MSS

pathology

LEC no.4

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MUSCULOSKELETAL PATHOLOGY-4 BONE TUMORS-1

Easy lecture; it was only ~25 minutes long!!

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(in this modified, anything in light blue is extra info from the internet for further understanding. NOT mentioned by the doctor!!)

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

When the tumor arises from the bone itself, we call it **primary**.
In contrast to metastasis, which is the development of **secondary** malignant growths at a distance from a primary site of cancer.

Examples:
- Osteoid+malignant cells =osteosarcoma
- In cartilage: chondrosarcoma

Benign tumors in bone are more common than malignant, they peak in the first three decades of life.
If a tumor arises after that, it is malignant for most cases.

*We'll start with **benign** tumors of the bone (osteoid tumors). Here we have two diseases that share the same morphology, but they are different clinically & the place they arise from:

Osteoma means benign

OSTEOID OSTEOMA (OO) & OSTEOBLASTOMA (OB)

- Similar histology but differ in clinical & radiologic features
- **OO** is < 2cm (small), 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 [1]surgically or by [2]radioablation.

"هاي حطّوا تحتها عشرين خط!!"
Most of tumors arise from medulla. But this one is peripheral, from the cortex of the bone (special characteristic).

Another special characteristic, especially in face.
انتفاخ في الوجه

Spreads outside cortex and affects the adjacent bone(s), activating a second-bone growth.
This **isn't** a special characterestic. Any tumor makes a reaction with the adjacent bone (thickening), which appears in x-ray.

- **OB**: large, posterior part of vertebrae, painful but not responsive to pain killers, no cortical bone reaction, treated by surgery
- Both (OO & OB) appear round and well-circumscribed in X-ray

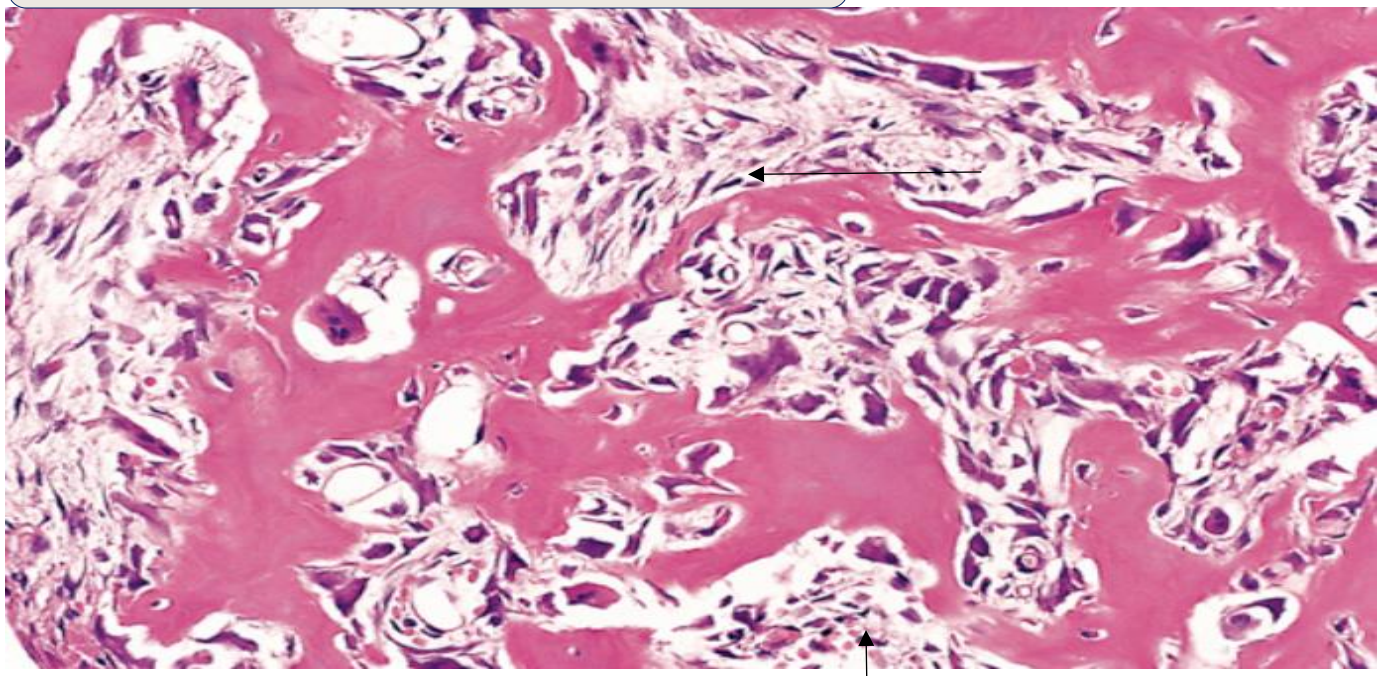
Characteristic of benign tumors. On the other hand, malignant cause invasion.

