Professor Tariq Aladily

Department of Pathology

The University of Jordan

tnaladily@ju.edu.jo

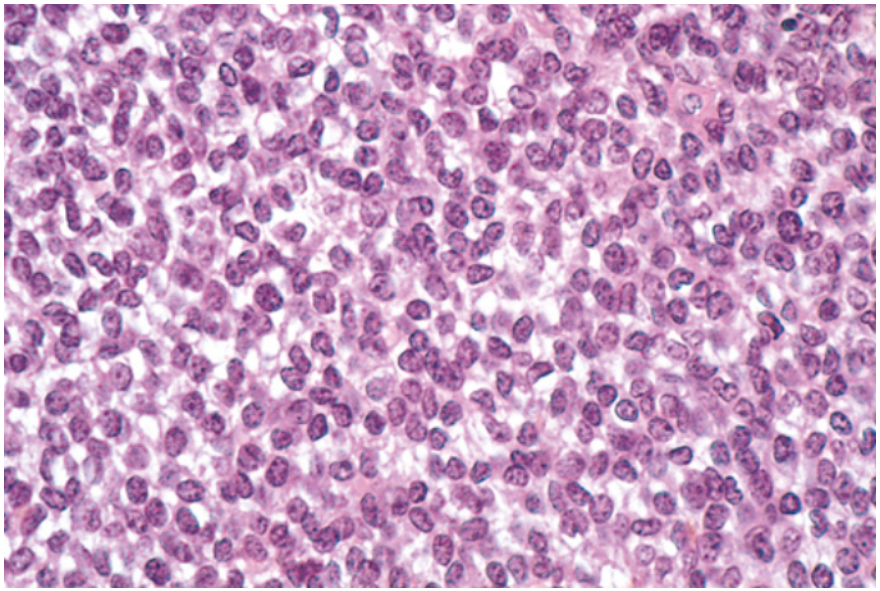
EWING SARCOMA

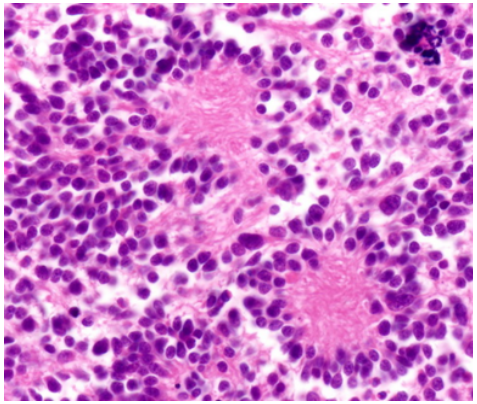
- Uncommon malignant, undifferentiated tumor
- 10% of primary malignant bone tumors
- Second most common bone sarcoma in children
- 80% of patients are <20 year-old
- M>F
- 20% of cases arise extra-skeletal

PATHOGENESIS

- Arise from primitive cell (mesenchymal stem cell vs neuroectodermal cell)
- >90% have balanced translocation
- Fusion of EWSR1 gene (chr 22) and FLI1 gene (chr 11).
- The resultant protein binds DNA, dysregulate transcription and lead to uncontrolled growth and abnormal differentiation
- Tumor arise in the medulla, diaphysis
- Severe necrosis and destruction, periosteal reaction of multiple layers, appear in X-ray as “onion skin”

