MSS

pathology

LEC no.7

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MUSCULOSKELETAL PATHOLOGY-7 SOFT TISSUE TUMORS

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GANGLION CYST

The name of disease is incorrect ,it has nothing to do with ganglion cell's in nervous system

It is not tumor it is a tumor like mass in the tissue
It is normal soft tissue undergoes cystic degeneration)cavity filled with fluid)

- Misnomer, not related to ganglion cells of nervous system
- Appears near joint capsule or tendon sheath
- The soft tissue undergoes cystic degeneration
- No cellular lining, does not communicate with joint space
- Most common site: wrist joint, foot
- Appears firm, pea-sized translucent nodule
- Treatment :surgery

Under the microscope there is no cellular lining in this cavity so it does
not communicat with joint space
We don't see synovium under this cyst

SYNOVIAL CYST

- Herniation of synovium through joint capsule into soft tissue
- Appears in the setting of rheumatoid arthritis or osteoarthritis
- Histologically: synovial lining(communicating with joint space), inflammation, fibrin
- Most common site: popliteal space (called Baker cyst)the name clinically

There is synovium within the cyst
Herniation of synovium results from disease in joints as well as pressure

TENOSYNOVIAL GIANT CELL TUMOR

Similar to giant cell tumor in bones but this arises from synovium of joints and tendon sheath

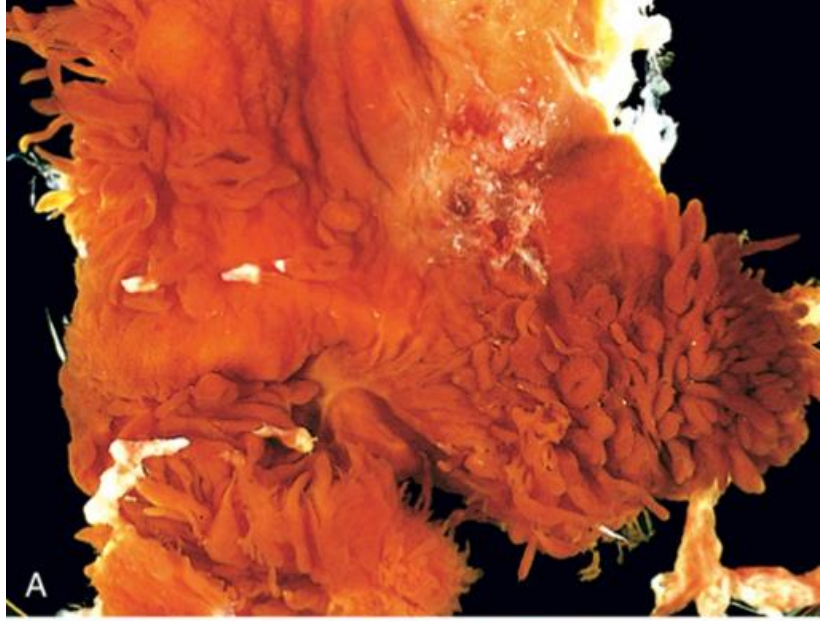
- Benign tumor that arises in synovium of joints and tendon sheath
- Can be localized (benign) (small tumor, commonly in the hand, painless, well-circumscribed), or diffuse (large tumor, knee joint, called "pigmented villonodular synovitis"(old name, it was thought that is an inflammation and not true tumor), causing pain, swelling, limitation of movement, sometimes a palpable mass)
- Appears in middle age adults
- t(1;2)(p13;q37),gene of type IV-collagen fuses with monocyte colony-stimulating factor gene, result in production of large amount of macrophages(that's why under microscope we will see a lot of histeocytes)