OO & OB appear similar under the microscope

How to differentiate OO from OB?
OB is:
1- large
2- forms in the vertebrae
3- doesn't make a bone reaction because it's already big (مش محتاجة)
4- painful but not responsive to medicine
5- treatment: surgery ONLY
(if exposed to radiation, that will cause exacerbation, worsening)

Osteolytic lesions are areas of damaged bone that most often occur in people with certain cancers. On an X-ray, they appear as tiny holes, giving the bone a "moth-eaten" or "punched-out" appearance.

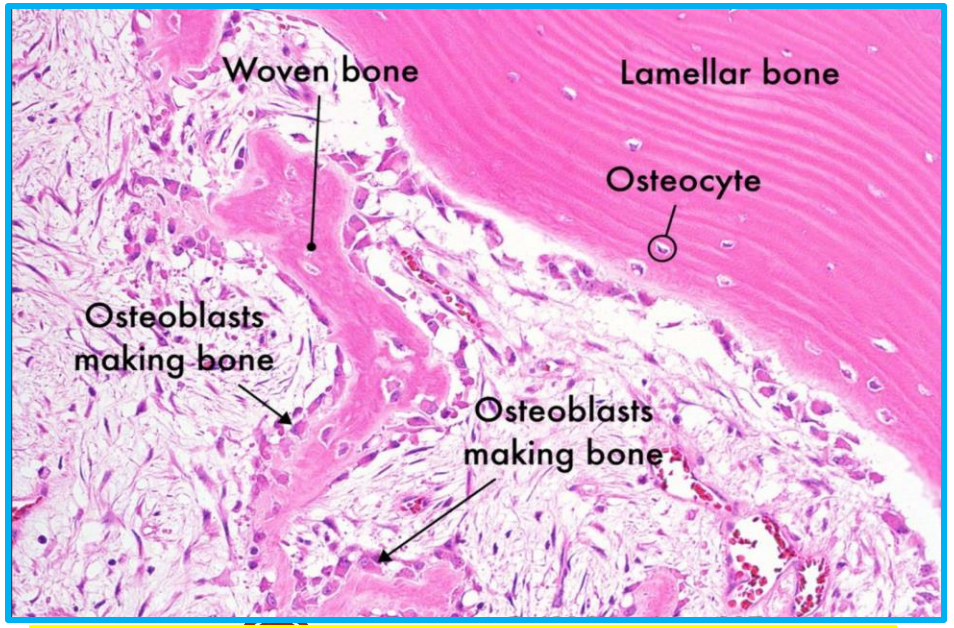
This is how OO & OB look like:



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

Notice how it's woven bone + osteoblasts all embedded in connective tissue.
The white areas contain fibroblasts, instead of bone marrow that are found normally.

In a histological section, we see woven bone. Which is thin and anastomosing ماسك ببعض. We **don't see** the lamella/lines of the bone.
So, when you see woven bone, it is pathologic, not normal.



Extra NOTE: (demonstrating the difference between lamellar & woven bones)

Okie dokie, now for **malignant**:
Osteosarcoma is the most common primary malignant tumor of the bone.

OSTEOSARCOMA

- Malignant tumor that produces osteoid matrix.
- Most common primary bone sarcoma/cancer.
- M>F
- 75% of cases arise in **childhood & adolescence.** Because most growth occurs at that time.
- a second small peak occurs in elderly with predisposing factors **(secondary osteosarcoma)**

In general, bone tumors are more common in males (boys,adults) than in females.
One of them is this one, osteosarcoma.

Most cases are children.
Sarcoma, in general, arises in young age/children (cancer of soft tissue, still growing). While in adults, carcinoma would arise (cancer of epithelial cells, secondary sarcoma).

Why are bone tumors more common in males?
Genetics, hormones, lifestyle, detection and reporting bias...etc.

Because it's the fastest growing bone, most exposed to mutations.

(continued)

- Can arise anywhere, but most common site is around **knee joint:** distal femur, proximal tibia (metaphysis of long bone)
- Patient complains of pain, enlarging mass, fracture.
- X-ray: **mass**, mixed osteolytic and sclerosis, infiltrative margin (infiltrating the soft tissue, not well-circumscribed, you can't see the borders).
- Most tumors arise in the medulla, invade the cortex, raise the periosteum, resulting in a wedge-shaped mass **(Codman triangle)**

Tumors Start in medulla then spread around it. They invade the cortex, push the periosteum, penetrate it sometimes, and this results in the wedge-shaped mass. Appears as a triangle, But the borders aren't clear.

We can see Codman triangle in two cases:

1. Osteosarcoma (mass, outside bone)
2. Subchondral osteonecrosis (seen as different coloring)

PATHOGENESIS

Genetic mutations of osteosarcoma:

