BONE TUMORS

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Table 26-6 Classification of Major Primary Tumors Involving Bones

Category and fraction (%)	Behavior	Tumor type	Common locations	Age (yr)	Morphology
Hematopoietic (20)	Malignant	Myeloma Lymphoma	Vertebrae, pelvis	50-60	Malignant plasma cells or lymphocytes replacing marrow space
Cartilage forming (30)	Benign	Osteochondroma	Metaphysis of long bones	10-30	Bony excrescence with cartilage cap
		Chondroma	Small bones of hands and feet	30-50	Circumscribed hyaline cartilage nodule in medulla
		Chondroblastoma	Epiphysis of long bones	10-20	Circumscribed, pericellular calcification
		Chondromyxoid fibroma	Tibia, pelvis	20-30	Collagenous to myxoid matrix, stellate cells
	Malignant	Chondrosarcoma (conventional)	Pelvis, shoulder	40-60	Extends from medulla through cortex into soft tissue, chondrocytes with increased cellularity and atypia
Bone forming (26)	Benign	Osteoid osteoma	Metaphysis of long bones	10-20	Cortical, interlacing microtrabeculae of woven bone
		Osteoblastoma	Vertebral column	10-20	Posterior elements of vertebra, histology similar to osteoid osteoma
	Malignant	Osteosarcoma	Metaphysis of distal femur, proximal tibia	10-20	Extends from medulla to lift periosteum, malignant cells producing woven bone
Unknown origin (15)	Benign	Giant cell tumor	Epiphysis of long bones	20-40	Destroys medulla and cortex, sheets of osteoclasts
		Aneurysmal bone cyst	Proximal tibia, distal femur, vertebra	10-20	Vertebral body, hemorrhagic spaces separated by cellular, fibrous septae
	Malignant	Ewing sarcoma	Diaphysis of long bones	10-20	Sheets of primitive small round cells
		Adamantinoma	Tibia	30-40	Cortical, fibrous , bone matrix with epithelial islands
Notochordal (4)	Malignant	Chordoma	Clivus, sacrum	30-60	Destroys medulla and cortex, foamy cells in myxoid matrix

Adapted from Unni KK, Inwards CY: Dahlin's Bone Tumors, 6th ed. Philadelphia, Lippincott-Williams & Wilkins, 2010, p 5; by permission of Mayo Foundation.

Variations in age-specific incidence rates with morphology, England, 1998-2007

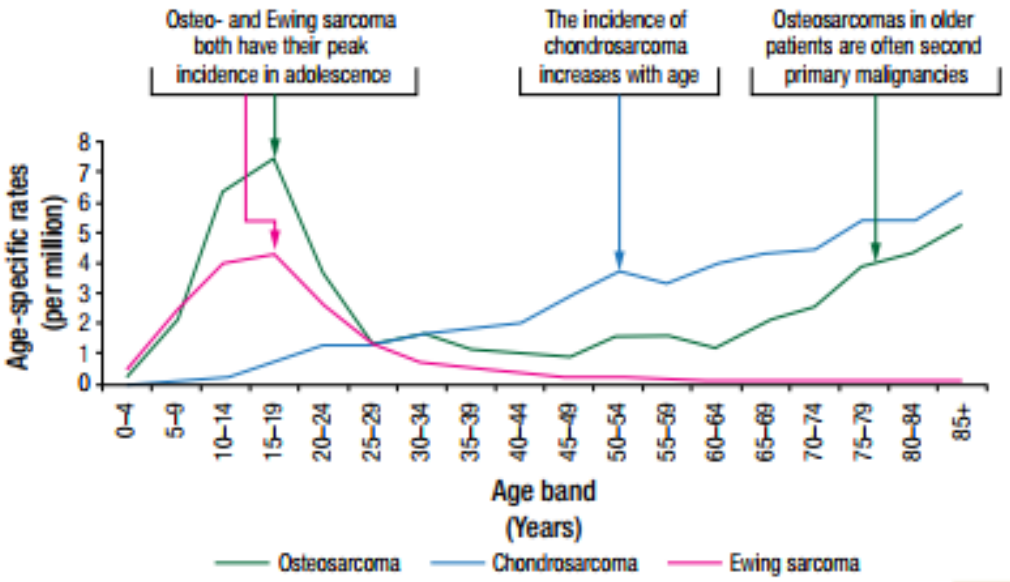


Fig. 4.1

Common x-ray locations of tumor in long bones

- Intrademullary:
- Ewing's sarcoma
- Lymphoma
- Myeloma
- Subcortical:
- Fibrous dysplasia (diaphysis)
- Adamantinoma (diaphysis)
- Chondromyxoid fibroma (diaphysis-metaphysis)
- Non-ossifying fibroma (metaphysis)

Common x-ray locations of tumor in long bones

- Periosteal:
- Osteoid osteoma
- Intracortical:
- Bone cyst
- Osteoblastoma (metaphysis)
- Enchondroma
- Chondrosarcoma
- Osteosarcoma (metaphysis-epiphysis)
- Giant cell tumor
- Chondroblastoma (epiphysis)

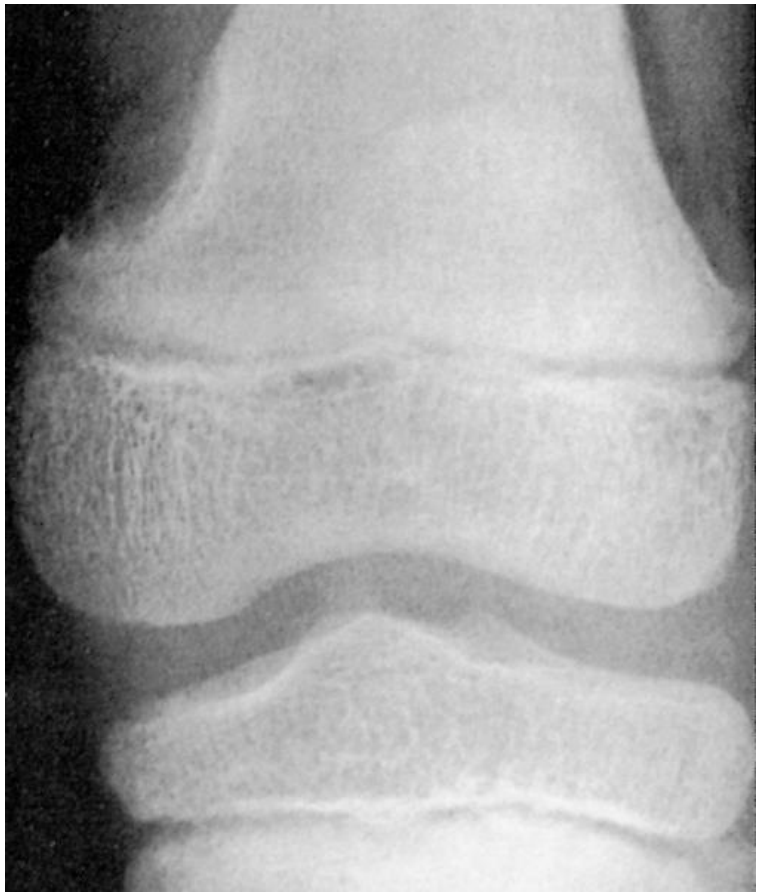
MRI characteristics

- Weighted: T1 short (time to recovery, time to echo); T2 is long.
- Gradient echo inversion recovery compatible with fat saturation.
- Proton dense lesions have long TR, short TE.
- Fibrous dense have low T1, T2
- Cysts have low T1, bright T2
- Fat is bright T1, gray T2
- Marrow is brighter than muscle on T1
- Free water is iso-intense on T1, bright on T2 (usually this represents tumor)

Fibrous cortical defect

- Found in 30% to 50% of all children older than age 2 years.
- The vast majority arise eccentrically in the metaphysis of the distal femur and proximal tibia; almost half are bilateral or multiple
- They are believed to be developmental defects rather than neoplasms.
- Often, they are small.
- Those that grow to 5 or 6 cm in size develop into nonossifying fibromas and are usually not detected until adolescence.

Fibrous cortical defect



This radiograph reveals a sharply demarcated cortical defect in the femoral metaphysis of an 8-year-old boy. Note the absence of periosteal new bone formation and the intact inner margin of the cortex. The vast majority arise eccentrically in the metaphysis of the distal femur and proximal tibia, and almost one half are bilateral or multiple.

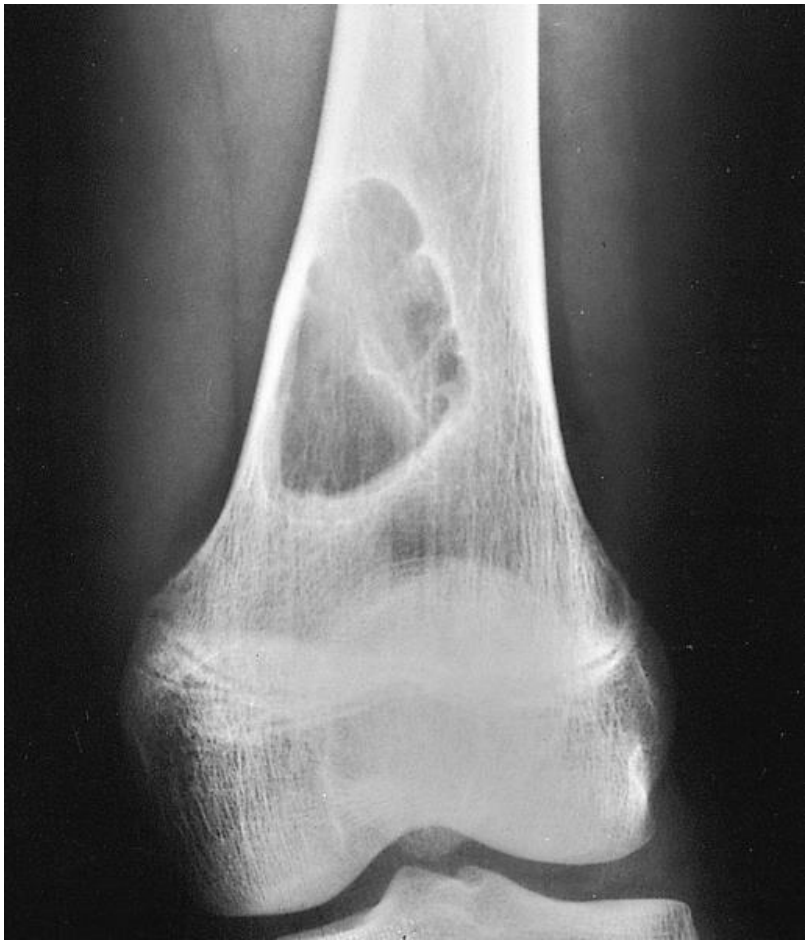
Fig. 282

Fechner, FE, Mills, SE. , “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Fibrous cortical defect

- Gray and yellow-brown tissue.
- Non-neoplastic proliferation.
- Cellular lesions composed of benign fibroblasts and histiocytes (activated macrophages).
- The fibroblasts are frequently arranged in a storiform (pinwheel) pattern, and the histiocytes are either multinucleated giant cells or clusters of foamy macrophages.
- Part of the spectrum that includes non-ossifying fibroma.

Non-ossifying fibroma

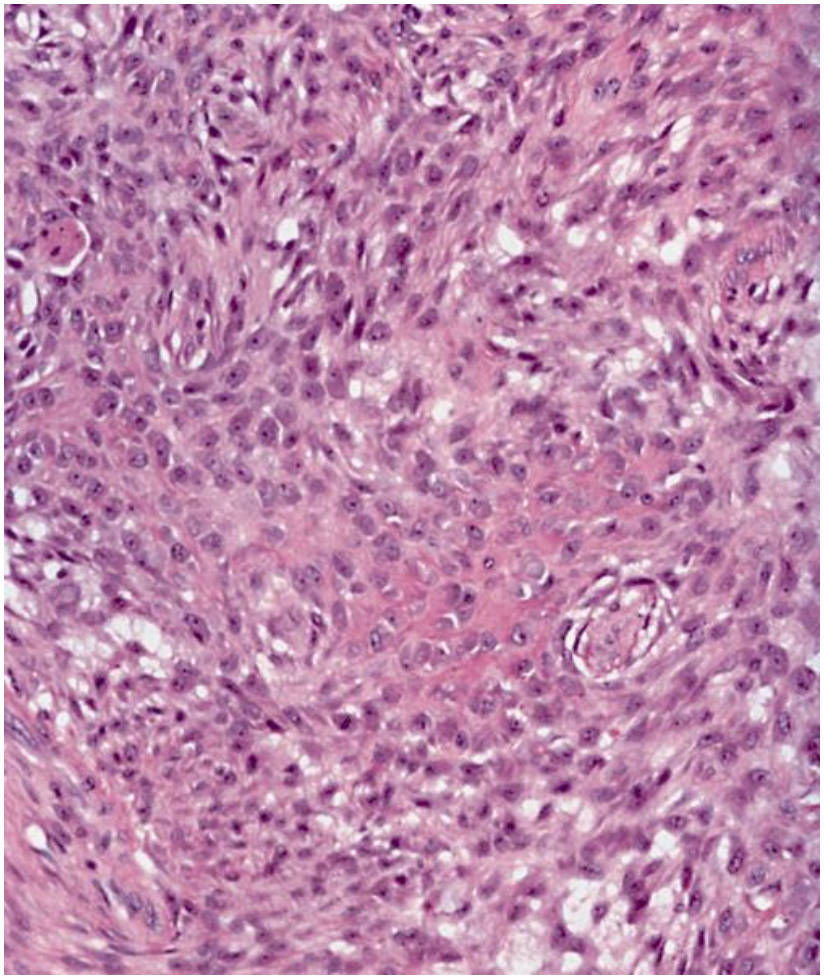


A 14-year-old boy had an non-ossifying fibroma discovered when a radiograph was taken following trauma to his knee. The lesion is lytic, irregular in outline, and has a sclerotic rim. Because of the size, the surgeon elected to curette the lesion and pack it with bone chips

Fig. 170

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Non-ossifying fibroma

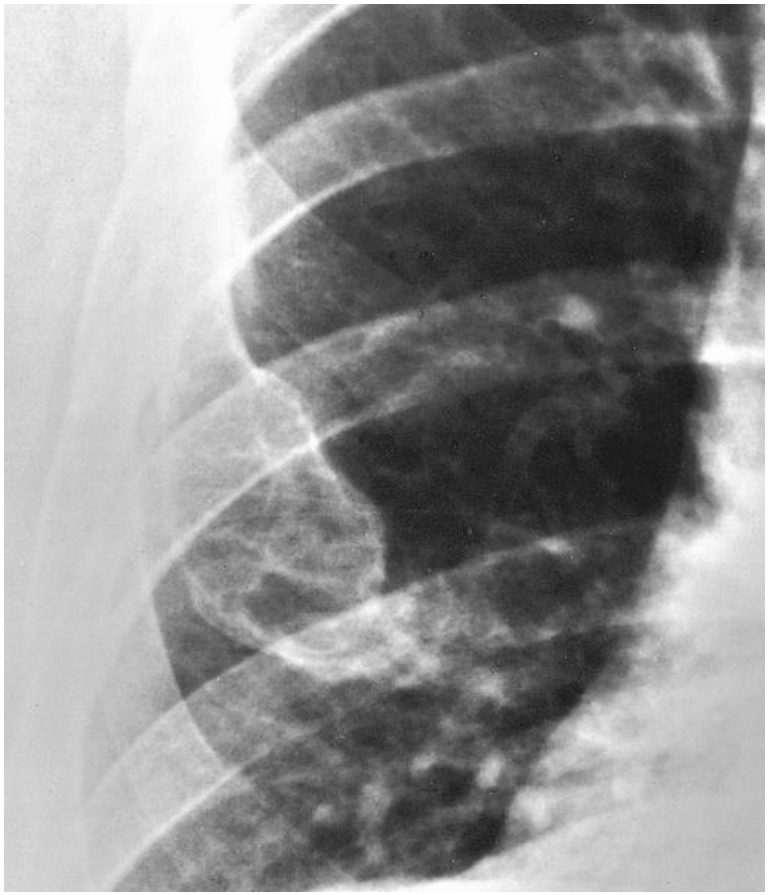


The cellular stroma is composed of spindle-to ovoid-shaped fibrocytic cells. An incipient focus of osteoid matrix formation is in the center.

Fig. 7-17

Sciubba, James J, Fantasia, John E, Kahn, Leonard B., "Tumors and cysts of the jaws." Atlas of Tumor Pathology, Third Series, Fascicle 29. Armed Forces Institute of Pathology. Washington, D.C. (2001)

Fibrous dysplasia



This expanded rib was an incidental finding on the chest radiograph of a 57-year-old man.

Fig. 172

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Fibrous dysplasia

- Benign tumor that has been likened to a localized developmental arrest.
- All of the components of normal bone are present, but they do not differentiate into their mature structures.
- Three distinctive clinical patterns:
- (1) involvement of a single bone (monostotic)
- (2) involvement of multiple, but never all, bones (polyostotic)
- (3) polyostotic disease with endocrine abnormalities, especially precocious puberty.

Fibrous dysplasia

- Monostotic fibrous dysplasia
- 70% of all cases.
- It occurs equally in boys and girls
- Usually in early adolescence
- Often stops growing at the time of growth plate closure.
- The ribs, femur, tibia, mandible, skull, and humerus are most commonly affected.

Fibrous dysplasia

- Polyostotic fibrous dysplasia without endocrine dysfunction
- 27% of all cases.
- It manifests at a slightly earlier age than the monostotic type and may continue to cause problems into adulthood.
- All forms of polyostotic disease have a propensity to involve the shoulder and pelvic girdles.
- Craniofacial involvement is present in 50% of patients who have a moderate number of bones affected and in 100% of patients with extensive skeletal disease.

Fibrous dysplasia

- Polyostotic fibrous dysplasia with endocrine abnormalities is the McCune-Albright syndrome and accounts for 3% of all cases.
- The bone lesions are often unilateral, and the skin pigmentation is usually limited to the same side of the body.
- The cutaneous macules are classically large; are dark to café au lait; have irregular serpiginous borders; and are found primarily on the neck, chest, back, shoulder, and pelvic region.
- Occurs principally in girls.