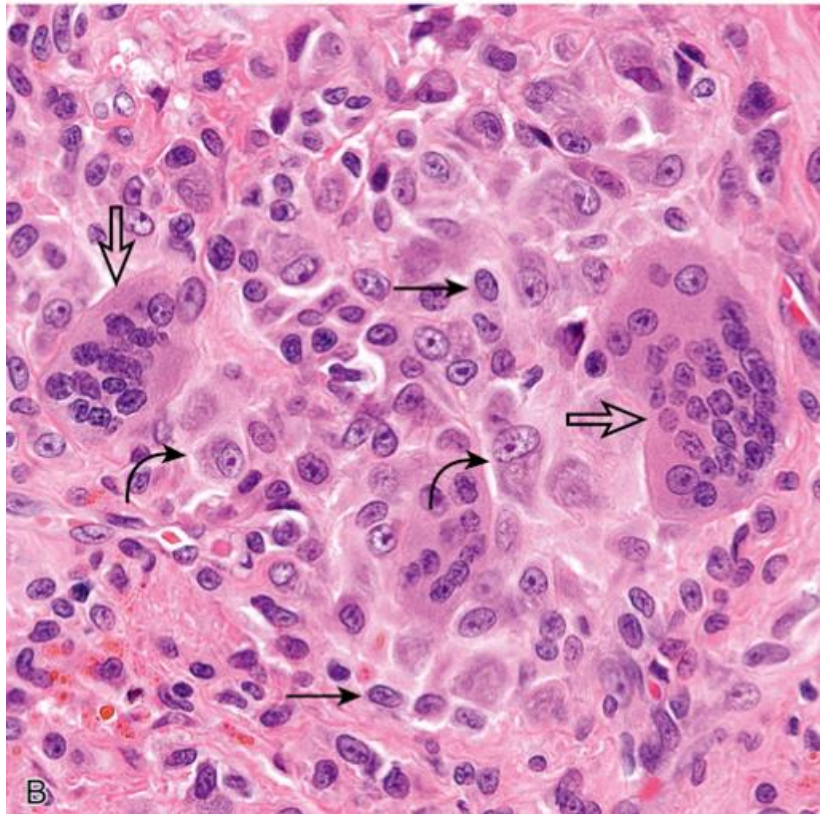
It is a tumor due to mutation (translocation between chr1 and chr2)

MORPHOLOGY

- Grossly: red or brown (pigmented)
- Tumors show nodules and finger-like projections(don't have smooth surface so it is called pigmented villonodular synovitis)
- Diffuse tumors fill the knee join space
- Neoplastic cells form a minority of tumor cells, appear polygonal and medium size (similar to synoviocytes). The majority of tumor cells are macrophages (containing hemosiderin) and multinucleated giant cells

Many of macrophages fuse to multinucleated giant cells





- enosynovial giant cell tumor. (A) Diffuse type: excised synovium with fronds and nodules. (B) Histologically, there is a mixed cell population, including epithelioid cells(largest cells وهي عباره عن monocytes) (curved arrow), mononuclear stromal cells (small neoplastic)(thin arrow), and osteoclast-like giant cells (multinucleated)(thick arrow)

fig A
shows irregular projections for this tumor

SOFT TISSUE TUMORS

They are tumors in skeletal system other than bone or hematologic tumors

- Benign tumors are more common than malignant (except for skeletal muscle tumors)
- Sarcomas (malignant tumors) are generally rare tumors, aggressive (tend to metastasis by blood), lack effective treatment
- Most common site: extremities (especially thigh deeply)
- 15% of cases arise in children, carry germline mutations
- Most cases are sporadic, rarely associated with syndromes (Li-Fraumeni, neurofibromatosis)
- In contrast to carcinoma and lymphoma, most tumors arise from pluripotent mesenchymal stem cells that acquire genetic mutations (sarcoma doesn't raise from a mature cells)
- 80% of sarcomas show complex karyotype (multiple chromosomal gains or losses) (three or more mutations at the level of chromosome while 15% show simple karyotype