MORPHOLOGY



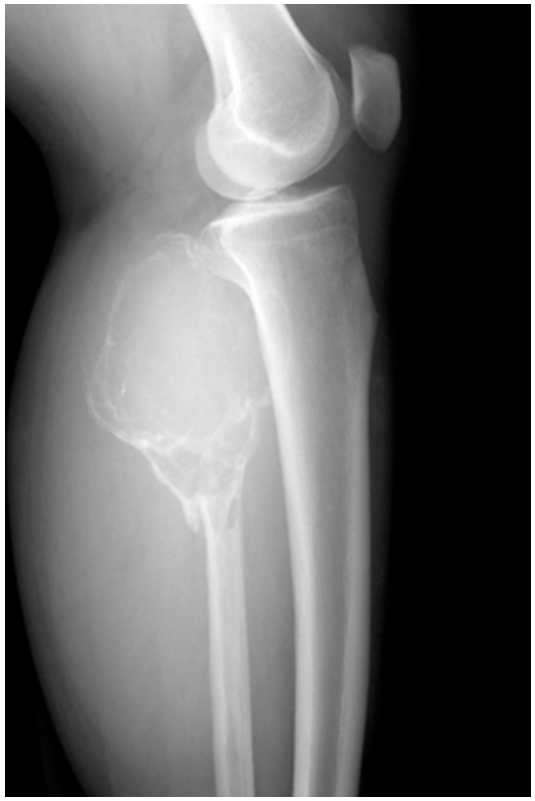


- Left: Ewing sarcoma composed of sheets of small round cells with minimal clear cytoplasm
- Right: Homer-Wright rosettes: circular arrangement of cells with a central fibrillary material

GIANT CELL TUMOR

- Mostly benign tumor, but locally aggressive (may recur)
- Third decade of life
- Epiphyseal tumor, causes destruction of overlying cortex and bulge into soft tissue (arthritis-like symptoms)
- Most common site: distal femur and proximal tibia
- 4% develop lung metastasis, but controlled by surgical removal
- Tumor is composed of two population of cells: primitive osteoblast precursors (neoplastic) that secrete RANKL, and reactive osteoclasts (non-neoplastic)

- Radiographically, giant cell tumor of the proximal fibula is predominantly lytic and expansile with destruction of the cortex. A pathologic fracture is also present.



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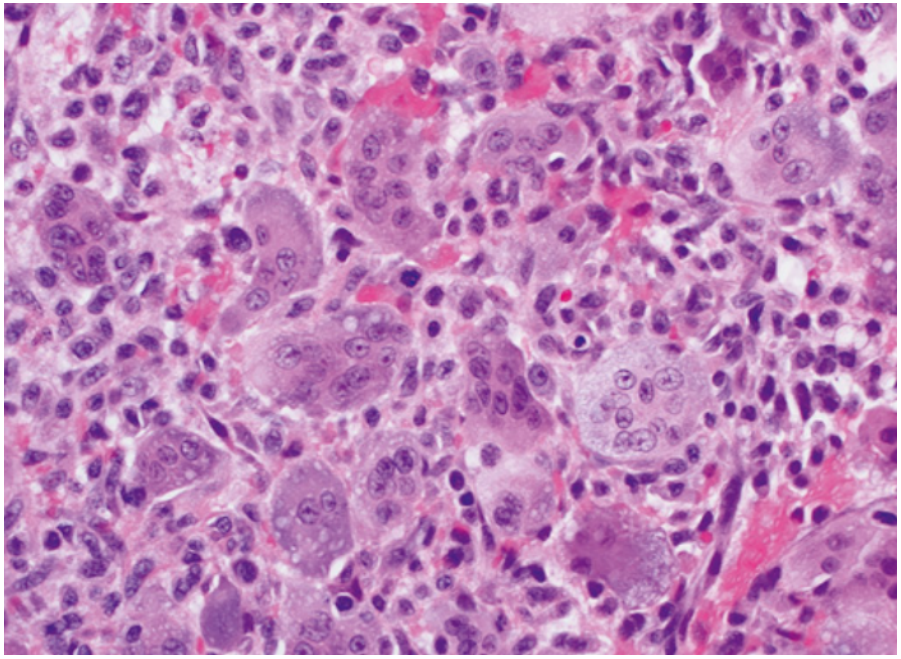


- Giant cell tumor illustrating an abundance of multinucleate giant cells with background mononuclear stromal cells.