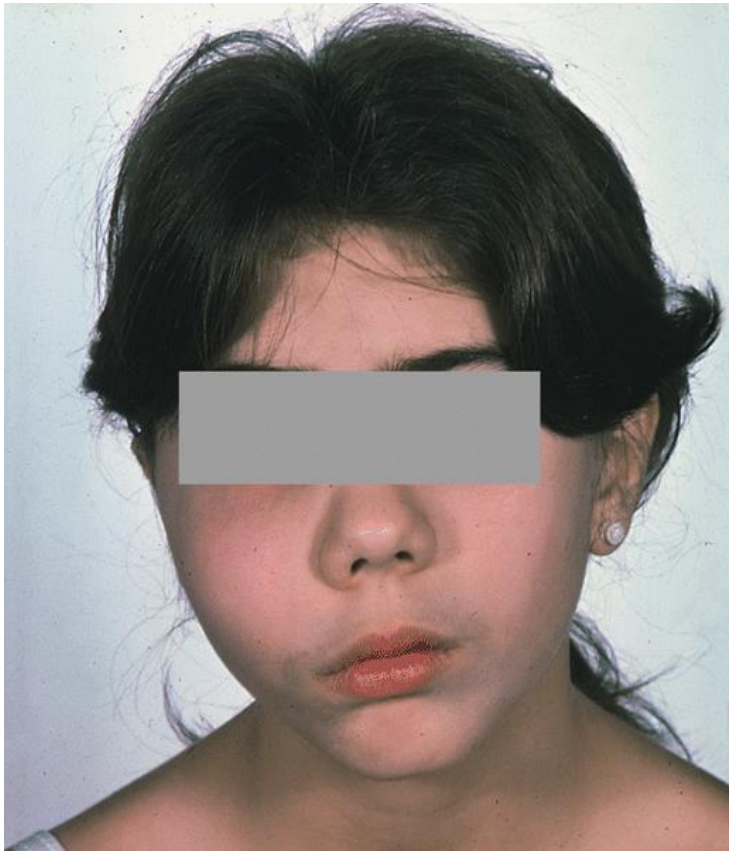
Fibrous dysplasia

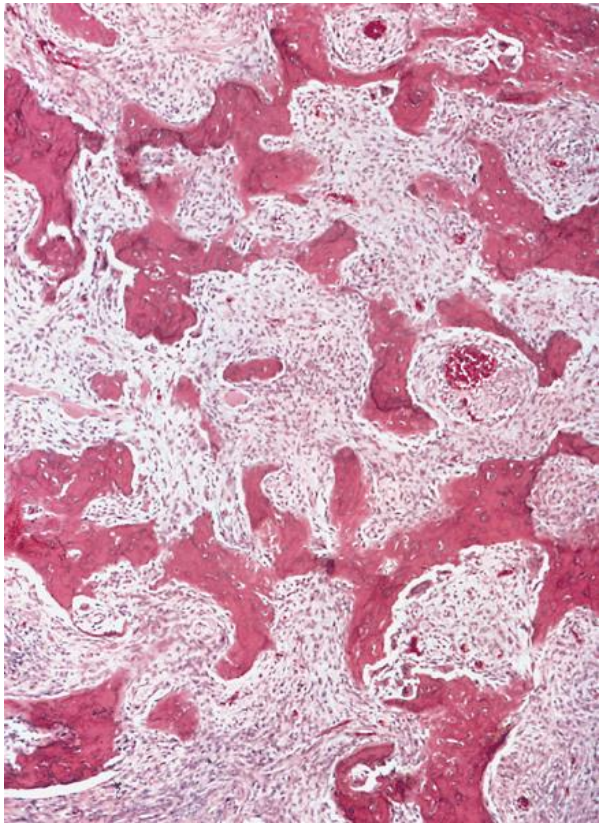
- The skeletal, skin and endocrine lesions result from a somatic mutation occurring during embryogenesis that involves a gain of function of the GNAS gene at 20q13.32 (encodes for a guanine nucleotide-binding protein).
- The mutation results in constitutive activation of adenyl cyclase so that excess production of cAMP occurs, leading to hyperfunction of cells in the involved tissues (usually endocrine glands)
- Normally regulates osteogenesis, blocking ectopic bone formation.

Fibrous dysplasia

- Tan, gritty, composed of curvilinear trabeculae of woven bone surrounded by a moderately cellular fibroblastic proliferation.
- The shapes of the trabeculae mimic Chinese characters, and the bone lacks osteoblastic rimming.
- Nodules of hyaline cartilage with the appearance of disorganized growth plate are also present in 20% of cases.
- Cystic degeneration, hemorrhage, and foamy macrophages are other common findings.

Fibrous dysplasia of the maxilla





Figs. 7-4 and 7-5

Sciubba, James J, Fantasia, John E, Kahn, Leonard B., “Tumors and cysts of the jaws.” Atlas of Tumor Pathology, Third Series, Fascicle 29. Armed Forces Institute of Pathology. Washington, D.C. (2001)

Variously shaped spicules of woven bone (resembling Chinese characters) separated by moderately cellular fibrovascular stroma are noted.

Osteoid osteoma

- Less than 2 cm in greatest dimension.
- Seventy-five per cent of patients are under age 25
- Men outnumber women 2:1.
- Can arise in any bone but have a predilection for the appendicular skeleton.
- Fifty percent of cases involve the femur or tibia, where they commonly arise in the cortex and less frequently within the medullary cavity.
- Usually, there is a thick rind of reactive cortical bone that may be the only clue radiographically

Osteoid osteoma

- Those that arise beneath the periosteum, usually elicit a tremendous amount of reactive bone formation that encircles the lesion.
- The actual tumor, known as the nidus**,** manifests radiographically as a small round lucency that is variably mineralized.
- Osteoid osteomas are painful lesions.
- The pain is characteristically nocturnal
- Proliferating osteoblasts produce prostaglandin E_2
- Responds to NSAIDS

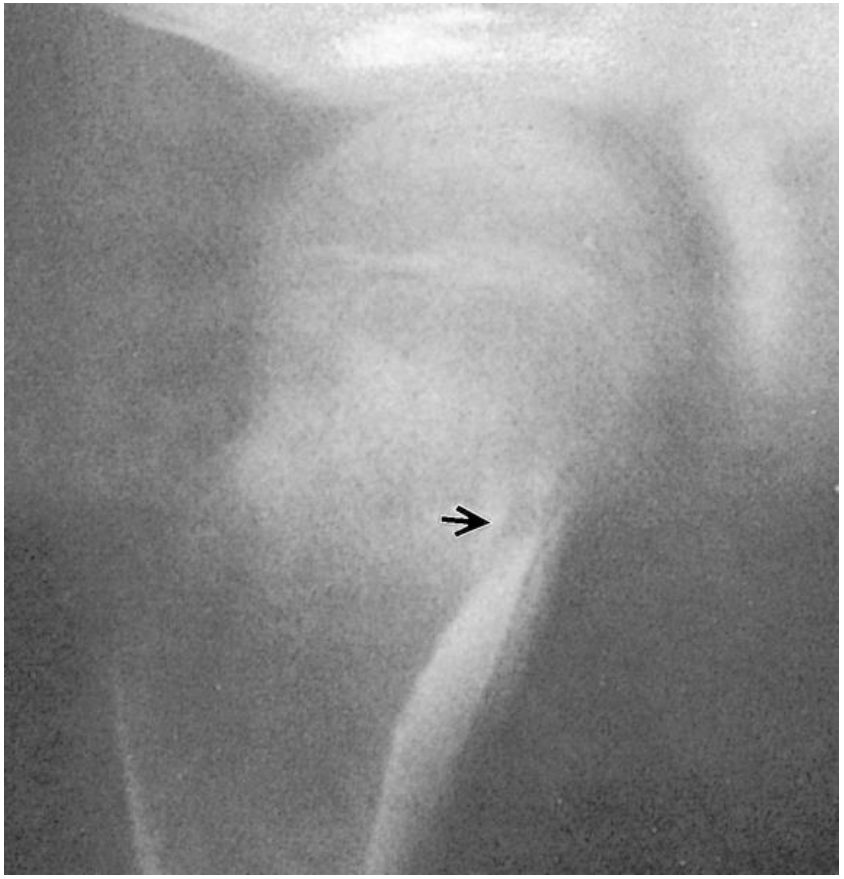
Osteoblastoma

- Frequently involves the spine
- Does not induce a marked bony reaction.
- The pain is dull, achy
- Does not respond to NSAIDs
- Resembles osteoid osteoma

Osteoid osteoma and osteoblastoma

- Grossly, both osteoid osteoma and osteoblastoma are round to oval masses of hemorrhagic gritty tan tissue.
- Histologically, they are well circumscribed and composed of a morass of randomly interconnecting trabeculae of woven bone prominently rimmed by single layer of osteoblasts.
- The stroma surrounding the tumor bone consists of loose connective tissue that contains many dilated and congested capillaries.
- Elicit the formation of reactive bone about the tumor (“nidus”).

Osteoid osteoma



This tomogram shows an osteoid osteoma in the femoral neck of a 12-year-old girl treated for arthritis because of a painful effusion. After several months, this radiograph was taken demonstrating sclerosis around the nidus (arrow). There is also periosteal new bone formation that corresponds with the extracapsular reaction to the lesion. Intracapsular reactive bone is lacking.

Fig. 15

Fechner, FE, Mills, SE. , “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

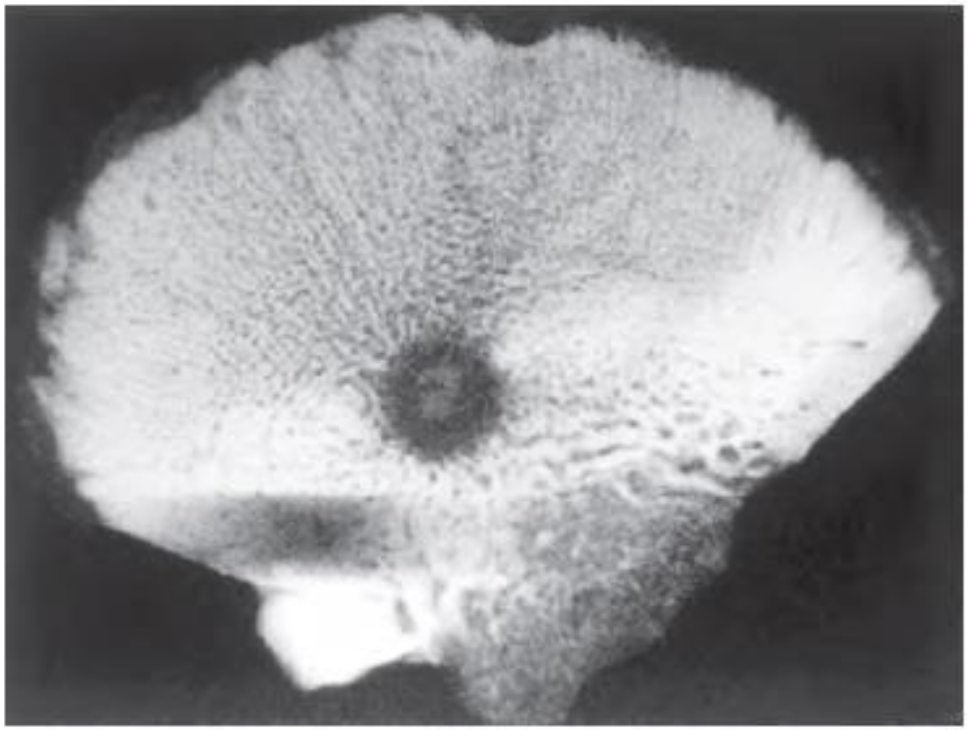
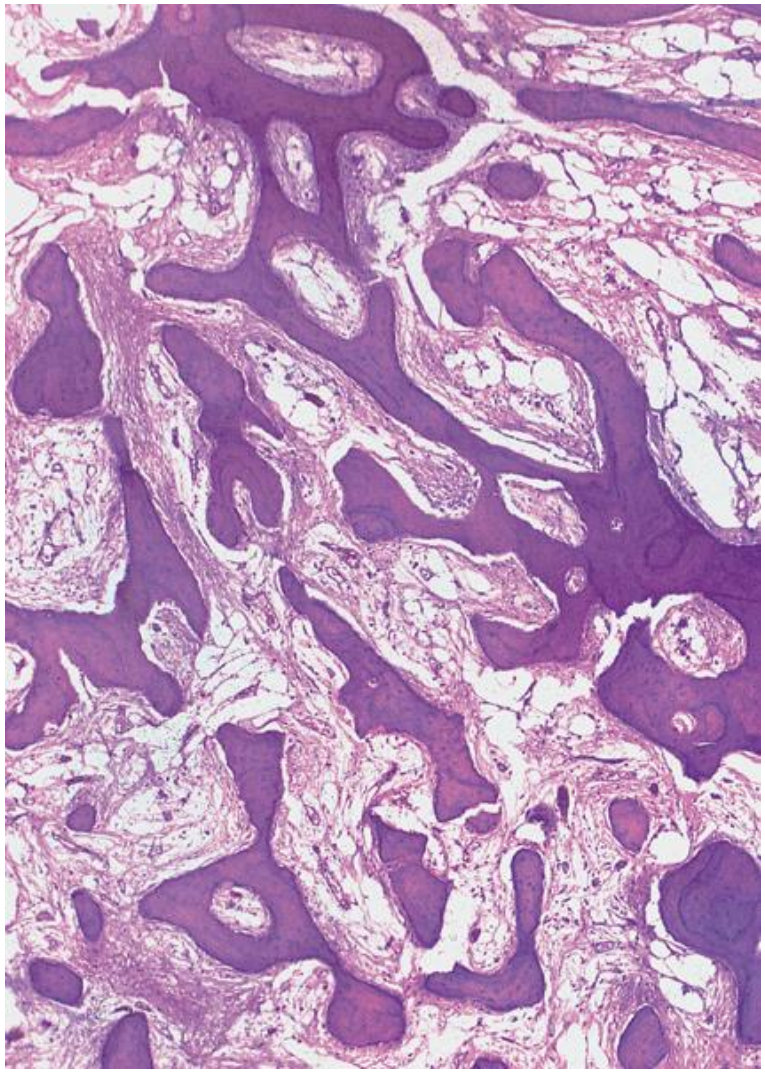


Figure 26-22 Specimen radiograph of intracortical osteoid osteoma. The round radiolucency with central mineralization represents the lesion and is surrounded by abundant reactive bone that has massively thickened the cortex.

Osteoid osteoma



A well-circumscribed nodule of mature dense bone is the characteristic feature. Bony trabeculae sometimes are rimmed by osteoblasts. Between bony trabeculae there may be fibrous tissue or fatty stroma with varying amounts of hematopoietic elements. Occasionally, there are foci of mature cartilage.

Fig. 11-6

Mills, SE, Gaffey, MJ, Frierson, HF. , “Tumors of the upper aerodigestive tract and ear.” Atlas of Tumor Pathology, Third Series, Fascicle 26. Armed Forces Institute of Pathology, Washington, D.C. 2006.

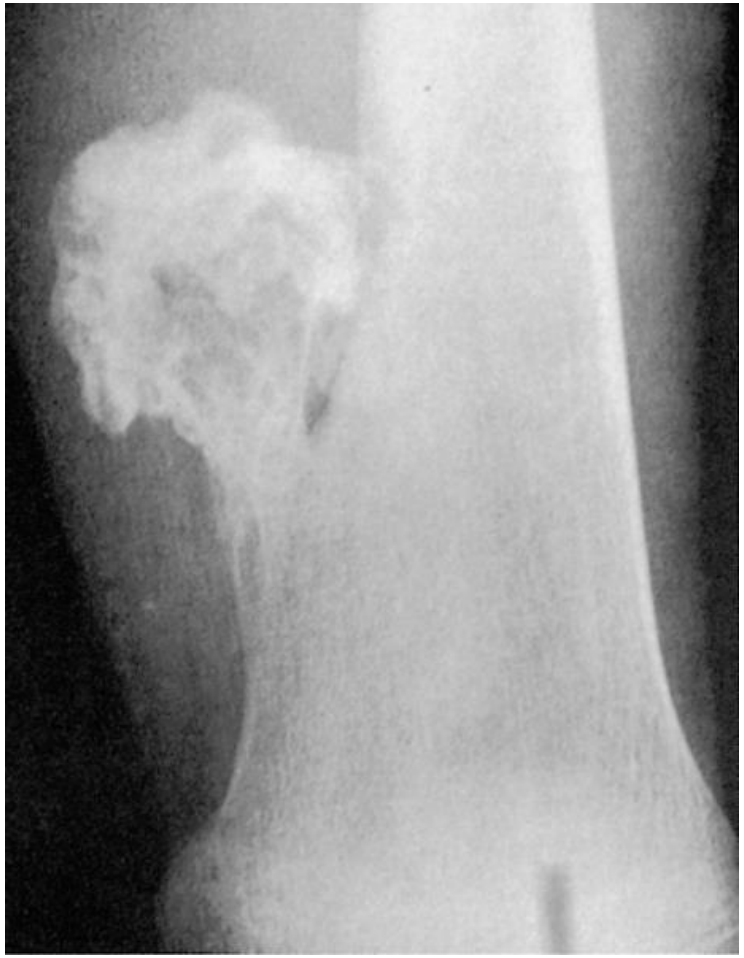
Osteochondroma

- Most common bone tumor.
- Also known as an exostosis.
- Benign cartilage-capped outgrowth that is attached to the underlying skeleton by a bony stalk.
- 10-15% of all bone tumors found on x-ray
- May be solitary or multiple.
- Multiple osteochondromas occur in hereditary multiple exostosis or in Trevor disease (arise in epiphysis)
- Both are autosomal dominant
- Symptomatic if fracture or impinge on another structure

Osteochondroma

- Germline mutation
- Inactivation of both copies of the EXT 1 gene at 8q24.11 (65%) or EXT 2 gene at 11p11.2 (35%) in growth plate chondrocytes.
- EXT1 encodes protein in Golgi that bind to EXT2 gene product
- Function in the biosynthesis and binding of heparan sulfate proteoglycans.

