MSS

PATHOLOGY

#9

WRITER:
Mohammad Al-Shamasneh

CORRECTOR:
Rawan Aqaileh

DOCTOR:
Mousa Al-Abbadi

In the last lecture we talked about the first type of soft tissue tumors, **the tumors of adipose tissue,** now we will discuss the second type, **the fibrous tumors**. let us deep in…

FIBROUS TUMORS:

- **Nodular fasciitis**
- **Fibromatoses:**
  - **Superficial**
  - **Deep (Desmoid tumor)**
- **Fibromas and Fibrosarcoma**

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1. Nodular Fasciitis:

is a very characteristic soft tissue tumor, it's believed that it's a true neoplasm (could be reactive), there are monoclonal changes in the process, a self-limited fibroblastic and myo-fibroblastic proliferation that typically occurs in the upper extremities of young adults.

- **Nodular fasciitis: thought to be reactive process.**
- **Now, clonal, t(17;22) producing MYH9-USP6 fusion gene.**

Initially thought as a reactive process, however the recent studies are now confirming that this process is actually **clonal**, because there is a molecular change of **t(17;22)** translocation producing a MYH9-USP6 fusion gene ,that was an indicator that Nodular fasciitis is a tumor **not** an inflammatory proliferative reaction .

- **Maybe self-limiting**

Nodular fasciitis maybe **self-limiting**, and this is the excuse of the people who believe that nodular fasciitis is not a true tumor even though it has a clonal signature change.

- **Trauma history, recent rapid size increase**

The classic clinical scenario is ⟶ previous history of trauma ⟶ recent rapid increase of that soft tissue mass at the site of tumor (chest wall , hand , leg …they can occur anywhere) .

A Case: 35 or 45 years old patient, who had a chest trauma, after couple of weeks, he came with a mass ⍰ nodular fasciitis. (recent trauma history).

Wait a minute, can the trauma cause a mutation so producing a tumor? Actually, we still do not know but in somehow, they are related as the doctor said, and keep in your mind that trauma also means burning or radiation.

- **IMPORTANT: not to diagnose it malignant**

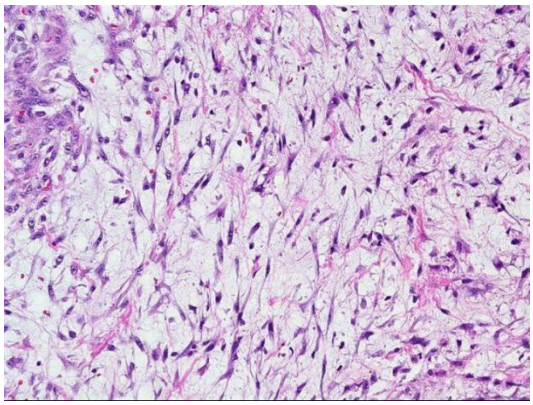
The most important thing about nodular fasciitis is not to diagnose it as a malignant tumor, exposing the patient to unnecessary aggressive harmful treatment.

So, misdiagnose of this tumor as sarcomas must be avoided by digging in the patient's history look whether he was exposed to trauma or not.

It could be neoplasm reactive trauma. It's important to remember that it's a benign disease.

- **Culture-like histology**

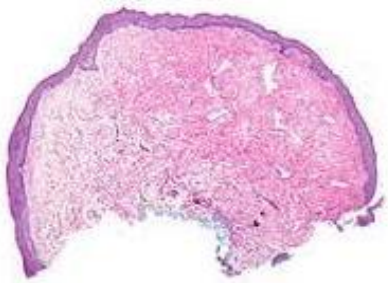
In the histology, under the microscope, it gives a classic appearance of **culture-like histology**.



They are spindle cells, they have frequent mitosis , the white area and spindle cell look like cell culture in petri dish ,sometimes there are inflammatory cell ,plasma cells , lymphocytes and this is why its name ends with **itis**, nodular fasci**itis** .

