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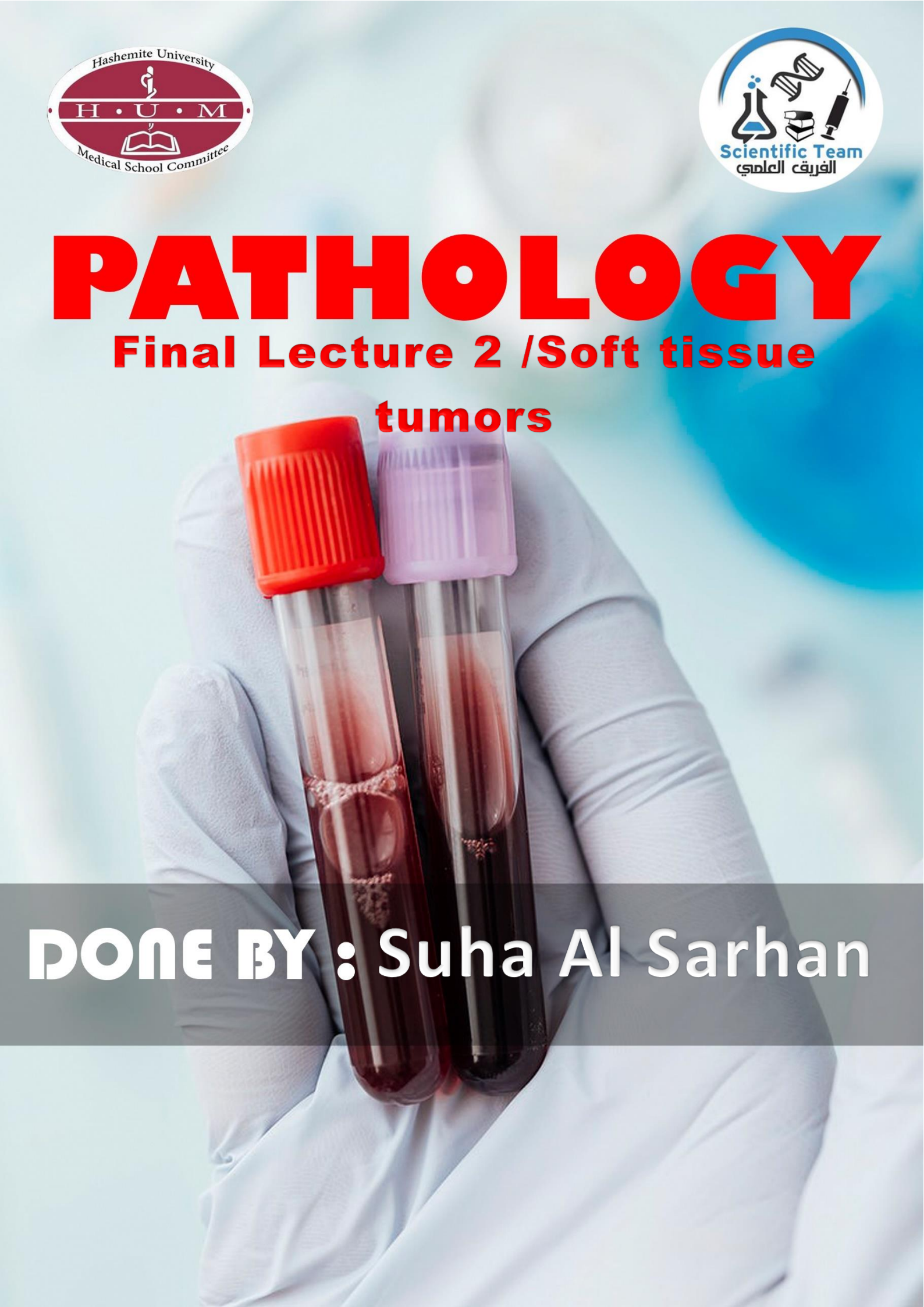
PATHOLOGY

Final Lecture 2 /Soft tissue tumors



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SOFT TISSUE TUMORS (26 Ones):

T of Adipose Tissue	Lipomas + Liposarcoma
T & T-like Lesions of Fibrous Tissue	Nodular fasciitis+ Superficial & Deep Fibromatoses + Fibrosarcoma
Fibrohistiocytic T	Fibrous histiocytoma + Dermatofibro sarcoma protuberans + Malignant fibrous histiocytoma (MFH)
T of Skeletal Muscle	Rhabdomyoma + Rhabdomyosarcoma
T of Smooth Muscle	Leiomyoma + Smooth muscle tumors of uncertain malignant potential + Leiomyosarcoma
Vascular T	Hemangioma + Lymphangioma + Kaposi T.Hemangioendothelioma + Hemangiopericytoma+ Angiosarcoma
Peripheral Nerve T	Neurofibroma + Schwannoma+ Malignant peripheral nerve sheath T
T of Uncertain Histogenesis	Synovial sarcoma + Alveolar soft part sarcoma + Epithelioid sarcoma + Granular cell T.