Osteochondroma

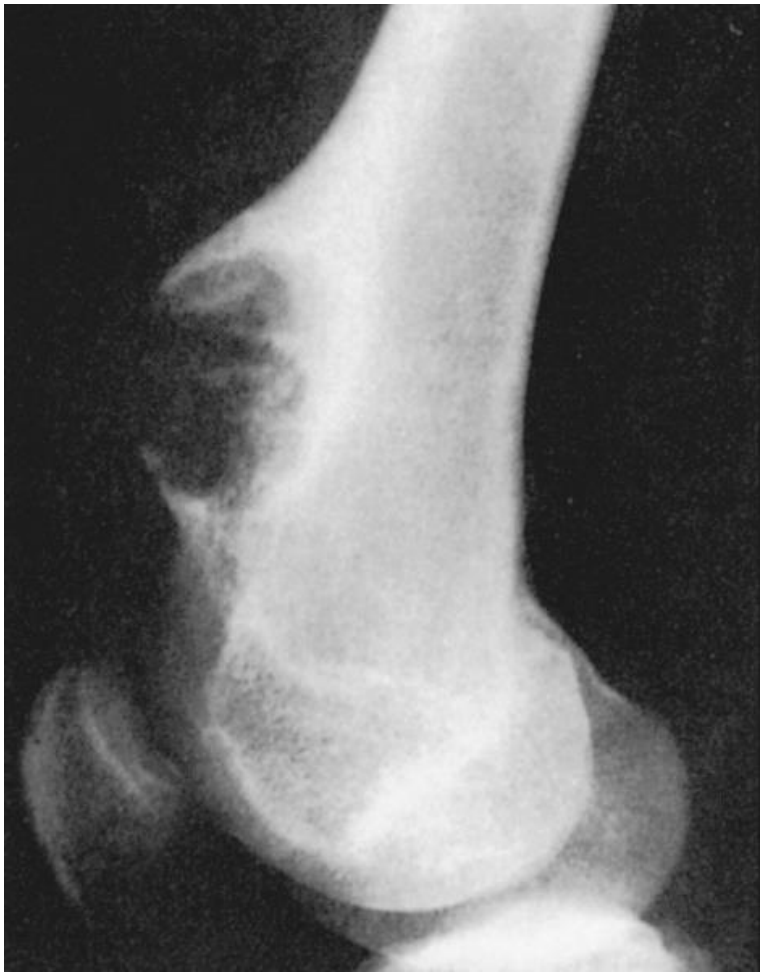


An osteochondroma involving the distal portion of the femur in a 13-year-old boy has a well-circumscribed, knobby surface. The lesion forms an acute angle with the cortex of the femur, and the cartilaginous cap is pointed away from the adjacent epiphysis.

Fig. 76

Fechner, FE, Mills, SE. , “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Periosteal chondroma

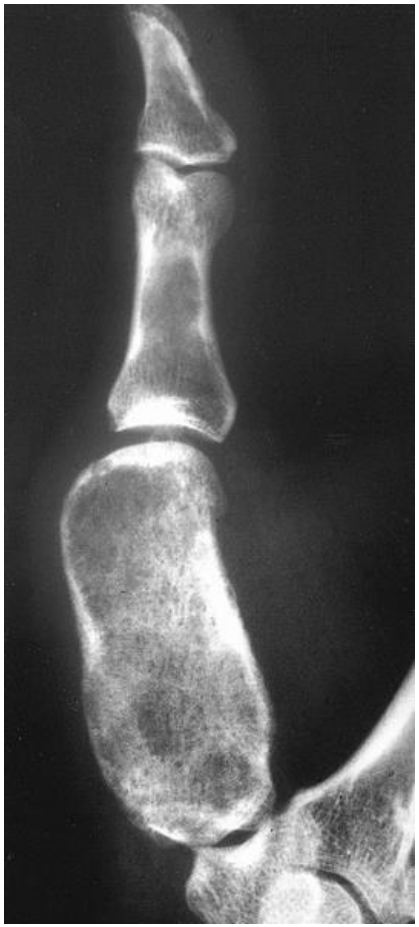


This metaphyseal femoral lesion from a 25-year-old man has the characteristic radiographic appearance of a periosteal chondroma. The lytic mass appears confined to the cortex and sits within a cup formed by buttresses of reactive bone. The patient complained of pain and swelling for several months.

Fig. 81

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Enchondroma



A 33-year-old woman noted discomfort and slight swelling in her finger for 2 months. An enchondroma expands the proximal phalanx and focally thins, but does not penetrate the cortex.

The radiographic features are characteristic, as the unmineralized nodules of cartilage produce well-circumscribed oval lucencies that are surrounded by a thin rim of radiodense bone (O ring sign). If the matrix calcifies, it is detected as irregular opacities. The nodules scallop the endosteum, and in long bones they do not result in complete cortical destruction

Fig. 84

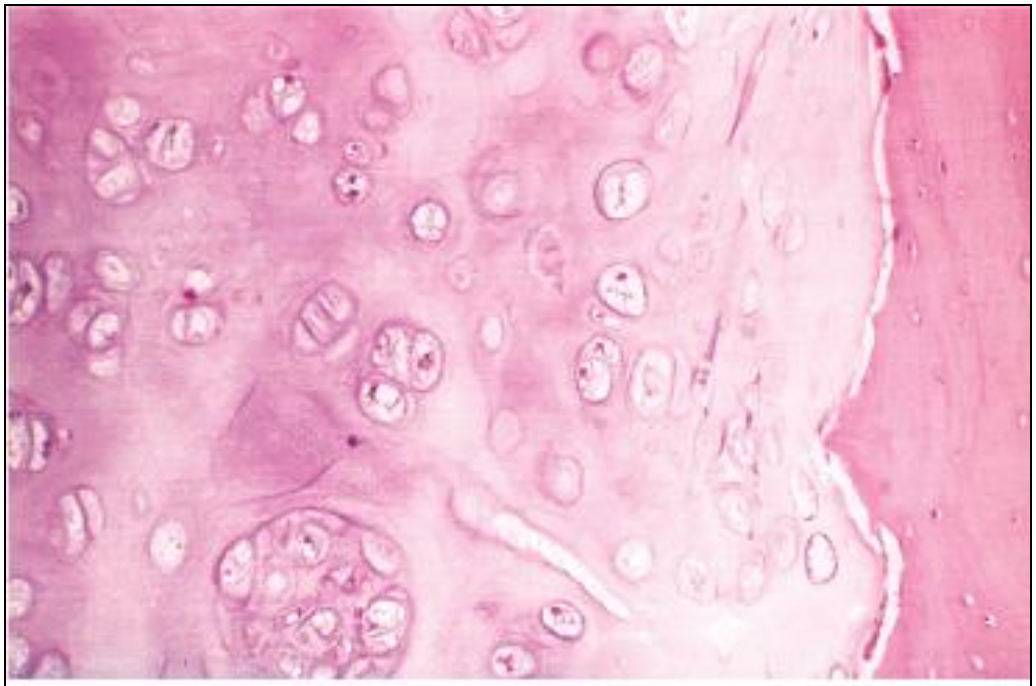
Fechner, FE, Mills, SE., "Tumors of the bones and joints." Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Enchondroma

- Most common intraosseous cartilage tumor
- Typically solitary metaphyseal lesions of tubular bones of the hands and feet.
- 20-50 years of age
- Ollier disease and Marfucci syndrome are non-hereditary disorders associated with multiple enchondromas. Marfucci syndrome also has associated spindle cell hemangiomas.
- Radiographically:
- Circumscribed lucency with central irregular calcifications, a sclerotic rim, and an intact cortex

Enchondroma

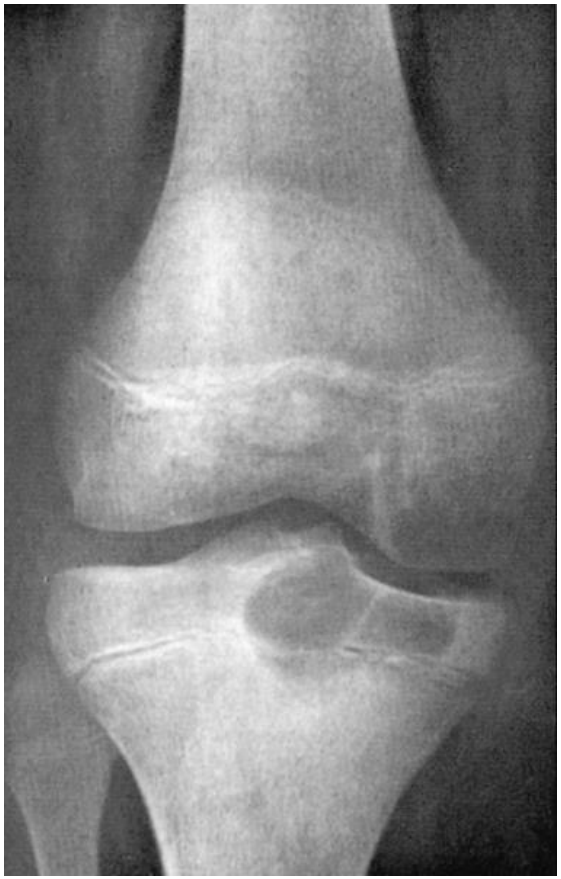
- Microscopically:
- The nodules of cartilage are well circumscribed and have a hyaline matrix, and the neoplastic chondrocytes that reside in lacunae are cytologically benign.
- At the periphery of the nodules, the cartilage undergoes enchondral ossification, and the center frequently calcifies and dies.
- Heterozygous mutations in the IDH1 and IDH2 genes are present within enchondromas.
- Acquire a new enzymatic activity that leads to the synthesis of 2-hydroxyglutarate. This “oncometabolite” interferes with regulation of DNA methylation



Chondroblastoma

- It usually occurs in young patients in their teens with a male-to-female ratio of 2:1.
- Most arise near the knee.
- Less common sites such as the pelvis and ribs are affected in older patients.
- Chondroblastoma has a striking predilection for epiphyses and apophyses (epiphyseal equivalents such as iliac crest).

Chondroblastoma



This radiograph of the tibia of a 12-year-old girl shows a sharply demarcated, radiolucent area located mainly in the epiphysis and extending for a short distance into the metaphysis.

Fig. 94

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

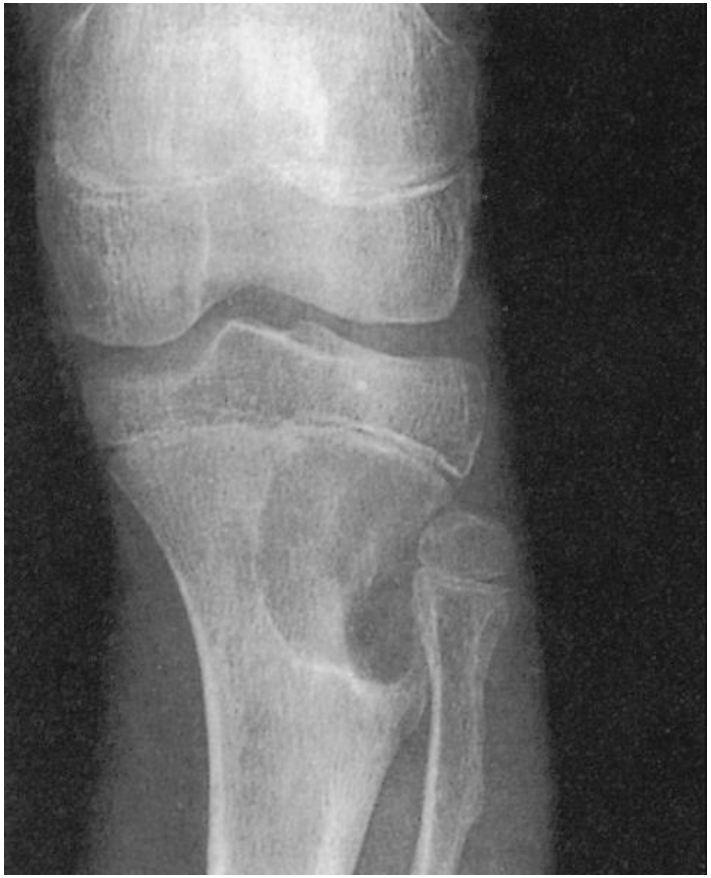
Chondroblastoma

- Composed of sheets of compact polyhedral chondroblasts that have well-defined cytoplasmic borders, moderate amounts of pink cytoplasm, and nuclei that are hyperlobulated with longitudinal grooves.
- Mitotic activity and necrosis are frequently present.
- The tumor cells are surrounded by scant amounts of hyaline matrix that is deposited in a lacelike configuration

Chondroblastoma

- Scattered through the lesion are non-neoplastic osteoclast-type giant cells.
- Nodules of well-formed hyaline cartilage are distinctly uncommon.
- When the matrix calcifies, it produces a characteristic chicken-wire pattern of mineralization.
- Occasionally the tumors undergo prominent hemorrhagic cystic degeneration.

Chondromyxoid fibroma



This chondromyxoid fibroma produced a radiolucent defect with sharply demarcated, slightly sclerotic margins in the tibial metaphysis.

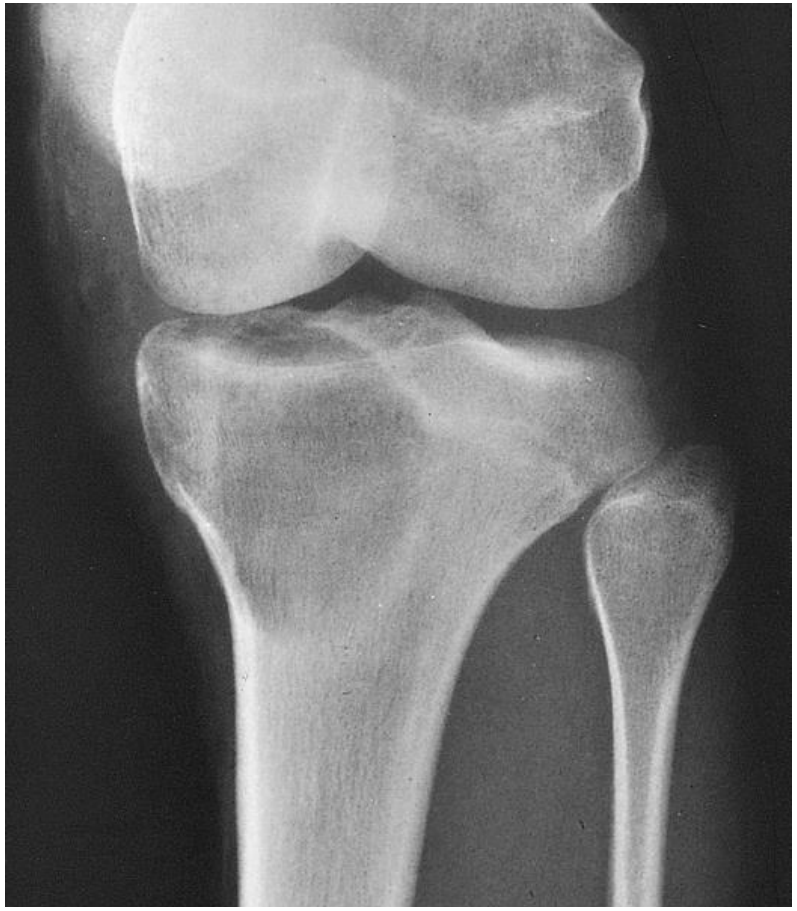
Fig. 101

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Chondromyxoid fibroma

- Microscopically:
- There are nodules of poorly formed hyaline cartilage and myxoid tissue delineated by fibrous septae.
- The areas of greatest cellularity are at the periphery of the nodules.
- In the cartilaginous regions, the tumor cells are situated in lacunae
- However, in the myxoid areas, the cells are stellate, and their delicate cell processes extend through the mucinous ground substance and approach or contact neighboring cells.
- Occasional osteoclast-type giant cells are also present.

Giant cell tumor



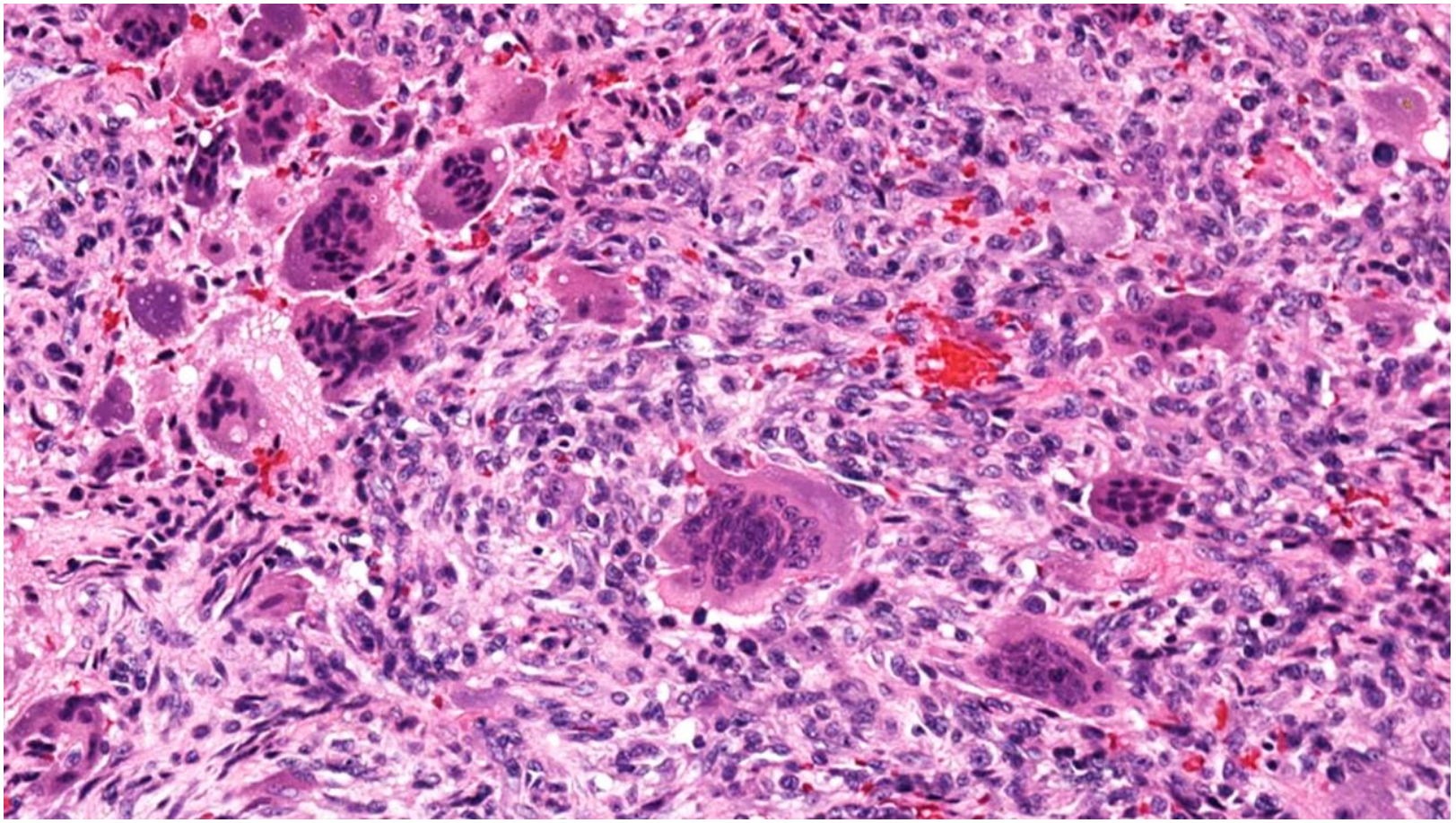
This tibial giant cell tumor from a 19-year-old woman with discomfort in her knee involves both the metaphysis and epiphysis, with extension to the articular cartilage. It is a purely lytic defect, confined to the normal bone contours, with sharply defined borders, except for some "blurring" at the metaphyseal margin.

