MSS

Musculoskeletal System

Doctor 2019 | Medicine | JU

9

Pathology

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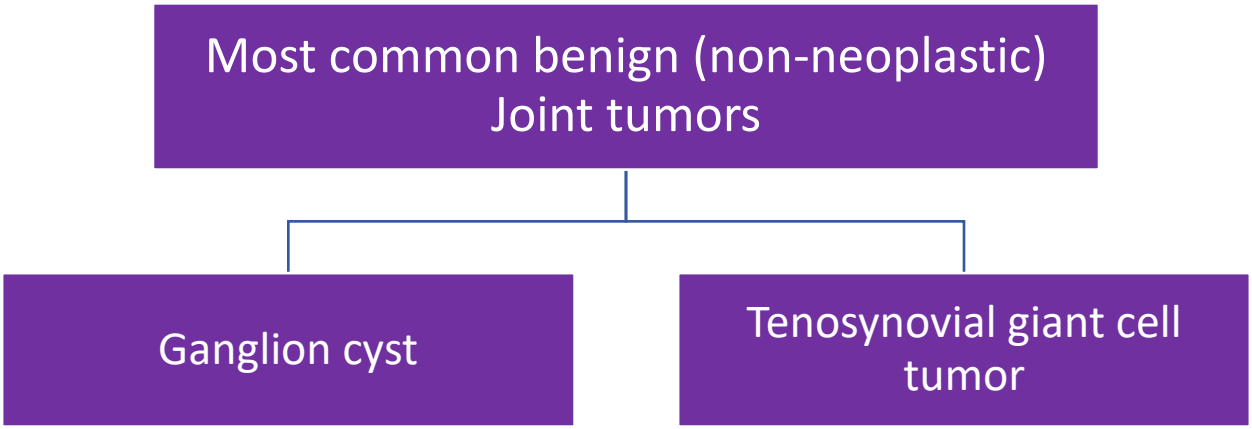
Joint tumors and tumor like conditions

Not as common as bone and soft tissue tumors. (**rare**)



1. **Ganglion cyst: common** condition, a cystic bulge which occurs **around the joint** and **mainly in the dorsum of the wrist**. Mostly asymptomatic, but sometimes it gets bigger causing pressure on a nerve which is painful.

It is **not a true cyst** because it does not have a lining, it is a bulge with many theories about its pathogenesis. Two of these theories are:

a. Degeneration of joint space leading to pseudocyst formation. (fluid containing bulge)
b. Herniation of synovial membranes.

Ganglion cyst is probably not a true tumor, it is either herniation or degenerative type of cyst.

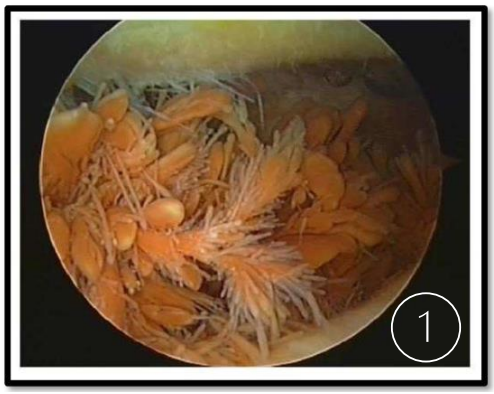
Treatment: aspiration of tissue (surgical removal). Under the microscope it is a dense fibrovascular connective tissue with myxoid degeneration.

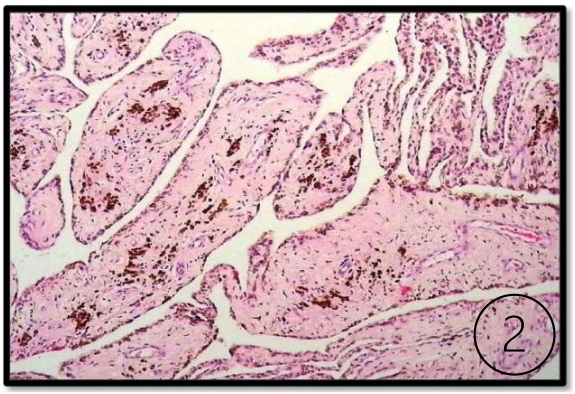
Note: The word ganglion is a misnomer, there is no actual ganglion.