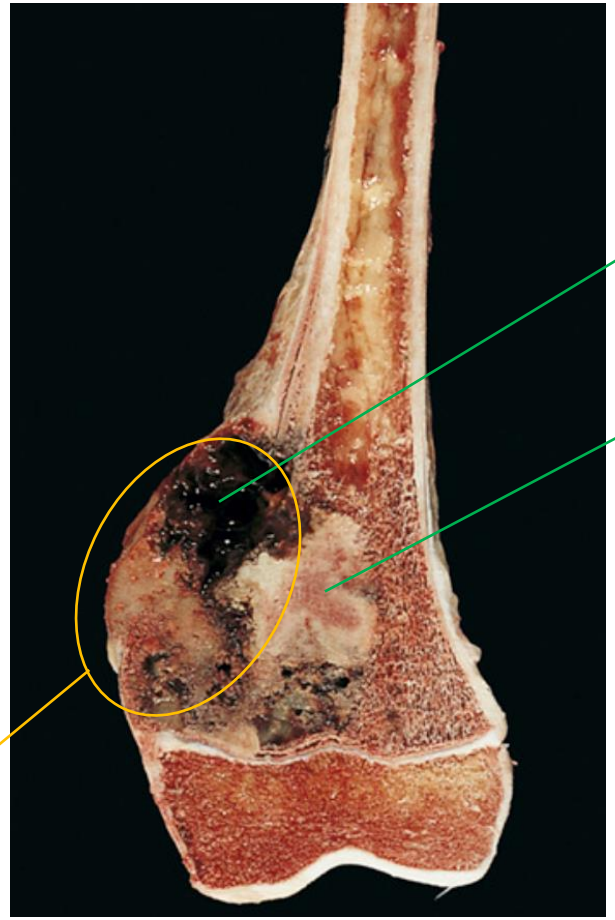
- Arise in rapidly growing bones
- **RB** gene mutation (tumor suppressor) is present in 70% of cases
- **TP53** mutation, common (guardian of the genome, fixes/repairs mutations)
- **MDM2 and CDK4** are overexpressed (inhibit normal RB and P53). These two are special for osteosarcoma. They also activate the cell cycle/proliferation.
- **CDKN2A** is inactivated, normally encodes tumor suppressors (P14 and P16)
- **MYC** (normally causes rapid proliferation of the cell cycle) amplification in 50% of cases.

Most common gene mutation:
Retinoblastoma (RB) gene.
Some people have this mutation present in their germline since birth. They develop tumors of the eye and the bone.

Remember: we always have a mass, not just fracture

MORPHOLOGY: MACROSCOPIC

- Osteosarcoma of distal femur. There is extensive cortical disruption and subperiosteal expansion, then it reaches the soft tissue. 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



Notice the bulge taking a triangular shape (cortical disruption)

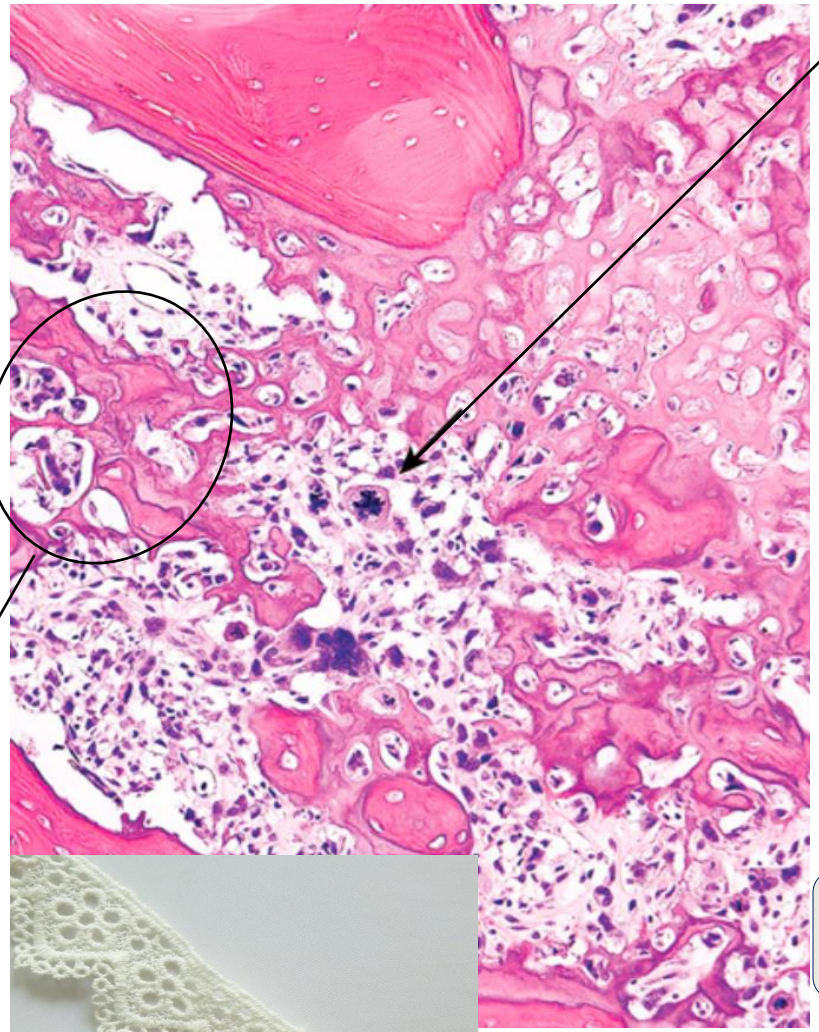
- damage & hemorrhage regions, different in color
- white area, starting from medulla (cancer)

Growth that pushes the periosteum

For unknown reason, osteosarcoma doesn't invade vertically to the direction of the joint. So, epiphyseal/joint invasion is not a frequent characteristic. Rather, it likes to invade soft tissue.