General Principles:

*the term soft tissue describes any non-epithelial tissue other than bone, cartilage, CNS, hematopoietic ,lymphoid tissues.

*Soft tissue T are classified according to the tissue type they recapitulate, including fat, fibrous tissue, & neurovascular tissue
However, In some soft tissue T no corresponding normal counterpart is known.

*With the exception of skeletal muscle T, benign soft tissue T are more than 100 times more than their malignant counterparts
*In the US, 8000 soft tissue sarcomas are diagnosed annually, representing less than 1% of all invasive malignancies; but causes 2% of all cancer deaths, reflecting their lethal nature. (highly malignant tumor)

*Most soft tissue T arise without antecedent causes, rarely radiation, burn injury, or toxin exposure is implicated.

*Although Kaposi sarcoma is associated with the HHPV 8, but viruses are not important in the pathogenesis of most sarcomas.

*A small minority of sarcomas are associated with genetic syndromes, e.g.,

1. neurofibromatosis type 1 (neurofibroma, malignant schwannoma)
2. Gardner syndrome (fibromatosis)
3. Li-Fraumeni syndrome (soft tissue sarcoma)
4. Osler-Weber- Rendu syndrome (telangiectasia).

*Even in sporadic soft tissue sarcomas, characteristic chromosomal abnormalities can be detected. These provide insight into pathogenesis, as well as diagnostic markers, e.g,.
Ewing sarcoma & synovial sarcoma, are eventually defined by their translocation t(11;22)مهم

*40% of soft tissue T occur in the lower extremities, especially the thigh.
The incidence increased with age, although 15% arise in children.

*Certain sarcomas tend to appear in certain age groups, e.g.,

1. rhabdomyosarcoma in children
2. synovial sarcoma in young adulthood (20-40 y.)
3. liposarcoma & (MFH) in later adult life (60-80 y.)

*Accurate histologic classification is critical.
Although cell morphology & architectural arrangement are important, these features are often inadequate to distinguish different sarcomas, particularly if they are poorly differentiated.

*immunohistochemistry, EM, cytogenetics ,molecular genetics are indispensable in assigning the correct diagnosis in some cases.

*Sarcoma grade (well, moderate, poorly differentiated) is important for predicting behavior Grading, (I to III) is based on the degree of differentiation, cellularity, pleomorphism.

*but the most important predictors are
1. the Mitotic counts (the average number of mitoses per HPF)
2. Necrosis extent.

*Sarcoma staging helps determine the prognosis. With T>20cm metastases develop in 80% of cases; in contrast, for T<5cm metastases occur in only 30% of cases.

*In general, T arising in superficial locations (e.g., skin) have a better prognosis than deep-seated lesions

*overall, the 10-year survival rate for sarcomas is 40%.

FATTY TUMORS

1. Lipoma

*are benign T of fat, They are the most common soft tissue tumors of adulthood. مهم جدا

Most lipomas are solitary lesions; multiple lipomas usually suggest the presence of rare autosomal dominant syndromes.

Lipomas can be sub classified based on their histologic features e.g.,

1. conventional the most common subtype→ composed of mature fat cells or adipocytes
2. myolipoma 3. spindle cell 4. Myelolipoma 5. Pleomorphic
6. Angiolipoma → (combination of fat, smooth ms cell and vascular tissue)

Grossly:
lipomas are soft, yellow, well-encapsulated mobile, slowly enlarging & painless masses (angiolipomas can present with local pain); vary considerably in size.

H. Features:
they consist of mature adipocytes (fat cells) with no pleomorphism.

Treatment:
Complete excision is usually curative.

2. Liposarcoma

- are malignant T of adipocytes.
- Occur most commonly in the fifth & sixth decades.
- Arise mostly in the deep soft tissues or in visceral sites.

Grossly:
usually present as relatively well-circumscribed lesions

*Several different histologic subtypes are recognized, including two low-grade variants:

1. the well-differentiated liposarcoma
2. myxoid liposarcoma → characterized by abundant, mucoid extracellular matrix

Some well-differentiated liposarcomas can be difficult to distinguish histologically from benign lipomas; whereas very poorly differentiated liposarcomas can resemble various other high-grade sarcomas.

H. Features:
in most cases, lipoblasts cells, indicative of fatty differentiation are present; they recapitulate fetal fat cells with cytoplasmic lipid vacuoles that scallop the nucleus

الlipoblasts cells مشابهة للي موجودة في الجنين.

Prognosis:
is greatly influenced by the histologic subtype;

- well-differentiated & myxoid variants tend to grow slowly & have a more favorable outlook
  the more aggressive round cell & pleomorphic variants, which tend to recur after excision & metastasize to lungs.

FIBROUS TUMORS AND TUMOR-LIKE LESIONS

Fibrous tissue proliferations are heterogeneous group of lesions :

- At one end of the spectrum, nodular fasciitis is not a true T but rather a reactive, self-limited proliferation.

