

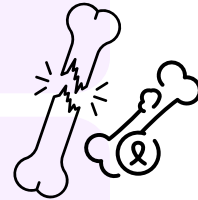
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FINAL | Lecture 1

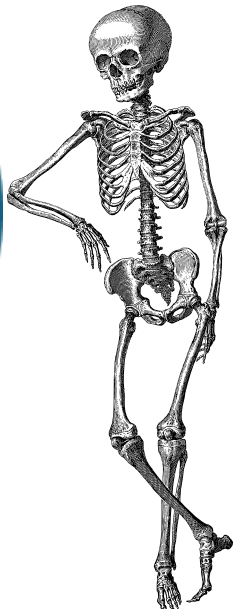
MSS & Skin Tumors (Pt.6)

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وَإِن تَتَوَلَّوْا يَسْتَبَدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَلَكُمْ
اللهم استعملنا ولا تستبدلنا



رَمَضَانَ مُبَارَكٌ



PATHOLOGY



Introduction

- The clinical and radiological features of the following three conditions can sometimes appear similar:
 1. [Giant Cell Tumor of Bone](#)
 2. [Aneurysmal Bone Cyst](#)
 3. [Non-Ossifying Fibroma](#)
- These conditions often present with similar clinical manifestations, including pain and local pathological fractures. Additionally, their radiological appearances may overlap, making accurate diagnosis challenging.
- Some underlined words are hyperlinks—you can click on them to access additional information about the topic.

GIANT CELL TUMOR OF BONE:

Mostly benign

- Sometimes can be a locally aggressive neoplasm of adults, destroying the surrounding bone, periosteum & soft tissues.
- Epiphyses of long bones
- Composed mainly of numerous Osteoclast-like giant cells
- Rare malignant behavior in 5-10% of patients
- Cells contain high levels of RANKL, as expected, as it is an osteoclast tumor.
- Trx: curetting with bone cementing, cut and replace, or cut and leave. The primary reasons for intervention include localized pain, pathological fracture, or suspicion of an underlying malignant or benign pathology.

Trx: Treatment

Giant cell tumors often destroy the overlying cortex, producing a bulging soft tissue mass delineated by a thin shell of reactive bone (Fig. 21.25). Grossly, they are red-brown masses that frequently undergo cystic degeneration. Microscopically, the tumor conspicuously lacks bone or cartilage, consisting of numerous osteoclast-type giant cells with 100 or more nuclei with uniform, oval mononuclear tumor cells in between (Fig. 21.26).



FIG. 21.25 Radiographically, giant cell tumor of the proximal fibula is predomi...

