Soft Tissue Tumor

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MSS lectures 2022

- By convention, the term soft tissue describes any nonepithelial tissue other than bone, cartilage, central nervous system, hematopoietic, and lymphoid tissues.

- Although soft tissue tumors are classified based on recognizable lines of differentiation, current evidence indicates that these tumors arise from pluripotent mesenchymal stem cells and are not the result of malignant transformation of mature mesenchymal cells.

What are the causes of soft tissue tumor ???

- Most soft tissue tumors arise without antecedent causes. Rarely, radiation exposure, burn injury, or toxin exposure is implicated.
- Virus: Kaposi sarcoma is associated with the human herpesvirus 8.
- A small minority of soft tissue tumors are associated with genetic syndromes, most notably:

❑ Neurofibromatosis type 1 (neurofibroma, malignant schwannoma).

❑ Gardner syndrome (fibromatosis).

❑ Li-Fraumeni syndrome (soft tissue sarcoma).

- Soft tissue tumors can arise in any location, but approximately 40% of sarcomas occur in the lower extremities, especially the thigh.
- While the overall incidence of sarcomas increases with age, 15% arise in children.
- Certain sarcomas tend to appear in certain age groups—for example, Rhabdomyosarcoma in childhood, synovial sarcoma in young adulthood, and liposarcoma and pleomorphic fibroblastic or undifferentiated sarcomas in later adult life.
- Soft tissue sarcomas usually are treated with wide surgical excision (frequently limb-sparing), with irradiation and systemic therapy reserved for large high-grade tumors.

Several features of soft tissue sarcomas influence prognosis :

• ***Diagnostic classification*.** This is based not only on histology, but also on immunohistochemistry, electron microscopy, cytogenetics, and molecular genetics, which are indispensable in assigning the correct diagnosis in some cases.

. ***Grading*.** Grading, usually on a scale of I to III, is based on the degree of differentiation, the average number of mitoses per high-power field, cellularity, pleomorphism, and an estimate of the extent of necrosis.

• ***Staging*.** With tumors larger than 20 cm, metastases develop in 80% of cases; by contrast, for tumors 5 cm or smaller, metastases occur in only 30% of cases.

• ***Location***. In general, tumors arising in superficial locations (e.g., skin) have a better prognosis than deep seated Lesions.

Table 20–4 Soft Tissue Tumors

Tumors of Adipose Tissue
Lipomas
Liposarcoma
Tumors and Tumor-Like Lesions of Fibrous Tissue
Nodular fasciitis
Fibromatoses Superficial fibromatoses Deep fibromatoses
Fibrosarcoma
Fibrohistiocytic Tumors
Fibrous histiocytoma
Dermatofibrosarcoma protuberans
Pleomorphic fibroblastic sarcoma/pleomorphic undifferentiated sarcoma (malignant fibrous histiocytoma)
Tumors of Skeletal Muscle
Rhabdomyoma
Rhabdomyosarcoma
Tumors of Smooth Muscle
Leiomyoma
Smooth muscle tumors of uncertain malignant potential
Leiomyosarcoma
Vascular Tumors
Hemangioma
Lymphangioma
Hemangioendothelioma
Angiosarcoma
Peripheral Nerve Tumors
Neurofibroma
Schwannoma
Granular cell tumor
Malignant peripheral nerve sheath tumors
Tumors of Uncertain Histogenesis
Synovial sarcoma
Alveolar soft part sarcoma
Epithelioid sarcoma

1- TUMORS OF ADIPOSE TISSUE

- LIPOMA: are benign tumors of fat

✓ The most common soft tissue tumors in adults.

✓ Most lipomas are solitary lesions; multiple lipomas usually suggest the presence of rare hereditary syndromes.

✓ Lipomas can be subclassified on the basis of their histologic features and/or characteristic chromosomal rearrangements.

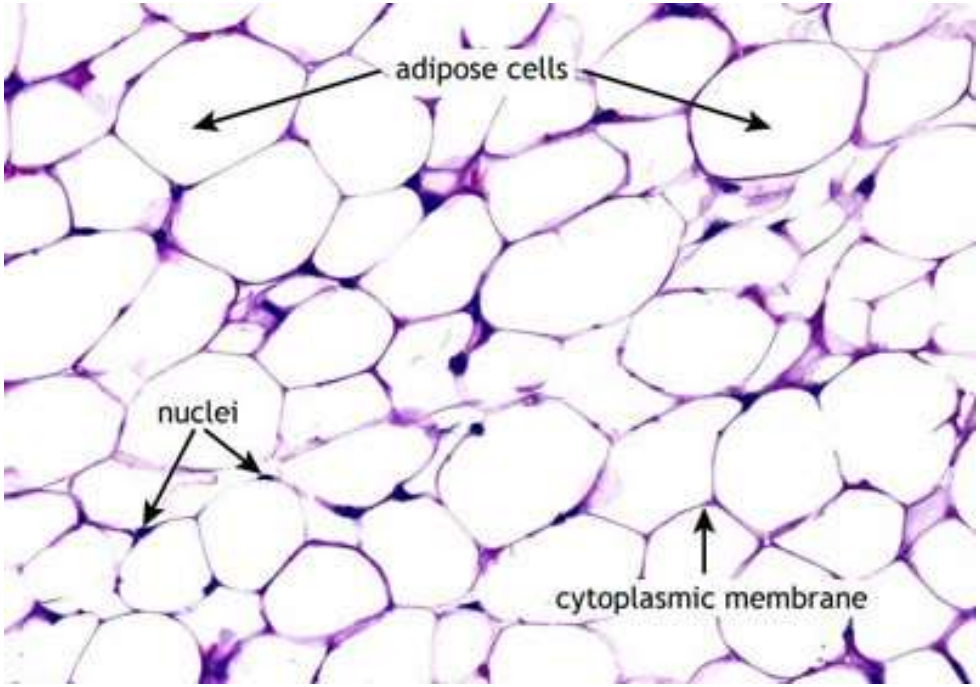
✓ Most lipomas are mobile, slowly enlarging, painless masses (although angiolipomas can manifest with local pain).

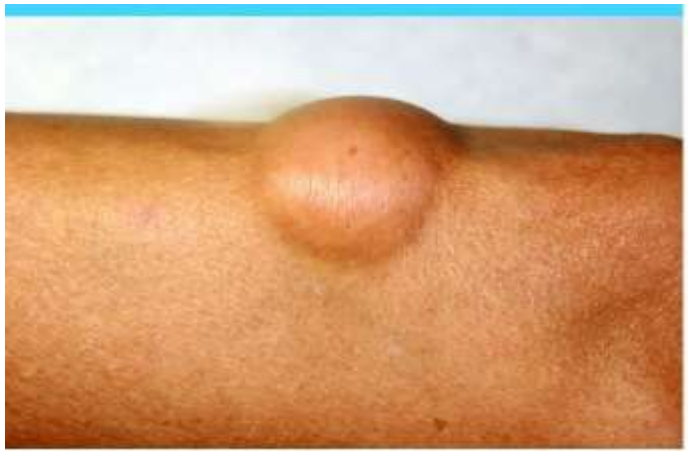
✓ Complete excision usually is curative.