Fig. 205

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

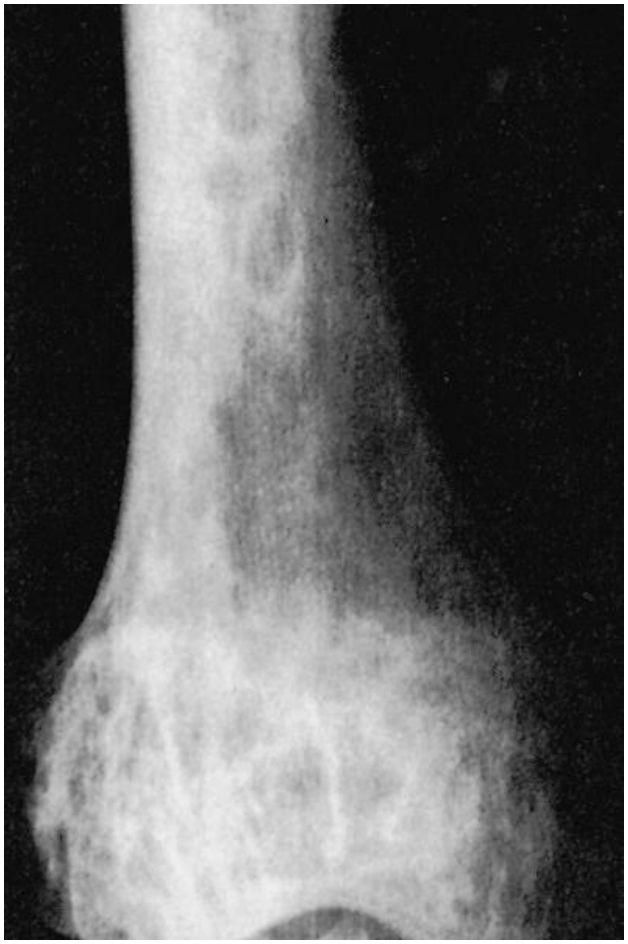
Giant cell tumor

- Composed of uniform oval mononuclear cells that have indistinct cell membranes and appear to grow in a syncytium.
- Mitoses are frequent.
- Numerous osteoclast-type giant cells having 100 or more nuclei that have identical features to those of the mononuclear cells are found in background.
- Express RANKL.
- Necrosis, hemorrhage, hemosiderin deposition, and reactive bone formation are common secondary features.
- H3F3A mutation at G34 position
- 40-60% recurrence after curettage. May metastasize.



http://ilovepathology.com/wp-content/uploads/2017/10/giant-cell-tumor-small.jpg
Accessed 05/10/2020

Skeletal angiomatosis

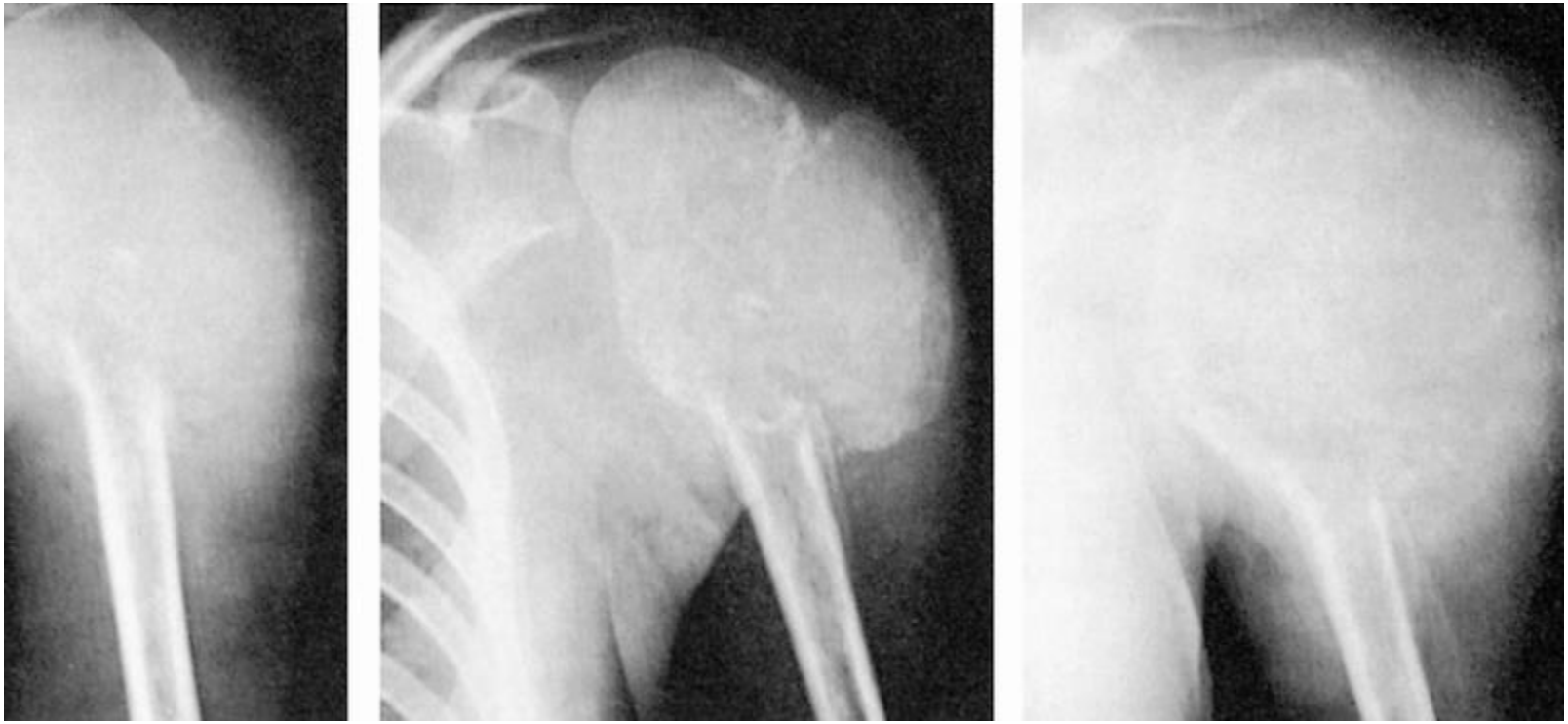


The lower end of the femur has numerous cyst-like lucencies traversed by dense bony trabeculae. A chest radiograph demonstrated similar lesions in the upper end of both humeri. There were no symptoms related to the skeletal lesions. The patient subsequently died and one femur was removed at autopsy.

Fig. 156

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Aneurysmal bone cyst



The radiographs (from left to right) were taken over a three month period. The lesion was locally resected and a prosthesis inserted.

Fig. 273

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

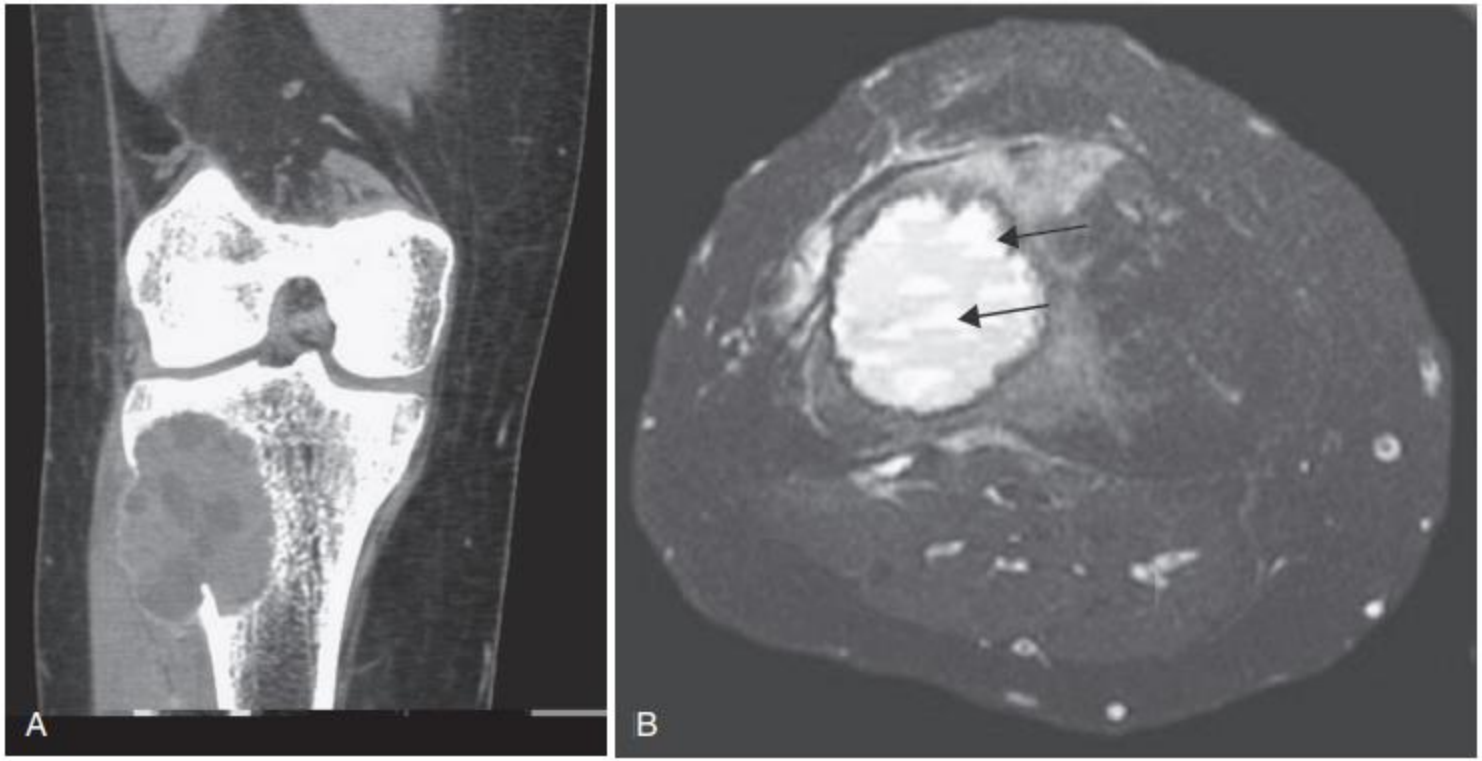


Figure 26.33 (A) Coronal computed axial tomography scan showing an eccentric aneurysmal bone cyst of the tibia. The soft tissue component is delineated by a thin rim of reactive subperiosteal bone. (B) Axial magnetic resonance image demonstrating characteristic fluid levels *(arrows)*.

Aneurysmal bone cyst

- In the initial or incipient phase, there is a small, often eccentric, lytic lesion that does not grossly expand the bone but may have an alarming, permeative growth pattern.
- In the growth phase there is rapid, destructive growth characterized by massive lysis of bone and cortical destruction.
- There is little or no bony circumscription.
- Codman's triangle may be prominent.
- The interface between a rapidly growing lesion and normal bone presenting on x-ray as an incomplete triangle bounded by periosteum

Aneurysmal bone cyst

- These naked margins may lead to confusion with malignancy but the "blowout" appearance is characteristic, and the intramedullary component usually has a well-circumscribed margin.
- In the stable phase, the radiograph has the classic appearance of aneurysmal bone cyst with expanded, grossly distorted bone and a distinct bony shell surrounding a lesion that contains numerous internal trabeculations.

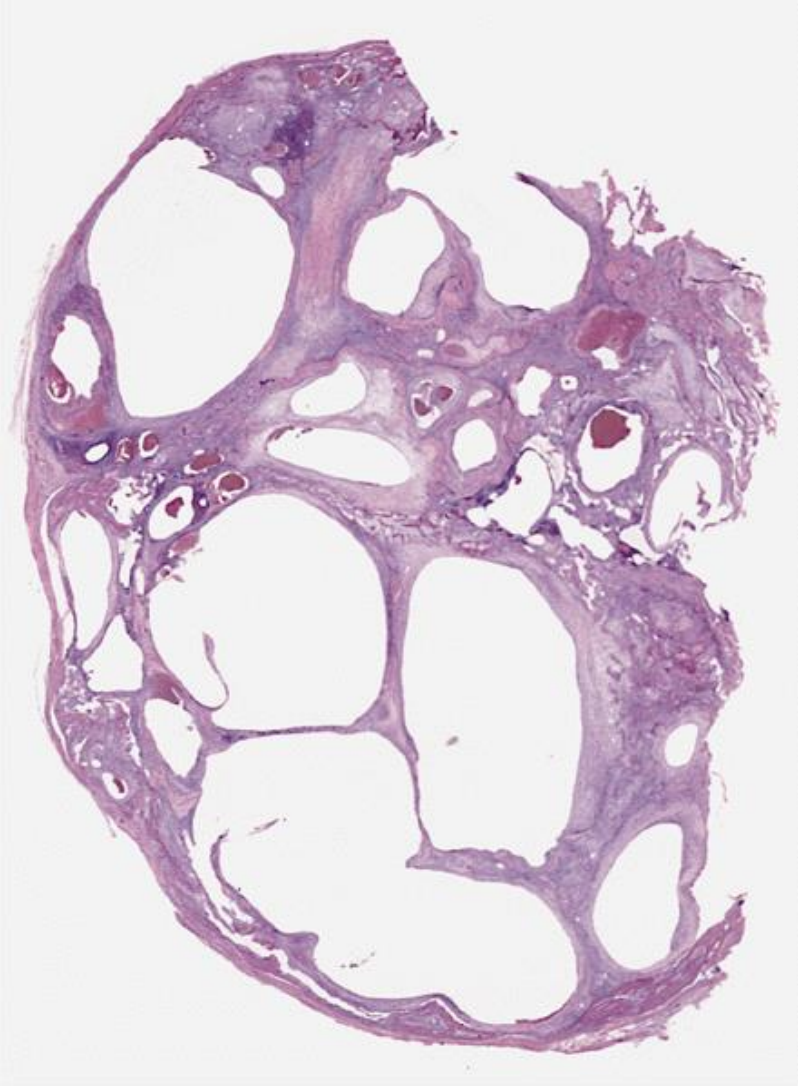
Aneurysmal bone cyst

- Finally, in the healing phase, there is progressive ossification of the bony trabeculae to form an irregular, coarsely trabeculated, bony mass.
- ABC presents with localized pain and swelling that may result in a limp, vertebral lesions, and nerve compression.
- Recurrence up to 50% following curettage but 10% following en bloc resection.

Aneurysmal bone cyst

- 70% have 17p13 gene rearrangements within spindle cells
- Fusion of the USP6 coding region with promoter genes such as CDH11 that are found in osteoblasts.
- USP6 encodes a ubiquitin-specific protease that regulates the activity of the transcription factor NF-κB, which in turn up-regulates expression of proteins, such as matrix metalloproteases, that lead to cystic bone resorption.

Aneurysmal bone cyst



The essential histologic feature is the presence of many cavernous spaces that are filled with blood but lack the smooth muscle walls and endothelial lining of normal vessels.

Fig.8-25

Sciubba, James J, Fantasia, John E, Kahn, Leonard B., "Tumors and cysts of the jaws." Atlas of Tumor Pathology, Third Series, Fascicle 29. Armed Forces Institute of Pathology. Washington, D.C. (2001)

Tenosynovial giant cell tumor

- It usually arises in patients in their twenties to forties.
- Monoarticular
- 80% of cases involve the knee.
- Hip, ankle and calcaneocuboid may also be involved.
- Once known as giant cell tumor of tendon sheath (localized) and as pigmented villonodular synovitis (diffuse)
- Nodular proliferation of synovial tissue
- Hyperplastic

Tenosynovial giant cell tumor

- Red-brown
- Composed of uniform oval mononuclear cells (CD68+) that have indistinct cell membranes and appear to grow in a syncytium.
- Mitoses are frequent.
- Scattered within this background are numerous giant cells (CD68+) believed to form via fusion of the mononuclear cells.
- RANKL present on cells
- Necrosis, hemorrhage, hemosiderin deposition, and reactive bone formation are common secondary features.

Tenosynovial giant cell tumors

- Recur
- Localized tumors are well circumscribed.
- May be locally invasive with bone cyst formation and loss of bone and cartilage
- In nodular tumors, the cells grow in a solid aggregate that may be attached to the synovium by a pedicle.
- In diffuse tumors the normally smooth joint synovium is converted into a tangled mat by red-brown folds, finger-like projections, and nodules.
- In the diffuse variant they spread along the surface and infiltrate the sub-synovial issue.

Tenosynovial giant cell tumors

- t(1;2)(p13;q37), resulting in fusion of the type VI collagen α-3 promoter upstream of the monocyte colony-stimulating factor (M-CSF) gene.
- Stimulates proliferation of macrophages

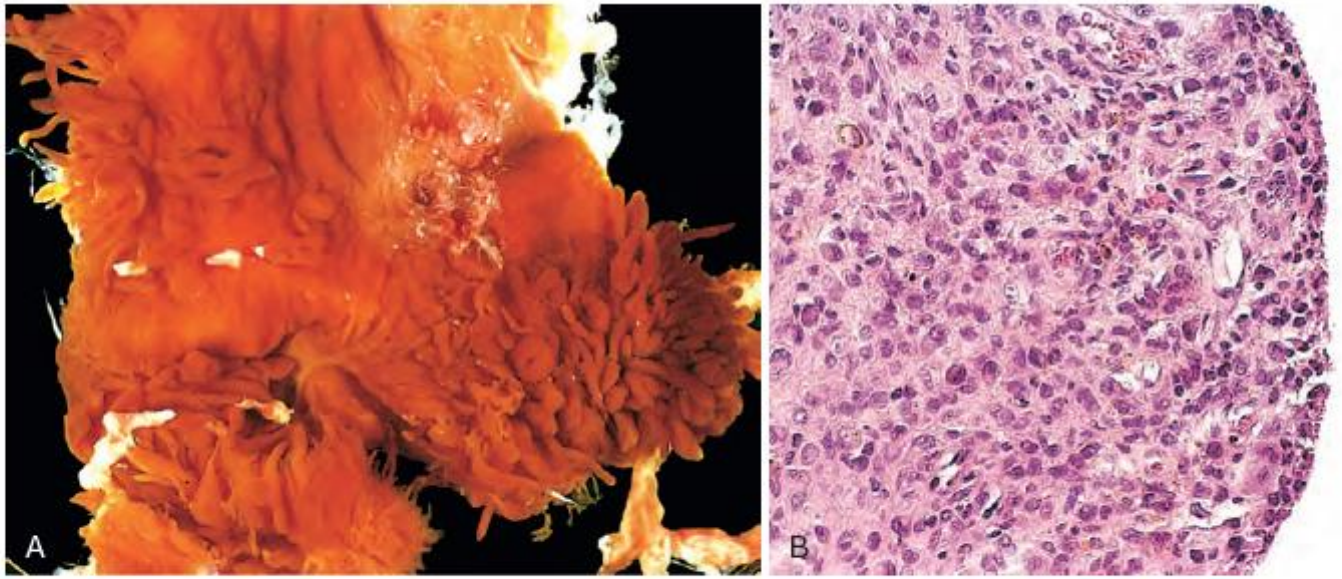


Figure 26-49 Tenosynovial giant cell tumor, diffuse type. **A,** Excised synovium with fronds and nodules typical of pigmented villonodular synovitis *(arrow)*. **B,** Sheets of proliferating cells in tenosynovial giant cell tumor bulging the synovial lining.

