MUSCULOSKELETAL PATHOLOGY-4 BONE TUMORS-1

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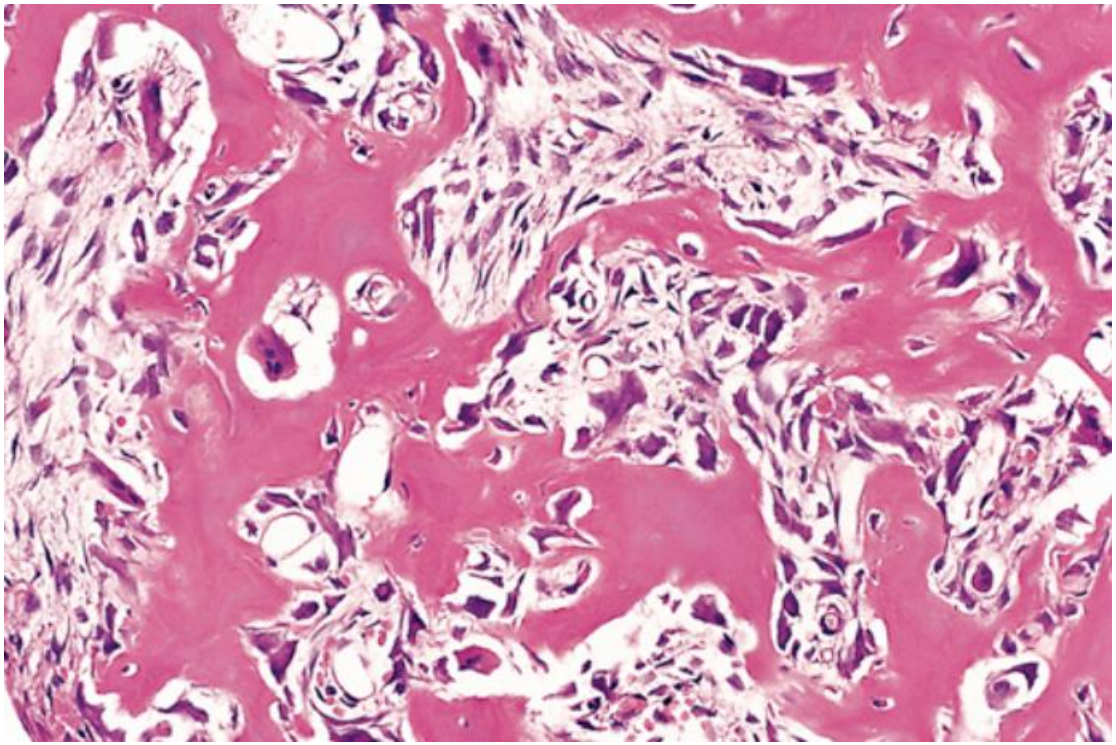
BONE TUMORS

- Primary bone tumors are rare and disfiguring
- Radiologic examination is essential
- Classified according to matrix production and shape of cells
- Benign tumors outnumber malignant tumors
- Benign tumors peak within the first three decades of life
- Most tumors that arise in old adults are malignant

OSTEOID OSTEOMA (OO) & OSTEOBLASTOMA (OB)

- Similar histology but differ in clinical & radiologic features
- OO is < 2cm, most common in young men, 50% arise in the cortex of femur or tibia, causes cortical bone reaction that appears in X-ray. Painful (osteoblasts secrete prostaglandin E2, relieved by aspirin and COX inhibitors), treated by radioablation
- OB: large, posterior part of vertebrae, painful but not responsive to pain killers, no cortical bone reaction, treated by surgery
- Both appear round and well-circumscribed in X-ray



- Osteoid osteoma composed of anastomosing trabeculae of woven bone rimmed by osteoblasts and embedded in a hypocellular fibrovascular connective tissue stroma