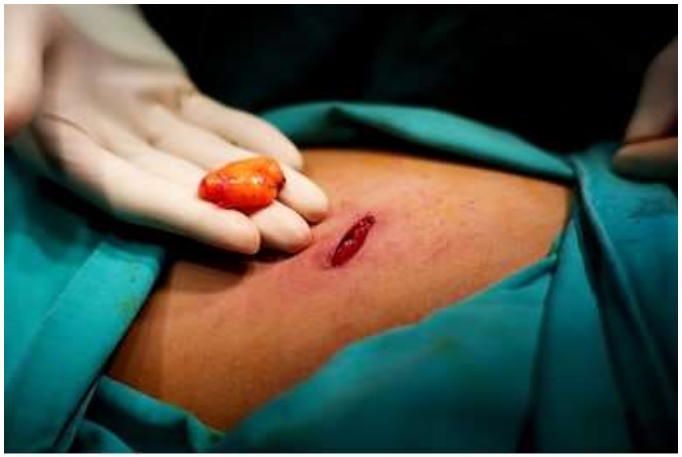
✓ Macroscopically: soft, yellow, well-encapsulated masses.

✓ Microscopically: On histologic examination, they consist of mature white fat cells with no pleomorphism.

Normal adipose tissue







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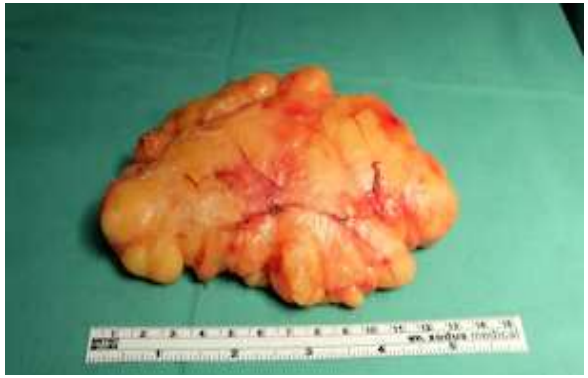
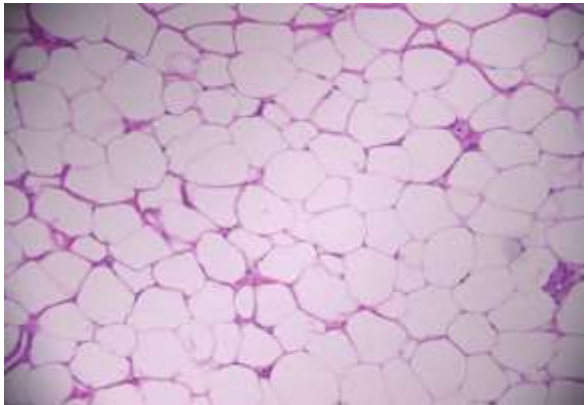
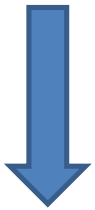




LIPOMYOSARCOMA:

- Liposarcomas are malignant neoplasms with adipocyte differentiation.
- They occur most commonly in the fifth and sixth decades of life.
- Most liposarcomas arise in the deep soft tissues or in the retroperitoneum.
- The prognosis of liposarcomas is greatly influenced by the histologic subtype:

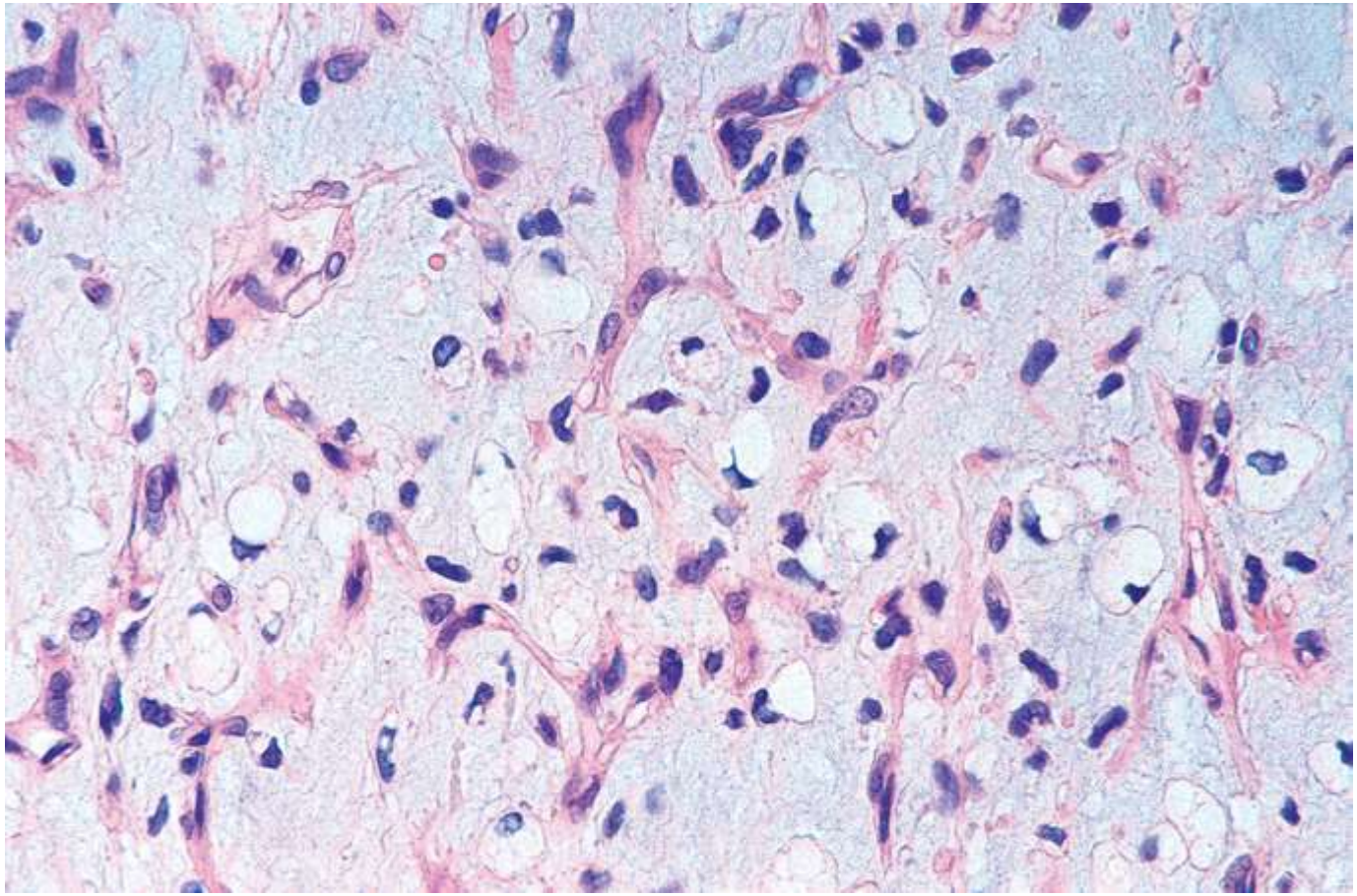
1. Well-differentiated .
2. Aggressive myxoid/round cell.
3. Pleomorphic variants



- In most cases, cells indicative of fatty differentiation known as lipoblasts are present; they have cytoplasmic lipid vacuoles

that scallop the nucleus and appearance recapitulating that of fetal fat cells.