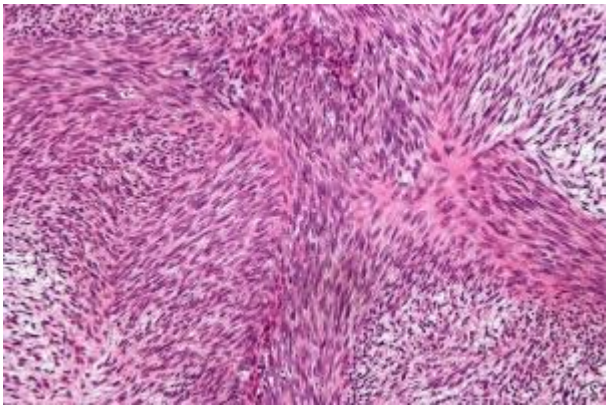
2. Fibromas and Fibrosarcoma:

- **Fibromas: benign proliferation of fibroblasts, very common, skin and subcutaneous tissue.**



Near to skin and mucosal surfaces (oral mucosal surface, vagina... etc)

- **Fibrosarcoma: malignant counterpart. usually, superficial cutaneous tumors of fibroblasts, cellular, storiform pattern with increased mitosis.**



It looks very cellular due to frequent mitosis of fibroblasts giving what we

called herringbone histologically appearance or storiform pattern .

Low grade sarcomas, they can be cured by just complete remove, they can metastasize, usually detected early because they are superficial (you can feel them, they pressure on the nerve causing pain).

3. Fibromatoses:

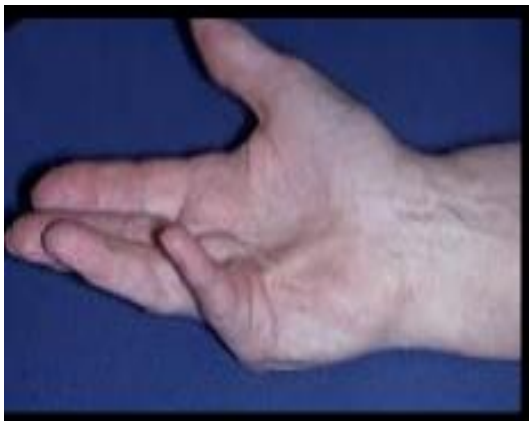
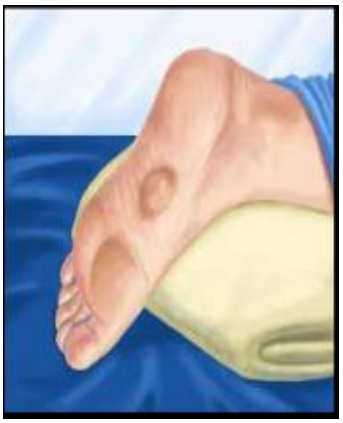
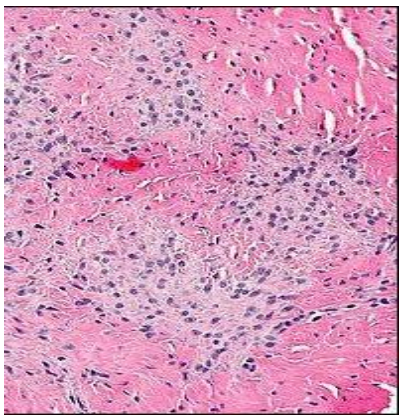
A group of diseases that can be divided into **superficial** and **deep** forms, let us explain…

A. Superficial fibromatoses:

• Infiltrative benign fibroblastic proliferation

Although it is a benign tumor, it is locally **infiltrative** too, which is usually a characteristic feature of malignancy, so this is an exception. What makes its diagnosis a little bit difficult.

• May run in families; may impact function

Palmer (DUPUYTREN CONTRACTURE)	PLANTAR **FIBROMATOSES**	PENILE **(PEYRONIE DISEASE)**
Palmar fascia	Sole of foot	Dorsolateral aspect of the penis
		
Palmer contraction, flexion of finger and you cant open it, so interfers with the function.	they are painful.	Very painful especially in erections and very difficult to treat.