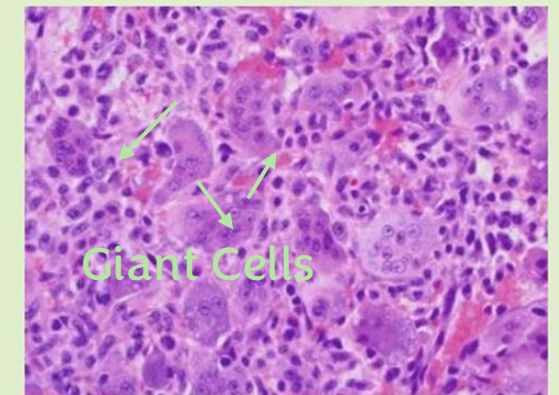


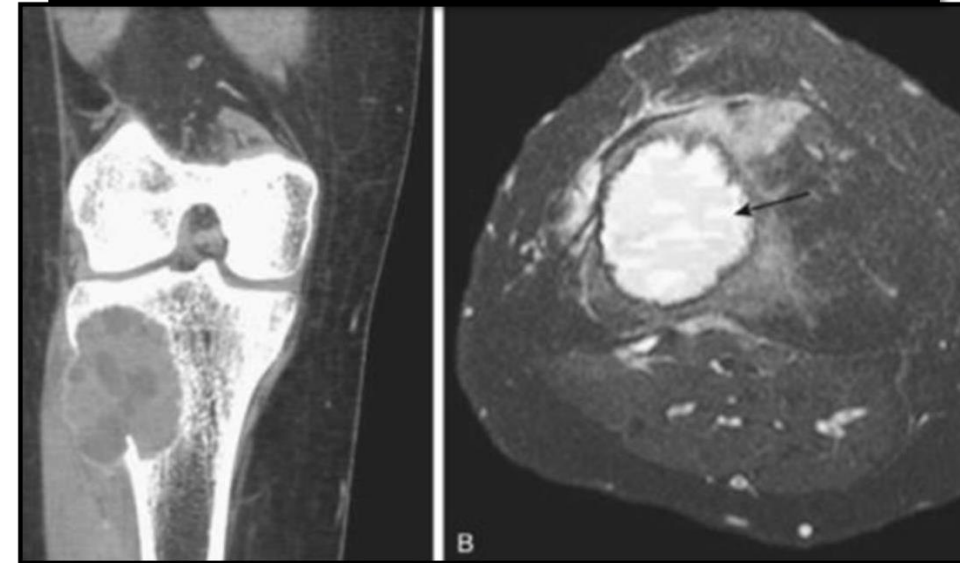
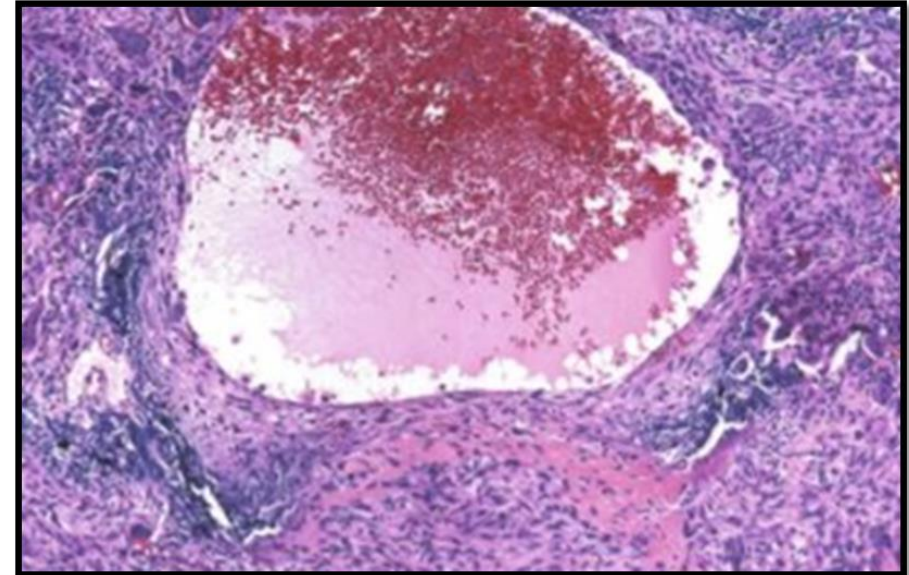
FIG. 21.26 Giant cell tumor illustrating an abundance of multinucleated giant c...

Giant Cell Tumor of Bone: Histological Features and Diagnostic Criteria

- The presence of osteoclast-like giant cells can be observed in various tumors, such as chondrosarcoma and osteosarcoma. However, in cases of giant cell tumor of bone, these multinucleated cells are a prominent histological feature and are distributed throughout the tumor in a relatively uniform pattern. One of the diagnostic features of giant cell tumors is the even distribution and consistent density of these giant cells within a background of mononuclear stromal cells.

ANEURYSMAL BONE CYST:

- Benign tumor (Common)
- Aneurysmal bone cysts (ABCs) are thought to not be true tumors. Some theories suggest they result from localized reactive processes, such as trauma or viral infections, forming blood-filled sacs. Osteoclast-like giant cells are often present, emphasizing their reactive nature and the potential for similar cells to appear in other tumor types.
- Blood filled cyst (Aneurysm: Sac)
- Metaphysis of long bones; adults, not seen in children.
- Curettage with bone cement is performed to treat aneurysmal bone cysts (ABCs) by stabilizing the bone and reducing the risk of recurrence. Histopathological examination is essential to distinguish ABCs from metastatic lesions.



