جامعة الملك سعود
King Saud University

Pathology practical

Med435.

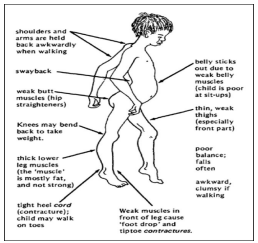
Muscular Dystrophies, Duchenne Muscular Dystrophy (DMD)

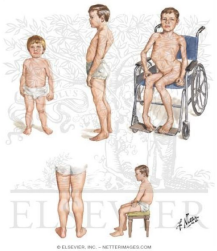
Case #1: A 3 - year- old boy presented to his pediatrician with complaint of his parents from difficulty in walking, poor balance, and frequent falls .

- Laboratory investigation shows elevated creatine kinase .
- Muscle biopsy show absence of dystrophin by western blot analysis

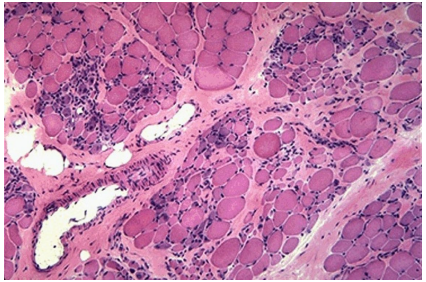
What is your provisional diagnosis? Duchenne Muscular Dystrophy (DMD).

- DMD is the most severe and common type of muscular dystrophy.
- DMD is characterized by the wasting away of muscles.
- DMD affects mostly males at a rate of 1 in 3,500 births
- Diagnosis in boys usually occurs between 16 months and 8 years.
- Death from DMD usually occurs by age of 30.
- DMD is a Genetic disorder.
- Mutation in Dystrophin.

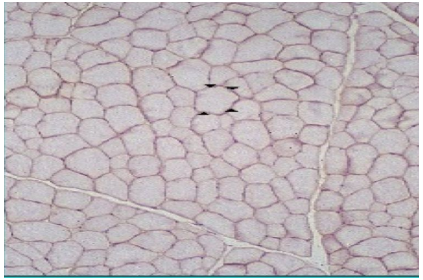




Muscular Dystrophies, Duchenne Muscular Dystrophy (DMD)

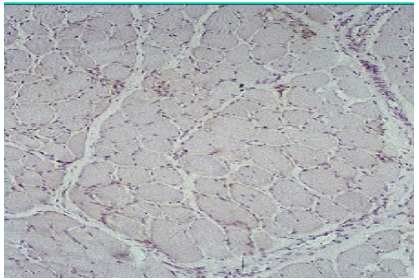


Duchenne Muscular Dystrophy - LPF
1- Variation in muscle fiber size *(Atrophy)*
2- Increased endomysial connective tissue
3- Blue regenerating fibers
*(*no inflammation present).



Normal Ms

(Normal muscle, brown border stains present)
POSITIVE TEST RESULT



DMD

(Brown borders of muscle fibers are absent)
NEGATIVE TEST RESULT

Stain: Immunohistochemistry for dystrophin shows dystrophin* brown
Note: Positive in normal individuals and negative in DMD
Confirmation by: Western blot analysis

Dystrophin*: sarcolemmal membrane protein that is **absent** in patients with muscular dystrophies

Dermatomyositis

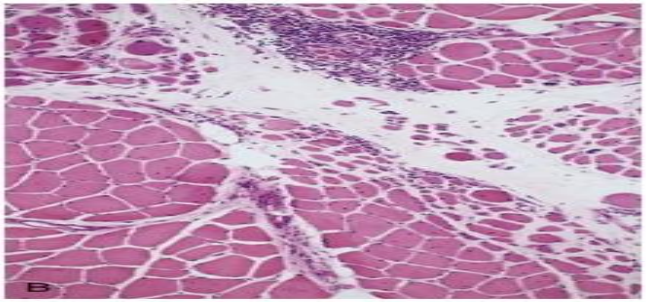
Case #2: A 52-year-old woman presents with 6-month history of progressive muscle weakness and a skin rash.

- Physical examination is remarkable for a diffuse purple/red discoloration of the skin over her cheeks, nose, and eyelids.
- Examination confirms proximal muscle weakness
- Laboratory findings show an increase in creatine kinase (10 times the normal).