Myxoid liposarcoma. Adult-appearing fat cells and more primitive cells, with lipid vacuoles (lipoblasts), are scattered in abundant myxoid matrix and a rich, arborizing capillary network.



2- FIBROUS TUMORS AND TUMOR-LIKE LESIONS

Fibrous tissue proliferations are a heterogeneous group of lesions.

It includes:

1- Reactive Proliferations:- Nodular Fasciitis

2- In the middle :- Fibromatoses

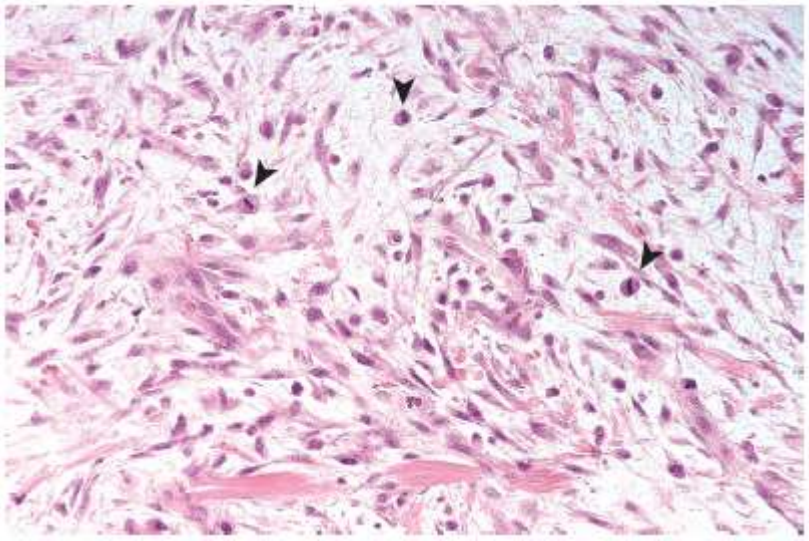
3- Neoplasm:-Fibrosarcoma

Reactive Proliferations

Nodular Fasciitis

- ✓ Nodular fasciitis is a self-limited fibroblastic proliferation that typically occurs in adults on the forearm, the chest, or the back.
- ✓ Patients characteristically present with a several-week history of a solitary, rapidly growing, and occasionally painful mass.
- ✓ Preceding trauma is noted in 10% to 15% of cases.
- ✓ Nodular fasciitis rarely recurs after excision.

Nodular fasciitis. A highly cellular lesion composed of plump, randomly oriented spindle cells surrounded by myxoid stroma.
Note the prominent mitotic activity



Fibromatoses

- The fibromatoses are a group of fibroblastic proliferations distinguished by:
- Their tendency to grow in an infiltrative fashion.
- To recur after surgical removal.
- Locally aggressive.
- They do not metastasize.

- Macroscopically: Fibromatoses are gray-white, firm to rubbery, poorly demarcated, infiltrative masses 1 to 15 cm in greatest dimension.

- Microscopically:

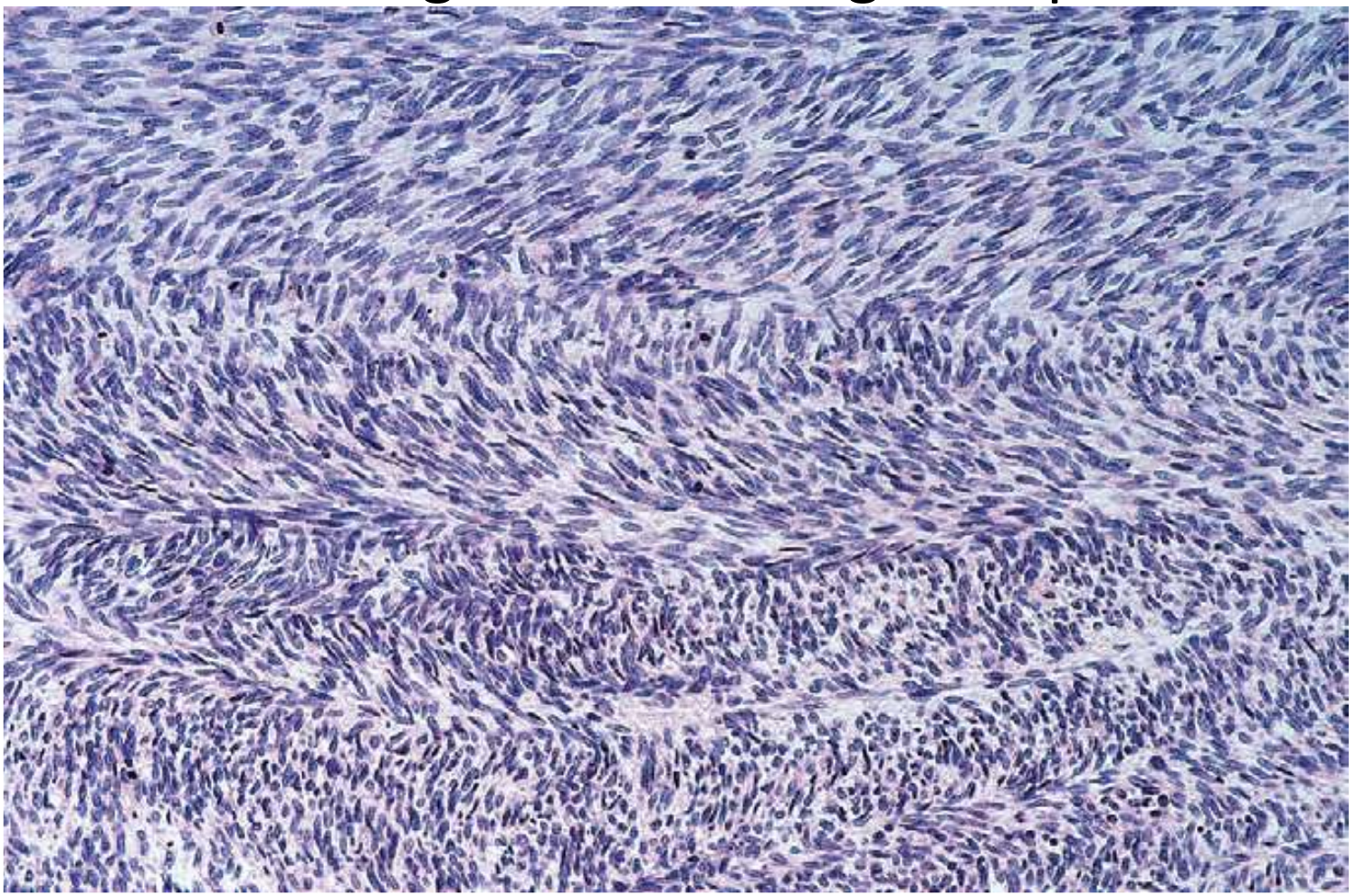
- On histologic examination, they are composed of plump spindle cells arranged in broad sweeping fascicles that penetrate the adjacent tissue; mitoses are few in number.