True synovial cyst can occur and is called **baker cyst**. Baker cyst usually occurs around the knee joint, it presents with large swelling in the posterior aspect of the knee joint (in the popliteal fossa). It is usually a **big cyst filled with fluid or a herniation process**. Sometimes it causes severe pain, it might also cause pressure

on venous structures of the lower limb leading to deep vein thrombosis. For these reasons, baker cyst must be treated.

2. **Tenosynovial giant cell tumor:** so called to differentiate it from giant cell tumor of bone. It is a **benign neoplasm of synovium** (benign synovial tumor) characterized by a specific translocation: **<u>T(1;2)(p13q;37) which affects type IV collagen α-3 (signature marker of the genetic abnormality in this tumor).</u>** Has two types:
   a. **Diffuse**: more dangerous. called pigmented villonodular synovitis (PVNS) because under the microscope brown pigment is seen which is an evidence of previous bleeding. These brown pigments (seen in picture 2) are hemosiderin macrophages. Picture 1 is an arthroscopic picture of PVNS. PVNS are finger-like projections into the joint (proliferation of the synovium with hemosiderin macrophages and few giant cells in the stroma). Usually affects **large joints** and **most commonly the knee** but can affect any joint.



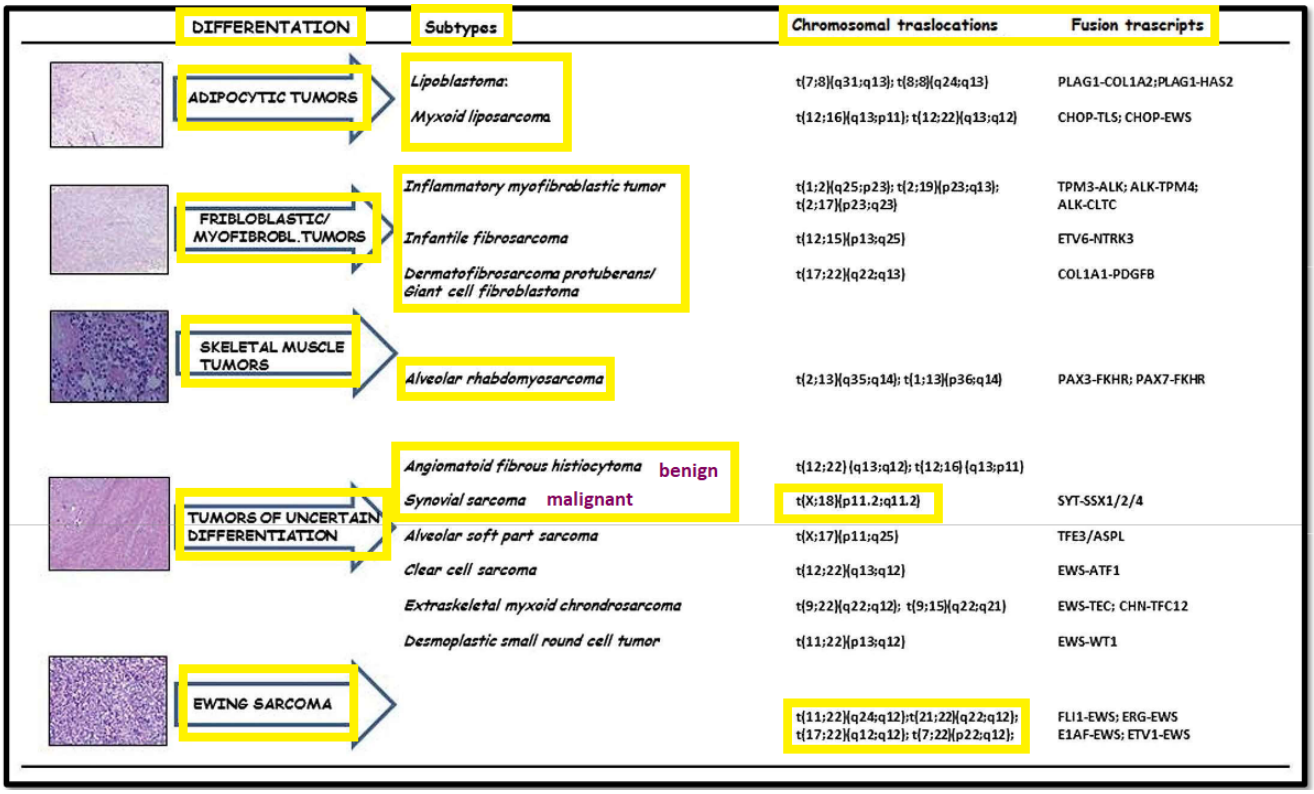


   b. **Localized giant cell tumor of tendon sheath (localized small hands tendons):** commonly occurs in the **distal aspect of joints of the hand**. Sometimes causes pain due to pressure on a nerve. Only treated when symptomatic.