Tenosynovial tumor

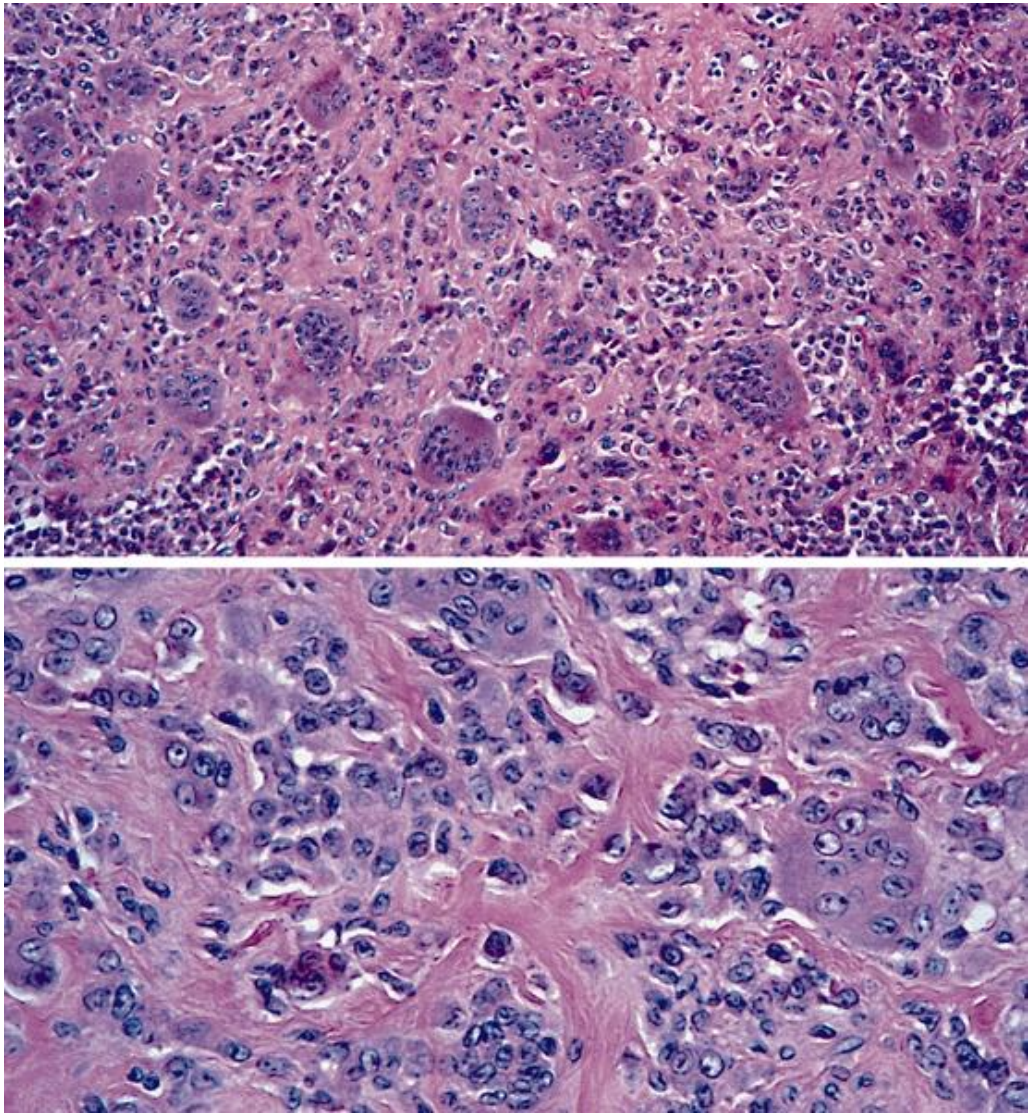
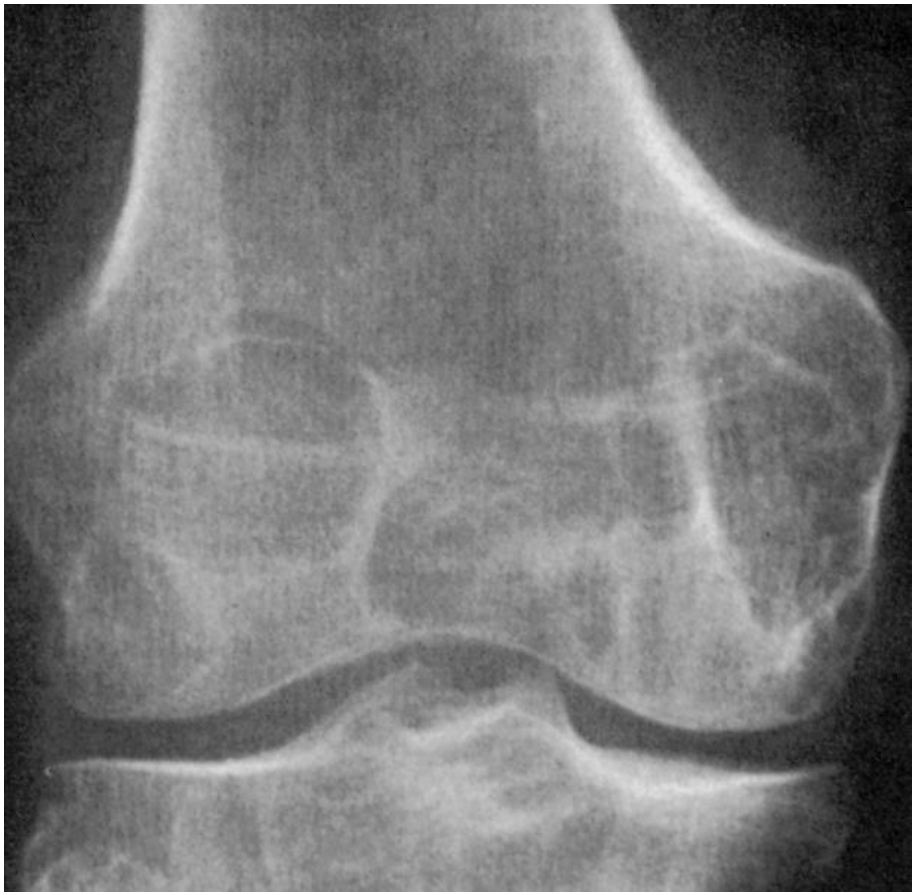


Fig. 9-3 Kempson, Richard L., Fletcher, Christophr DM, Evans, Harry L, Hendrickson, Michael R, and Sibley, Richard K, Tumors of the Soft Tissues, Fascicle 30, Atlas of Tumor Pathology. 3rd Series. Armed Forces Institute of Pathology, Washington, DC (2001).

Tenosynovial giant cell tumor

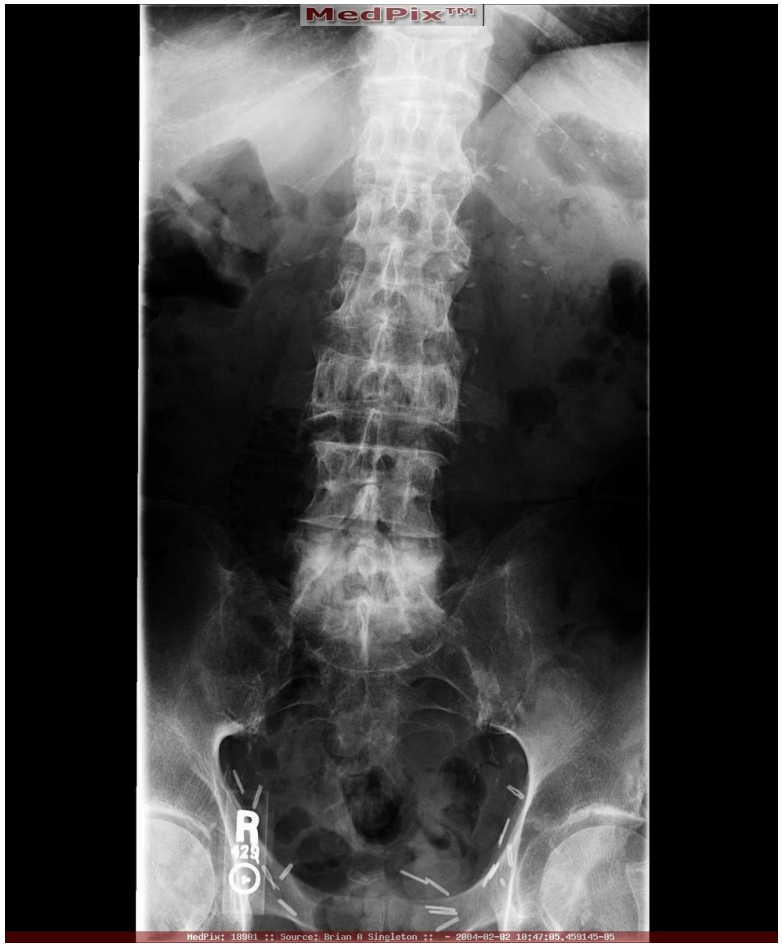


Several lytic defects are present in the distal portion of the femur. These contained pigmented villonodular synovitis that had invaded bone.

Fig. 314

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Paget's disease of bone

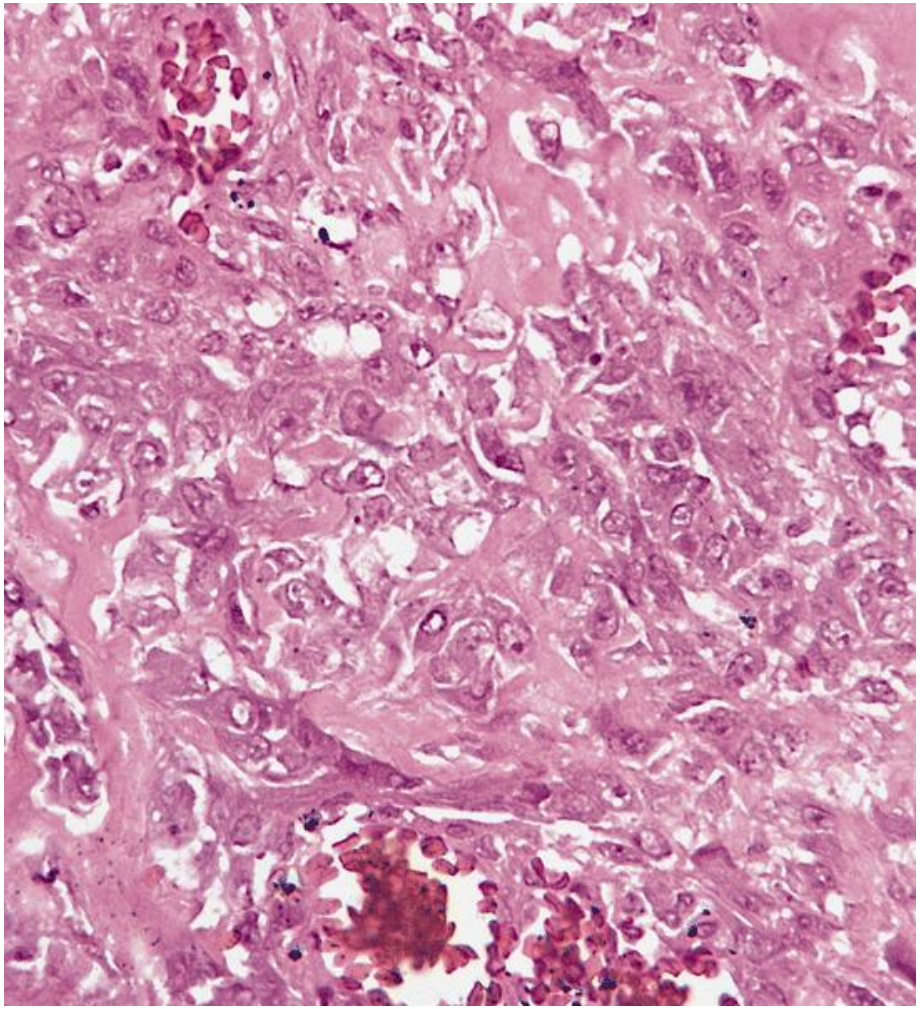


Incidental discovery. Often suggestive of metastasis. There is expansile widening of L3 with a central compression fracture. There are increased trabecular markings at L2. L5 has an "ivory" appearance. Spondylosis is present at multiple levels. A "vacuum disc" phenomenon is noted at L5-S1.

Medepix18901.

Contributed by Dr. Brian A. Singleton.
http://rad.usuhs.edu/medpix/kiosk_image.html?mode=kiosk&imageid=18901&pt_id=6848#pic
Accessed 07/14/2010.

Paget’s disease



Typical pattern of Paget's disease showing appositional cement lines, fibrovascular stroma, and tunneling resorption of bone.

Fig.8-25

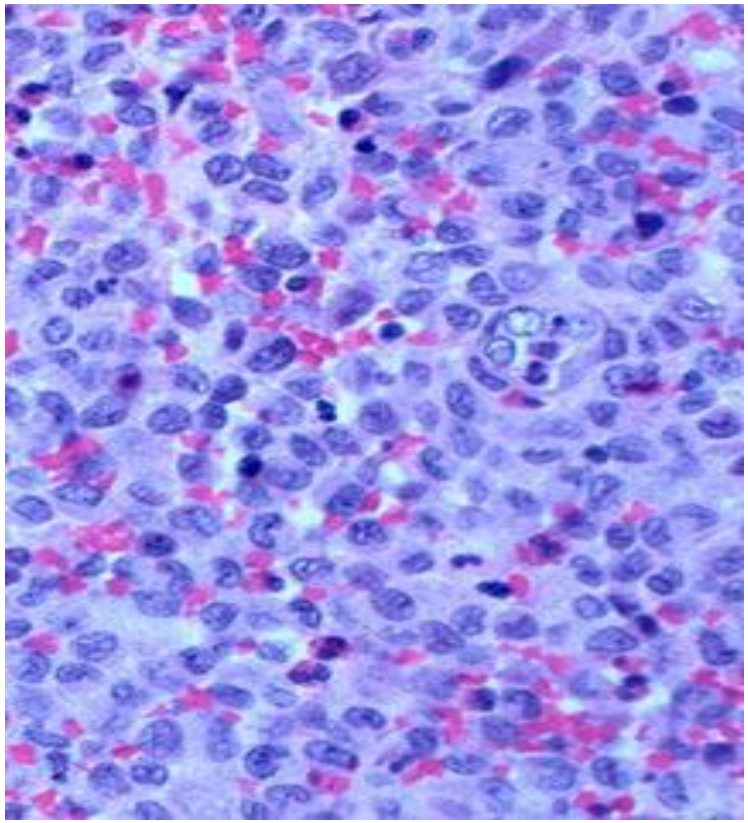
Sciubba, James J, Fantasia, John E, Kahn, Leonard B., “Tumors and cysts of the jaws.” Atlas of Tumor Pathology, Third Series, Fascicle 29. Armed Forces Institute of Pathology. Washington, D.C. (2001)

Histiocytosis

- May arise from any bone and any site within a bone (usually, skull)
- Eosinophilic granuloma.
- 70% of cases consist of a solitary lesion (lytic)
- Seldom leads to disseminated systemic disease
- Disorder of immune regulation
- Benign proliferation of Langerhans cells usually accompanied with eosinophils, lymphocytes, neutrophils and scattered plasma cells.
- Langerhans cells have abundant, powdery, eosinophilic cytoplasm. The diagnostic nuclei are bean shaped with convoluted nuclear grooves.

Histiocytosis

- Hand-Schuller-Christian Disease
- 1-5 years of age
- Chronic disseminated histiocytosis
- Exophthalmos
- Diabetes insipidus
- Hepatosplenomegaly
- Adenopathy
- Fever
- Letterer-Siwe disease
- <1 year of age
- Disseminated histiocytosis
- Small bone lesions common
- Uniformly fatal



http://www.tumorsurgery.org/tumor-education/bone-tumors/types-of-bone-tumors/eosinophilic-granuloma.aspx
Accessed 05/10/2020

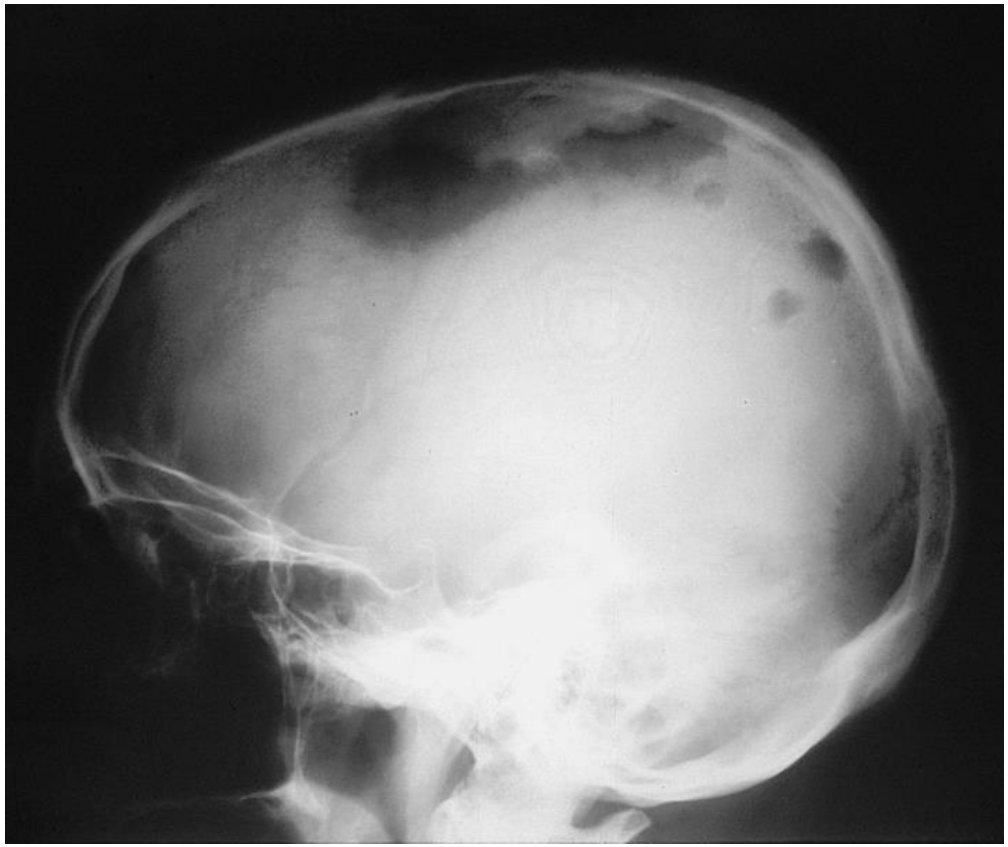


Fig. 11-24
Mills, SE, Gaffey, MJ, Frierson, HF. , “Tumors of the upper aerodigestive tract and ear.” Atlas of Tumor Pathology, Third Series, Fascicle 26. Armed Forces Institute of Pathology, Washington, D.C. 2006.

