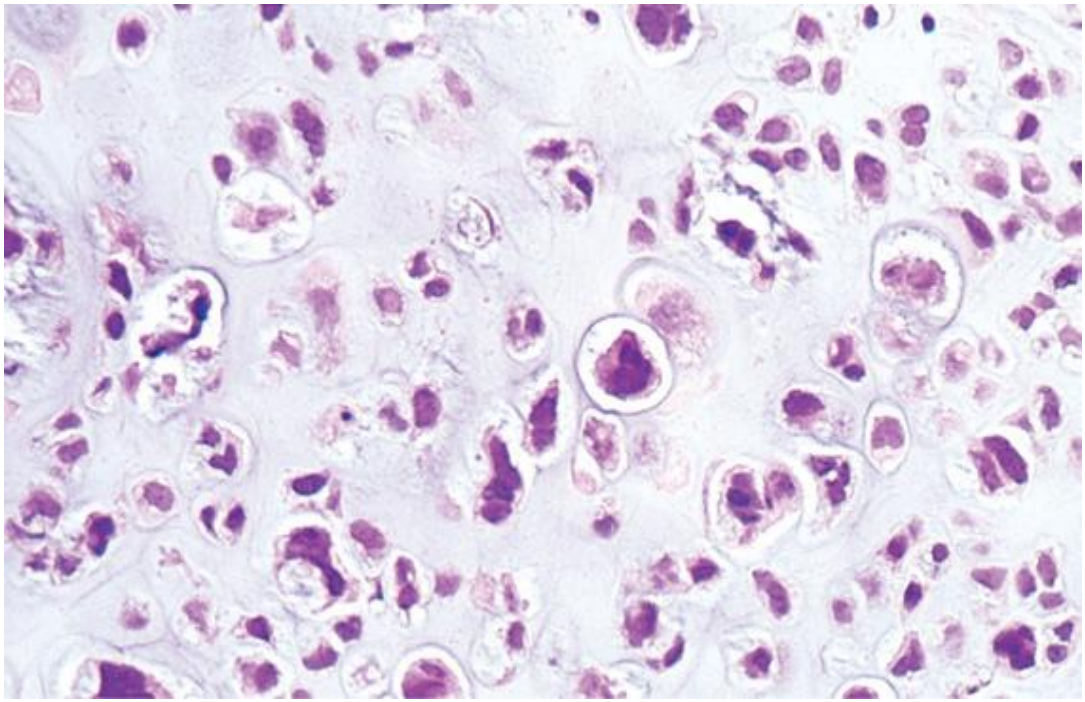
- Most patients are age 40 or older, with men affected twice as frequently as women.

- Microscopically: Tumor grade is determined by cellularity, degree of cytologic atypia, and mitotic activity

Chondrosarcoma. A, Islands of hyaline and myxoid cartilage expand the medullary cavity and grow through the cortex to form a sessile paracortical mass.

B, Anaplastic chondrocytes within a chondroid matrix.





Clinical Features

- Chondrosarcomas commonly arise in the pelvis, shoulder, and ribs; in contrast with enchondromas, chondrosarcomas rarely involve the distal extremities.
- They typically manifest as painful, progressively enlarging masses.
- There is also a direct correlation between grade and biologic behavior of the tumor.
- Fortunately, most conventional chondrosarcomas are indolent and low-grade, with a 5-year survival rate of 80% to 90% (versus 43% for grade 3 tumors); grade 1 tumors rarely metastasize, whereas 70% of the grade 3 tumors disseminate.
- Chondrosarcomas metastasize hematogenously, preferentially to the lungs and skeleton.
- May variants, including clear cell chondrosarcoma, mesenchymal chondrosarcoma, and dedifferentiated chondrosarcoma.
- Conventional chondrosarcomas are treated with wide surgical excision.
- Chemotherapy is added for the mesenchymal and dedifferentiated Variants.