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**



Malignant cells
appear large, pleomorphic, mitotic.

Diagnosis under histology:
We can see bone deposition.
Malignant cells produce abnormal osteoid (lacelike).

Pink area: abnormal osteoid, lacelike

Lacelike osteoid ≠ woven bone

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%

You're doing amazing, keep going!!

Sarcomas in general don't go to lymph nodes. Rather, they spread by blood, causing distant metastasis. Hematogenous metastasis mostly in lung and heart.

Occult means small, cannot be seen with radiology.

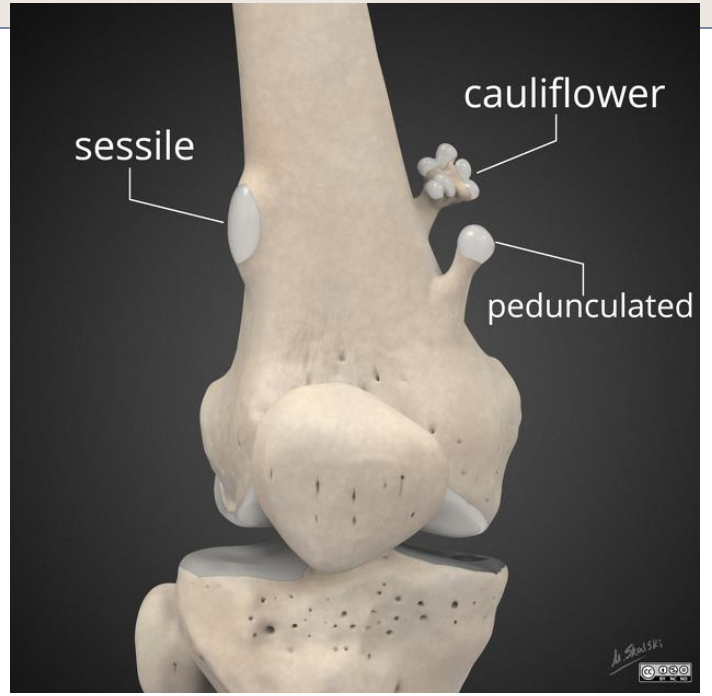
Neoadjuvant means pre-surgery. Neoadjuvant chemotherapy causes shrinkage of tumor.

We treat osteosarcoma and metastasis patients the same technique of therapy.

OSTEOCHONDROMA (EXOSTOSIS)

another name of osteochondroma: exostosis
It's a mix between bone and cartilage (bone with a cartilaginous cap)

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



More explanation:
85% of cases are sporadic
15% syndromic (which comes early in life, born with)

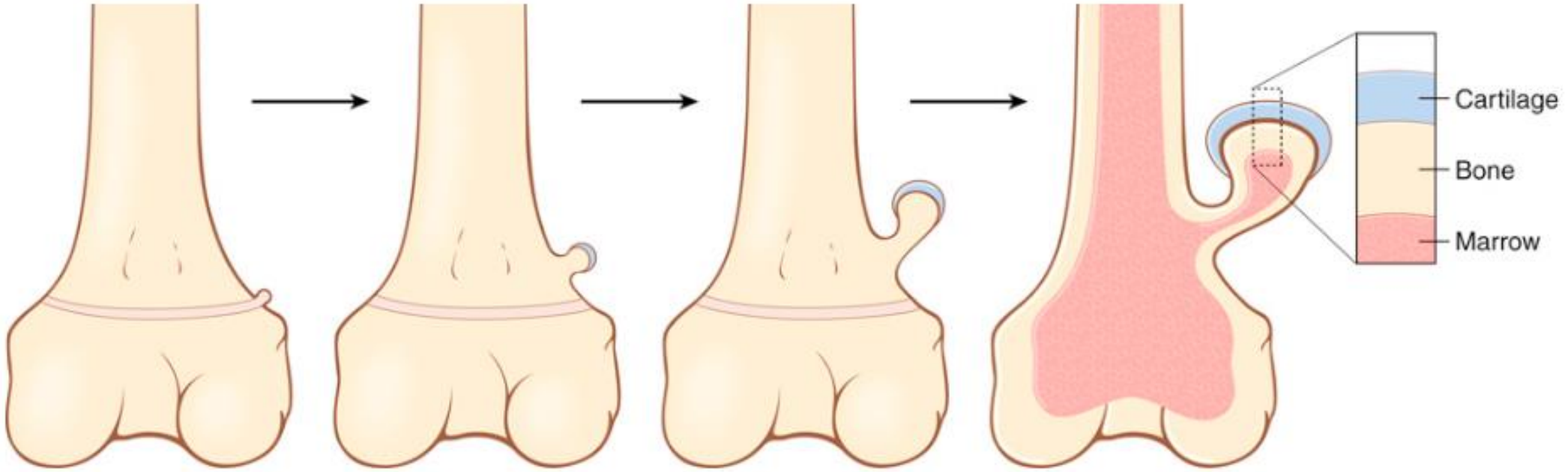
Sessile :attached or established on the bone itself
Pedunculated: has a stalk like mushroom:)
Which means the bone looks like stalk then having a cartilage

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.