What is your provisional diagnosis? Dermatomyositis

Gross description:

1) Purple/violet colored upper eyelids Skin rash
2) Periorbital edema



The histologic appearance of muscle shows:

1) Inflammatory cell infiltrate (Lymphocytes)
2) Perifascicular muscle atrophy *in the periphery*

Characteristics:

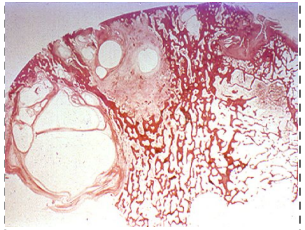
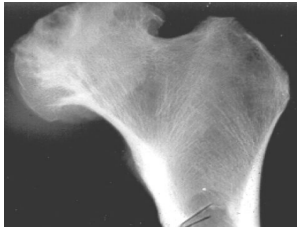
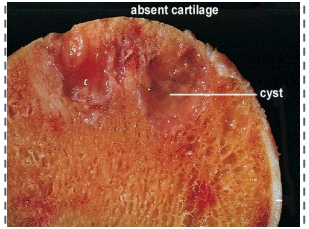
- Its an autoimmune disorder characterized by inflammation of muscle tissue and skin rash.
- Occurs more frequently in women.
- Can occur in any individual with peak age patterns at: 5-15 years of age 40-60 years of age.
- Dermatomyositis can be associated paraneoplastic disorder (Internal malignancies) in adults.
  - A **paraneoplastic syndrome** is a syndrome (a set of signs and symptoms) that is the consequence of cancer in the body.

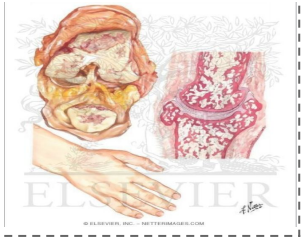
Lab tests:

1. Anti nuclear antibodies (ANA)
2. Creatinine kinase (CK)

NON INFECTIOUS ARTHRITIS: Osteoarthritis

Case #3: An obese 56-year-old woman presented with bilateral localized pain to her knees, hands and difficulty in walking .



- Osteoarthritis is a degenerative disorder.
- Treatment: joint replacement
- Arthritis is inflammation in joints

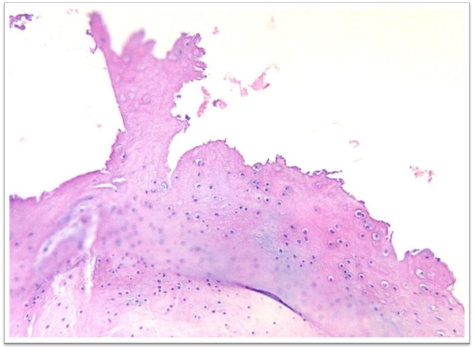
Osteoarthritis - Gross description


1) Progressive erosion of articular cartilage.
2) eburnated articular surface.
3) Subchondral cyst.
4) residual articular cartilage.

Osteoarthritis - LPF

Histologic description:

1) bony outgrowths (osteophyte)
Mushroom-shaped
2) Absence of inflammation



- erosion: تآكل
- eburnated: إستعاجة

NON INFECTIOUS ARTHRITIS: Rheumatoid Arthritis

Case # 4 : A 45 year old woman complains of low grade fever, malaise, and stiffness in her joints each morning

- Affects small joints
- Rheumatoid nodules

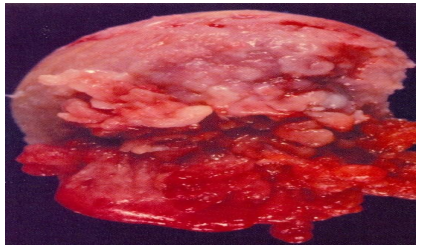
What is your provisional diagnosis? Rheumatoid arthritis

Swelling and deformity of the metacarpo-phalangeal joints and ulnar deviation of the fingers.

Serological tests which are somewhat specific for this disease:

1- Rheumatoid factor (RF)
2- Antibodies to citrullinated peptides in the serum (Anti CCP)
3- C-Reactive protein (CRP)
4- ESR (Non specific)