➢ The fibromatoses are divided into two major clinicopathologic groups: superficial and deep.

Fibrosarcomas

- ✓ Fibrosarcomas are malignant neoplasms composed of fibroblasts.
- ✓ Most occur in adults, typically in the deep tissues of the thigh, knee, and retroperitoneal area.
- ✓ Fibrosarcomas often recur locally after excision and can metastasize hematogenously , usually to the lungs.
- ✓ Macroscopically:Fibrosarcomas are soft unencapsulated, infiltrative masses that frequently contain areas of hemorrhage and necrosis.
- ✓ Microscopically:Histologic examination discloses all degrees of differentiation, from tumors that closely resemble fibromatoses, to tumor which are highly cellular neoplasms exhibiting architectural disarray (Herringbone Fashion), pleomorphism, frequent mitoses, and necrosis.

Fibrosarcoma. Malignant spindle cells here are arranged in a herringbone pattern.



3- FIBROHISTIOCYTIC TUMORS

Fibrohistiocytic tumors are composed of a mixture of fibroblasts and phagocytic, lipid-laden cells resembling activated tissue macrophages (also called histiocytes by morphologists).

- ✓ These tumors span a broad range of histologic patterns and biologic behavior, from self-limited benign lesions to aggressive high-grade sarcomas.

1-Benign Fibrous Histiocytoma (Dermatofibroma)

2- Pleomorphic Fibroblastic Sarcoma/Pleomorphic Undifferentiated Sarcoma

Skeletal Muscle Tumors

Rhabdomyosarcoma

- ✓ Rhabdomyosarcoma is the most common soft tissue sarcoma of childhood and adolescence, usually appearing before age 20.

- ✓ Of interest, it occurs most commonly in the head and neck or genitourinary tract.

- ✓ Rhabdomyosarcoma is histologically subclassified into the embryonal, alveolar, and pleomorphic variants.

- ✓ Macroscopically: The gross appearance of these tumors is variable.
- ✓ Microscopically : The rhabdomyoblast is the diagnostic cell in all types; it has granular eosinophilic cytoplasm rich in thick and thin filaments. The rhabdomyoblasts may be round or elongated; the latter are known as tadpole or strap cells and may contain cross-striations visible by light microscopy.

- ✓ The diagnosis of rhabdomyosarcoma is based on the demonstration of skeletal muscle differentiation, either in the form of sarcomeres under the electron microscope or by immunohistochemical demonstration of skeletal muscle specific transcription factors such as myogenin and MYOD-1, and the muscle-associated intermediate filament desmin.

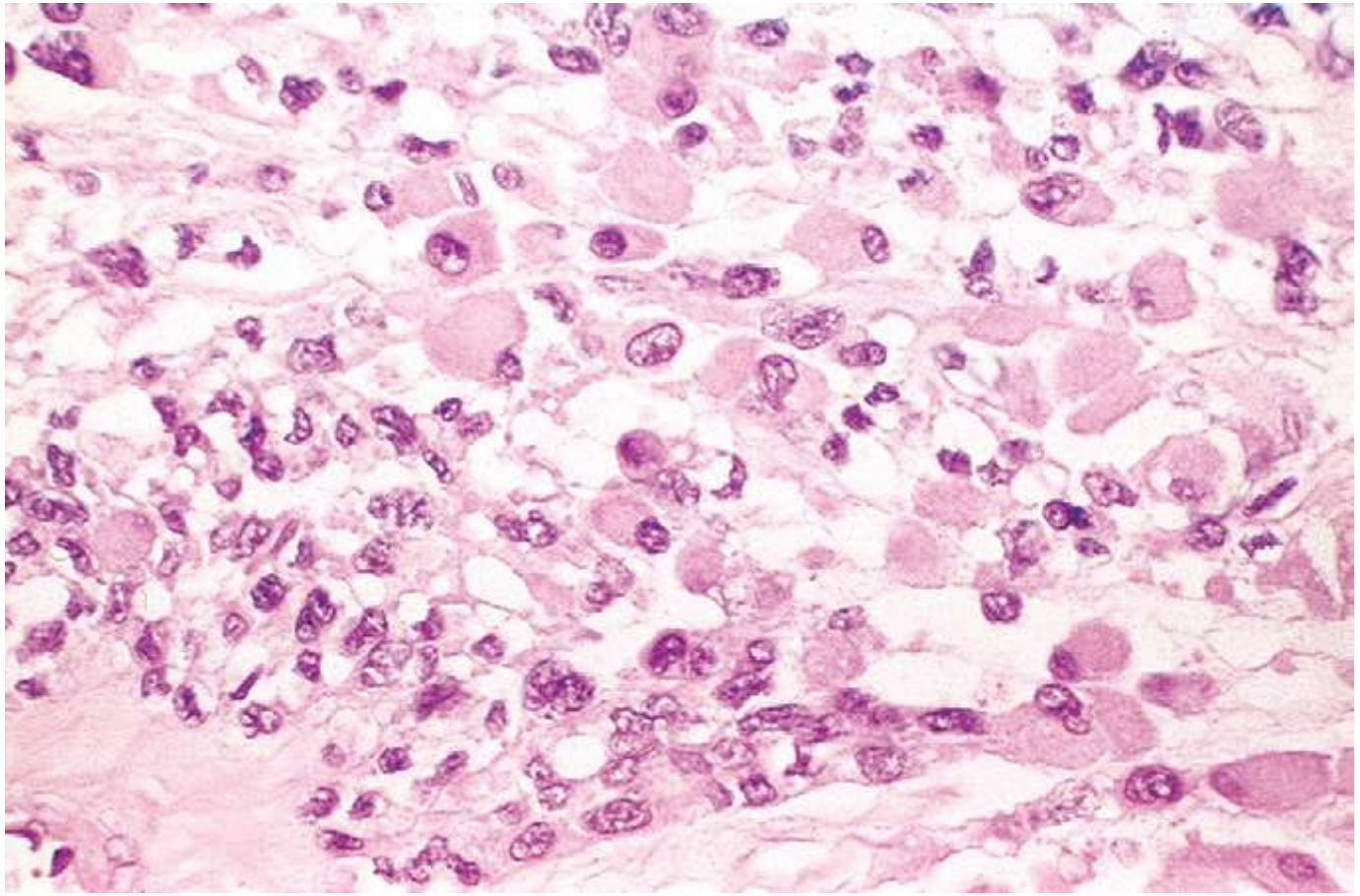
- Chromosomal translocations are found in most cases of the alveolar variant; the more common t(2;13) translocation fuses the PAX3 gene on chromosome 2 with the FKHR gene on chromosome 13.