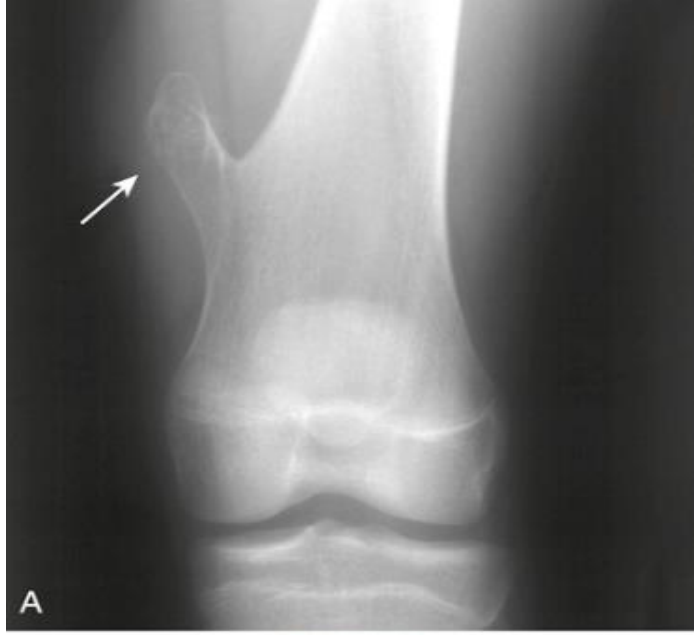
What kind of mutation??
EXT: this gene's name came from exostosis.
The first allele of EXT1 or EXT2 is mutated from the germline (inherited, born with), while the second allele will be mutated by somatic (مكتسبة) mutation.

What is the relationship between EXT mutation and bones??
Decrease EXT causes decrease the synthesis of the matrix itself (heparan sulfate glycosaminoglycans)...it affects a normal pathway important to bone and cartilage formation "**Indian Hedgehog**" pathway which is responsible for normal growth and formation of bone and cartilage (disruption!!)



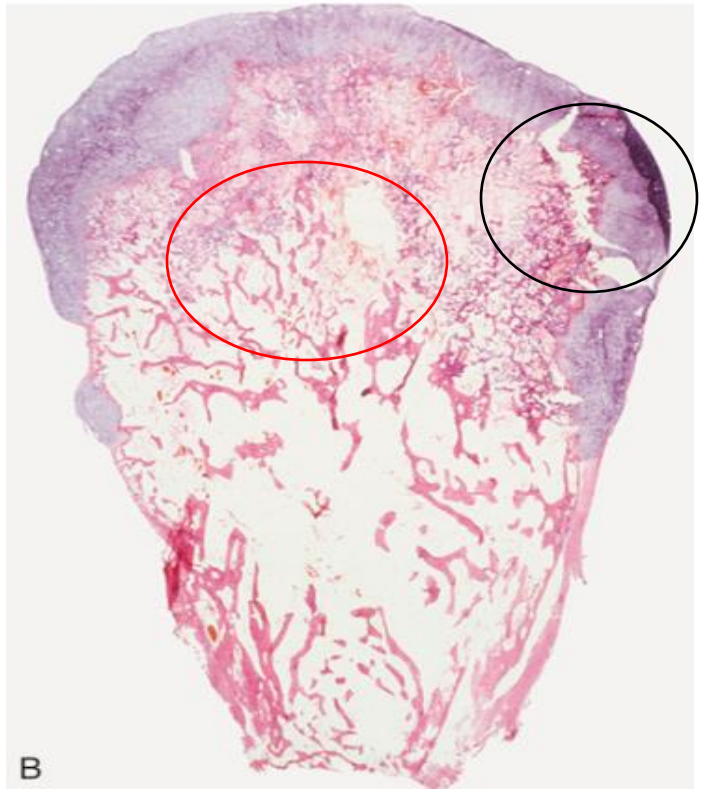
- The development of an osteochondroma, beginning with an outgrowth from the epiphyseal cartilage.

This is how osteochondroma looks like:
Metaphysis of the long bone around the knee
Starts as **small growth** ----> Looks like a **stalk** and **cartilage** from outside



- Osteochondroma. (A) Radiograph of an osteochondroma (arrow) arising from the distal femur.

A) In x rays: osteochondroma appears as a fungus, stalk grown outside the bone.



- (B) Whole mount section of narrow-pedicled osteochondroma with surface cartilage cap

B) In histologic examination: normal bone with bone marrow (red color)
And outermost part is cartilage (big lumen)

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.

Sensed by the person

لما يصور يعني الشخص بكتشفها بالصدفة صورة أشعة

Which means after teen age it will stop growing (because of growth plate closure)

It starts as benign but later, it will be converted to malignant chondrosarcoma (in syndromic cases)

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 (young or middle age)
- Sporadic cases are usually single lesion, asymptomatic
- Ollier disease and Maffucci syndrome show enchondromatosis (multiple)
- Solitary enchondromas rarely undergo secondary chondrosarcoma-malignant- sarcomatous transformation; by contrast, those associated with enchondromatosis do so more frequently(syndromes - Ollier disease and Maffucci syndrome – frequently transform to malignant)

CHONDROMA

- Next disease: chondroma it's benign cartilage tumor of hyaline cartilage.
- Affects bone that grow in endochondral growth method (proliferation of cartilage.. ossification)
- There are two types of chondroma:

  1-tumor from center of bone(medulla) called enchondroma.