Soft tissue tumors

- Benign is much more common than malignant.
- Incidence is 1% with 2% cancer death. (2% cancer mortality rate)
- Sarcomas, which are malignant tumors of soft tissue:
  - are usually aggressive and **metastasize** via the hematogenous pathway **into the lungs.** The lung is the most common site of metastasis of sarcomas. Therefore, when a patient is diagnosed with a sarcoma a CT scan must be done to check if the lungs are involved at the time of the diagnosis.
  - **The most common site** for sarcomas is in the **extremities**, especially the thigh.
  - Sarcomas are **usually sporadic** but very few **can arise from genetic mutations** such as tumor suppressor gene mutations. Patients with neurofibromatosis type 1 (NF1) are at higher risk of neurofibrosarcomas. Patients with Gardner syndrome, Li-Fraumeni syndrome, Osler-Webber-Rendu Syndrome are at higher risk of soft tissue tumors, especially sarcomas.
  - Few of these sarcomas can occur after exposure to radiation, burns, and toxins. Radiation is becoming a more frequent cause because many patients are receiving radiation for cancer treatment.
- Soft tissue tumors in general have no precursor or preneoplastic lesions, unlike dysplasia of the cervix, skin, or colon. Theory is that they arise from pluripotent mesenchymal stem cell which acquires somatic mutation producing these tumors.
- 15-20% of these tumors (especially sarcomas) have a simple karyotype or a single signature mutation. Examples are Ewing and synovial sarcoma. Scientists use these mutations as target therapy and for prognosis.
- 80-85% of sarcomas in general or aggressive malignant soft tissue tumors have a complex karyotype, which means there is genomic instability and a lot of mutations. Investigating these tumors for genetic abnormality is not useful because there will be multiple and many of these mutations specifically in leiomyosarcoma (LMS) and pleomorphic sarcoma.
- There is a wide range of these tumors from benign to highly malignant.

- Diagnosis: grading and staging are important.
  - Grade: how much the tumor looks like the primary cell of origin. Divided to:
    - well-differentiated: low grade, good prognosis.
    - moderately differentiated.
    - poorly differentiated: high grade, bad prognosis
  - Stage: The extent to which a cancer has developed by growing and spreading. stages 1, 2, 3, 4. pleomorphic sarcoma with multiple lung metastasis is an example of stage 4.
- If the tumor is low grade and localized surgical excision would probably be curative.