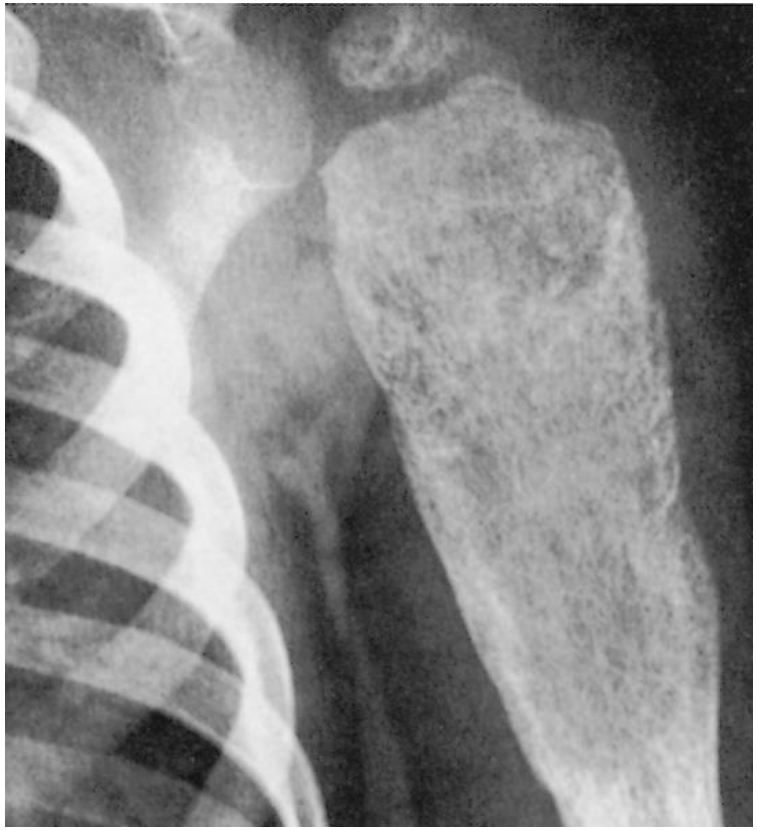
Ewing’s sarcoma

- Ewing’s sarcoma and primitive neuroectodermal tumor account for approximately 6% to 10% of primary malignant bone tumors.
- Follow osteosarcoma as the second most common group of bone sarcomas in children.
- Most patients are 10 to 15 years old. Unusual after age 20.
- Boys are affected slightly more frequently than girls, and there is a striking predilection for whites; those of sub-Saharan ancestry are rarely afflicted.

Ewing's sarcoma

- Usually arise in the diaphyses of long tubular bones, especially the femur and the flat bones of the pelvis.
- May be extraosseous.
- They present as painful enlarging masses, and the affected site is frequently tender, warm, and swollen. Some patients have systemic findings.
- Plain x-rays show a destructive lytic tumor that has permeative margins and extension into the surrounding soft tissues.
- The characteristic periosteal reaction produces layers of reactive bone deposited in an onionskin fashion.

Ewing’s sarcoma



Radiograph from a 2-year-old boy. There is diffuse loss of the normal contour of bone and destruction of the cortex. At operation, a large hemorrhagic, cystic cavity was encountered. Curettings from the wall revealed the primitive neuroectodermal cells of Ewing’s sarcoma.

Fig. 219

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Ewing’s sarcoma

- 85% of cases, t(11;22)(q24;q12)
- 5%-10% of cases, t(21;22)(q21;q12)
- <1% of cases, t(7;22)(q22;q12)
- The most common fusion gene (FLI1-EWS) generated from the t(11;22) translocation acts as a dominant oncogene, and the fusion protein acts as a constitutively active transcription factor.
- ERG-EWS fusion gene in t(21;22); ETV1-EWS fusion gene in t(7;22).
- STEAP1 mutation associated with good prognosis.

Ewing's sarcoma

- Composed of sheets of uniform small, round cells that are slightly larger than lymphocytes. They have scant cytoplasm, which may appear clear because it is rich in glycogen.
- The presence of Homer-Wright rosettes (where the tumor cells are arranged in a circle about a central fibrillary space) is indicative of neural differentiation.
- There is generally little stroma, although the tumor contains fibrous septae. Necrosis may be prominent.
- Few mitotic figures in relation to the dense cellularity of the tumor.
- Nearly all patients have micro-metastases

Ewing's sarcoma

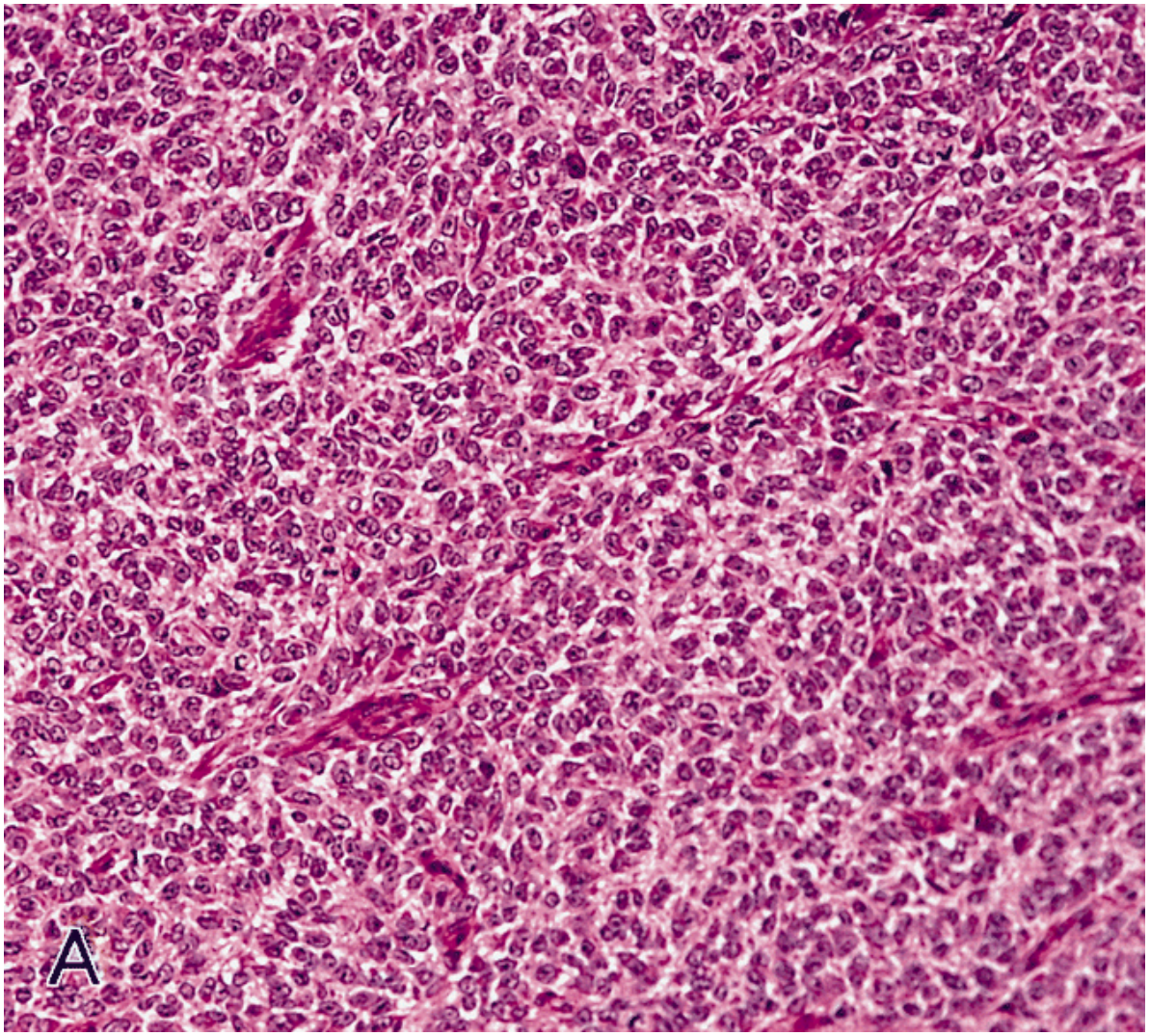


Fig. 11-47A Kempson, Richard L., Fletcher, Christophr DM, Evans, Harry L, Hendrickson, Michael R, and Sibley, Richard K, Tumors of the Soft Tissues, Fascicle 30, Atlas of Tumor Pathology. 3rd Series. Armed Forces Institute of Pathology, Washington, DC (2001).

Metastatic lesions

- Metastatic tumors are the most common form of skeletal malignancy.
- The pathways of spread include (1) direct extension, (2) lymphatic or hematogenous dissemination, and (3) intraspinal seeding (Batson plexus of veins).
- In adults, more than 75% of skeletal metastases originate from cancers of the prostate, breast, kidney, and lung.
- In children, metastases to bone originate from neuroblastoma, Wilm's tumor, osteosarcoma, Ewing's sarcoma, and rhabdomyosarcoma.

Metastatic lesions

- Skeletal metastases are typically multifocal.
- Carcinomas of the kidney and thyroid may produce a solitary lesion.
- Metastases most commonly involve the axial skeleton (vertebral column, pelvis, ribs, skull, sternum), proximal femur, and humerus.

Metastatic lesions

- Carcinomas of the kidney, lung, and gastrointestinal tract and malignant melanoma produce lytic bone destruction through stimulation of osteoclast activity.
- Metastases that elicit a sclerotic response, particularly prostate adenocarcinoma, do so by stimulating osteoblastic bone formation.
- Most metastases induce a mixed lytic and blastic reaction.

Osteosarcoma

- The most common primary malignant tumor of bone, exclusive of myeloma and lymphoma.
- 20% of primary bone cancers.
- Occurs in all age groups but has a bimodal age distribution
- 75% occur in patients younger than age 20.
- The tumors usually arise in the metaphyseal region of the long bones of the extremities
- 60% occur about the knee.
- Any bone may be involved, however, and in persons over age 25, the incidence in flat bones and long bones is almost equal.

Osteosarcoma

- A malignant mesenchymal tumor in which the cancerous cells produce bone matrix.
- Osteosarcomas are bulky tumors that are gritty, gray-white, and often contain areas of hemorrhage and cystic degeneration
- The tumors frequently destroy the surrounding cortices and produce soft tissue masses.
- They spread extensively in the medullary canal, infiltrating and replacing the marrow surrounding the pre-existing bone trabeculae.

Osteosarcoma

- Infrequently, they penetrate the epiphyseal plate or enter the joint.
- When joint invasion occurs, the tumor grows into it along tendino-ligamentous structures or through the attachment site of the joint capsule.
- May present with sudden fracture.
- At the time of diagnosis, approximately 10% to 20% of patients have demonstrable pulmonary metastases.

Osteosarcoma

- Radiographs usually show a large destructive, mixed lytic and blastic mass with infiltrative margins.
- The tumor frequently breaks through the cortex and lifts the periosteum, resulting in reactive periosteal bone formation.
- The triangular shadow between the cortex and raised ends of periosteum on x-ray is known as Codman's triangle.

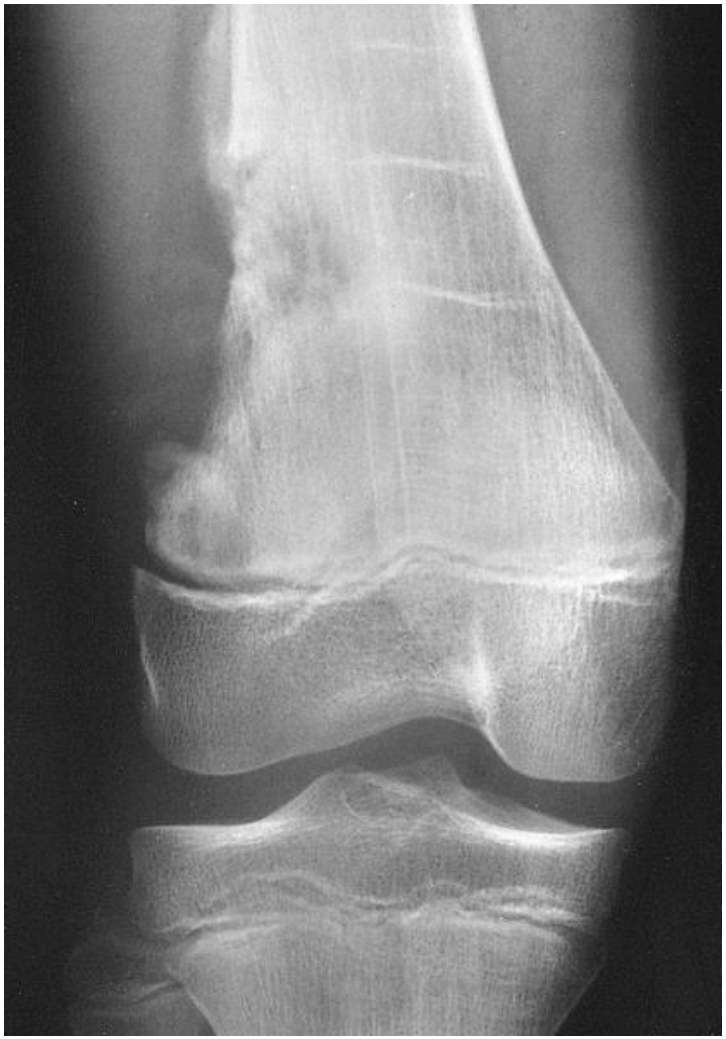
Osteosarcoma

- Frequently have large hyperchromatic nuclei. Bizarre tumor giant cells are common, as are mitoses.
- The formation of bone by the tumor cells is characteristic of osteosarcoma.
- The neoplastic bone has a coarse, lacelike architecture but is also deposited in broad sheets or as primitive trabeculae.
- Cartilage or fibrous tissue may be present in varying amounts.
- Chondroblastic sarcoma if cartilage is abundant in tumor.
- Vascular invasion common.
- Tumor may be necrotic.

Osteosarcoma

- When malignant cartilage is abundant, the tumor is called chondroblastic osteosarcoma**.**
- Loss of heterozygosity, structural rearrangements, or point mutations in the RB gene.
- Abnormalities in genes that regulate cell cycling, such as p53 or MDM2, CDK4, p14 and p16/INK4A, CYCLIN D1, and have also been implicated in the genesis of non-hereditary osteosarcomas.

Osteosarcoma

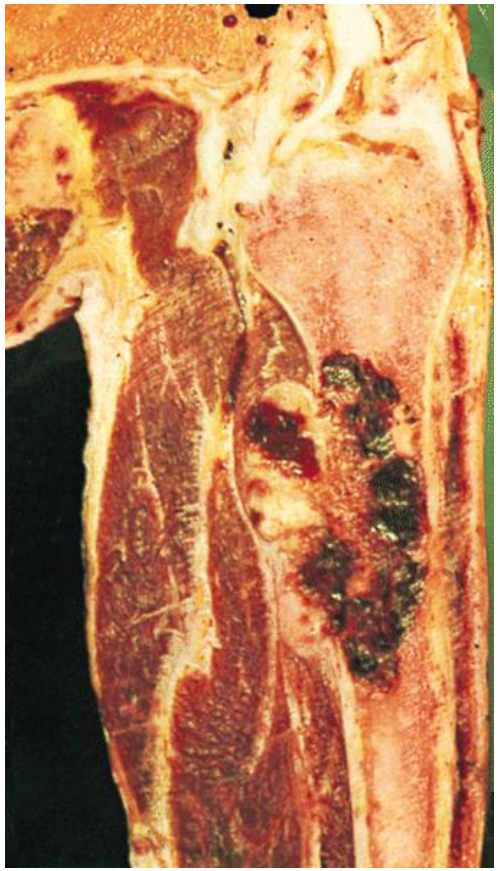


A part of the cortex is destroyed with osteosarcoma. The tumor breaks through the cortex and lifts the periosteum, resulting in reactive periosteal bone formation (“sunburst”). A Codman triangle (the triangular shadow between the cortex and raised ends of periosteum at the margin of the lesion) is seen proximal to the cortical break. The medullary portion of the bone contains irregular calcified matrix.