OSTEOSARCOMA

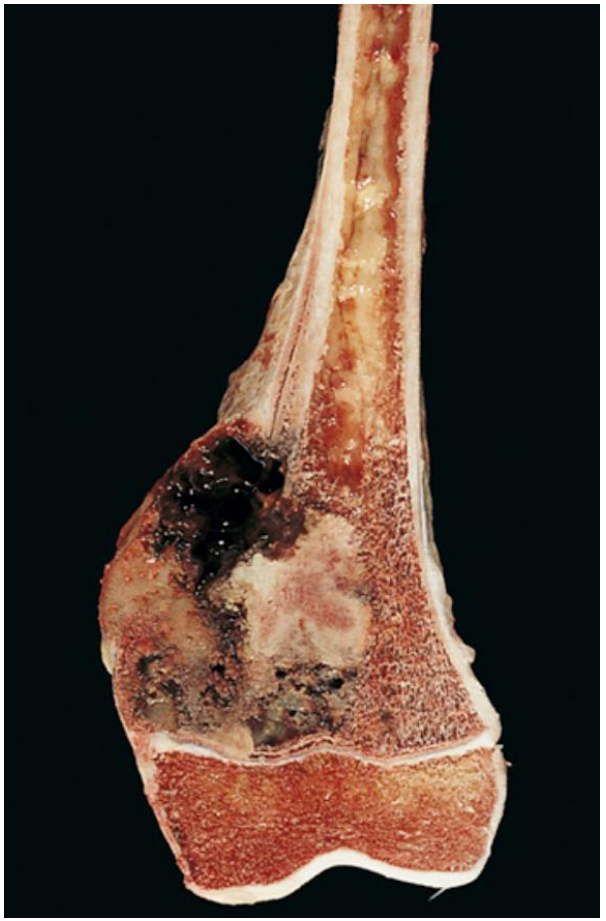
- Malignant tumor that produces osteoid matrix
- Most common primary bone sarcoma
- M>F
- 75% of cases arise in childhood & adolescence, a second small peak occurs in elderly with predisposing factors
- Can arise anywhere, but most common site is around knee joint (metaphysis of long bone)
- Patient complain of pain, enlarging mass, fracture
- X-ray: mass, mixed osteolytic and sclerosis, infiltrative margin
- Most tumors arise in the medulla, invade the cortex, raise the periosteum, resulting in a wedge-shaped mass (Codman triangle)

PATHOGENESIS

- Arise in rapidly growing bones
- RB gene mutation (tumor suppressor) is present in 70% of cases
- TP53 mutation
- MDM2 and CDK4 are overexpressed (inhibit normal RB and P53)
- CDKN2A is inactivated, normally encodes tumor suppressors (P14 and P16)
- MYC amplification in 50% of cases