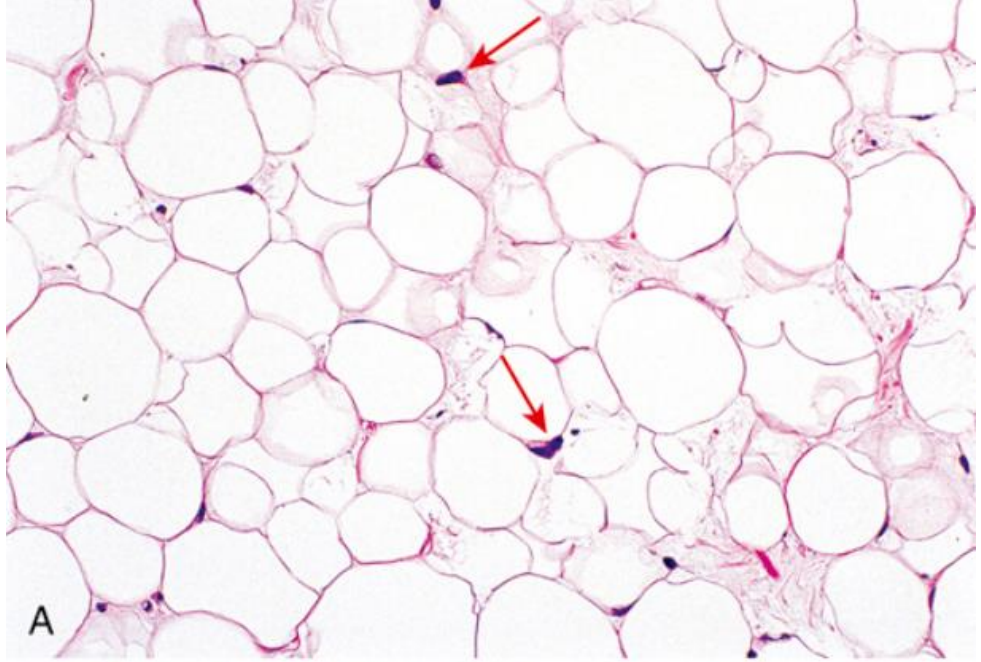
Extra information: karyotype is the general appearance of the complete set of chromosomes in the cells of a species or in an individual organism

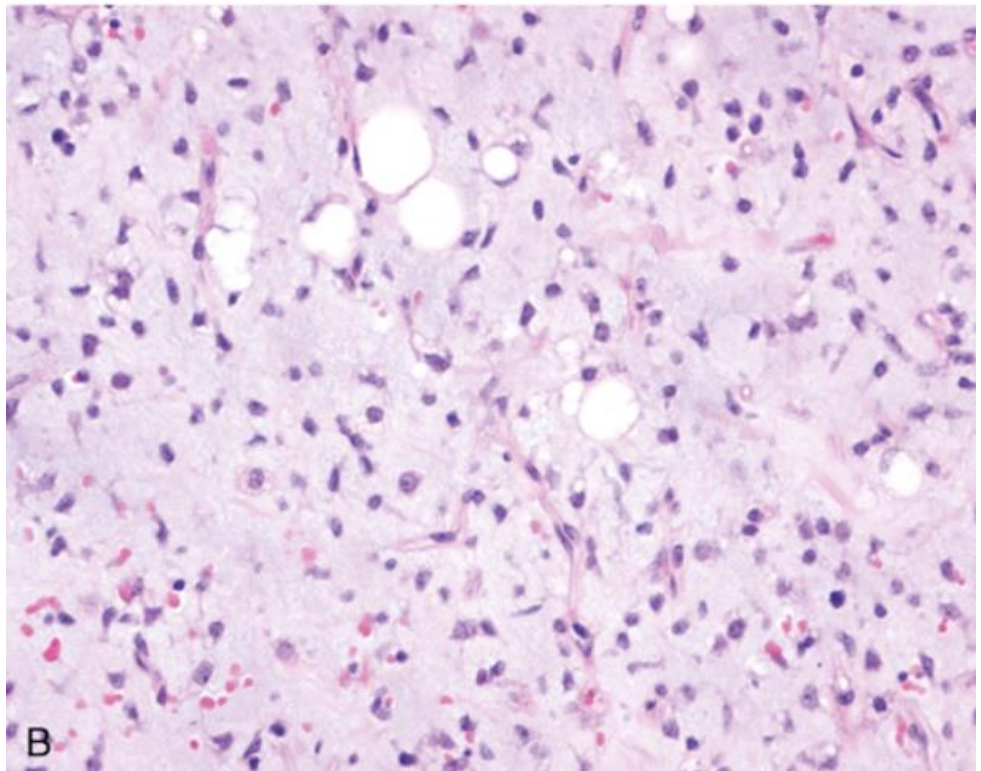
LIPOMA

- Benign tumor with adipose tissue differentiation
- The most common soft tissue tumor in adults
- Well-circumscribed tumor, appears in subcutis of extremities or trunk, middle age adults
- Histologically appears like normal adipose tissue