B. Deep fibromatoses (Desmoid tumor):

- **Deep infiltrative but bland fibroblastic proliferation; doesn't metastasize but recur.**
- **20-30years, females more common**
- **Abdominal wall, mesentery and limbs**

Most common in the intra-abdominal wall and thigh, but in any location can occurs.

- **Mutations in CTNNB1 (β-catenin) or APC genes leading to increased Wnt signaling.**

Immuno-histo-chemical stain for CTNNB1 (β-catenin) is applied when we suspect desmoid tumor.

- **Mostly are sporadic; but patients with Gardner (FAP) syndrome are susceptible.**

APC genes (adenomatous polyposis coli) is translated to APC protein that acts as a tumor suppressor, which means that it keeps cells from growing and dividing too fast or in an uncontrolled way.

If you have an APC gene mutation, this will affect the behavior of **cancer stem cells**, which are considered by most to be responsible for establishment of the tumor via **WNT signaling cascade**, so you have a greater risk of developing gastrointestinal polyps (pre-cancerous growths also known as adenomas) such as FAP (Familial Adenomatous Polyposis). Which is a risk factor for developing desmoid tumor.

- **Complete excision is needed to prevent recurrence which is very common.**

Treatment is very difficult because the surgeon cannot tell where the tumor starts and ends, so he has to remove extra, extra, extra 5-10 cm margins away from the lesion!

Even though, most of the patients come with recurrence.

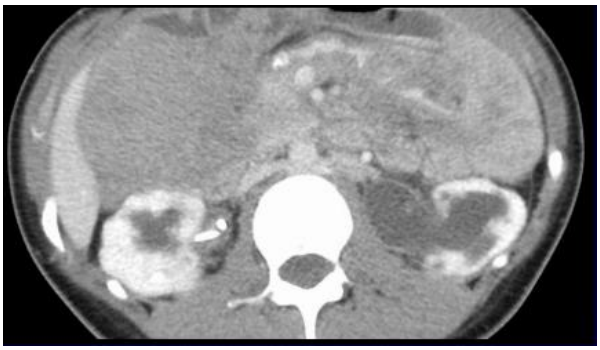
That was just for clarification not memorizing

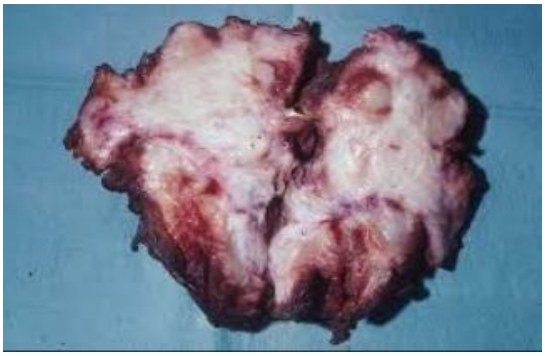
- **These tumors kill by local infiltration NOT metastasis**

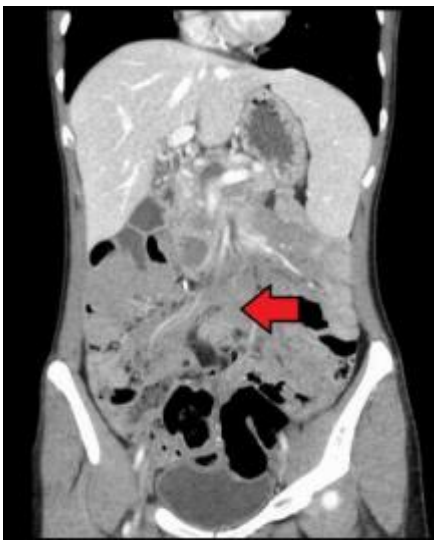
(benign but infiltrative). Because this mass, especially in the abdominal wall, will destroy the vital organs; liver, spleen and kidneys.