- Rhabdomyosarcomas are aggressive neoplasms treated with a combination of surgery, chemotherapy, and radiation.

- Location, histologic appearance, and tumor genetics all impact the likelihood of cure, with progressively worsening rates for embryonal, pleomorphic, and alveolar variants, in that order.

- The malignancy is curable in almost two thirds of children; the prognosis is much less favorable in adults with the pleomorphic type.

Rhabdomyosarcoma. The rhabdomyoblasts are large and round and have abundant eosinophilic cytoplasm.



SMOOTH MUSCLE TUMORS

Leiomyoma

- ✓ Benign smooth muscle tumors, or leiomyomas, are common, well-circumscribed neoplasms that can arise from smooth muscle cells anywhere in the body but are encountered most commonly in the uterus and the skin.

Leiomyosarcoma

- ✓ Leiomyosarcomas account for 10% to 20% of soft tissue sarcomas.
- ✓ They occur in adults, more commonly females.
- ✓ Skin and deep soft tissues of the extremities and retroperitoneum (inferior vena cava) are common sites.
- ✓ These neoplasms manifest as firm, painless masses; retroperitoneal tumors can be large and bulky and cause abdominal symptoms.
- ✓ Histologic examination shows spindle cells with cigar-shaped nuclei arranged in interwoven fascicles.
- ✓ Superficial or cutaneous leiomyosarcomas usually are small and carry a good prognosis, whereas retroperitoneal tumors are large and difficult to excise and cause death by both local extension and metastatic spread.

Synovial sarcoma

- Synovial sarcoma was originally believed to recapitulate synovium; however, the phenotype of the neoplastic cells bears no resemblance to a synoviocyte, and despite the name, less than 10% of tumors are intra-articular.
- Synovial sarcomas account for approximately 10% of all soft tissue sarcomas, typically occurring in persons in their 20s to 40s.
- They usually develop in deep soft tissues around the large joints of the extremities, with 60% to 70% occurring around the knee.
- Most synovial sarcomas show a characteristic (X;18) translocation that produces a fusion gene encoding a chimeric transcription factor.
- Synovial sarcomas are treated aggressively with limb sparing surgery and chemotherapy.
- Common metastatic sites are lung, bone, and regional lymph nodes.

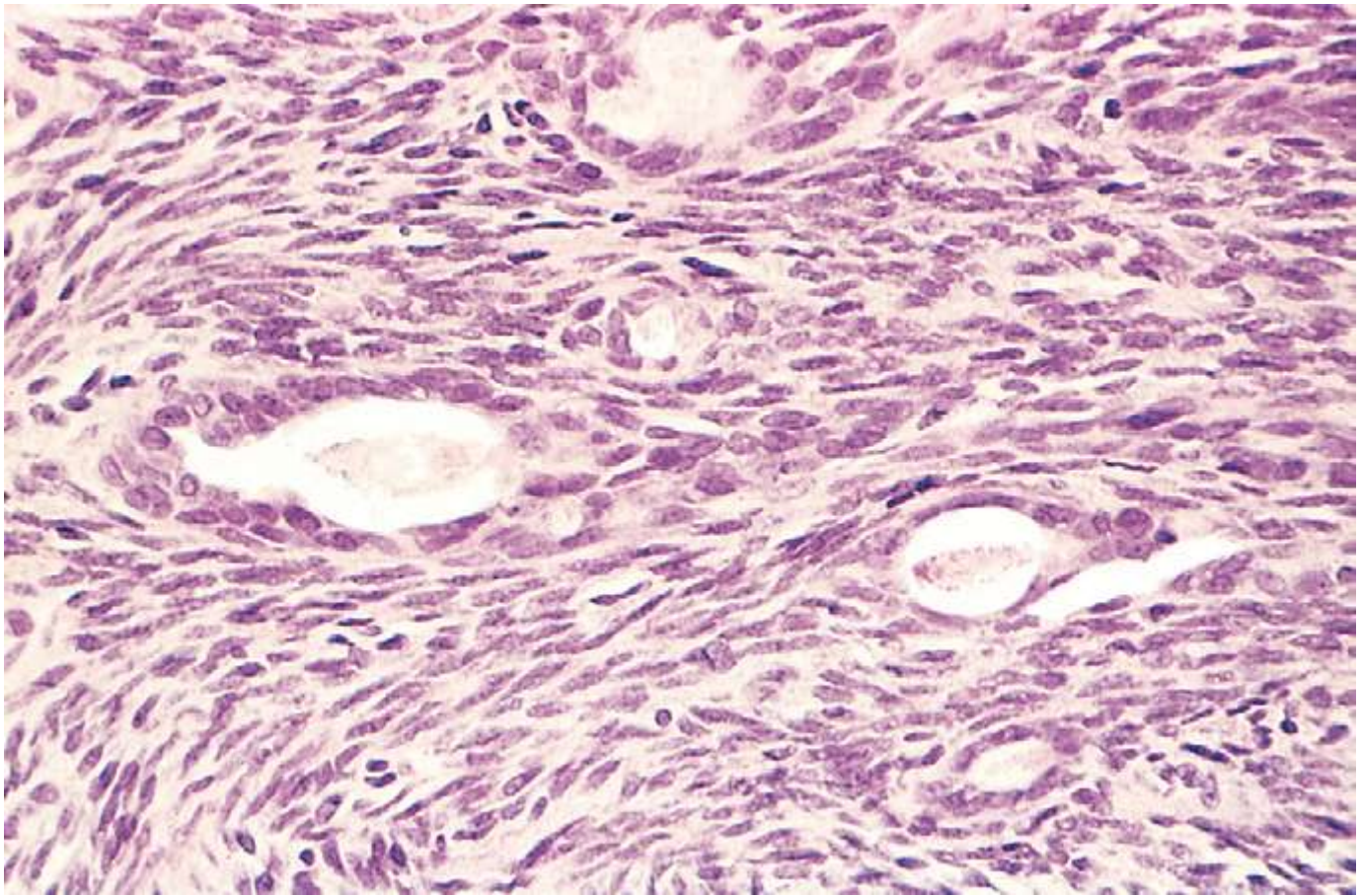
Microscopiacally:

On histologic examination, synovial sarcomas may be biphasic or monophasic.