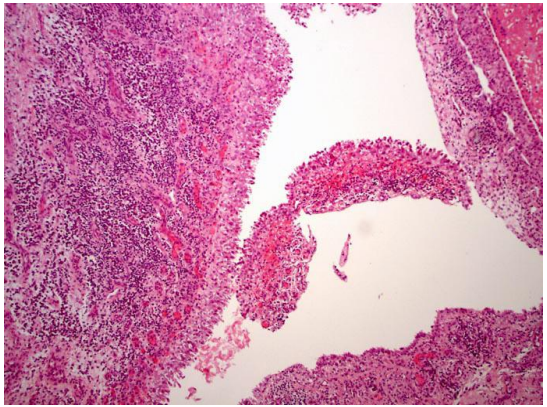
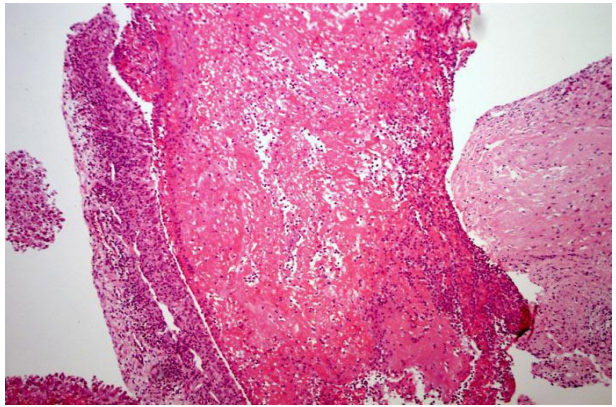
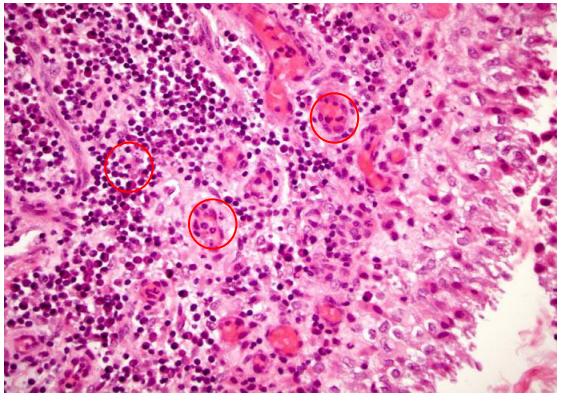
Cytokines are involved in the pathogenesis of the disease. Few of them are Interleukin 1, Tumor necrosis factor (TNF), Interleukin 6,8 and 17.



- **Rheumatoid arthritis affecting the head of the femur.**

Gross description:
1) Edematous synovium
2) Hyperplastic synovium
3) Bulbous fonds (finger like)

Hyperplastic Synovium In Rheumatoid Arthritis microscopically

LPF	LPF	HPF
		

- *Hyperplastic synovium*
- *Congested blood vessels*
- *Lympho-plasmacytic inflammatory infiltration*

GOUT

Gout is a syndrome caused by the inflammatory response to tissue deposition of monosodium urate crystals (MSU).

We have different types of gout, for example:

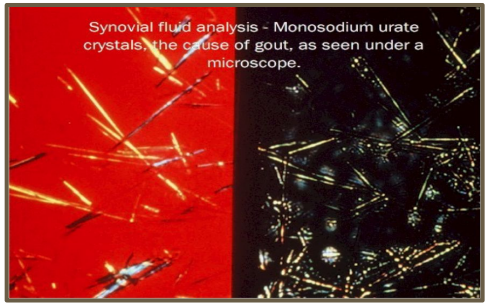
Acute gouty arthritis on the big toe of an elderly man

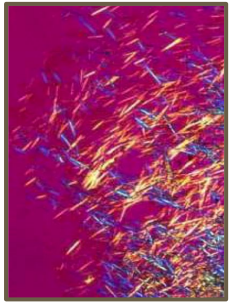
Severe gout in the fingers resulting in large, hard deposits of crystals of uric acid. These deposits are called **Tophi.**

Gross description (clinical features): Redness, Swelling, Edema

Test used to diagnose gout:

Polarizing microscope (You will see needle-shaped monosodium urate crystals)





Pyrophosphate overproduction or its decreased breakdown can give rise to similar joint disease called **Pseudogout or chondrocalcinosis.**

Gouty Arthritis can be associated with

- Leukemia (Because of increased turnover of cells),
- Chronic renal diseases

Osteomyelitis

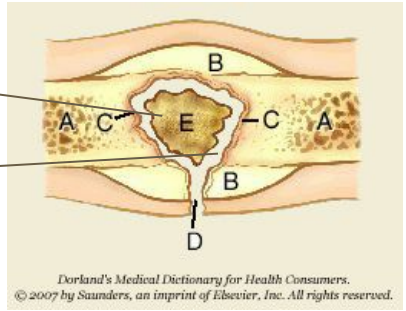
Case #5: A 22- year- old male presented with localized pain above his right knee joint with recurrent fever. Later, he had a discharging sinuses* from the skin overlying the right knee.

Gross description:

- Involucrum (New bone)
- Sequestrum (Dead bone)

Sequestrum (E)

Involucrum (C)



Tip: The fact that **sinuses** was mentioned gives us a hint that it's a bacterial infection.