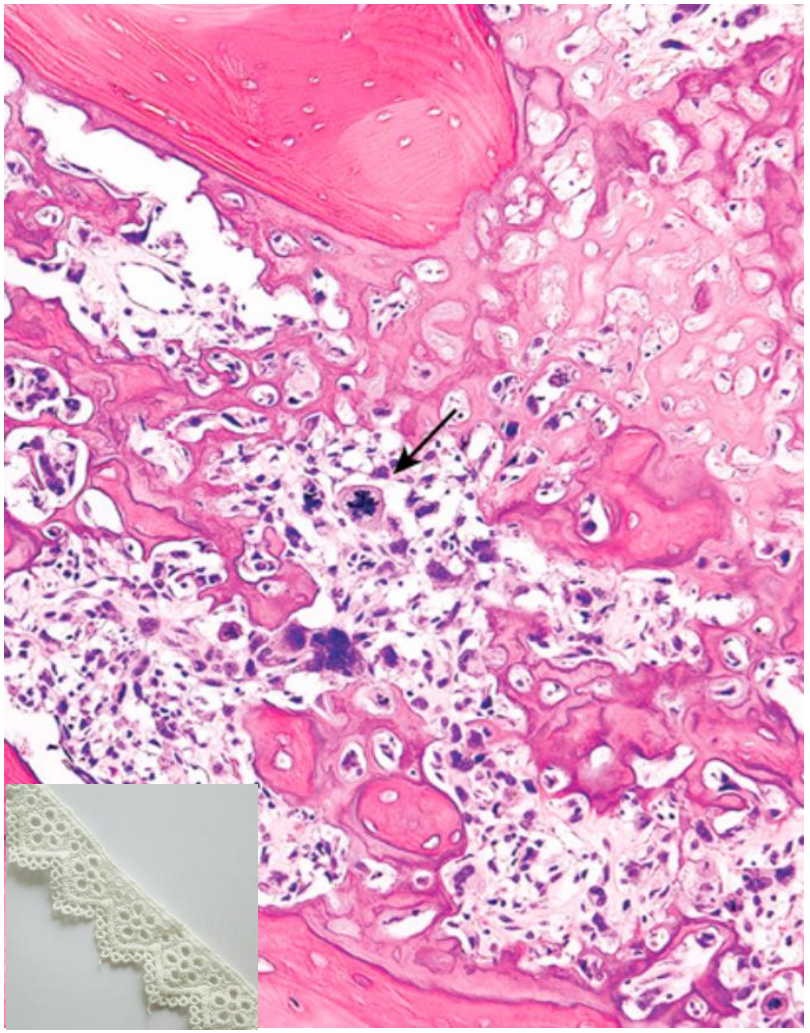
MORPHOLOGY: MACROSCOPIC

- Osteosarcoma of distal femur. There is extensive cortical disruption and subperiosteal expansion. Tumor is confined to the metaphyseal side of the cartilaginous growth plate. Hemorrhagic area represents biopsy site.
- Invasion of epiphysis and joint is NOT frequent



MORPHOLOGY: MICROSCOPIC

- Lacelike osteoid produced by pleomorphic malignant tumor cells bridges preexisting lamellar bone in an osteosarcoma. Note the abnormal mitotic figure (arrow)
- Most cases are high-grade, poorly differentiated



CLINICAL

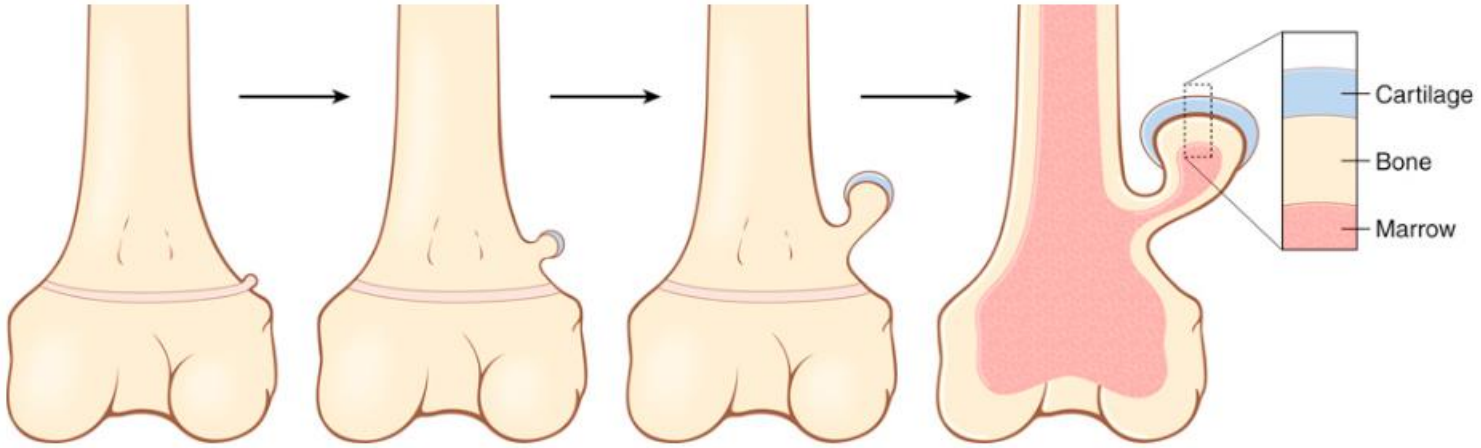
- Osteosarcoma have hematogenous metastasis, all cases at presentation are assumed to have occult metastasis
- Treatment: neoadjuvant chemotherapy, surgery, then adjuvant chemotherapy
- 5-year survival is 70%
- Patients with obvious metastasis, secondary osteosarcoma have poor prognosis, 5-year survival is 20%

OSTEOCHONDROMA (EXOSTOSIS)