Fig. 32

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Osteosarcoma

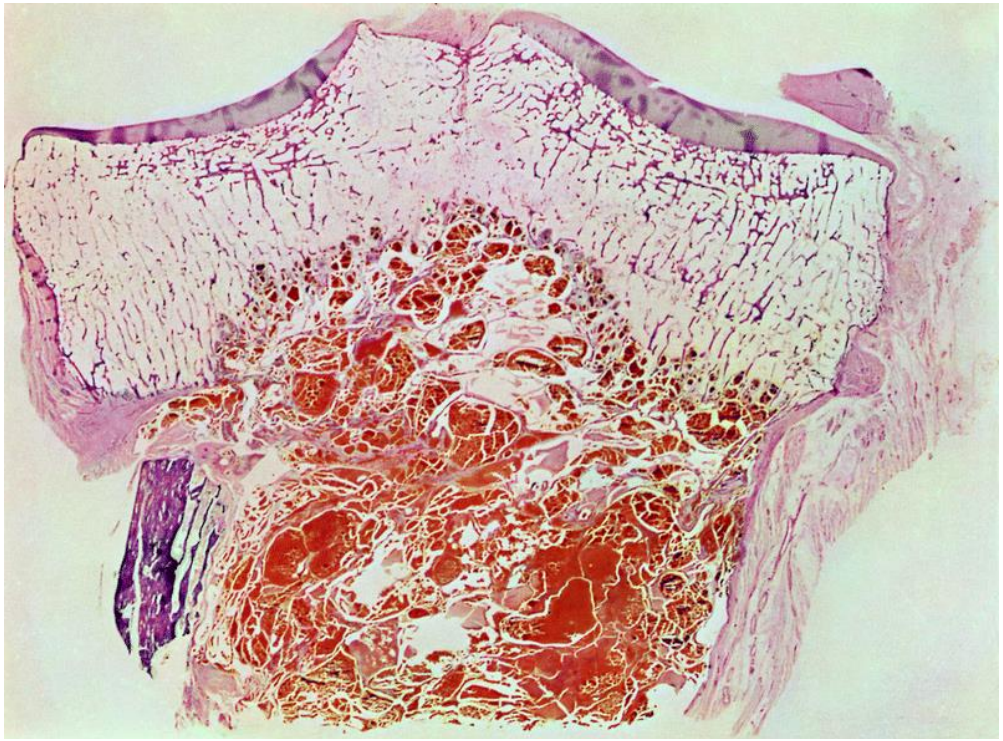


Osteosarcoma of the upper end of the tibia. The tan-white tumor fills most of the medullary cavity of the metaphysis and proximal diaphysis. It has infiltrated through the cortex, lifted the periosteum, and formed soft tissue masses on both sides of the bone. Tumoral osteoid appears yellow-white

Fig. PL1C

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Osteosarcoma

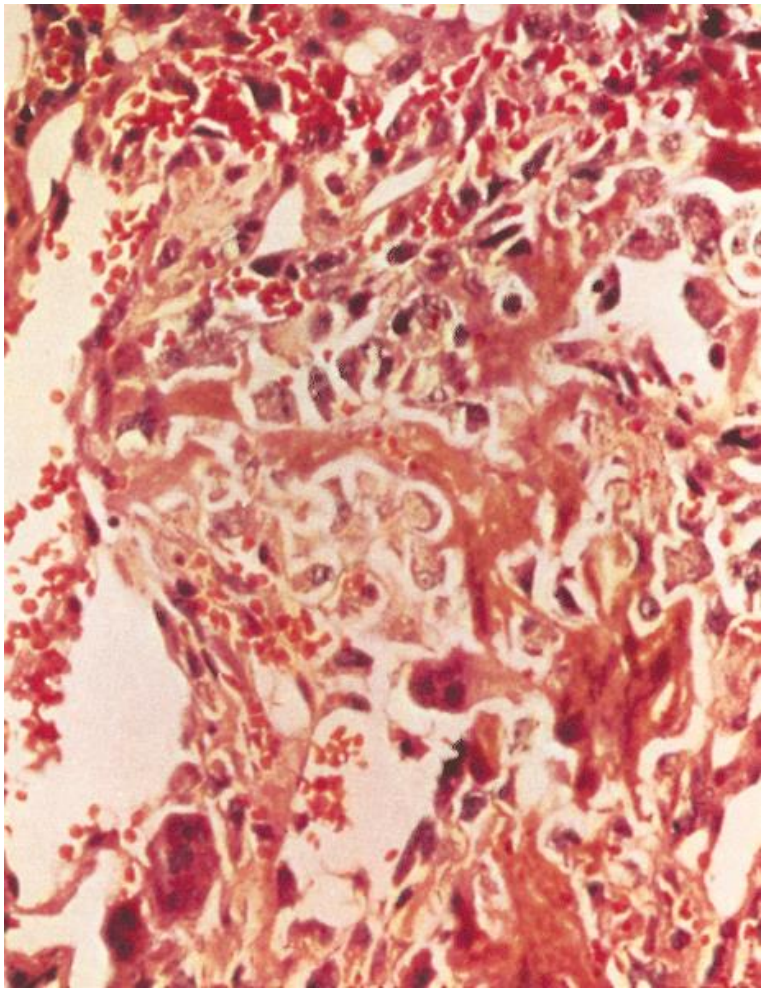


This coronal section through a telangiectatic osteosarcoma is from the upper end of the tibia in a 20-year-old woman. Numerous blood-filled spaces are evident with minimal solid tissue component.

Fig. PL1A

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

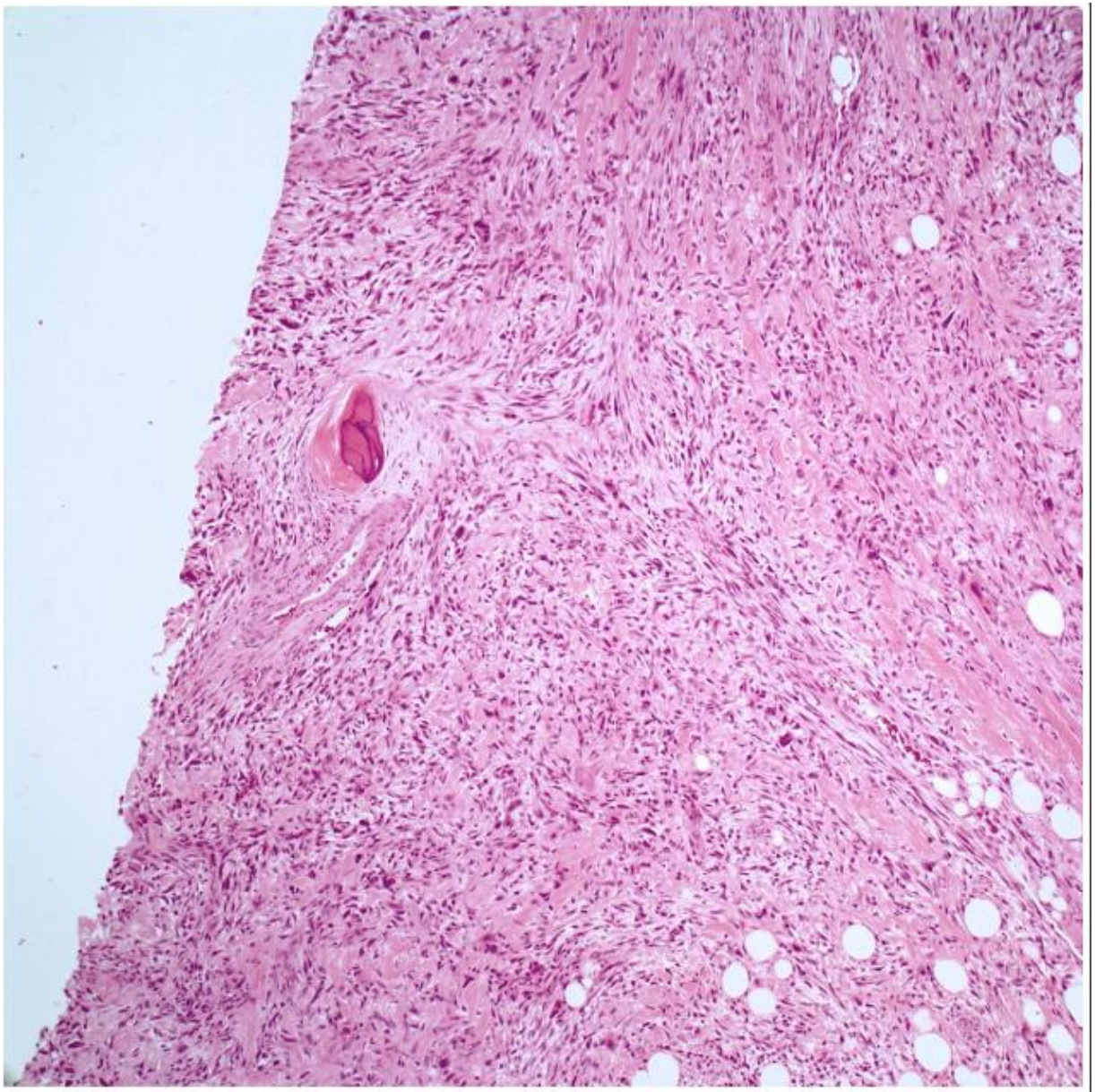
Osteosarcoma



The sparse solid areas of telangiectatic osteosarcoma show pleomorphic cells and irregular deposits of osteoid

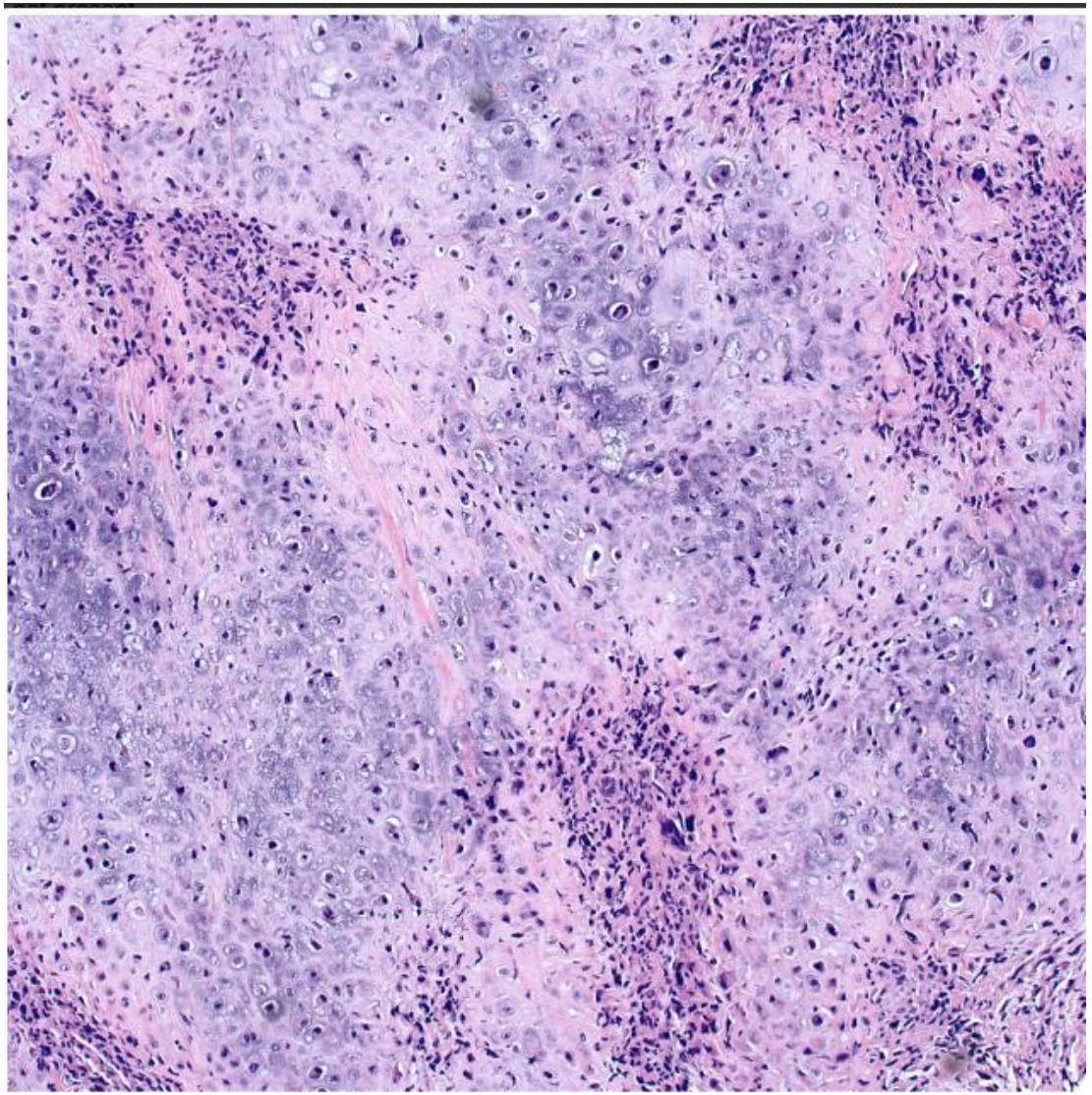
Fig. PL1B

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.



High grade fibroblastic osteosarcoma surrounding native bony traceculae

http://www.pathologyoutlines.com/topic/boneosteosarcomageneral.html



High grade cartilaginous differentiation in a chondroblastic osteosarcoma

http://www.pathologyoutlines.com/topic/boneosteosarcomageneral.html

Treatment strategy

- Preoperative chemotherapy is standard.
- Methotrexate in high doses with doxorubicin or cisplatin, ifosfamide with cisplatin, or doxorubicin and cisplatin are employed.
- En bloc excision of tumor and muscle compartment is the preferred surgical option.
- Amputation considered only if localized disease (negative MRI and bone scan) and not possible to achieve adequate margins.
- Postoperative chemotherapy follows with same drugs.
- 10-20% patients with recurrent disease may be salvaged and are treated with curative intent

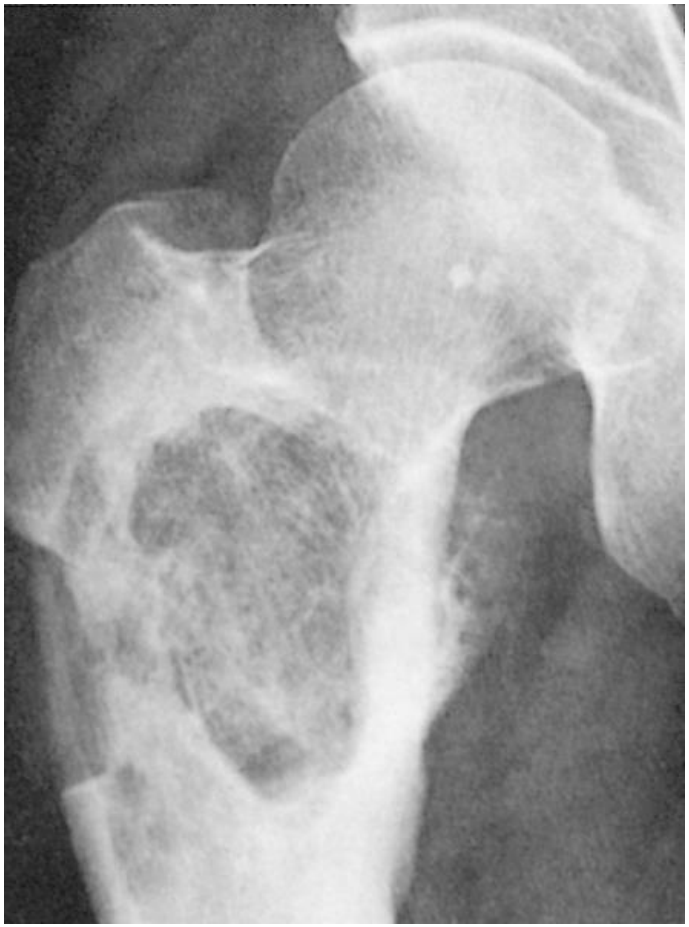
Chondrosarcoma

- Second most common malignant matrix-producing tumor of bone.
- Progressively enlarging painless mass.
- Patients are usually age 40 or older.
- The clear cell and the mesenchymal variants occur in younger patients, in their teens or twenties.
- The tumor affects men twice as frequently as women.
- Nodular growth implies poorer risk.

Chondrosarcoma

- Commonly arise in the central portions of the skeleton
- Pelvis, shoulder, and ribs
- Rarely involves the distal extremities.
- The clear cell variant is unique in that it originates in the epiphyses of long tubular bones.
- The nodular growth pattern of the cartilage produces prominent endosteal scalloping on x-ray.
- The calcified matrix appears as foci of flocculent density.
- The more radiolucent the tumor, the greater the likelihood it is high grade.

Chondrosarcoma



A slow-growing, low-grade tumor causes reactive thickening of the cortex, whereas a more aggressive high-grade neoplasm destroys the cortex and forms a soft tissue mass. A central chondrosarcoma has a predominantly lytic appearance in the medullary portion of the bone. Medially there is extraosseous extension. The cortical defect on the left is the biopsy site.

Fig. 111

Fechner, FE, Mills, SE., “Tumors of the bones and joints.” Atlas of Tumor Pathology, Third Series, Fascicle 8. Armed Forces Institute of Pathology, Washington D.C.1992.

Chondrosarcoma

- Conventional chondrosarcoma is composed of malignant hyaline and myxoid cartilage.
- The large bulky tumors are made up of nodules of gray-white, somewhat translucent glistening tissue.
- In predominantly myxoid variants, the tumors are viscous and gelatinous and the matrix oozes from the cut surface.
- Spotty calcifications are typically present; central necrosis may create cystic spaces.
- Mesenchymal chondrosarcoma is composed of islands of well-differentiated hyaline cartilage surrounded by sheets of primitive appearing small round cells.

Chondrosarcoma

- The adjacent cortex is thickened or eroded, and the tumor grows with broad pushing fronts into the surrounding soft tissue. The malignant cartilage infiltrates the marrow space and surrounds pre-existing bony trabeculae.