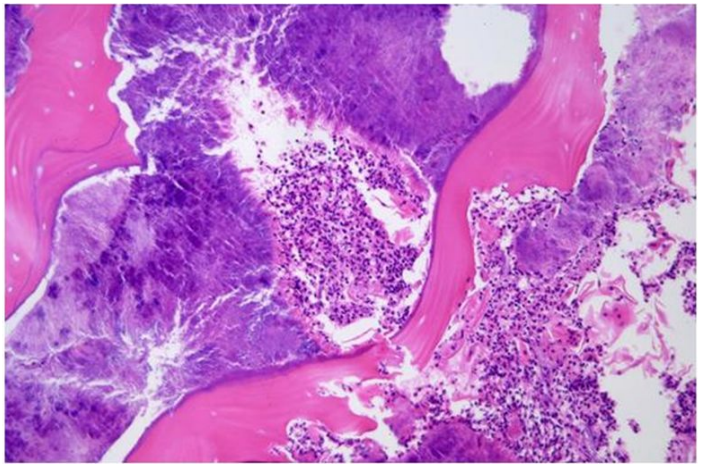
Direct infection of bone by:

Most common bacteria:

- Staphylococcus
- Salmonella in patients of Sickle Cell Disease
- Tuberculosis: Spine first

Osteomyelitis

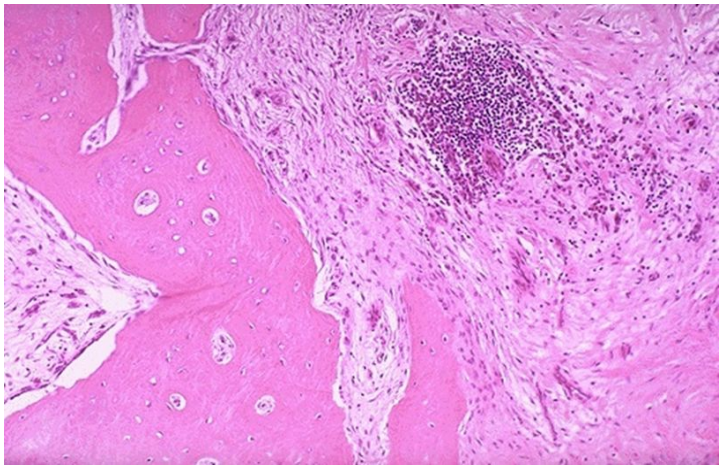
Acute Osteomyelitis - LPF



Description:

- Bacterial colonies
- Acute inflammatory cells " neutrophils"
- Sequestrum (dead bone)

Chronic Osteomyelitis - LPF



Description:

- Fibrosis
- Involucrum (new bone)
- Sequestrum (dead bone)
- lymphocytes and plasma cell

Spinal TB – Pott's Disease (Tuberculous Osteomyelitis)

Case #6: **A 30 -year-old debilitated man presented to the orthopedic clinic with back pain, low grade fever, marked elevation of sedimentation rate and recent kyphosis and scoliosis .**

The patient has a history of coughing up blood, fever, chills, night sweats, weight loss, pallor, and often a tendency to fatigue very easily.

Gross description:

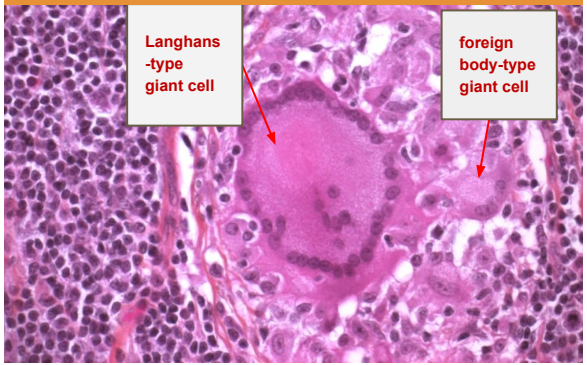
- Fractured
- Caseating necrosis of vertebral column

Gross description:

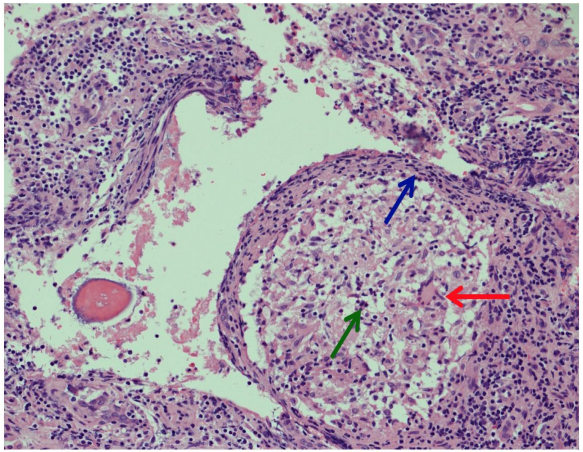
- Fractured
- Caseating necrosis of vertebral column