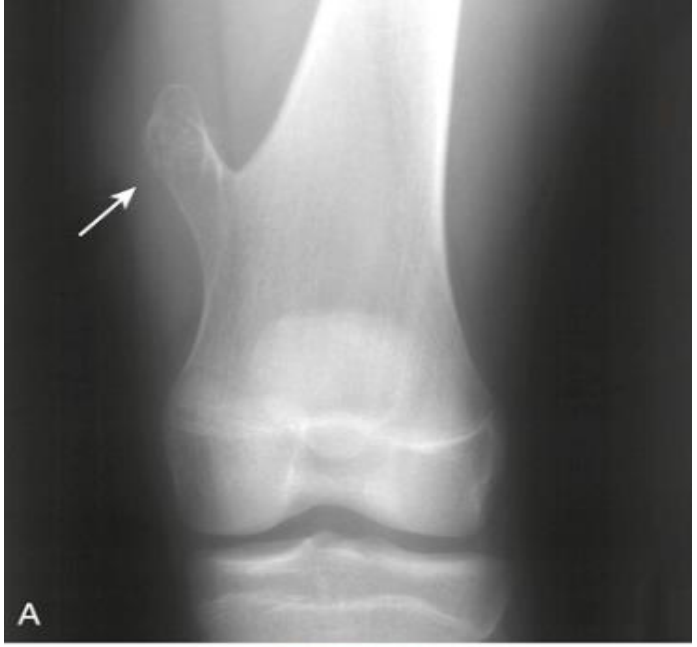
- Bone growth with a cartilage cap, sessile or pedunculated
- M>F (3 times)
- 85% of cases solitary (adolescence)
- 15% multiple (children, multiple hereditary exostosis)
- Arise around growth plate, most commonly around knee joint

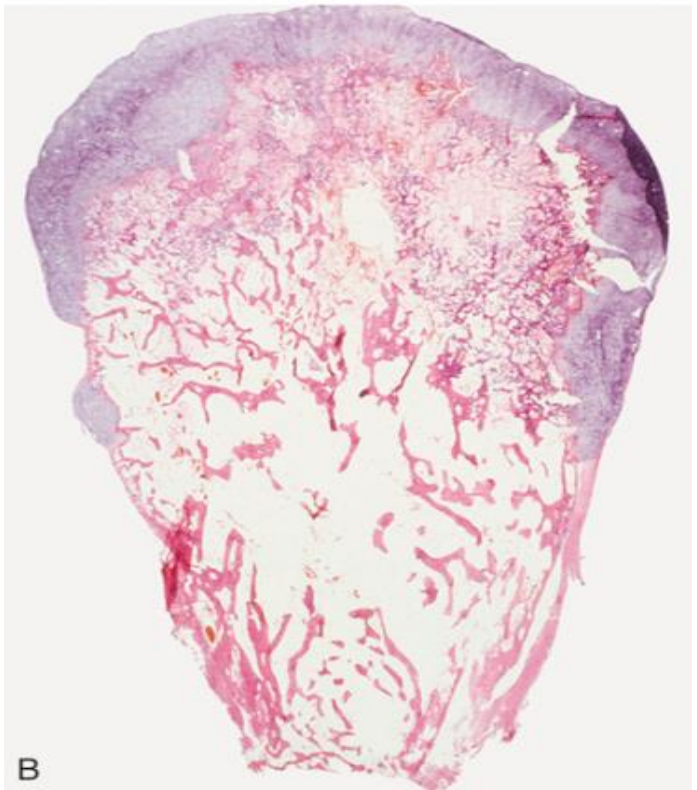
PATHOGENESIS

- In syndrome: EXT1 or EXT2 germline gene mutation, the second allele is mutated later
- In sporadic: decreased EXT expression
- Decreased synthesis of heparan sulfate glycosaminoglycans
- This interferes with "Indian Hedgehog" signaling proteins, that regulate cartilage growth



- The development of an osteochondroma, beginning with an outgrowth from the epiphyseal cartilage.





- Osteochondroma. (A) Radiograph of an osteochondroma (arrow) arising from the distal femur. (B) Whole mount section of narrow-pedicled osteochondroma with surface cartilage cap