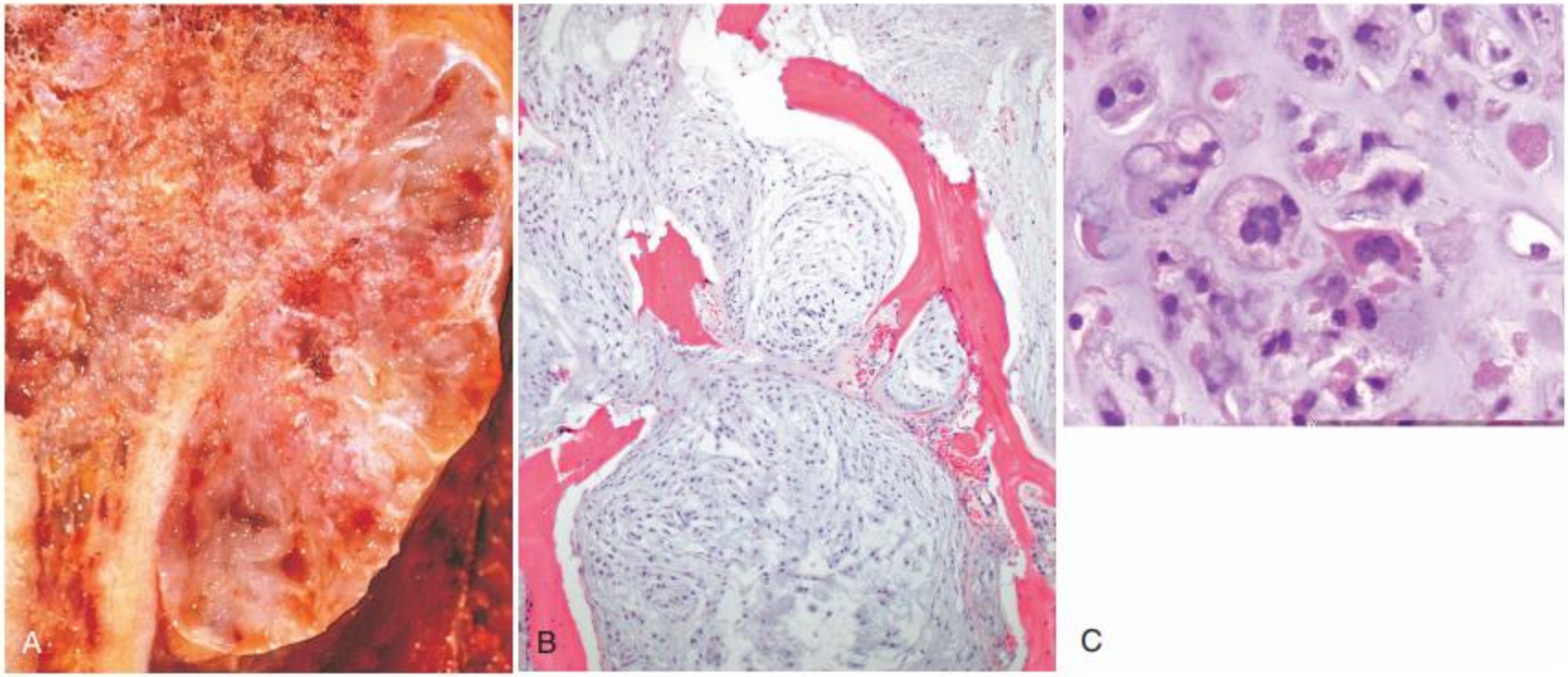


Figure 26.29 Chondrosarcoma. (A) Nodules of hyaline and myxoid cartilage permeate the medullary cavity, grow through the cortex, and form a relatively well-circumscribed soft tissue mass. (B) Conventional chondrosarcoma appearing as a hypercellular cartilaginous mass with entrapped normal bone trabeculae. (C) Anaplastic chondrocytes amid hyaline cartilage matrix in a grade 3 chondrosarcoma.

Myxoid chondrosarcoma

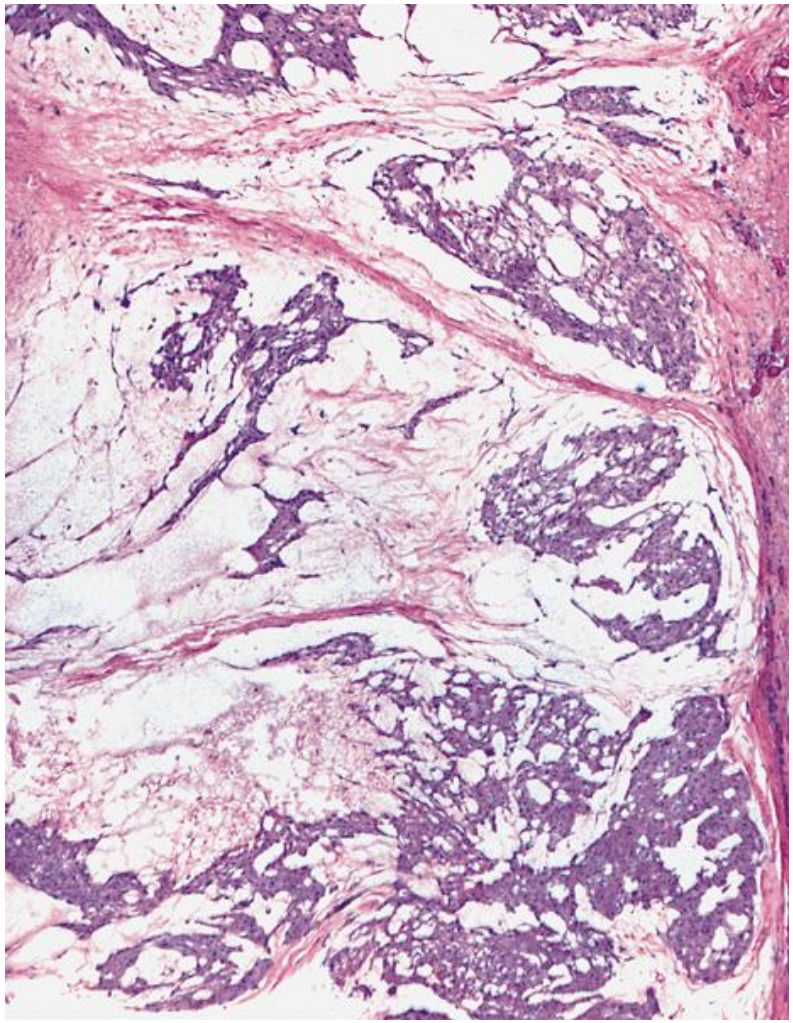
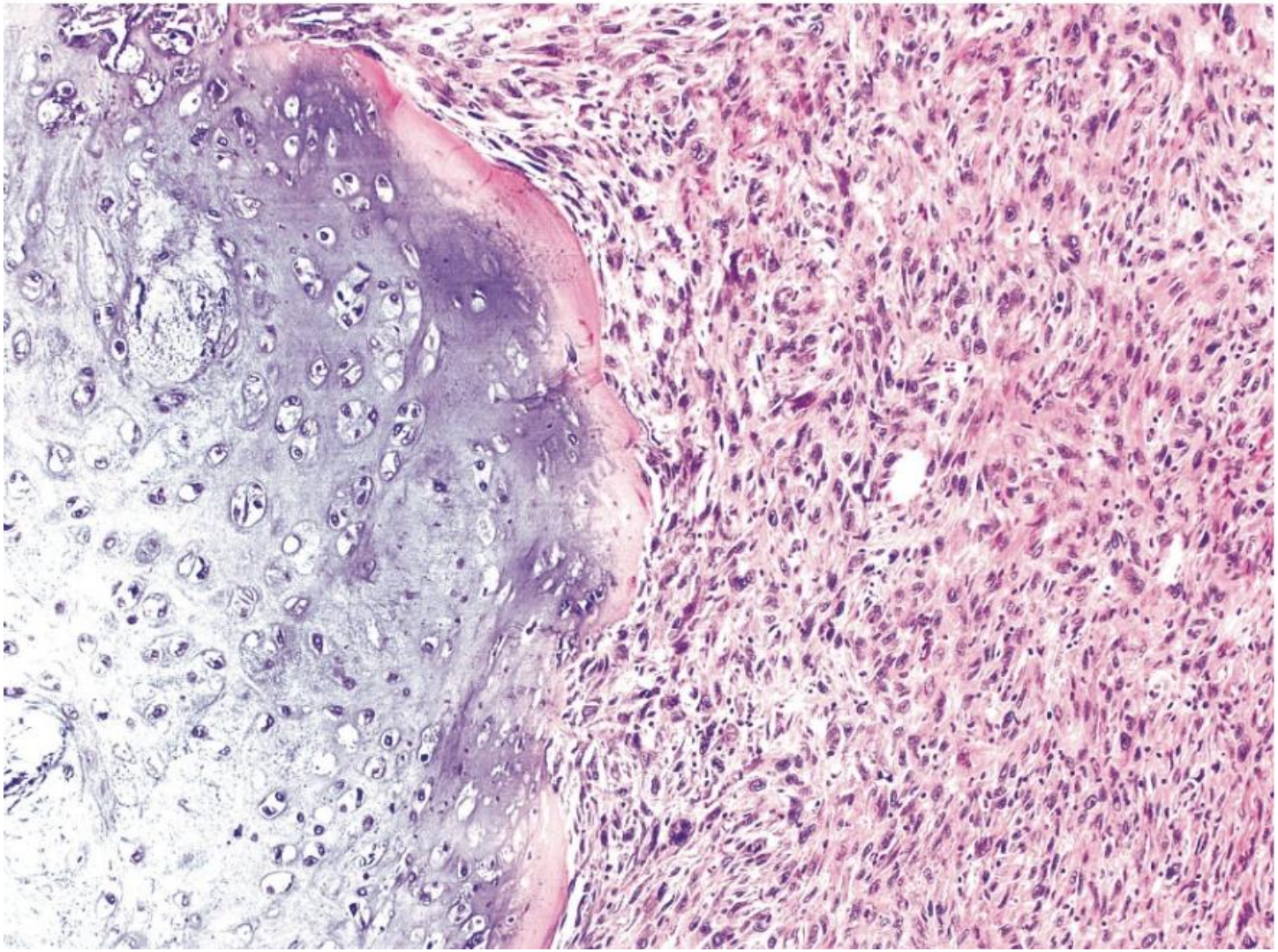


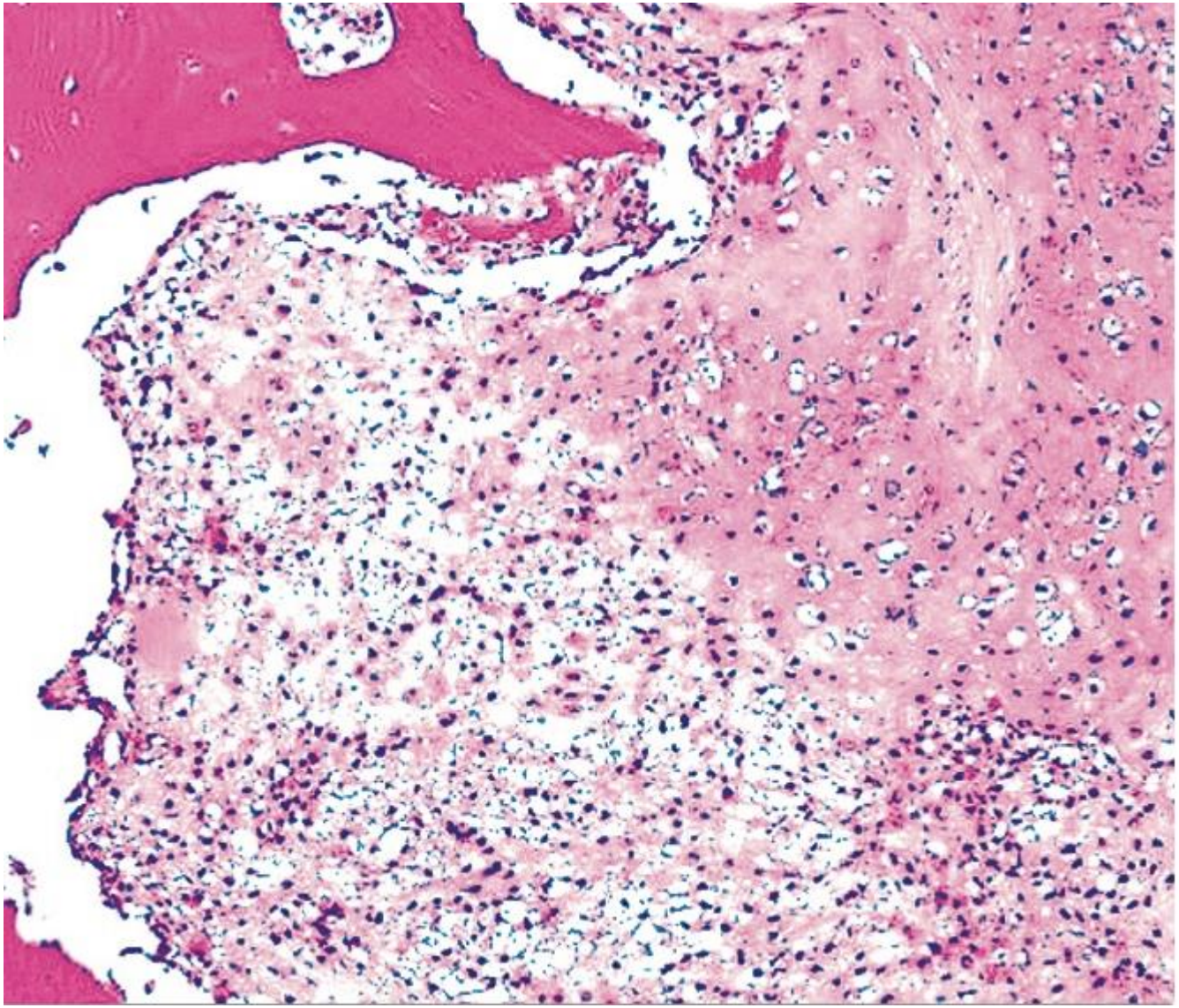
Fig. 10-3 Kempson, Richard L., Fletcher, Christophr DM, Evans, Harry L, Hendrickson, Michael R, and Sibley, Richard K, Tumors of the Soft Tissues, Fascicle 30, Atlas of Tumor Pathology. 3rd Series. Armed Forces Institute of Pathology, Washington, DC (2001).

Chondrosarcoma

- Dedifferentiated chondrosarcomas
- 10% of chondrosarcomas.
- They have a high-grade component that has the morphology of another poorly differentiated sarcoma.
- Clear cell chondrosarcoma
- Sheets of large malignant chondrocytes that have abundant clear cytoplasm, numerous osteoclast-type giant cells, and intralesional reactive bone formation.



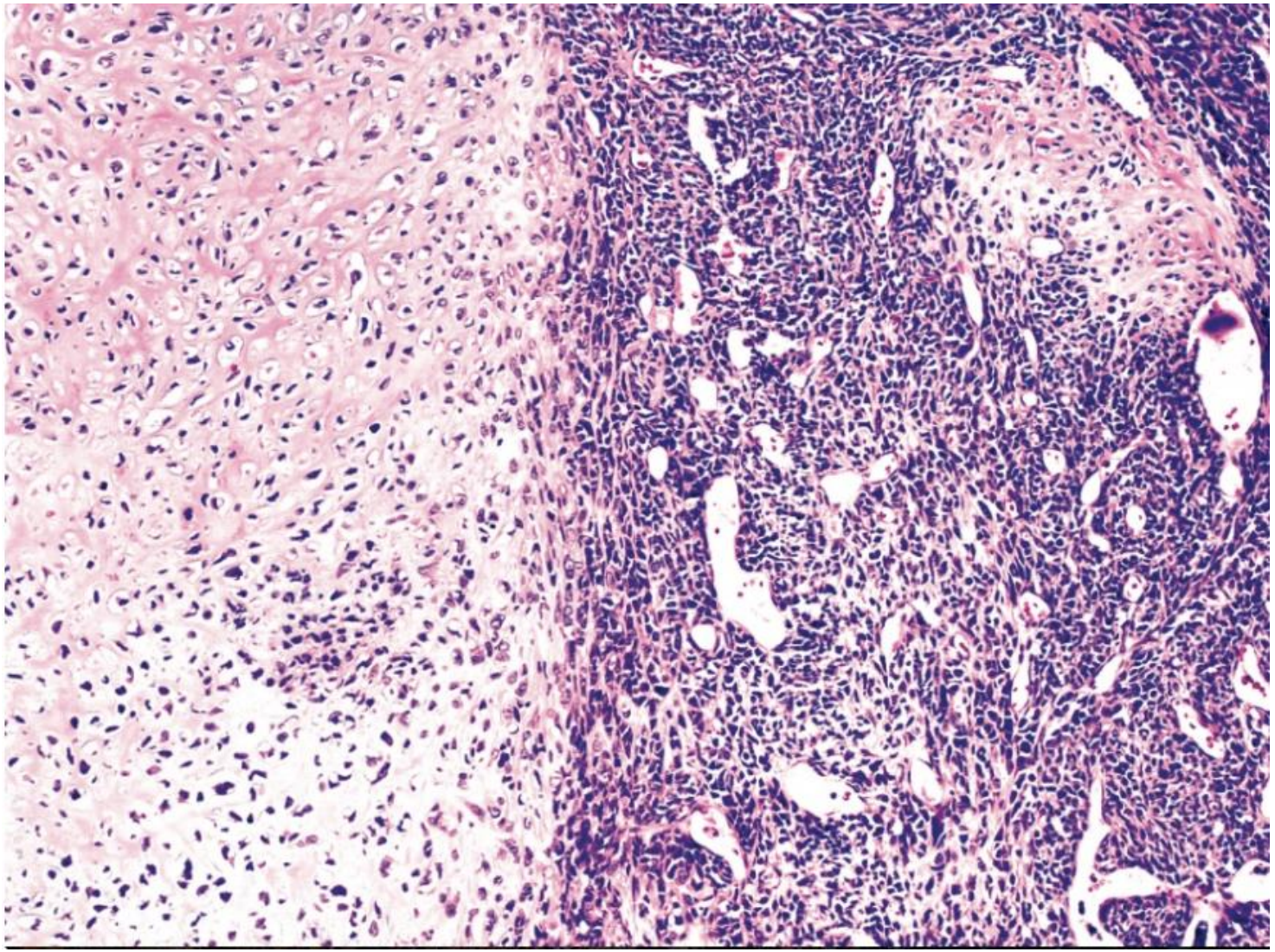
http://www.pathologyoutlines.com/topic/bonedediffchondrosarcoma.html



http://www.pathologyoutlines.com/topic/boneclearcellchondrosarcoma.html

Chondrosarcoma

- Mesenchymal chondrosarcoma
- Composed of islands of well-differentiated hyaline cartilage surrounded by sheets of small round cells.



https://www.pathologyoutlines.com/topic/bonemesenchymalchondrosarcoma.html

Treatment strategy

- En bloc, macro- and microscopically complete surgical excision of the gross tumor encompassing the biopsy scar is the treatment of choice.
- High grade disease regardless of location should be considered for neo-adjuvant dose-intensive anthracycline and isofosfamide combination chemotherapy.
- Excluded are those patients unable to tolerate an aggressive regimen as well as those with extraskeletal myxoid chondrosarcoma (resistant to chemotherapy generally).

Treatment strategy

- Amputation is seldom used as limb sparing surgery with post-operative radiation yields similar results.
- Neoadjuvant chemotherapy may be employed to reduce tumor bulk to permit resection without amputation.
- Isolated limb perfusion with hyperthermia and tumor necrosis factor is another approach that may permit tumor resection without amputation.

Response description	Response grade
Osteosarcoma (Huvos system)	
No vital tumour cells	IV
Less than 10% vital tumour tissue	III
10%-50% vital tumour tissue	II
No effect of chemotherapy	I
Ewing sarcoma (Picci)	
At least one residual macroscopic nodule of viable tumour (>10x)	I
Only isolated microscopic nodules of viable tumour cells are identified (<10x)	II
No viable nodules of tumour cells can be identified within the specimen	III

Fig. 2.13

Angiosarcomas the only subtype showing a response to paclitaxel.