- ✓ Classic **biphasic** synovial sarcoma exhibits

differentiation of tumor cells into both epithelial-type cells and spindle cells.

- ✓ Many of synovil sarcomas are **monophasic**—that is, composed of spindle cells only.



Bone Tumors

- 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

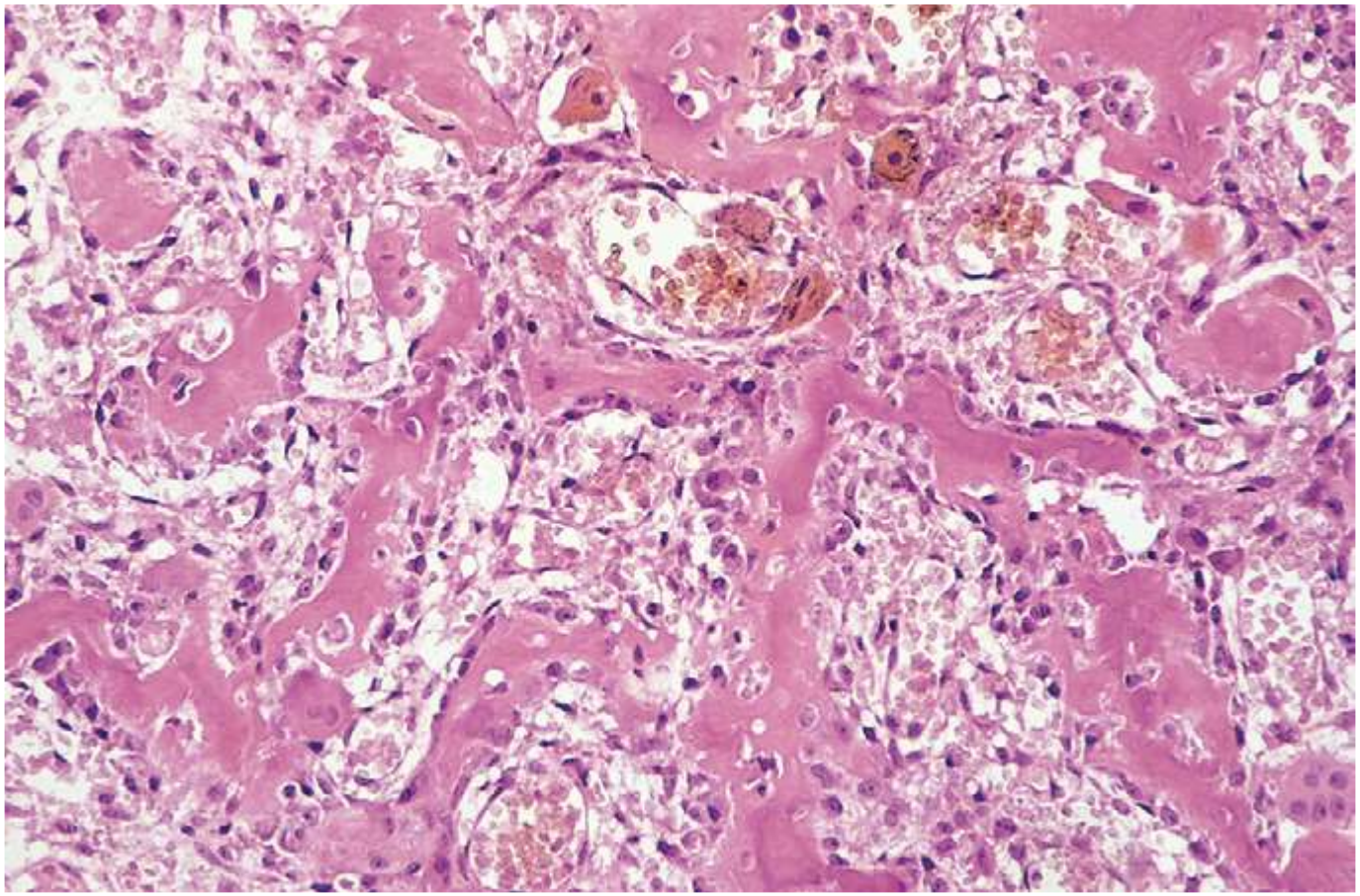
- Osteoid osteomas and osteoblastomas are benign neoplasms with very similar histologic features.
- Both lesions typically appear during the teenage years and 20s, with a male predilection (2 : 1 for osteoid osteomas).
- They are distinguished from each other primarily by their size and clinical presentation.
- 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.
- 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.