CLINICAL FEATURES

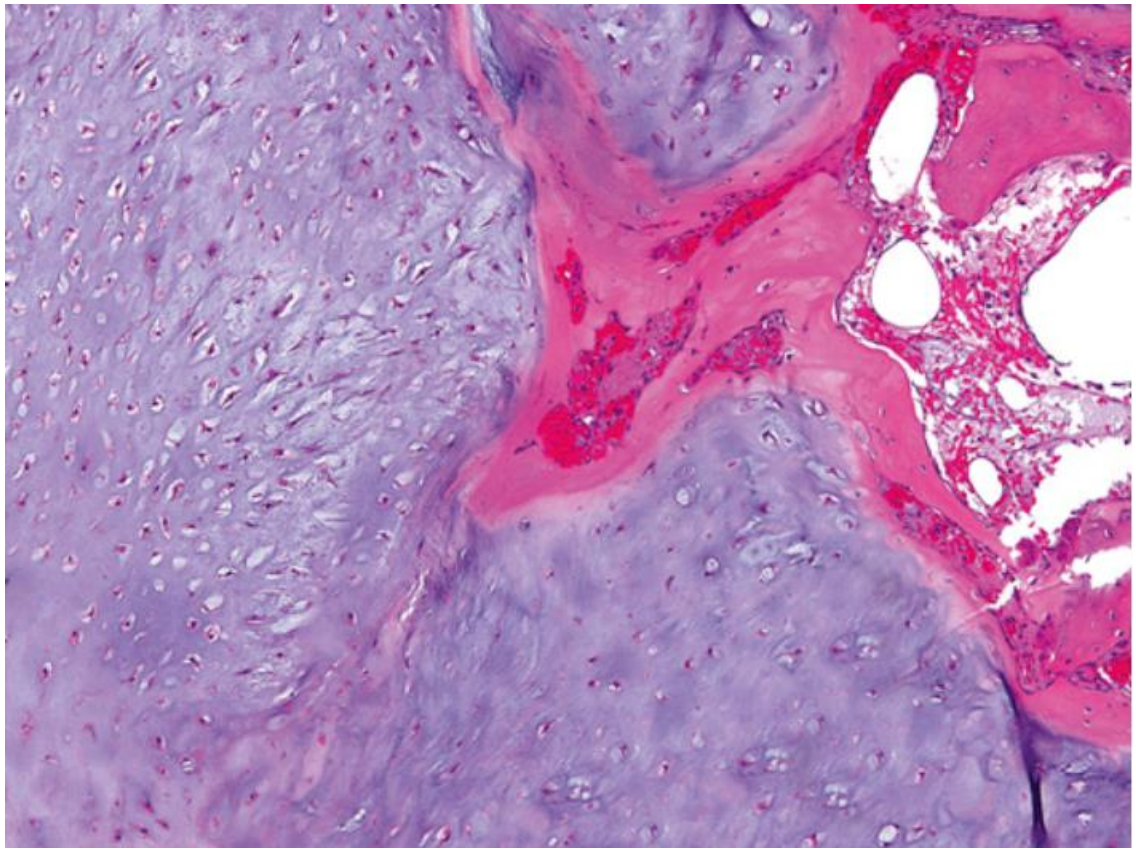
- Presents as a mass
- May cause pain if fractured or entrap a nerve
- May be painless and incidental finding
- Usually stop growing at the time of growth plate closure
- Secondary chondrosarcoma develops only rarely, usually in tumors associated with multiple hereditary exostosis.

CHONDROMA

- Benign tumor of hyaline cartilage that occurs in bones of endochondral origin
- May arises in the medullary cavity (enchondroma) or on the bone surface (juxtacortical chondroma)
- Metaphysis of long bones
- Age between 20-50 years
- Sporadic cases are usually single lesion, asymptomatic
- Ollier disease and Maffucci syndrome show enchondromatosis (multiple)
- Solitary enchondromas rarely undergo sarcomatous transformation; by contrast, those associated with enchondromatosis do so more frequently