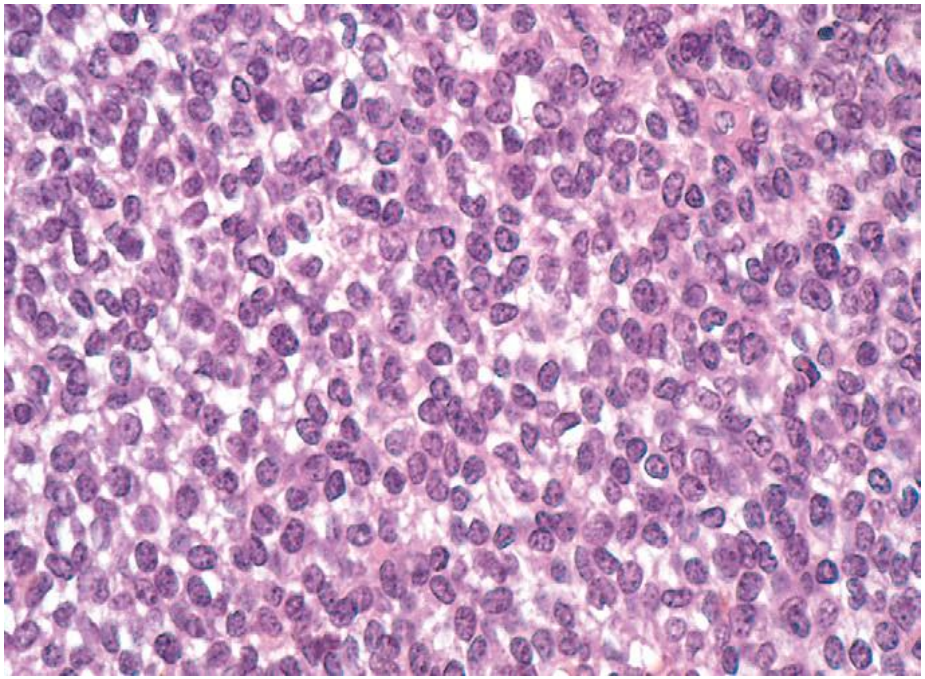
Miscellaneous Bone Tumors

Ewing Sarcoma and Primitive Neuroectodermal Tumor

- ✓ (PNETs) are primary malignant small round cell tumors of bone and soft tissue.
- ✓ They share certain molecular features, however; PNETs demonstrate clear neural differentiation, whereas Ewing sarcomas are undifferentiated.
- ✓ Ewing sarcoma accounts for 6% to 10% of primary malignant bone tumors.
- ✓ Most patients are 10 to 15 years of age, and 80% are younger than 20 years. Boys are affected slightly more frequently than girls.
- ✓ At a practical level, these translocations are of diagnostic importance, as approximately 95% of tumors have t(11;22)) ort(21;22).

Macroscopically: Ewing sarcoma/PNET arises in the medullary cavity and invades the cortex and periosteum to produce a soft tan white tumor mass, frequently with hemorrhage and necrosis.

Microscopically: t is composed of sheets of uniform small, round cells that are slightly larger than lymphocytes; The presence of Homer-Wright rosettes (tumor cells circled about a central fibrillary space) indicates neural differentiation.



Clinical Features

- Ewing sarcoma/PNET typically manifests as a painful enlarging mass in the diaphyses of long tubular bones (especially the femur) and the pelvic flat bones.

- There is a characteristic periosteal reaction with deposition of bone in an onion-skin pattern.

- Treatment includes chemotherapy and surgical excision with or without irradiation.

- The 5-year survival rate is currently 75% for patients presenting with localized tumors.