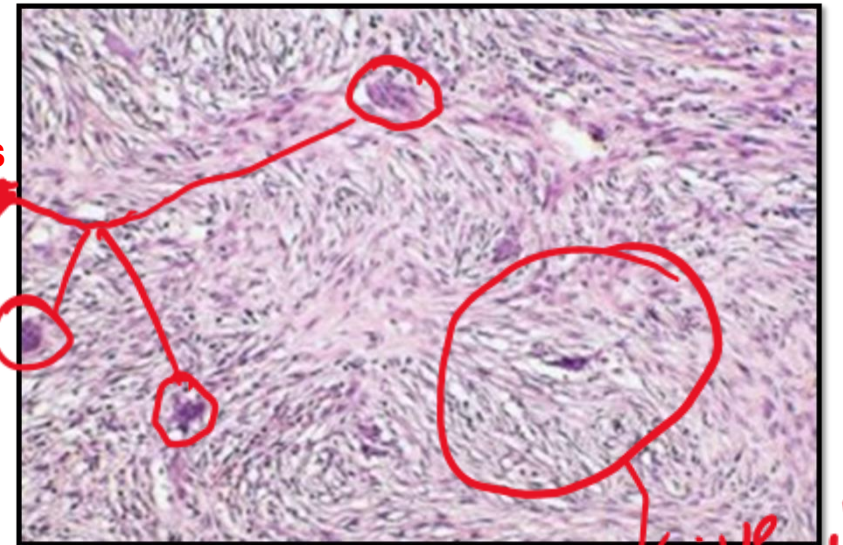
Radiological imaging can assess the nature of a tumor, determining whether it is infiltrative or locally destructive.

NON-OSSIFYING FIBROMA (benign):

- Non-ossifying: does not form mature bone tissue and is primarily composed of fibrous tissue.
- Benign lesion maybe reactive not a true neoplasm (other names: FCD, MFD)
- Metaphysis lesion.
- Histology: bland* fibroblastic proliferation
- May resolve spontaneously
- Bland: lack of atypia or malignancy-associated characteristics.



giant cells




Reactive
fibroblast

FCD: Fibrous Cortical Deficit
MFD: Metaphyseal Fibrous Defect

FIBROUS DYSPLASIA (FD):

- Dysplasia refers to abnormal cellular development and is considered a potential precursor to malignancy, which may progress to cancer over time if left untreated, although not all cases do.
- Dysplasia can also refer to developmental abnormalities, such as focal cortical dysplasia, a brain malformation. Similarly, fibrous dysplasia is a developmental bone disorder characterized by the replacement of normal bone with fibrous tissue and irregular, immature bone.
- Not a real tumor; rather a developmental abnormality of bone genesis due to mutations in GNAS1 gene (cAMP mediated osteoblast differentiation).

FIBROUS DYSPLASIA (FD):

- Forms of FD:
 - Monostotic: affecting one bone
 - Polyostotic: multiple bones Similar to Paget Disease
- Mazabraud syndrome: FD + soft tissue myxoma, benign spindle cell tumors which can occur in different parts of the body, including the heart, where cardiac myxoma represents the most common type of primary cardiac tumor.
- McCune-Albright syndrome: polyostotic FD (mainly in the face) + café-au-lait skin pigmentation (light to dark brown skin patches) + endocrine abnormalities (any type can occur, commonly precocious puberty).
 - The management of McCune-Albright syndrome focuses on treating its complications, including hormonal therapy for endocrine abnormalities and orthopedic interventions for bone deformities or fractures.

McCUNE-ALBRIGHT SYNDROME:

Abnormal proximal femur demonstrating mixed sclerotic and lytic changes, resembling Paget disease but also consistent with fibrous dysplasia.



- Woven bone with odd irregular shapes - **key feature**. Described as "Chinese characters".
- Fibrous tissue around bone.