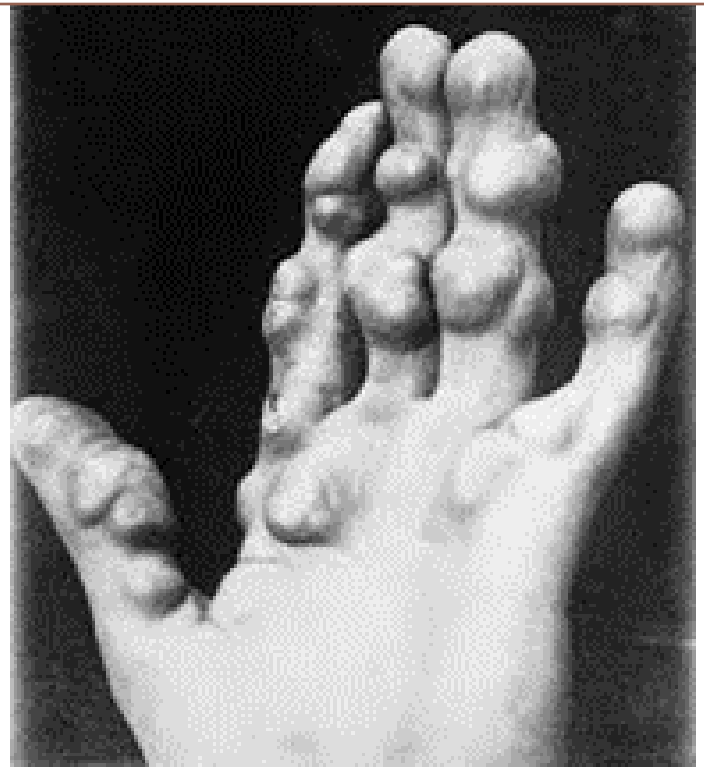
  2- from cortex called juxtacortical.

- It can be sporadic or syndromic, what's the difference??
- **Sporadic**: usually are very small and asymptomatic (incidental findings when doing X-rays)
- **Syndrome**: appears early and multiple, like:

  1-Ollier disease

  2-Maffucci syndrome (both usually have more tumors in body)