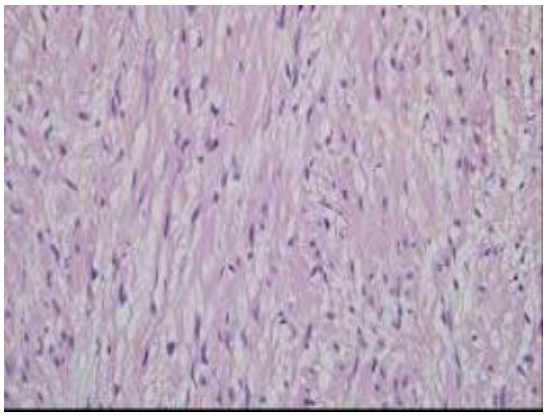
So, it doesn't metastasize but can kill you by a local destruction of an important organ. Histologically they are bland benign fibroblasts.

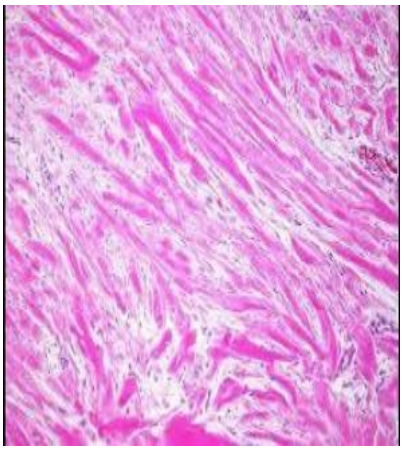
These following pictures hope show you how large this tumor and affecting other organs (included skeletal muscles in the last pic.):











Frozen abdomen

SKELETAL MUSCLE TUMORS

• Almost all malignant; except rhabdomyoma which is benign, rare, occurs with tuberous sclerosis

Rarely to find rhabdomyoma, and the most common location of it, if you find, in the heart and tongue.

• Rhabdomyosarcoma (RMS) is the malignant prototype; most common child sarcoma <15 yr.

More common than rhabdomyoma (the benign form).

• 3 types (embryonal 60%; alveolar 20%; pleomorphic 20%)

No need to remember these types, just know that there is histological variations.

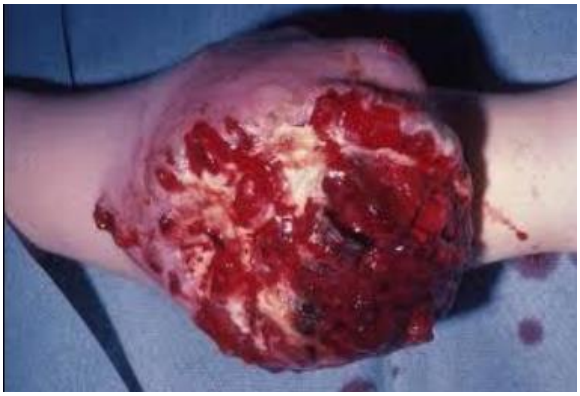
• Specific mutations are common

But not needed to make the diagnosis. No need for molecular testing.

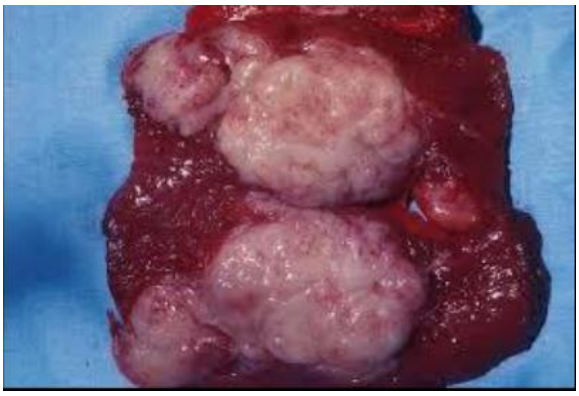
• Aggressive tumors; treated by surgery, CT +/-RT

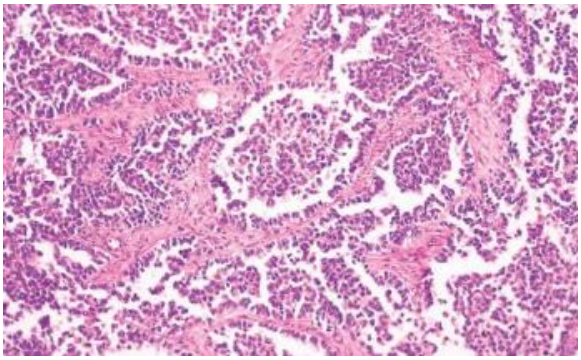
They are **high grade sarcoma**. And the **treatment is multi-modality** (chemotherapy followed by surgery with or without radiation therapy).