Cherubism



café-au-lait patches

METASTASIS OF TUMORS TO BONE:

- Bone metastases are much more common than primary bone tumors, particularly in adults.
- In adults, malignant tumors that metastasize to the bone are predominantly carcinomas, primarily originating in the lung, prostate, breast, kidney, thyroid, and liver. These tumors are often referred to as “osteotropic carcinomas” due to their tendency to spread to bone.
- This means that when bone metastasis is suspected, the most likely diagnosis is carcinoma, with adenocarcinoma being the most common subtype among carcinomas.
- Thyroid gland tumors can be benign or malignant, with benign tumors being the most common.
- Among malignant thyroid tumors, there are four main types. The most common is papillary thyroid cancer (PTC), accounting for approximately 80% of cases. The second most common type is follicular thyroid cancer (FTC), comprising about 10-15% of cases.

METASTASIS OF TUMORS TO BONE:

- It is much less common to see metastasis to the bone in children: Neuroblastoma, Wilms tumor, and rhabdomyosarcoma are the top malignant tumors in differential diagnosis.
- They are usually multiple lesions and present on the axial bone; mostly by hematogenous spread.
- They usually present as multiple lesions within the axial skeleton, primarily spreading through the bloodstream (hematogenous spread).
- Therefore, if multiple axial lesions are observed, especially in adults, the primary differential diagnosis is metastasis from a malignant tumor.
- Bone metastasis, as seen radiologically on X-ray, MRI, or CT scan, can appear as lytic (more common), blastic (commonly associated with prostate cancer.), or mixed lesions, depending on the mediators' secretions.

BLASTIC METASTASIS

more bone formation



LYTIC METASTASIS

more bone resorption



- In both cases, blastic and lytic bone lesions are mediated by cancer cells.
- In blastic lesions, mediators secreted by cancer cells activate osteoblasts, leading to increased bone formation.
- In lytic lesions, mediators secreted by cancer cells activate osteoclasts, resulting in increased bone resorption.

A 75-year-old male patient presents with chronic mild to moderate pelvic pain or a pelvic fracture following a fall. X-ray imaging reveals multiple whitish osteoblastic lesions in the pelvis. What is the most likely underlying condition that could explain these blastic lesions?

Diagnostic reasoning:

1. The patient's age (75 years) and presence of a pathological fracture suggest an underlying bone weakness, which could be due to metastasis.
2. The presence of multiple whitish osteoblastic lesions on X-ray indicates a metastatic tumor, with osteoblastic metastasis being common in prostate cancer.
3. As the patient is male, prostate cancer is the most likely primary tumor responsible for these findings.

The etiology of these lesions is metastatic prostate cancer.

- A simple and effective test to detect prostate cancer is measuring the prostate-specific antigen (PSA) level in the blood. The normal PSA level is less than 4 ng/mL. In this patient, the PSA level is expected to be significantly elevated, typically around 10 ng/mL or higher.



Summary

Bone Tumors and Tumorlike Lesions

Primary bone tumors are classified according to the cell of origin or the matrix that they produce. The remainder is grouped according to clinicopathologic features. Most primary bone tumors are benign. Metastases, especially from lung, prostate, kidneys, and breast, are far more common than primary bone neoplasms.

Major categories of primary bone tumors include

- **Bone forming:** Osteblastoma and osteoid osteoma consist of benign osteoblasts that synthesize osteoid. Osteosarcoma is an aggressive tumor of malignant osteoblasts, predominantly occurring in adolescents.
- **Cartilage forming:** Osteochondroma is an exostosis with a cartilage cap. Sporadic and syndromic forms arise from mutations in the *EXT* genes. Chondromas are benign tumors producing hyaline cartilage, usually arising in the digits. Chondrosarcomas are malignant tumors of chondroid cells that involve the axial skeleton in adults.
- **Ewing sarcomas** are aggressive, malignant, small round cell tumors most often associated with t(11;22).
- **Fibrous dysplasia** is an example of a disorder caused by gain-of-function mutations that occur during development.

For any feedback, scan the code or click on



Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slides 7, 8, and 9 had not been updated to reflect the recorded lecture at the time, they have since been updated accordingly.		
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

Reference Used:

(numbered in order as cited in the text)

1. Robbins & Kumar Basic Pathology - 11th Edition pages: 695-698
2. Carcinomas
3. Dysplasia
4. GNAS1 Gene
5. Precocious Puberty
6. Histology Picture, Slide 8