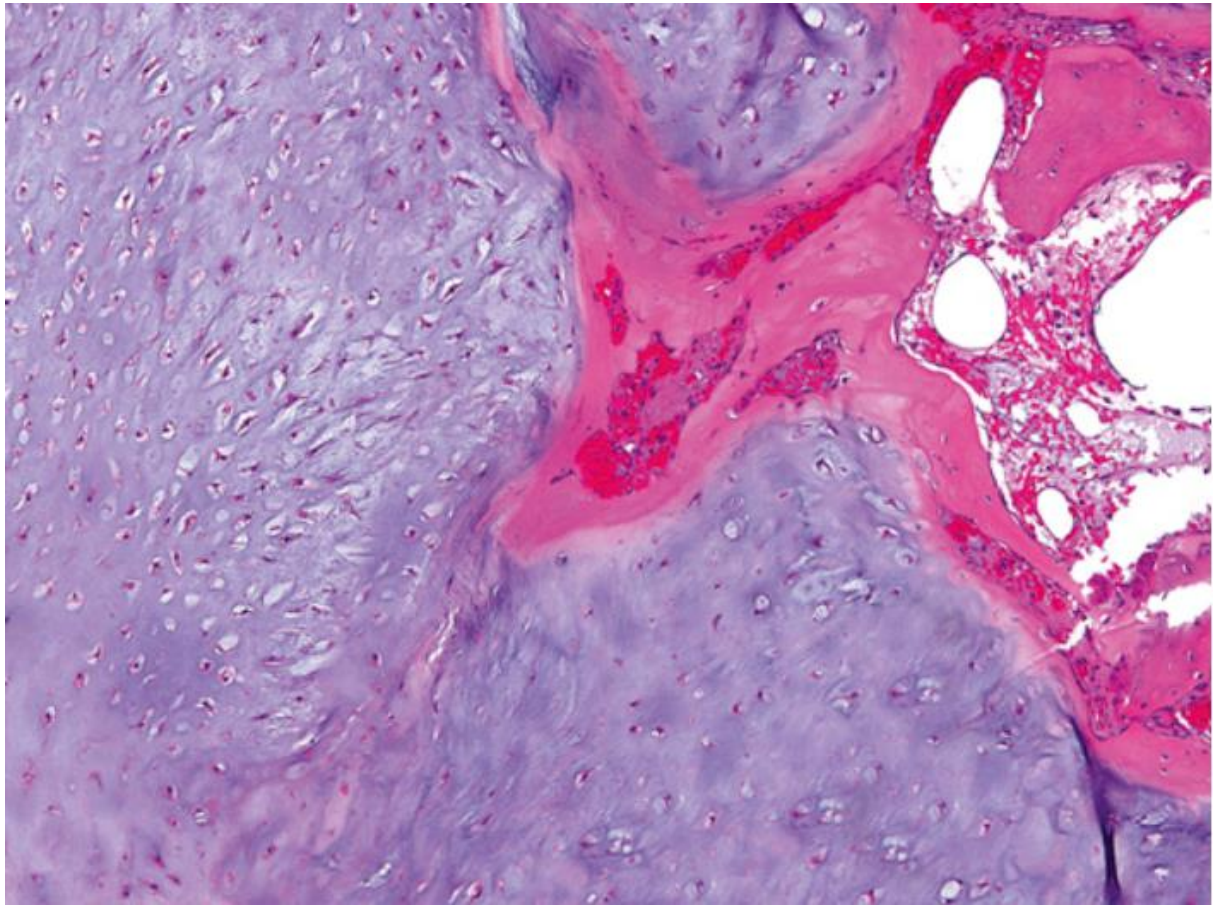
EXTRA: Multiple chondromas of fingers



PATHOGENESIS

What's the pathogen included in chondroma?
Isocitrate dehydrogenase enzyme gene deficiency (1 and 2 IDH)

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



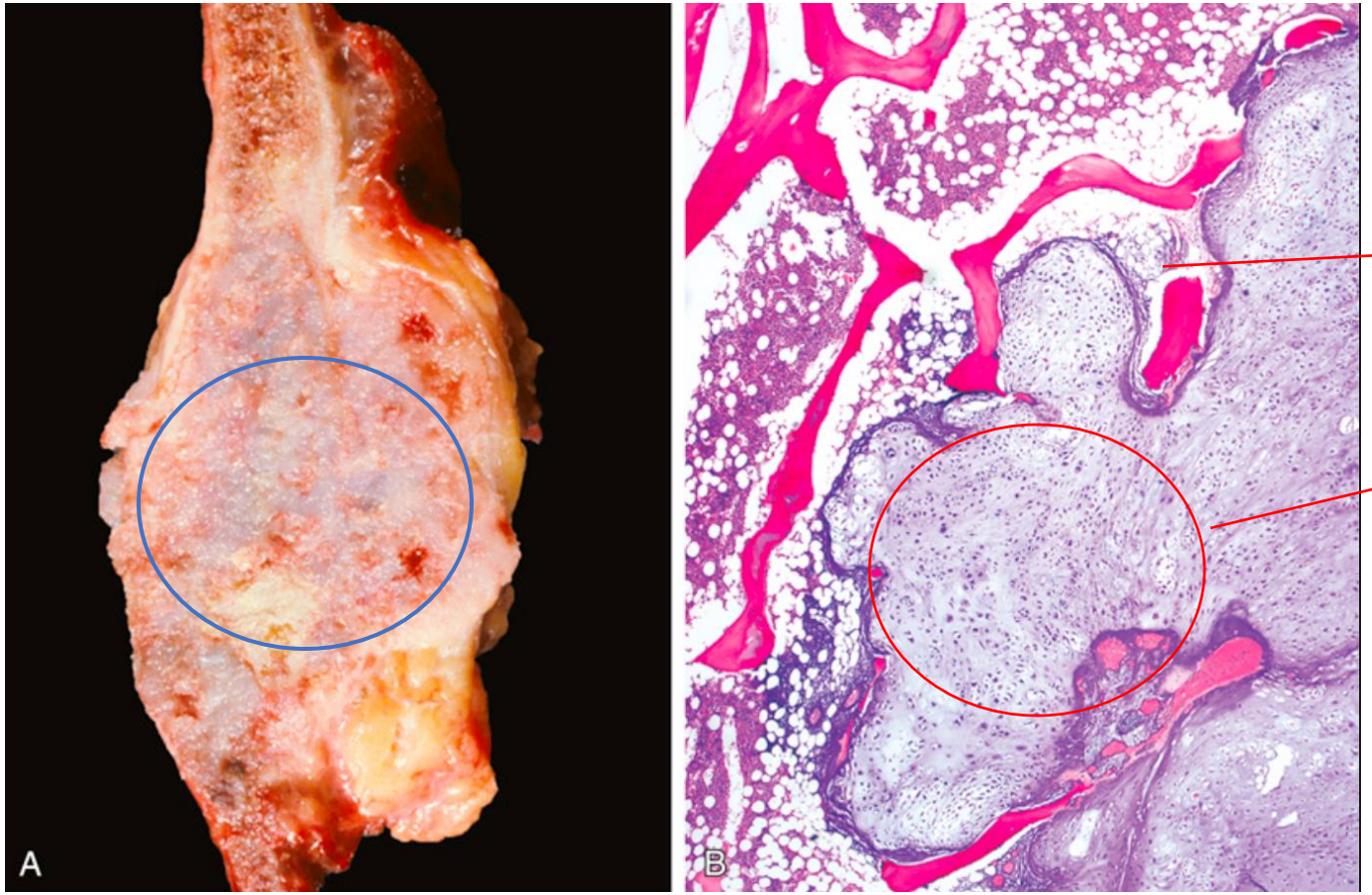
We can see chondroma as hyaline cartilage (bluey layer) but it will be presented in large amounts and has an abnormal location (in medulla of the bone).
Nodules: like balls

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

CHONDROSARCOMA

Chondrosarcoma: second malignant tumor in this lecture after osteosarcoma.