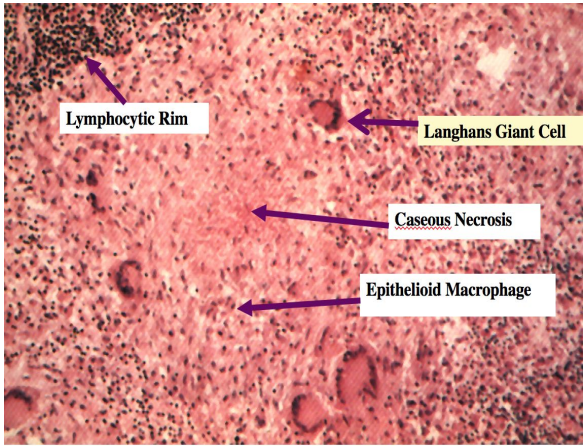
Spinal TB – Pott's Disease (Tuberculous Osteomyelitis)

Shows the difference between Langhans giant cell and foreign giant cell



Bone section shows Epithelioid cells fuse to form giant cells containing 20 or more nuclei. The nuclei arranged either peripherally (Langhans-type giant cell) or haphazardly (foreign body-type giant cell). These giant cells can be found either at the periphery or the center of the granuloma.





Histopathologic description:

Granuloma composed of:-

1) Langhans giant cell

2) Epithelioid macrophages/histiocyte

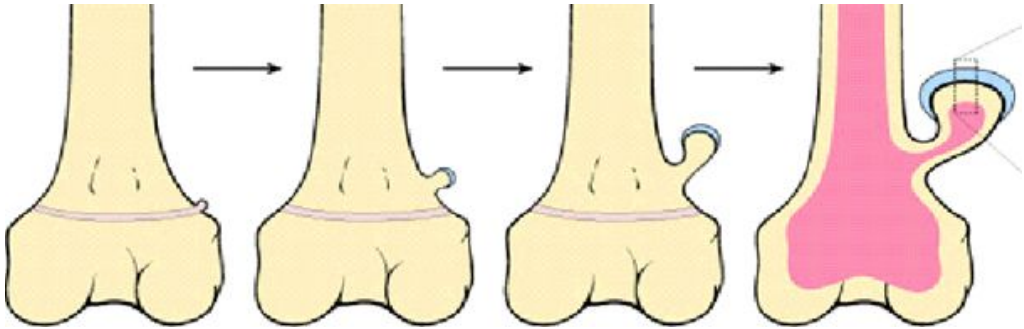
3) Caseous necrosis

4) Rim of lymphocytes

Osteochondroma

Case #7: A 16 -year-old male was found to have a small swelling protruding from the upper part of his leg with local pain .

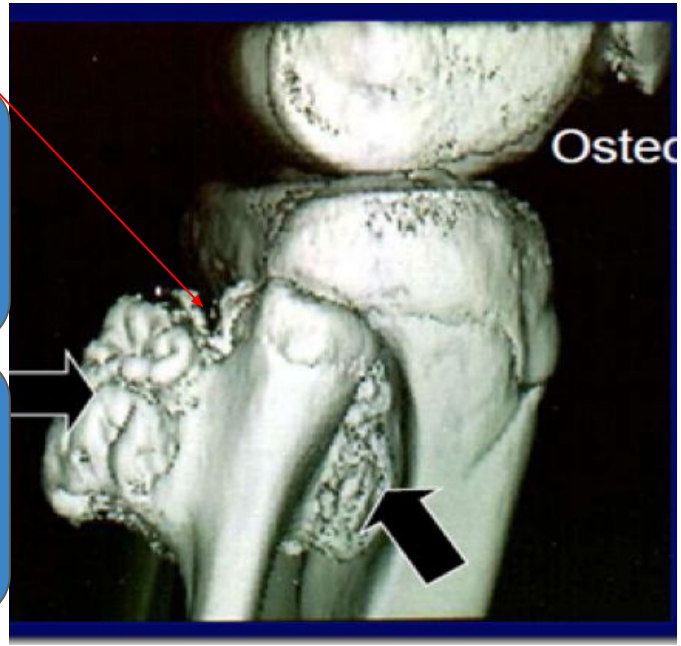
- The solitary osteochondroma is the most common benign bone tumors.
- Seen in patients aged from 10-30 years.
- Arise during skeletal growth.
- Equally in males and females.
- Etiology is unknown.