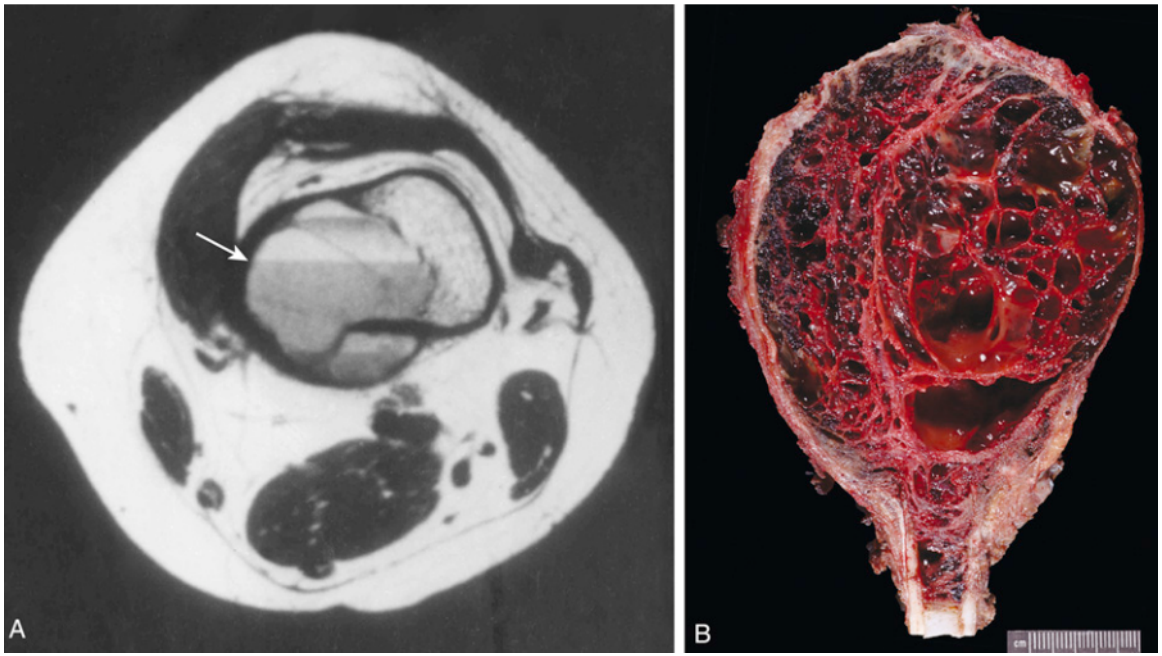
ANEURYSMAL BONE CYST (ABC)

- Multiloculated blood-filled spaces
- Affects all age groups, but most commonly in adolescents
- Affects femur, tibia or vertebra
- Arise in metaphysis
- Appear well-defined lesion with internal septa and filled with blood
- Septa are composed of plump uniform fibroblasts, multinucleated giant cells and woven bone
- Causes pain, swelling, pathologic fracture
- Locally aggressive (may recur)

PATHOGENESIS

- Neoplastic cells are spindle, unknown origin
- Rearrangement of chromosome 17p13
- Fusion of USP6 with COL1A1 genes
- Results in overexpression of USP6
- Activation of NF-kB pathway
- Increase in matrix metalloproteases, leading to cystic bone resorption

MORPHOLOGY



- Aneurysmal bone cyst. (A) Axial magnetic resonance image demonstrating characteristic fluid-fluid levels (arrow). (B) Gross appearance of aneurysmal bone cyst. The lesion appears hemorrhagic and spongelike in this bisected portion of proximal fibula