LIPOSARCOMA

- Malignant tumor with adipose tissue differentiation
- Most common sarcoma in adults
- Patients are in 50s-60s (older than patients with lipoma)
- Appears deep in the thigh or retroperitoneum (the second common site is retroperitoneum)
- Three types:
- 1) well-differentiated: MDM2 and P53 mutations, good prognosis (most common type and this type there is few malignant cells)
- 2) myxoid: t(12;16) (translocation mutation), intermediate prognosis (in this type there is hematoxylin deposition in background)
- 3) pleomorphic: complex karyotype, poor prognosis (here we can see anaplastic cells)





- Liposarcoma. (A) The well-differentiated subtype consists of mature adipocytes and rare, atypical stromal (red arrows) cells with hyperchromatic nuclei. (B) Myxoid liposarcoma with abundant basophilic background substance and a rich capillary network in which are scattered immature adipocytes.

NODULAR FASCIITIS

This is the most common fibrous tumor which arise from the fibroblast cells.

- Benign tumor of fibroblasts
- Arises in upper extremities of young adults
- t(17;22)(MYH9-USP9) gene fusion
- Self-limited proliferation, spontaneous regression

(T) Here refers to the translocation mutation.

-This tumor appears rapidly after trauma ,but it is self-limited and will regress by its own.
- It appears most commonly in the upper limbs and superficial area.

FIBROMATOSIS

- Benign tumor of fibroblasts
- Can be superficial or deep (called desmoid), abdomen
- Large mass with infiltrative margins, frequently recur but do not metastasize
- Carry mutation in CTNB1 (β-catenin) and APC (adenomatous polyposis coli) genes
- Most cases are sporadic, but may appear in Gardner syndrome (familial adenomatous polyposis coli)

Morphology: it's infiltrative and looks like malignant tissues so it needs resection in surgery.

-Can be superficial and appears in extremities or skin.
- It's benign but locally aggressive disease.

- Can be sporadic without previous disease, but a little may be syndromic like in Gardner Syndrome which has germ line mutation in APC gene with a polypes in colon (Desmoid fibromatosis).

RHABDOMYOSARCOMA

Remember that benign tumor of the skeletal muscle are very rare !

- Malignant mesenchymal tumor with skeletal muscle differentiation
- Four types: → This classification is according to histology
- Alveolar and embryonal: most common sarcomas in children and adolescents
- Pleomorphic: appears in adults
- Spindle cell: appears in any age groups
- Pediatric rhabdomyosarcoma arises in head and neck, or genitourinary areas
- Alveolar rhabdomyosarcoma carry a mutation in PAX3 gene (FOXO3-PAX3) that interferes with normal skeletal muscle differentiation