- Malignant tumor that produces cartilage only
- Most cases are conventional similar to cartilage known but malignant, other histologic types include dedifferentiated, mesenchymal and clear cell
- Patients are > 40 years old age
- M>F (twice) more common in men
- 15% of cases are secondary, follows osteochondroma or enchondroma, most cases are sporadic
- Most common sites: pelvis, shoulder and ribs (large joints of the body)
- X-ray: large mass that destroys the cortex and extends to soft tissue, flocculent calcification (commonly calcification occurs; appearing as white areas that are heterogenous -غير متجانش- in bones similar to شكل الصوف)



Trabecular bone

cartilage

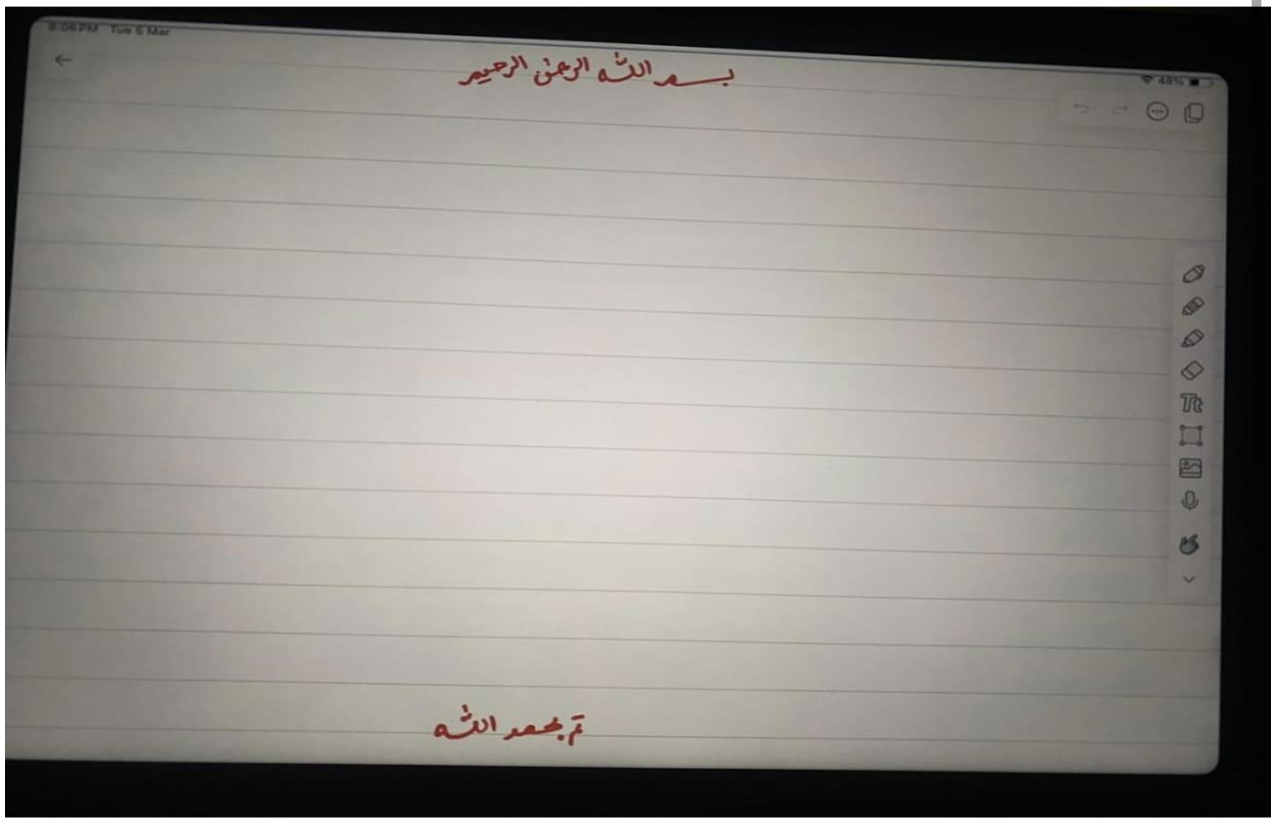
- Chondrosarcoma. (A) Nodules of hyaline cartilage permeate the medullary cavity of the sternum, grow through the cortex, and form a relatively well-circumscribed soft tissue mass in the parasternal soft tissue.
- (B) Chondrosarcoma permeating through preexisting trabecular bone.

Chondrosarcoma: large mass in bone stored in bone its growth outside, differs from osteosarcoma in which it is bluish in color.

In histologic examination: cartilage invading the bone and having malignant cells

دكتور 2022
Anonymous member · 1h ·

تفريغ محاضرتين اليوم للباثو:



Haha Comment Send

(: تم بحمد الله