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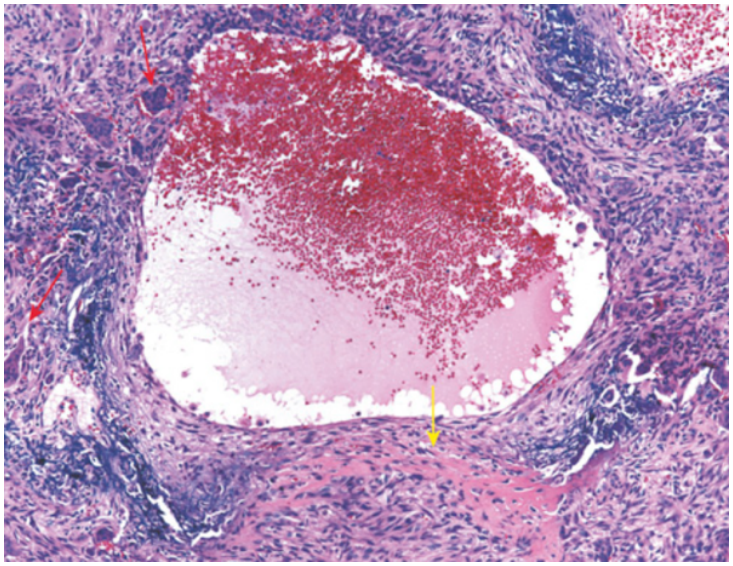
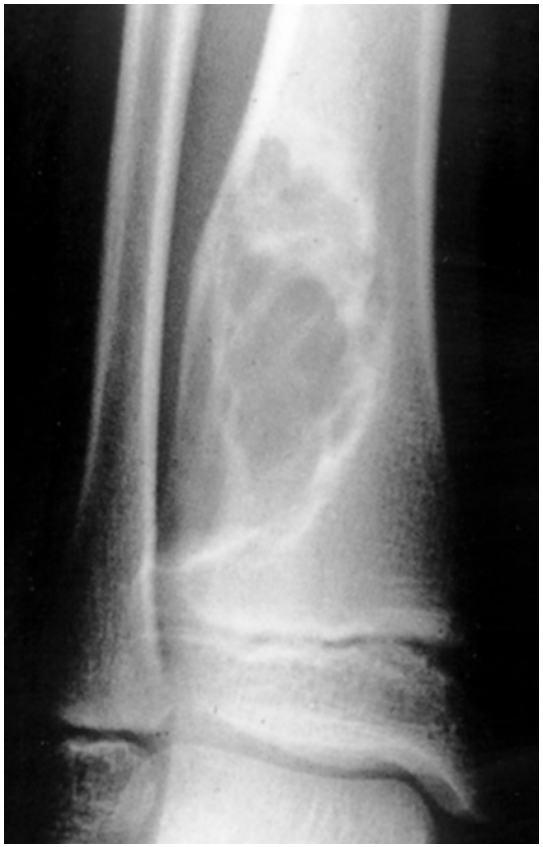


- Aneurysmal bone cyst with blood-filled cystic space surrounded by a fibrous wall containing proliferating fibroblasts, reactive woven bone (yellow arrow), and osteoclast-type giant cells (red arrows).

FIBROUS CORTICAL DEFECT AND NONOSSIFYING FIBROMA

- Developmental defects, where fibrous tissue replaces bone
- Present in 50% of children >2 years, incidental finding
- Most commonly in metaphysis of distal femur or proximal tibia
- 50% multiple and bilateral
- Fibrous cortical defect: small (<0.5 cm)
- Non-ossifying fibroma: large (may reach 5 cm)
- Both are well-demarcated, appear radiolucent in X-ray

- Nonossifying fibroma of the distal tibia metaphysis producing an eccentric lobulated radiolucency surrounded by a sclerotic margin.