Osteochondroma

Osteochondroma (X-ray)

osteochondroma (MRI)



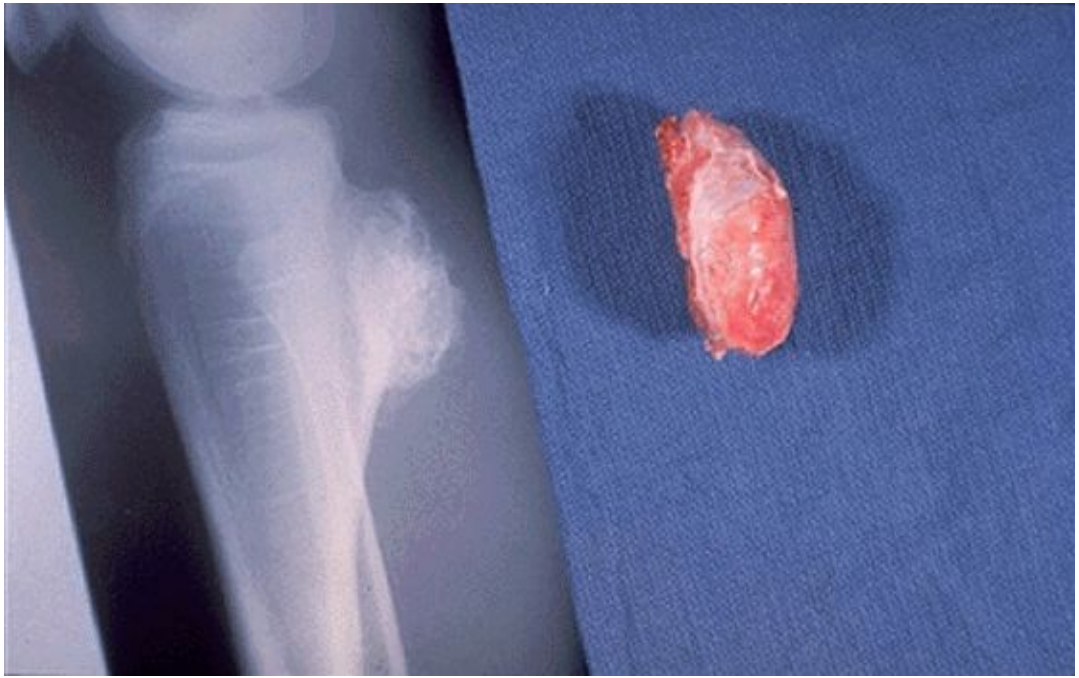
Bony outgrowth

MRI image showing:
- Multiple bony outgrowth (exostosis) around fibula.

X-ray image showing:
- Bony outgrowth (exostosis) in Tibia

Osteochondroma

Gross & X-ray



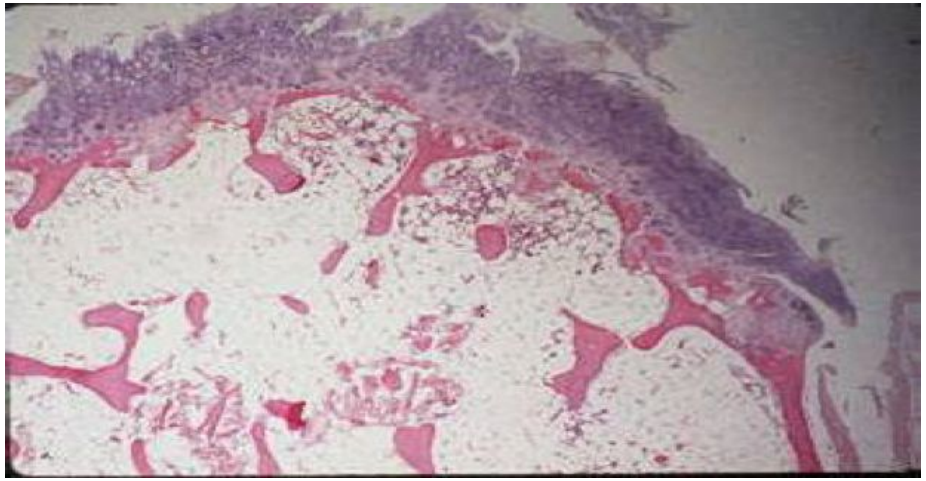
This is an osteochondroma of bone.
This benign lesion appears as a bony projection (exostosis).
Most are solitary, incidental lesions that may be excised if they cause local pain.
There is a rare condition of multiple osteochondromatosis marked by bone deformity and by a greater propensity for development of chondrosarcoma.