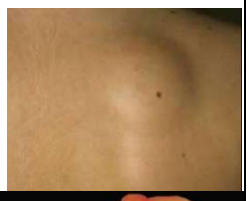
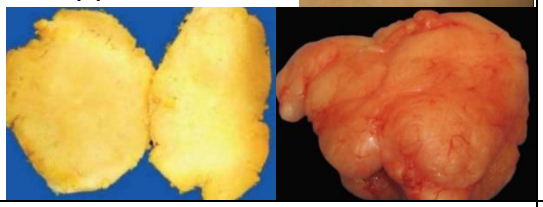
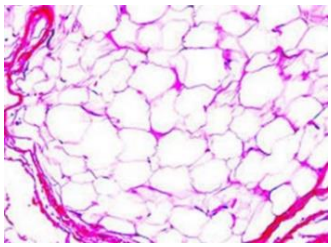
DIFFERENTATION	Subtypes	Chromosomal traslocations	Fusion trascripts
ADIPOCYTIC TUMORS	*Lipoblastoma*:	t(7;8)(q31;q13); t(8;8)(q24;q13)	PLAG1-COL1A2;PLAG1-HAS2
	Myxoid liposarcoma	t(12;16)(q13;p11); t(12;22)(q13;q12)	CHOP-TLS; CHOP-EWS
FRIBLOBLASTIC/ MYOFIBROBL.TUMORS	*Inflammatory myofibroblastic tumor*	t(1;2)(q25;p23); t(2;19)(p23;q13); t(2;17)(p23;q23)	TPM3-ALK; ALK-TPM4; ALK-CLTC
	Infantile fibrosarcoma	t(12;15)(p13;q25)	ETV6-NTRK3
	Dermatofibrosarcoma protuberans/ Giant cell fibroblastoma	t(17;22)(q22;q13)	COL1A1-PDGFB
SKELETAL MUSCLE TUMORS	*Alveolar rhabdomyosarcoma*	t(2;13)(q35;q14); t(1;13)(p36;q14)	PAX3-FKHR; PAX7-FKHR
TUMORS OF UNCERTAIN DIFFERENTIATION	*Angiomatoid fibrous histiocytoma* benign	t(12;22)(q13;q12); t(12;16)(q13;p11)	
	Synovial sarcoma malignant	t(X;18)(p11.2;q11.2)	SYT-SSX1/2/4
	Alveolar soft part sarcoma	t(X;17)(p11;q25)	TFE3/ASPL
	Clear cell sarcoma	t(12;22)(q13;q12)	EWS-ATF1
	Extraskeletal myxoid chrondrosarcoma	t(9;22)(q22;q12); t(9;15)(q22;q21)	EWS-TEC; CHN-TFC12
	Desmoplastic small round cell tumor	t(11;22)(p13;q12)	EWS-WT1
EWING SARCOMA		t(11;22)(q24;q12);t(21;22)(q22;q12); t(17;22)(q12;q12); t(7;22)(p22;q12);	FLI1-EWS; ERG-EWS E1AF-EWS; ETV1-EWS

Notes regarding the previous table:

1. This table gives an idea about common soft tissue tumors.
2. Only the yellow boxes are mentioned by the doctor.

3. Adipocytic tumors arise from adipose tissue. Chromosomal translocations are sometimes used to confirm the diagnosis especially in well-differentiated lipomatous tumor.
4. Chromosomal translocations of **Ewing sarcoma** and **synovial sarcoma** ***must be memorized.***
5. Any cell in the soft tissue can give rise to benign and malignant tumors.
6. Extra video recommended by the doctor: https://www.youtube.com/watch?v=qpkPKk3HxUQ

Adipose tissue tumors

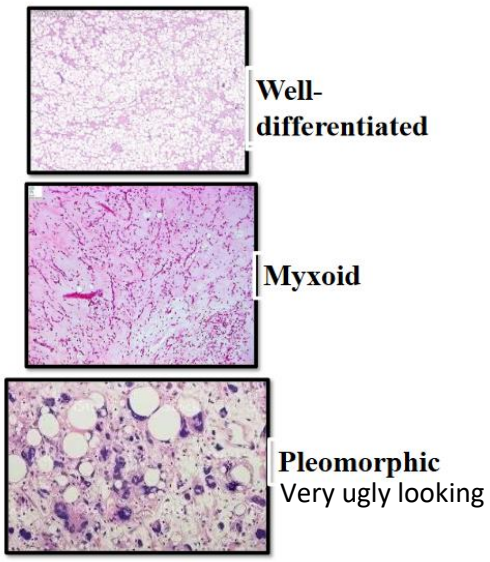
	Lipoma	liposarcoma
Prevalence	MOST COMMON SOFT TISSUE TUMOR. Much more common than liposarcoma.	MOST COMMON SARCOMAS IN ADULTS **above the age of 50.**
Pathogenicity	A clone that forms a benign tumor.	A clone that forms a malignant tumor.
Site	The most common location is subcutaneous tissue. (subcutis)	The most common location is the Extremities and retroperitoneum.
Size	Smaller	Larger
Gross appearance	1. Well-encapsulated and well-circumscribed 2. Soft shiny yellow appearance.  	
Histological appearance	Mature fat cells (adipocytes) 	Three types: 1. Well-differentiated: also called atypical lipomatous tumor. Difficult to diagnose because it looks like lipoma under the microscope. better prognosis.