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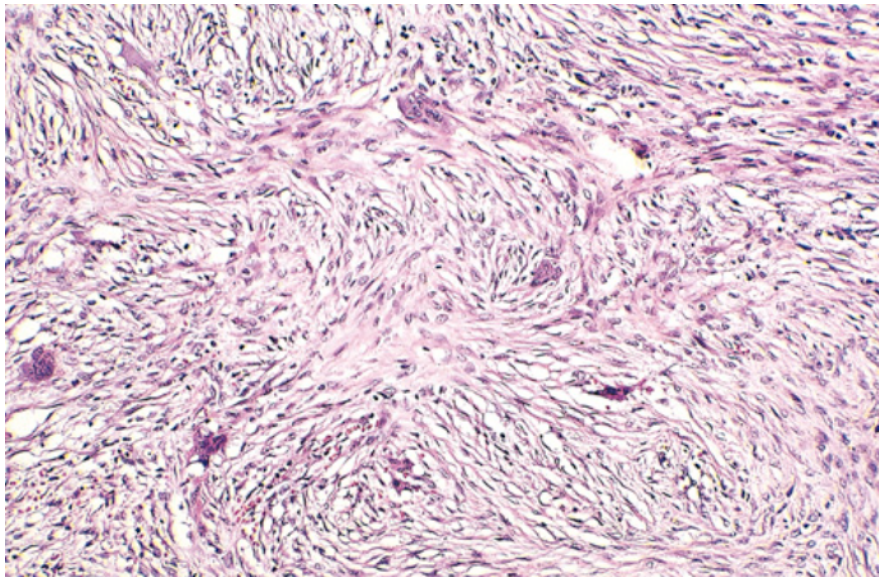


- Pinwheel (storiform) fibroblasts and multinucleated giant cells

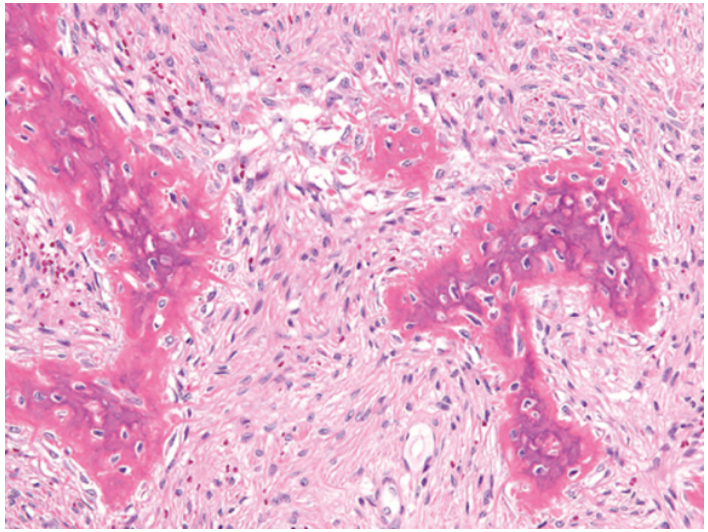
FIBROUS DYSPLASIA (FD)

- Benign tumor, results from localized development arrest (components of normal bone are present but do not differentiate into mature structures)
- May grow and cause disfigurement
- Might be sporadic or syndromic
- Can be:
- Monostotic
- Polyostotic (may transform to osteosarcoma)
- Mazabraud syndrome: FD and soft tissue myxoma
- McCune Albright syndrome: polyostotic FD, endocrine diseases, skin pigmentation

PATHOGENESIS

- Gain of function mutation in GNAS1 gene
- Constitutively active Gs-protein
- Increase level of cAMP
- Promotes cell proliferation and disrupts osteoblast differentiation
- Tumor arise in medulla, causes cortical thinning and bowing

MORPHOLOGY



- Small curved woven bone trabeculae (Chinese letters), not rimmed by osteoblasts
- Abundant fibroblasts in between

BONE METASTASIS

- More common than primary bone tumors
- Any cancer can spread to bone (hematogenous, lymphatic or direct invasion)
- Commonly multifocal
- Can be bone destroying (lytic lesion), pure blastic (bone forming) or mixed
- Prostate cancer commonly cause osteoblastic lesion
- Malignant cells secreted prostaglandins, cytokines and PTH-like peptide, activating osteoclasts
- WNT proteins are secreted in osteoblastic metastasis