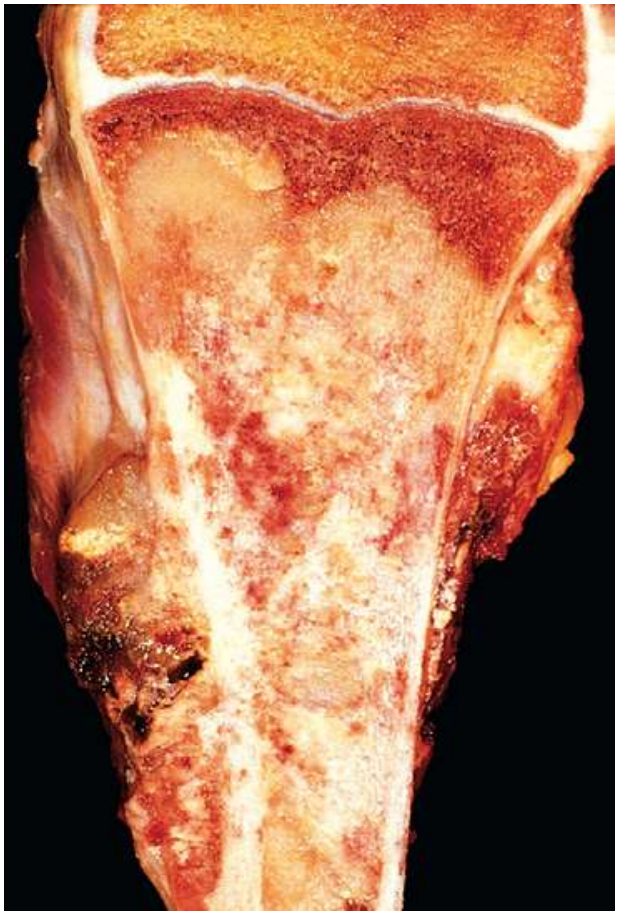


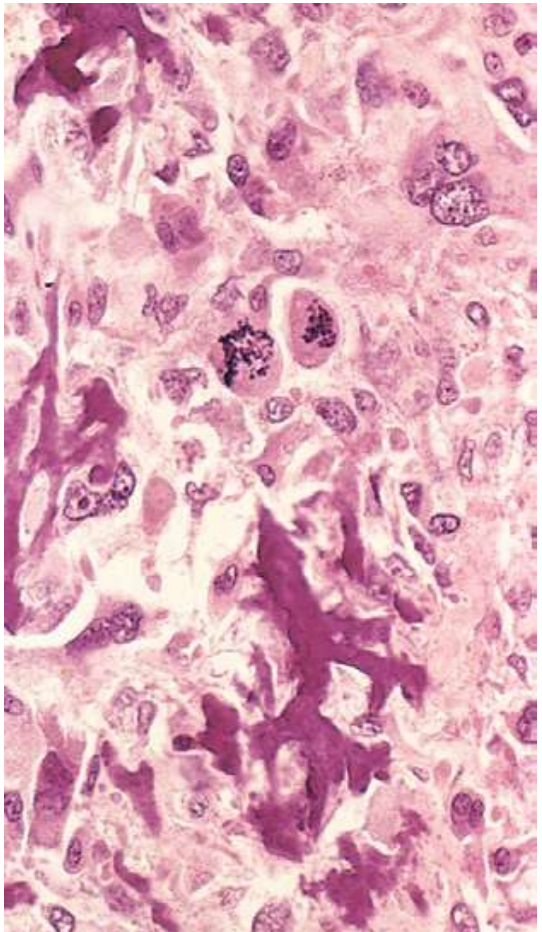
Osteosarcoma

- 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 (arrow) produced by anaplastic tumor cells. Note the wildly aberrant mitotic figures (arrowheads).





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

Variants of Chondrosarcomas:

- ✓ **Conventional chondrosarcoma, the most common variant**. It is composed of malignant hyaline and myxoid cartilage.

- ✓ **Myxoid chondrosarcomas**). Low-grade tumors may be difficult to distinguish from enchondroma. Higher-grade lesions contain pleomorphic chondrocytes with frequent mitotic figures.

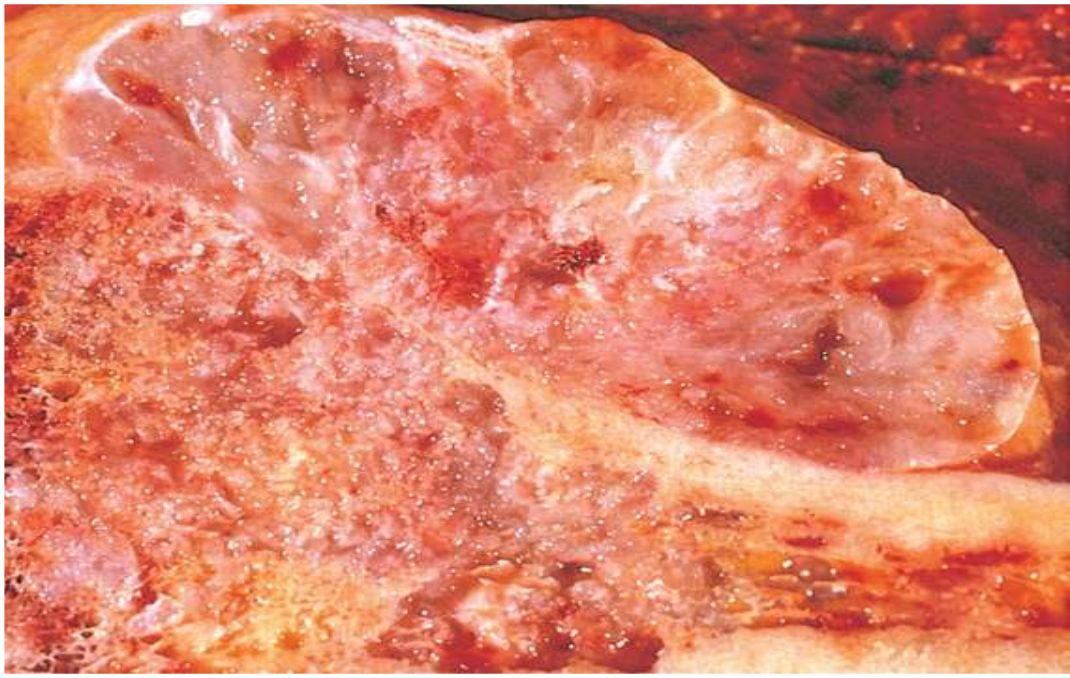
- ✓ Approximately 10% of patients with conventional lowgrade chondrosarcomas have a second high-grade poorly differentiated component **(dedifferentiated chondrosarcomas)**

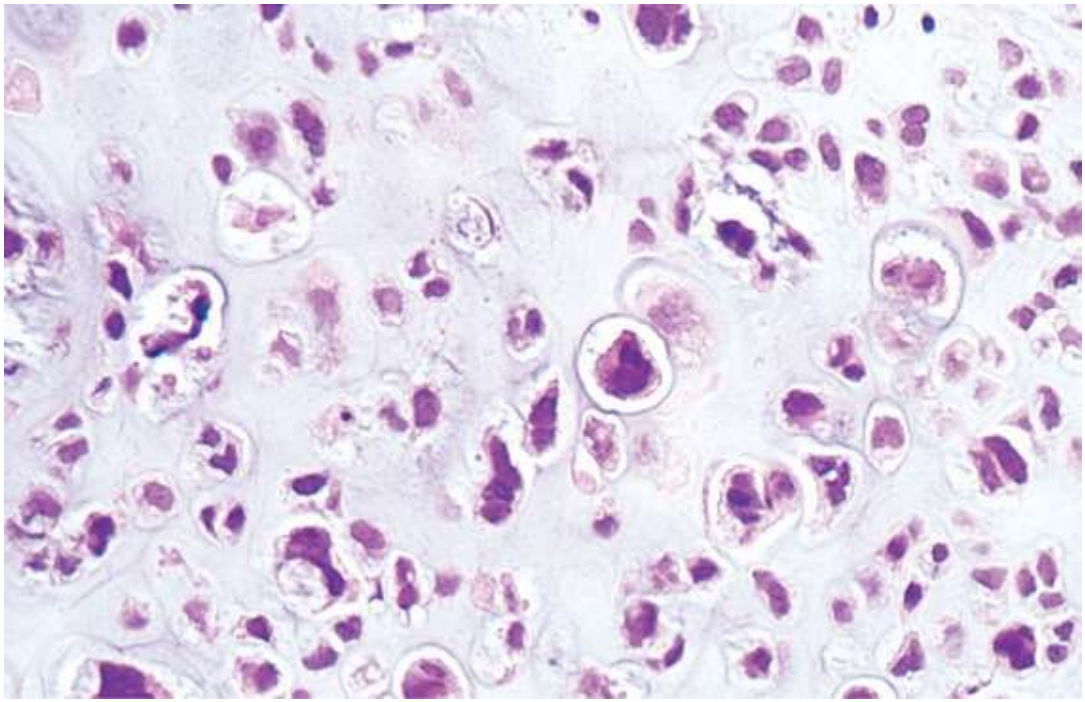
- ✓ **Clear cell chondrosarcomas.**

- ✓ **Mesenchymal chondrosarcomas.**

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.
- Conventional chondrosarcomas are treated with wide surgical excision.
- Chemotherapy is added for the mesenchymal and dedifferentiated Variants.