Hint: vowels letters (A-E) appears in children

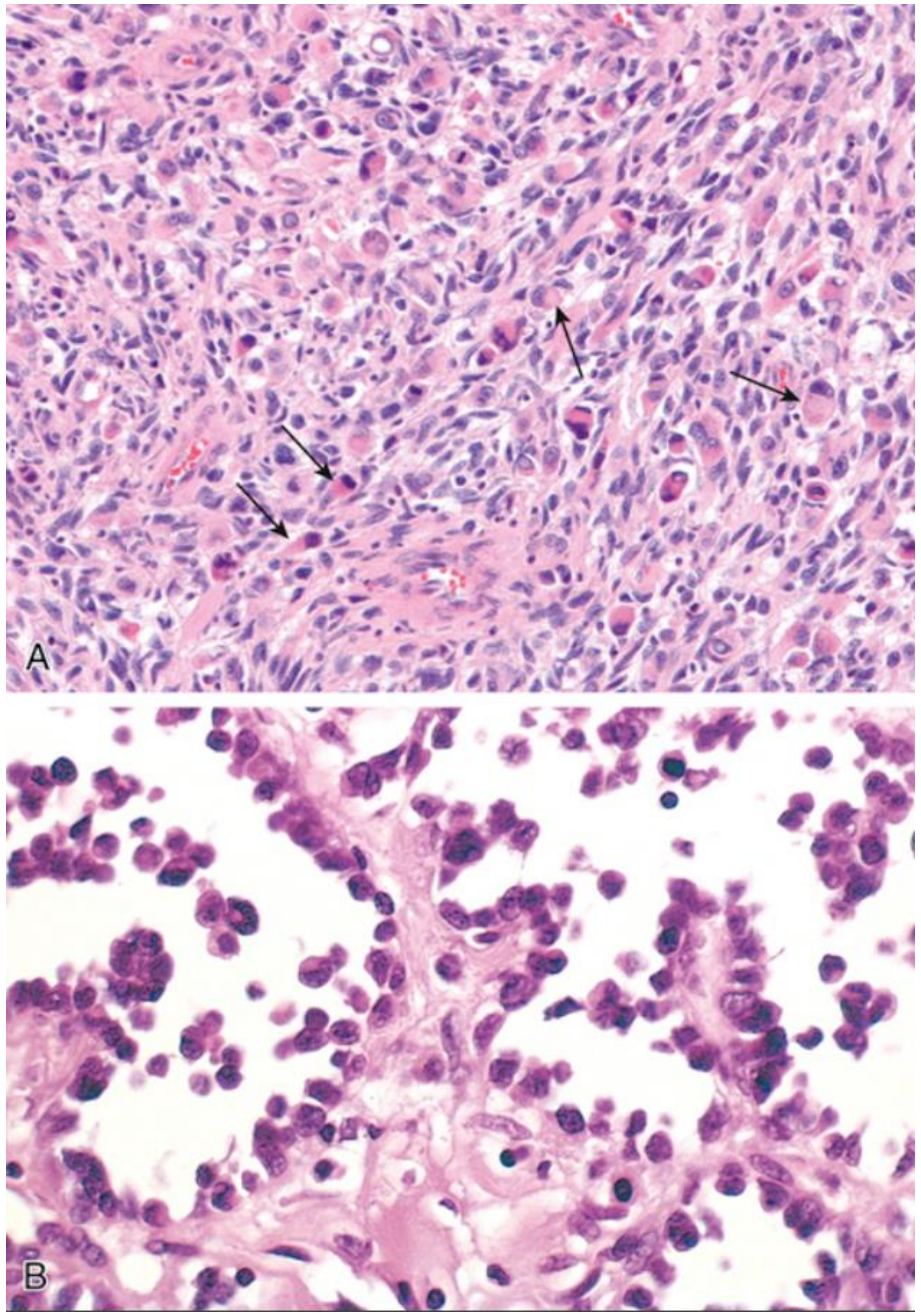
PAX3 gene has a role in the differentiation of skeletal muscles.

MORPHOLOGY

- **Embryonal rhabdomyosarcoma:** very cellular tumor, malignant cells appear as different stages of skeletal muscle maturation (from primitive to rhabdomyoblasts with cytoplasmic striation).
- **Alveolar rhabdomyosarcoma:** tumor shows empty spaces l lung alveoli, malignant cells are loosely cohesive

They take a shape of the emproyal phase of skeletal muscle start from a small , undifferentiated calls and become rhabdomyoblast cells with cytoplasmic straition due to myofibrilis , they are different from the mature skeletal muscle in histology and there will be a lot of cells (cellular tumor).

The cells won't bind to each other because they are loosely cohesive.



- Rhabdomyosarcoma. (A) Embryonal subtype composed of malignant cells ranging from primitive and round to densely eosinophilic with skeletal muscle differentiation (arrows). (B) Alveolar rhabdomyosarcoma with numerous spaces lined by dyscohesive, uniform round tumor cells

(A): Here you can see a very cellular tumor with a lot of nuclei (dark in Color), most of them are very small and you can't know the type of them because they are undifferentiated .
The larger cells in arrows reassemble the rhabdomyoblast .
Cytoplasm-> pink in color , in high magnification you can see the cytoplasmic straition.