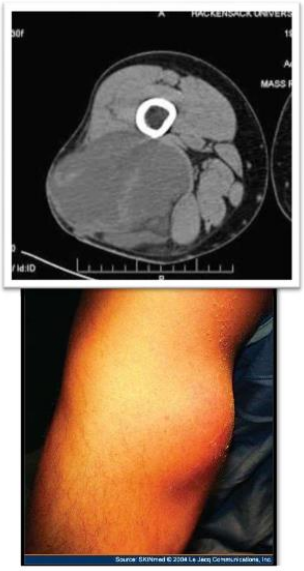
		2. Myxoid: classic, easy to diagnose under the microscope. also good prognosis. t(12,16) 3. Pleomorphic: the most aggressive type, easy to diagnose, ugly looking. Bad prognosis.
Treatment	Excision if they are big, start causing pressure, and their cosmetic appearance is not very good.	

How to differentiate between a low grade liposarcoma (well-differentiated) and benign lipoma (both are histologically similar)?

If the tumor is in the Extremities or retroperitoneum and is more than 10-15 cm in size further analysis to MDM2 gene mutations in chromosome number 12 is needed to confirm the diagnosis by immunohistochemistry (which is not that good) or FISH analysis (which is more sensitive and specific). IF IT TESTS POSITIVE for the **MDM2 gene** translocation $\longrightarrow$ Liposarcoma.

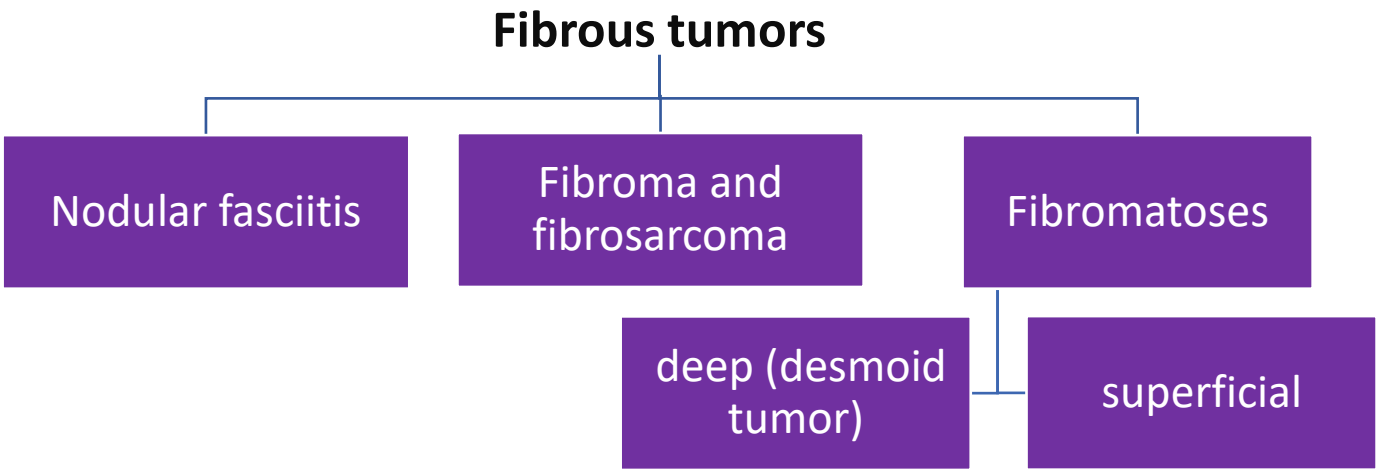
Liposarcoma features





Thigh big tumor

Big tumor behind the thigh or knee joint



Nodular fasciitis:

- Was thought to be a reactive process. However, recent studies confirm that this process is actually clonal, t(17;22) producing MYH9-USP6 fusion gene. People who found the translocation believe that nodular fasciitis is a tumor and not an inflammatory proliferative reaction.
- The classic clinical scenario for nodular fasciitis is previous **history trauma**, and **recent rapid increase in the size** of the tissue mass at the site of tumor. (can occur anywhere)
- 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.
- **The most important thing** about nodular fasciitis is **not to Mistakenly diagnose it as malignant** because this exposes the patient to unnecessary harmful treatment.
- There is a classic appearance of nodular fasciitis under the microscope called culture-like histology. It has spindle cells which are bland and sometimes have frequent mitosis. Inflammatory cells such as plasma cells, neutrophils, and lymphocytes are sometimes seen as well.