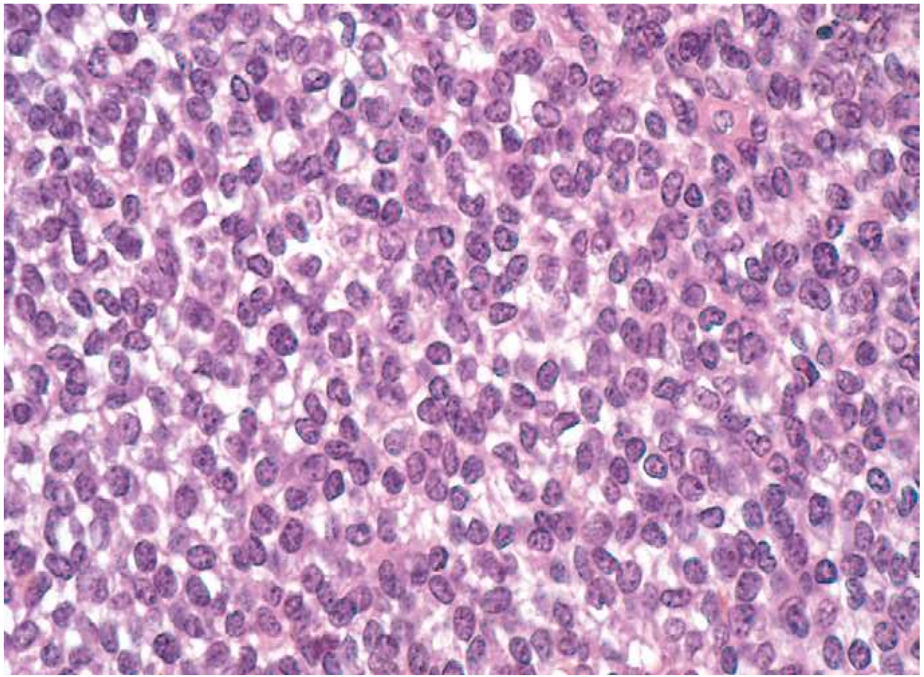
Miscellaneous Bone Tumors

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.
- **MORPHOLOGY**

GCTs are large and red-brown, and often show cystic degeneration.

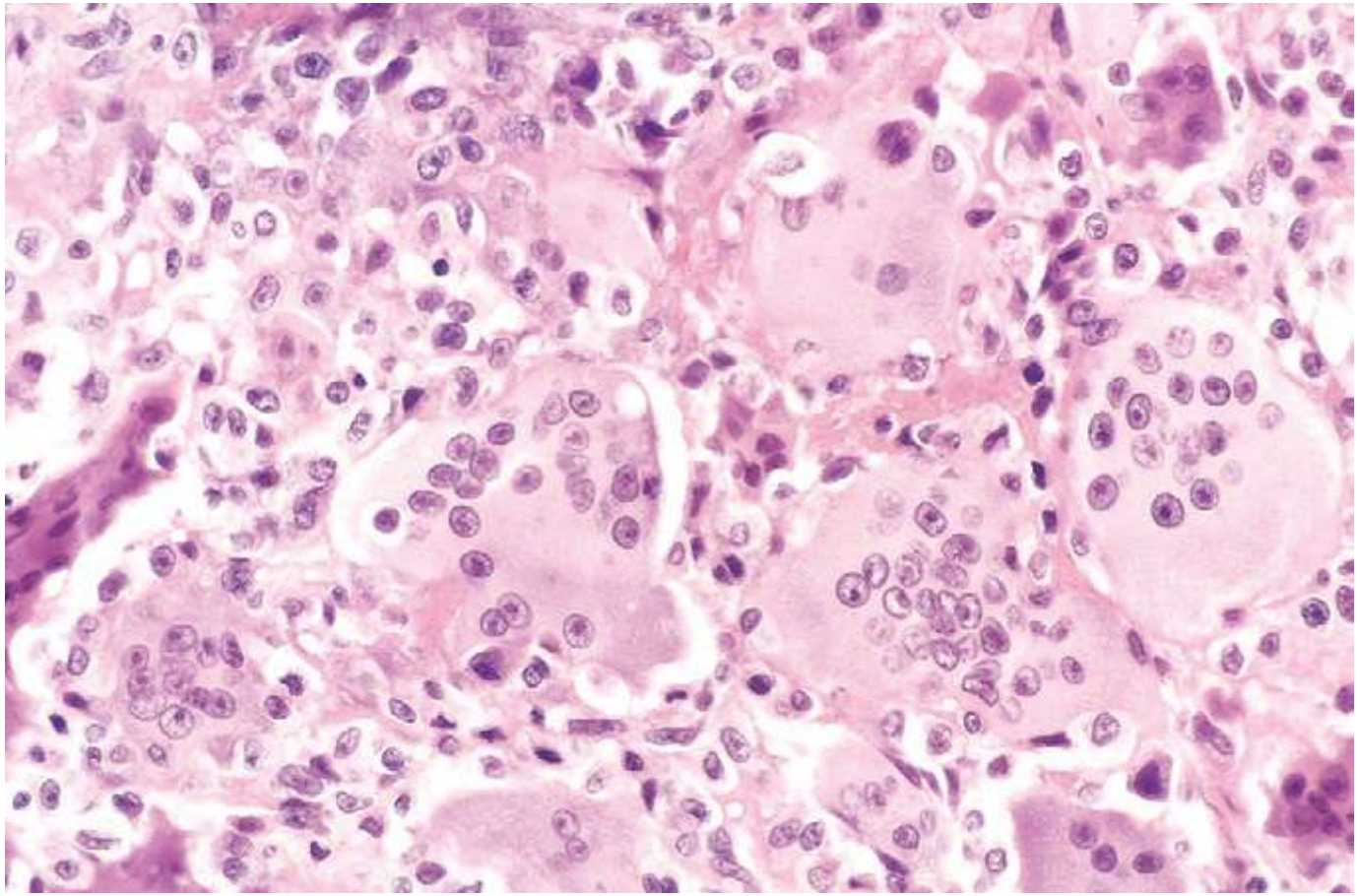
They are composed of uniform oval mononuclear cells and scattered osteoclast-type giant cells containing 100 or more nuclei. Mitotic figures are typically frequent. Necrosis, hemorrhage, and reactive bone formation also are commonly present.

- **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 from cancers 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 and melanoma),however; metastatic tumors that elicit an osteoblastic response (e.g., prostate adenocarcinoma).