Osteochondroma

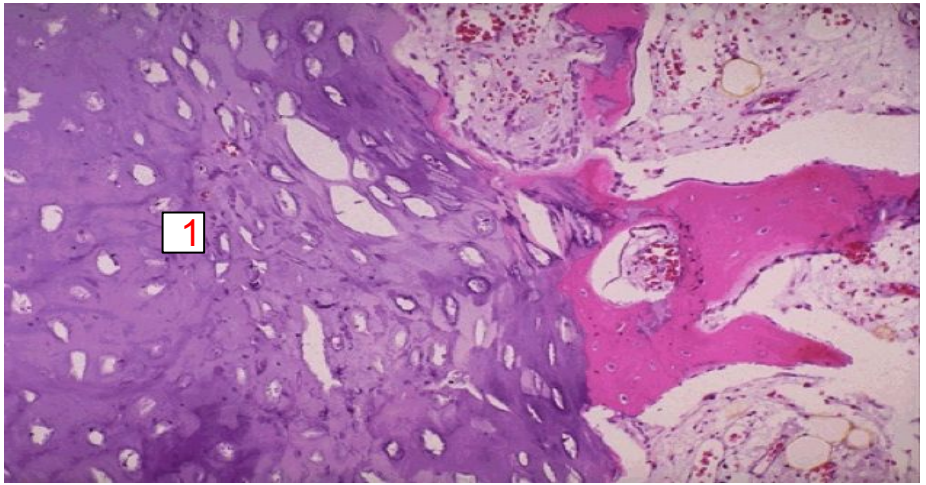
Multiple Cartilaginous Exostoses - Gross	Osteochondroma - Gross description
	
	We can see: - Well circumscribed lesion - Cartilaginous cap - Pale bony structure

Osteochondroma

LPF



HPF



We can see: - Bluish cartilaginous cap (1)
- Bone cortex

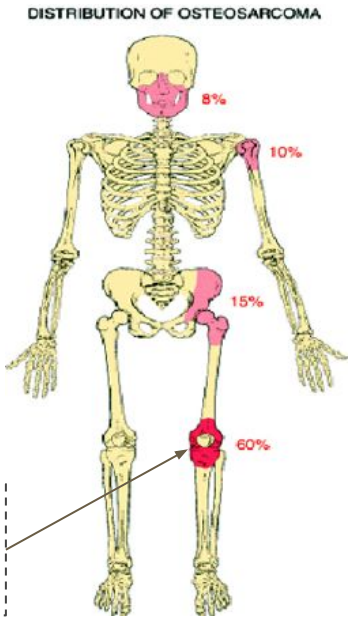
Osteosarcoma

Case #8: An 18-year-old female presented to the rheumatology clinic with 2 months history of pain and swelling in her upper thigh with weight loss .

Osteosarcoma, Primary Malignancy

What is the most common area?
- The knee joint

What are the gene mutations that are involved?
- RB and P53 genes

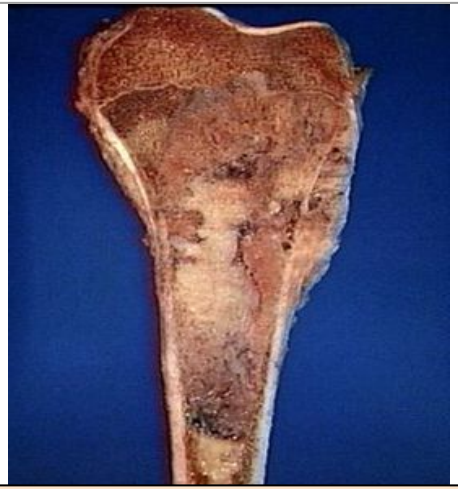


Usually affects long weight bearing bones.

Osteosarcoma

Osteosarcoma of the upper end of the tibia.