General features ⟶ **Bulky**, large with **hemorrhage** and **necrosis** by your naked eye, imaging and microscopic examination. However you look, you will see these features.

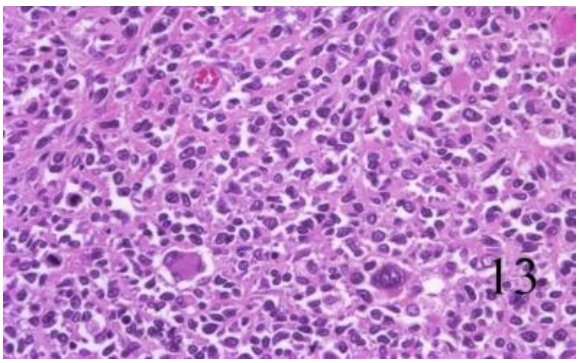


Don't be afraid, it is just someone's limb (usually a child).





The alveolar type of rhabdomyosarcoma, because it looks like the alveoli of the lung.



The pleomorphic rhabdomyosarcoma (Embryonal type).

SMOOTH MUSCLE TUMORS

1. Leiomyoma (benign) **2. leiomyosarcoma (malignant)**

• Leiomyoma (LYM): very common; any site but mostly uterus (fibroid) … menorrhagia and infertility.

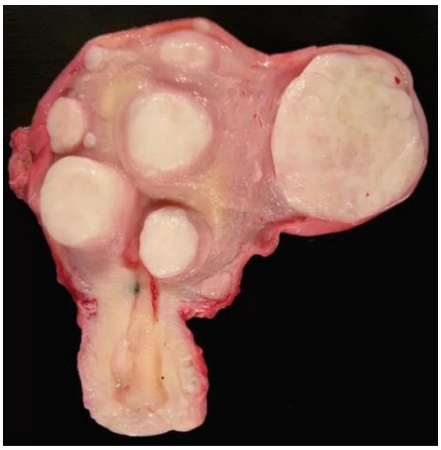
Women come with **menorrhagia** (heavy menstrual bleeding) and **infertility** (usually there are multiple masses that interfere with pregnancy) their best diagnose is leiomyoma .

• LYM vary in size and location

They can occur in any smooth muscle, but the most common location again is **uterus.** Even in the uterus itself, they have different locations.

- **Few can have specific mutations (Fumarate hydratase on chromosome 1q42.3).**

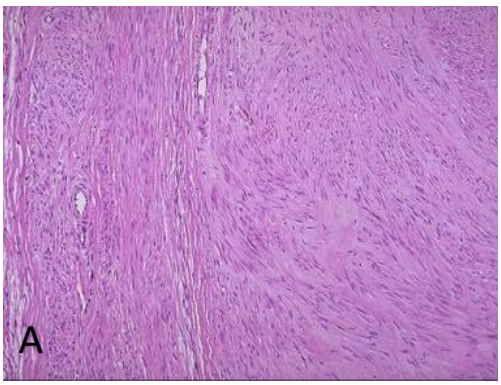
We don't need these mutations (molecular testing) to make the diagnosis, rather than, we make histological diagnosis.

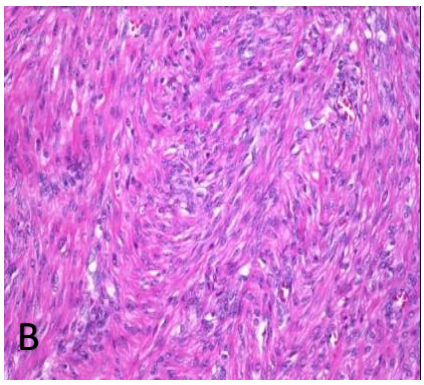


Coronal section of the uterus, these ball-like masses are leiomyoma, benign, well-circumscribed, no hemorrhage, without tissue necrosis and smooth muscle neoplasm.