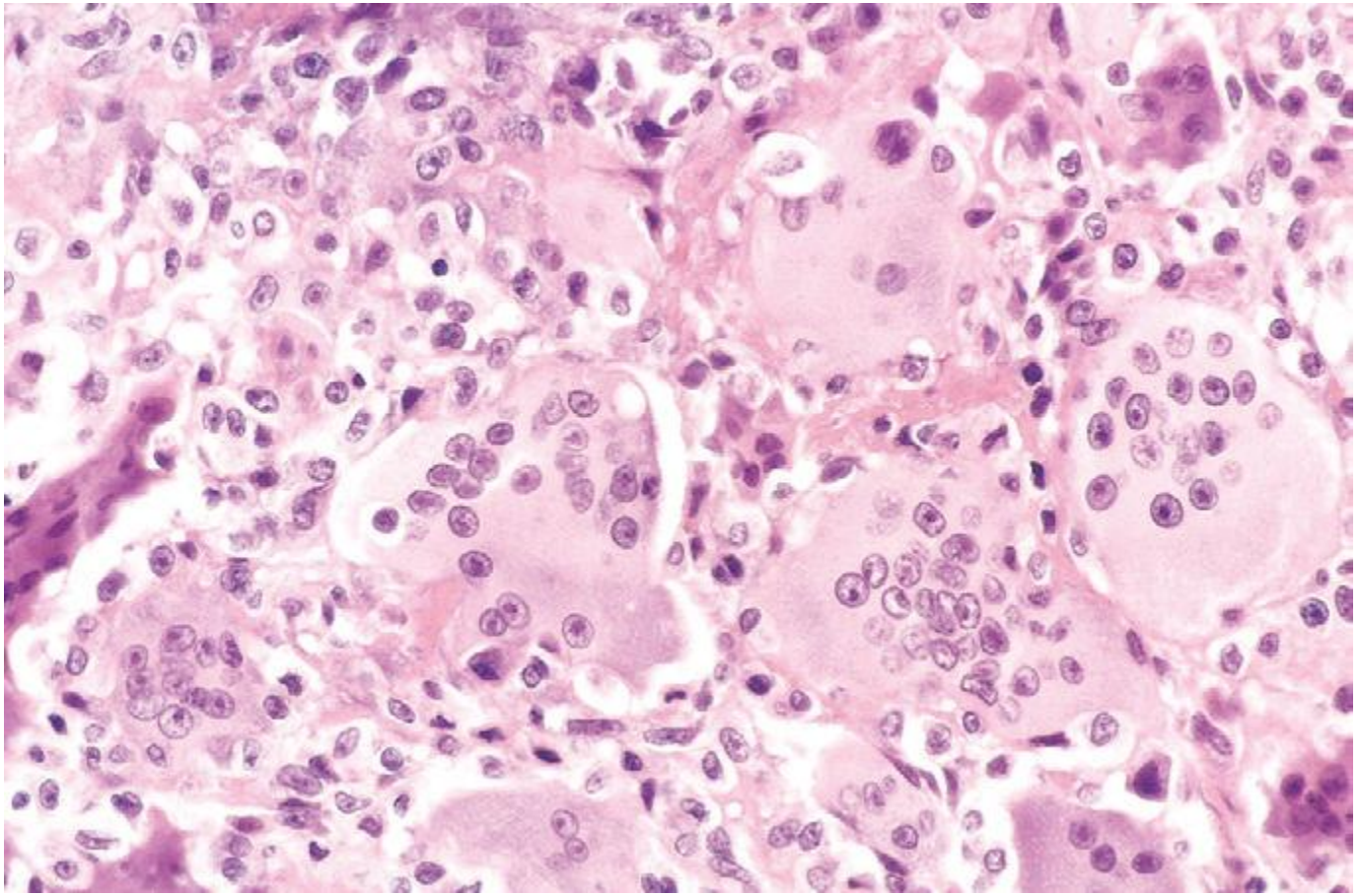
Giant Cell Tumor of Bone

- Giant cell tumors (GCTs) contain prominent by multinucleate osteoclast-type giant cells—hence the synonym osteoclastoma.
- GCT is a relatively common benign but locally aggressive bone tumor, usually arising in persons in their 20s to 40s.

Clinical Course

- Although almost any bone may be involved, a majority of GCTs arise in the epiphysis and involve the metaphysis of long bones around the knee.
- Most are solitary tumors.
- Although GCTs are considered benign, roughly half recur after simple curettage, and as many as 2% spread to the lungs as localized lesions that are cured by local excision.

Benign giant cell tumor showing abundant multinucleate giant cells and a background of mononuclear cells.



Metastatic Disease

- ✓ *Metastatic tumors are the most common malignant tumors involving bone.* Pathways of spread include:

  (1) Direct extension.

  (2) Lmphatic or hematogenous dissemination.

  (3) Intraspinal seeding.

- ✓ In adults more than 75% of skeletal metastases originate fromcancers of the prostate, breast, kidney, and lung.

- ✓ In children, neuroblastoma, Wilms tumor, osteosarcoma, Ewing sarcoma, and rhabdomyosarcoma are the common sources of bony metastases.

- ✓ The radiologic appearance of metastases can be purely lytic, purely blastic, or both. In lytic lesions (e.g., with kidney and lung tumors andmelanoma),however; metastatic tumors that elicit an osteoblastic response (e.g., prostate adenocarcinoma).