- 2nd most common primary bone tumor.
- Malignant tumor of mesenchymal origin



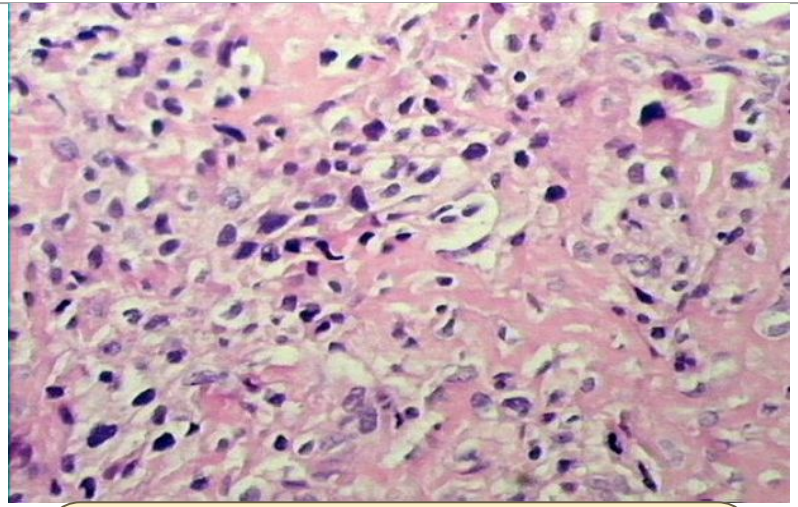
Conventional Osteosarcoma - Gross

We can see:

- Erosion of the epiphysis
- Tan-white tumor that fills the medullary cavity
- Invasion of cortex and soft tissue

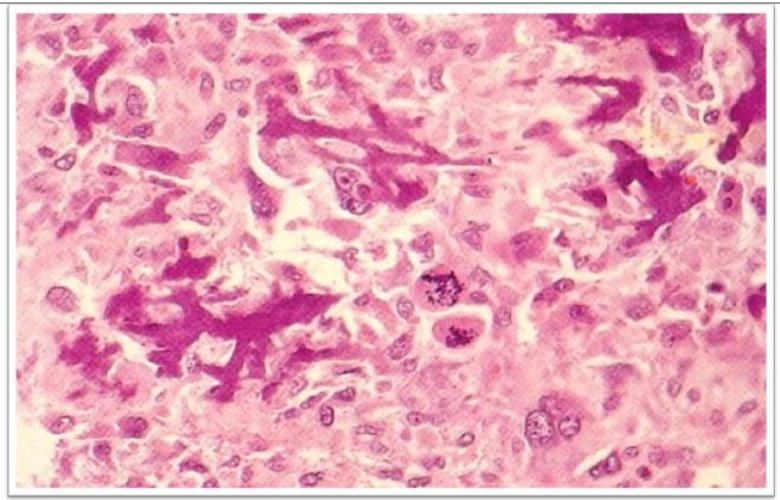
Osteosarcoma

Osteosarcoma - LPF



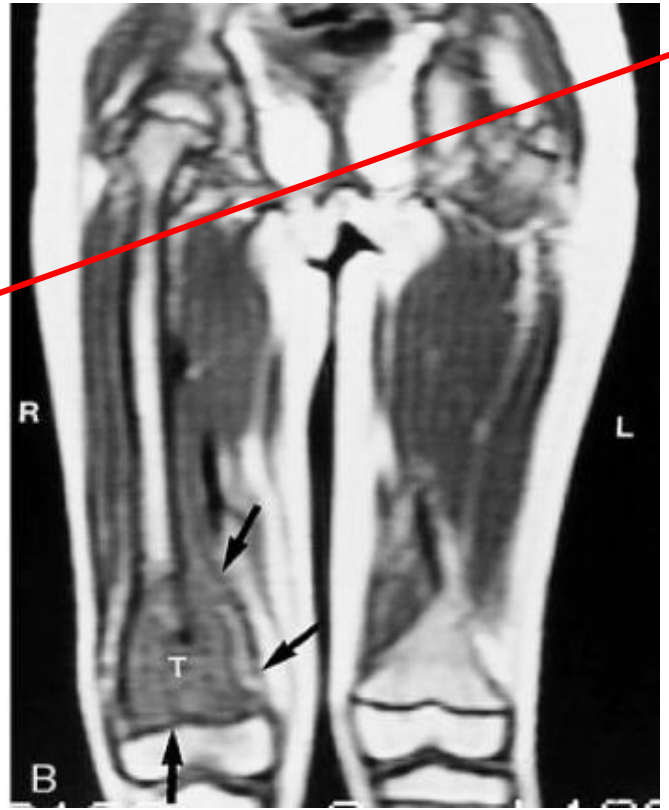
Spindle shaped malignant cells

Osteosarcoma - HPF



Spindle shaped malignant cells that produce osteoid
- Giant cells
- abnormal mitosis

Osteosarcoma



A: *Lytic* destructive lesion affecting lower femur is seen in the metaphysis on this anteroposterior view of the knee in a young teenager with pain.

B: MRI scan of both legs shows soft tissue extent of the tumor

Notes:

- the pictures are going to be the same

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