Histologically, (A) low power of resolution, (B) high power.

No increased mitosis, no hemorrhage, without necrosis or infiltration .





2. leiomyosarcoma

- **10-20% of soft tissue sarcomas**

If you collect all the soft tissue sarcomas, leiomyosarcoma constitutes 10-20% of them.

- **Adults; more in females**
- **Deep soft tissue, extremities and retroperitoneum or from great vessels**
- **Complex genotypes**

We don't need these mutations (molecular testing) to make the diagnosis, rather than, we make histological diagnosis and special staining.

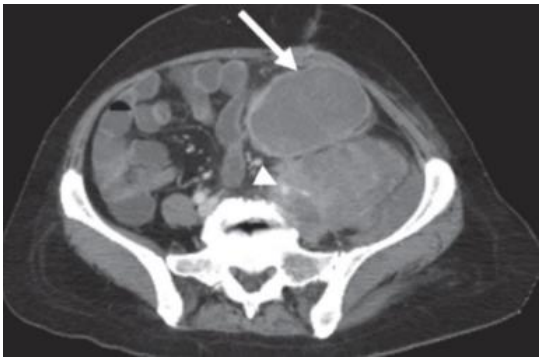
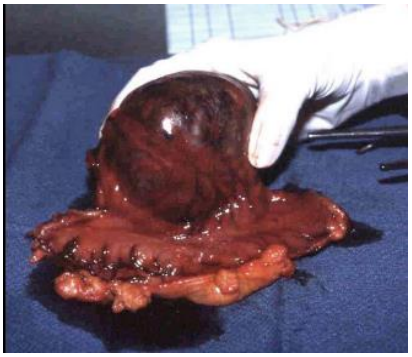
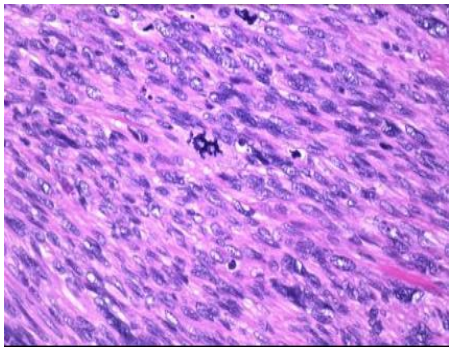
- **Hemorrhage, necrosis, increased mitosis and infiltration of surrounding tissue.**

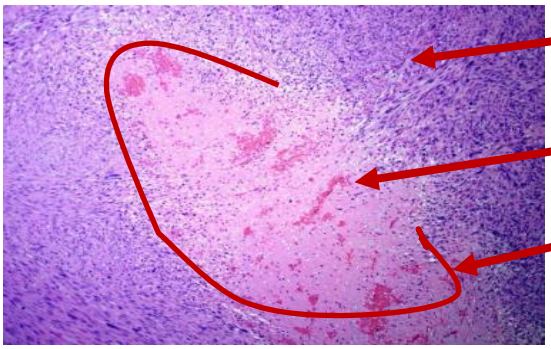
General features of any sarcoma

- **Trx: depends on location, size and grade.**

Nowadays, doctors use new adjuvant therapy (chemotherapy, surgery and then chemo or radiation).

Examples:



TUMORS OF UNCERTAIN ORIGIN:

They still soft tissue tumors

- **Uncertain mesenchymal lineage**
- **Synovial sarcoma**
- **Undifferentiated pleomorphic sarcoma**

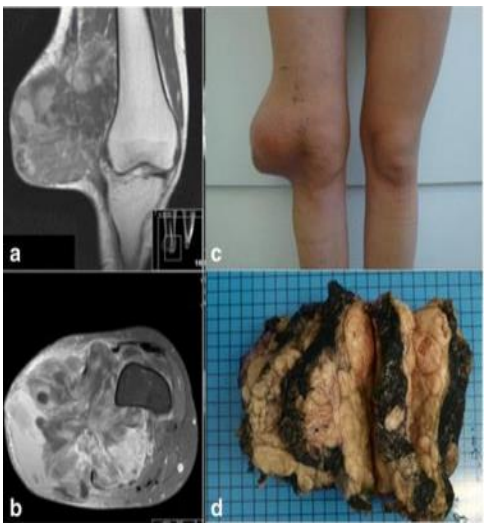
1. Synovial sarcoma

It can metastasize and be fetal.