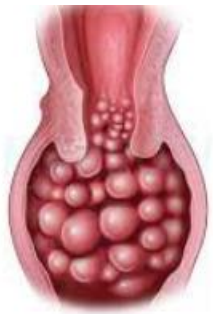
(B): The spaces between tumor cells looks like the alveoli of the lung .

SARCOMA BOTRYOIDES

-This is a clinical term of the embryonal rhabdomyosarcoma.
- Botryoides means grape's shape.

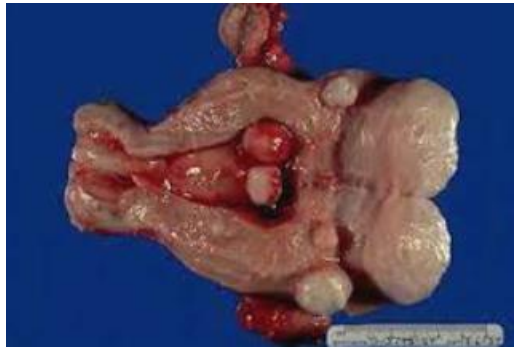
- A variant of embryonal rhabdomyosarcoma
- Affects children
- Arises in the walls of hollow organs (urinary bladder and vagina)
- Appears like a bunch of grapes
- Good prognosis

The second most common site is genitourinary tract.



LEIOMYOMA

- Benign tumor of smooth muscle differentiation
- Commonly arises in uterus (myometrium, called fibroids), but also in skin (erector pili muscle) and soft tissue
- Germ-line mutation in fumarate hydratase (FH) gene results in loss of function, patients develop multiple leiomyomas and renal cell carcinoma
- Leiomyomas are small, well circumscribed, similar morphology to normal smooth muscles (spindle cells, eosinophilic cytoplasm, monomorphic)



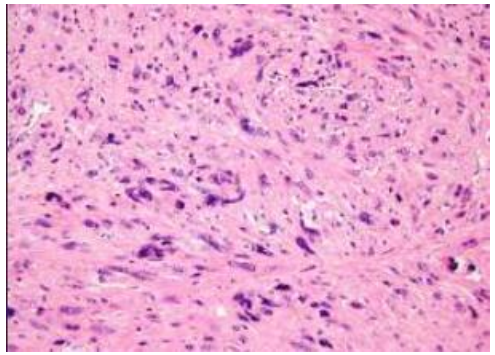
(تليفات أو ألياف الرحم)
The most cases are sporadic (individual tumor) but sometimes it arises with syndromes when they have germ line mutation in FH gene.

They have firm consistency because they are muscles .
Under microscope they are identical to the smooth muscles and spindle in shape.

Monomorphic : all cells are the same in shape and size .
- Fumarate is a part of the kerbs cycle .

LIOMYOSARCOMA

- Malignant tumor that shows smooth muscle differentiation
- 10%-20% of sarcomas
- Old age
- Arises in deep soft tissue of extremities, uterus, retroperitoneum, great blood vessels (inferior vena cava)
- Complex karyotype
- Morphology: spindle cells, pleomorphic, numerous mitosis



-This is a bad tumor !

- You can see the nuclei, most of them are very big and they are different from each other.