PATHOGENESIS

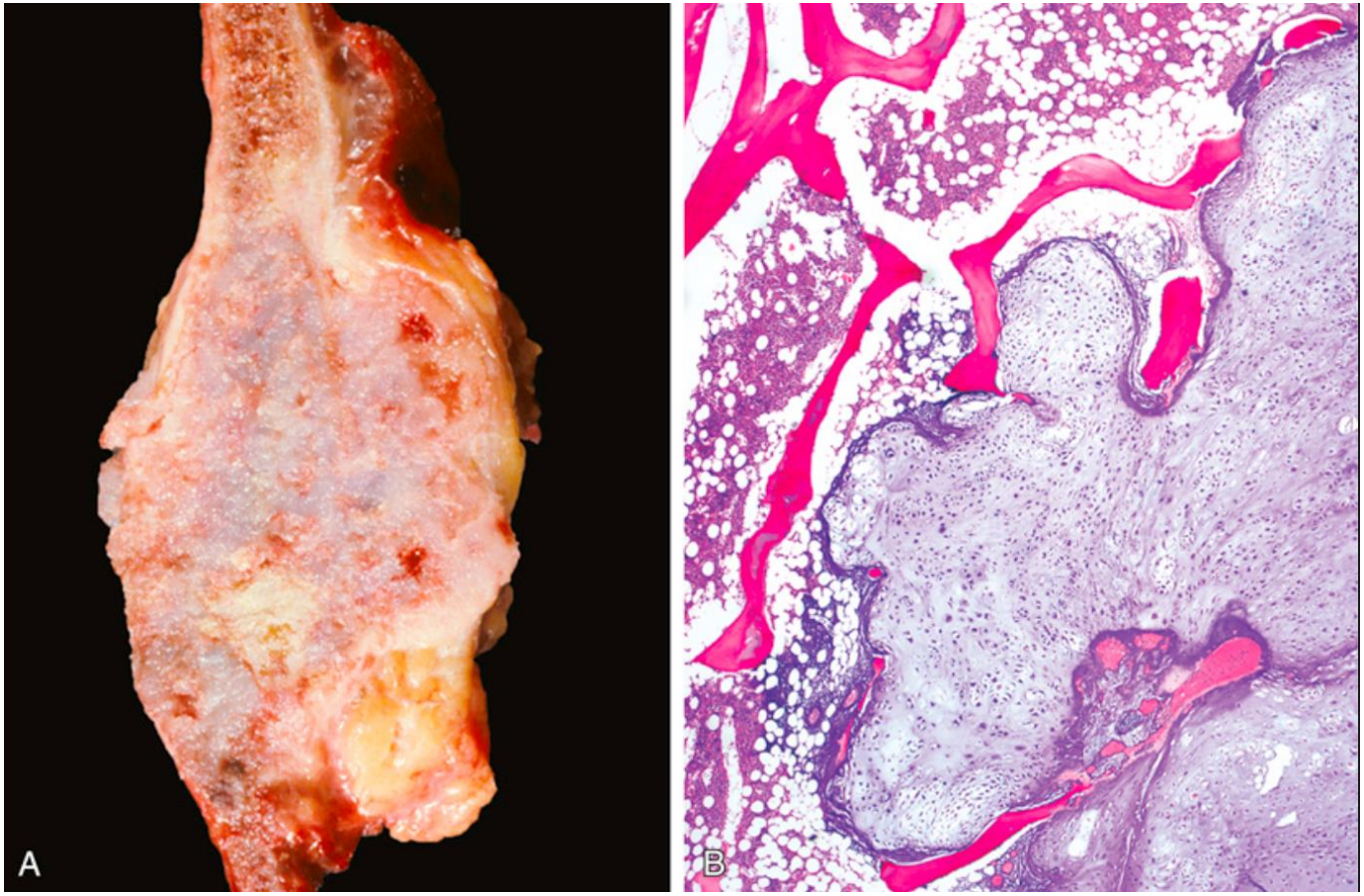
- IDH1 and IDH2 gene mutations
- Isocitrate dehydrogenase enzyme gain a new activity that leads to synthesis of 2-hydroxyglutarate (oncometabolite)
- The latter interferes with regulation of DNA- methylation, leading to expression of other oncogenes
- This mutation is detected in both sporadic and syndromic cases



- Enchondroma composed of a nodule of hyaline cartilage encased by a thin layer of reactive bone

CHONDROSARCOMA

- Malignant tumor that produces cartilage only
- Most cases are conventional, other histologic types include dedifferentiated, mesenchymal and clear cell
- Patients are > 40 years
- M>F (twice)
- 15% of cases are secondary, follows osteochondroma or enchondroma
- Most common sites: pelvis, shoulder and ribs
- X-ray: large mass that destroys the cortex and extends to soft tissue, flocculent calcification



- Chondrosarcoma. (A) Nodules of hyaline cartilage permeate the medullary cavity of the sternum, grow through the cortex, and form a relatively well-circumscribed soft tissue mass in the parasternal soft tissue. (B) Chondrosarcoma permeating through preexisting trabecular bone