- **Name is misnomer**

It doesn't arise from the synoviocytes, we don't know the cell of origin. It was named that because it was around the knee joint (beside the synovium).

(Although they occur most commonly around joints, they can occur anywhere).



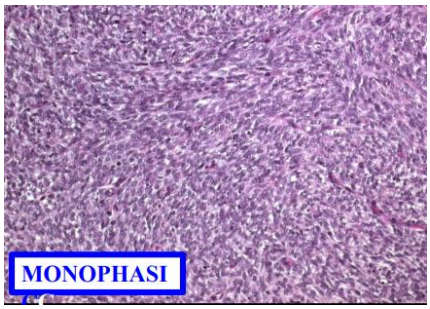
- **10% of all soft tissue sarcomas; 20-40s age**
- **Deep seated mass of long history**

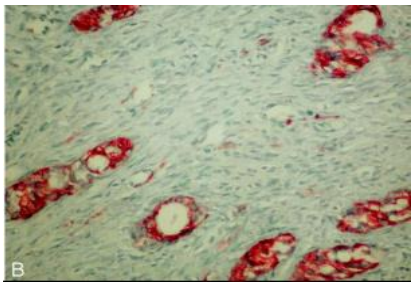
It is diagnosed late because it has low growth rate.

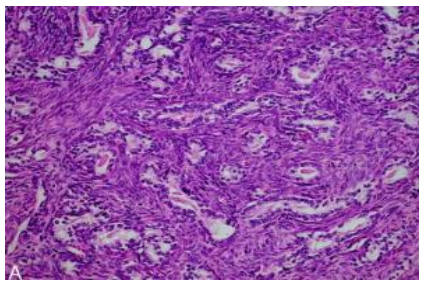
- **T(X;18) (p11;q11) fusion genes SS18…**

Translocation is important to memorize.

- **Monophasic (only spindle cells) or biphasic (spindle cells and glands).**







Biphasic (spindle cells and gland-like histologic appearance in between)

- **Trx: aggressive with limb sparing excision + CT**
- **5 year survival 25-65% depending on stage.**

Early-stage ⟶ better response ⟶ better survival.

- **Metastasis: lung and lymph nodes.**

In general, sarcomas hematogenously metastasize to the lungs, and carcinomas metastasize to the lymph nodes, so this one of the exceptions; **one of the sarcomas that can go to the lymph nodes**.

2. Undifferentiated pleomorphic sarcoma

Undifferentiated means it's with unknown origin, is it smooth muscle origin or skeletal muscle origin or fibroblast origin or adipocyte origin?

Hydrate undifferentiated, polymorphic, ugly, anaplastic sarcoma with unknown origin.

- **High grade mesenchymal sarcomas of pleomorphic cells that lack cell lineage.**

Ugly large mass with necrosis, with hemorrhage, rapidly growing, anywhere, very complex karyotype (many mutations).