SYNOVIAL SARCOMA

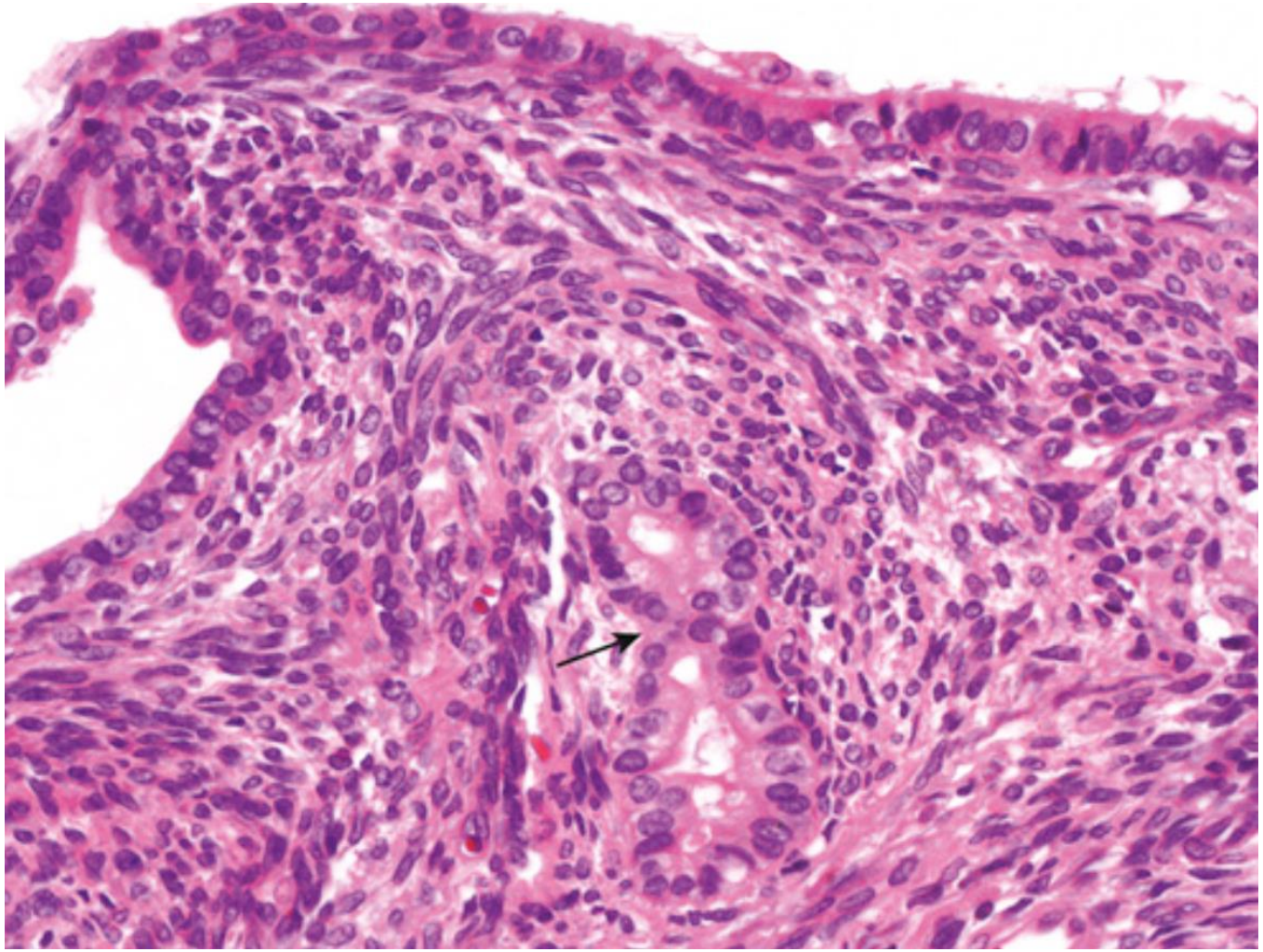
- Tumor that arises near joint
- Adolescents and middle age adults
- Carries translocation (X;18)(SS18;SSX), produces chimeric proteins that interfere with normal chromatin remodeling
- Morphology: monophasic: spindle cell sarcoma, or biphasic: spindle cell and gland-like structures

The origin cell and how the tumor formed is still unknown.
It can occur in any part of the body .

This is a special mutation, it involves the (X) chromosome.

Chimeric protein is not present normally.

Monophasic: all tumor cells are spindle in shape and looks like each other.



- Synovial sarcoma showing the classic biphasic spindle cell and glandlike (arrow) histologic appearance

This is a Biphasic synovial sarcoma

At arrows you can see the glands which have lumen at the centre and they are round in shape.
Also; the background cells all are elongated and spindle cells in shape .