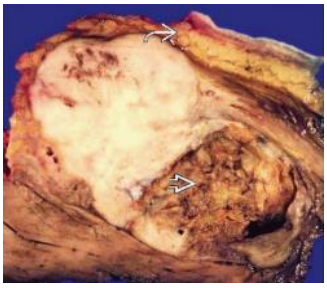
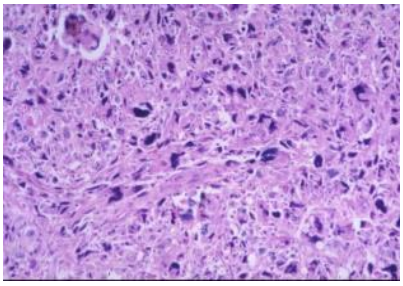
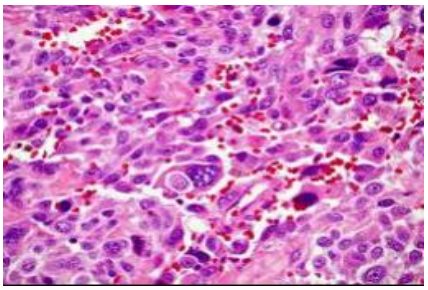
- **Deep soft tissue and extremities**

Usually in the thigh or the abdomen tissues.

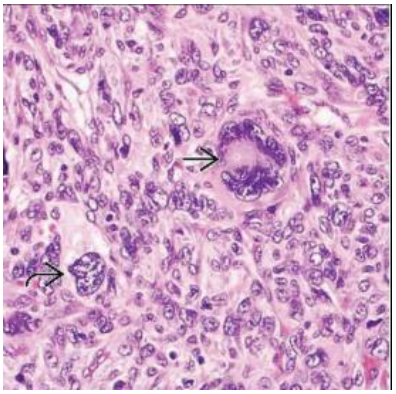
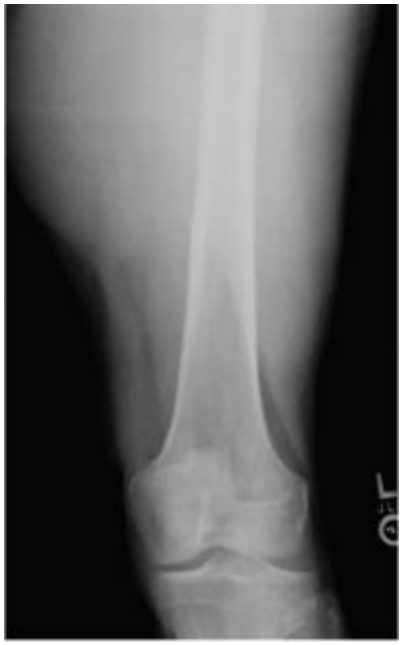
- **Old terminology: malignant fibrous histiocytoma (MFH)…not anymore.**
- **Aneuploid and complex genetic abnormalities.**

So I don't need any expensive molecular testing to diagnose. It's difficult to be treated (a tumor with bad news).

- **Large tumors; anaplastic and pleomorphic cells, abnormal mitoses, necrosis**
- **Trx: aggressive with surgery and adjuvant CT, +/- RT; poor prognosis**

when you look at these sections, you notice how hard is to differentiate this tumor (very ugly bizarre anaplastic cells, abnormal mitosis and hemorrhage).

SUMMARY

SOFT TISSUE TUMORS

- The category of soft tissue neoplasia describes tumors that arise from non-epithelial tissues, excluding the skeleton, joints, central nervous system, and hematopoietic and lymphoid tissues. A sarcoma is a malignant mesenchymal tumor.
- Although all soft tissue tumors probably arise from pluripotent mesenchymal stem cells, rather than mature cells, they can be classified as
  - Tumors that recapitulate a mature mesenchymal tissue (e.g., fat). These can be further subdivided into benign and malignant forms.
  - Tumors composed of cells for which there is no normal counterpart (e.g., synovial sarcoma, UPS).
- Sarcomas with simple karyotypes demonstrate reproducible, chromosomal, and molecular abnormalities that contribute to pathogenesis and are sufficiently specific to have diagnostic use.
- Most adult sarcomas have complex karyotypes, tend to be pleomorphic, and are genetically heterogeneous with a poor prognosis.

BEST WISHES

V2

THE ONE OF FIBROMATOSIS THAT CAN KILL YOU IS **THE DEEP ONE** NOT THE SUPERFICIAL.

as its name implies, deep fibromatosis, it is located deep to the vital organs, and due to its highly proliferative nature it could infiltrate too much and compress on the adjacent organs lead them to function abnormally, then death.