- At the other end, fibrosarcomas are highly malignant T that tend to recur locally & metastasize.
- Fibromatoses fall somewhere in the middle; these are characterized as benign lesions that, nevertheless, exhibit persistent local growth & can recurs.

1.Reactive Proliferations: Nodular Fasciitis → not tumor

*Is a self-limited, reactive fibroblastic proliferation that typically occurs in adults on the volar aspect of the forearm, followed in frequency by the chest & back.

*Patients characteristically present with a several-week history of a solitary, rapidly growing, and occasionally, painful mass.

*Preceding trauma is noted in 10% to 15% of cases.

لكن مش شرط ال trauma

*Lesions of nodular fasciitis rarely recur after excision.

Grossly:
characteristically, the lesion is few cms , nodular with poorly defined margins.

H. Features:
shows richly cellular fibroblastic lesion, consisting of immature, plump, spindle to stellate fibroblasts, vary in size, having conspicuous nucleoli & numerous mitoses, randomly arranged in an abundant myxoid stroma مهم

Myositis Ossificans التهاب العضلة المتعظم
*is distinguished from other fibroblastic proliferations by the presence of metaplastic bone. It usually develops in the proximal muscles of the extremities in athletic adolescents & young adults after trauma بصير عند راكبي الخيل اكتر شي .

*The involved area is initially swollen & painful, eventually evolving into a painless, hard, well-demarcated massلانه صار فيها تليف وتعظم .
It is critical to distinguish it from extra-skeletal osteosarcoma.

*Simple excision of myositis ossificans is usually curative.

2. Fibromatoses
*are a group of fibroblastic proliferations distinguished by:
1. their tendency to grow in an infiltrative fashion
2. to recur after surgical removal.

The fibromatoses are divided into two major clinicopathologic groups: superficial & deep.

a. Superficial fibromatoses :

arising in the superficial fascia & include planter & palmar fibromatosis (Dupuytren contracture) & penile fibromatosis (Peyronie disease)

*Superficial lesions are genetically distinct from their deep- seated cousins; are generally more innocuous بسيطة(they can be associated with trisomy 3 & 8)
*because they cause deformity of the involved structure, they come to clinical attention earlier

b. Deep fibromatoses:
*include the (desmoid tumors that arise in the abdominal wall) & muscles of the trunk , extremities, within the abdomen (mesentery & pelvic walls).

*They can be isolated lesions, or a component of Gardner syndrome, an autosomal dominant disorder including colonic adenomatous polyps osteomas.

*Mutations in the APC or β-catenin genes are present in the majority of these tumors.

Grossly:
Fibromatoses are gray-white, poorly demarcated, firm to rubbery, infiltrative masses 1-15 cm

H:
*fibromatoses composed of plump cells arranged in broad sweeping fascicles that penetrate the adjacent tissue; mitoses are infrequent.

*Immunohistochemical & ultrastructural studies show that these cells are probably myofibroblasts.

*Early lesions may be quite cellular, whereas others, especially the superficial fibromatoses, contain abundant dense collagen.

*Fibromatosis can be disfiguring, disabling & occasionally painful.

*Although curable by adequate excision, they frequently recur when incompletely removed. Some T respond to tamoxifen (anti estrogen) & in other cases chemotherapy or irradiation are effective.

3. Fibrosarcoma

- are malignant T of fibroblasts.
- Most occur in adults
- typically in the deep tissues of the thigh, knee ,retroperitoneal area.
- They grow slowly, & have usually been present for several years at the time of diagnosis.
- often recur locally after excision (in >50% of cases) & can metastasize hematogenously (in >25% of cases), usually to the lungs.

Grossly:
fibrosarcomas are soft infiltrative (unencapsulated masses, with areas of hemorrhage & necrosis; but, well differentiated ones can appear deceptively encapsulated!

H:
all degrees of differentiation are seen, from T that closely resemble fibromatosis, to densely packed T with spindled cells growing in a herringbone fashion to highly cellular neoplasms exhibiting architectural disarray, pleomorphism, frequent mitoses, necrosis فوضوي بدون ترتيب معين

FIBROHISTIOCYTIC TUMORS
*composed of a mixture of fibroblasts & phagocytic lipid-laden activated macrophages.
*The neoplastic cells in many cases are most likely fibroblasts.

a. Benign Fibrous Histiocytoma (Dermatofibroma)
are relatively common benign lesions in adults, presenting as circumscribed, small (<1 cm) mobile nodules in the skin dermis or subcutaneous tissue.
H:
*these typically consist of bland, interlacing spindle cells admixed with foamy, lipid-rich histiocyte-like cells.
*The borders of the lesions tend to be infiltrative, but extensive local invasion does not occur. The pathogenesis is uncertain.
*They are cured by simple excision

b. Malignant Fibrous Histiocytoma (MFH) highly malignant
MFH is a term rather loosely applied to a variety of soft tissue sarcomas characterized by
1. considerable cytologic pleomorphism,
2. bizarre multinucleate cells
3. storiform architecture

*Despite the name, the phenotype of many such tumors is fibroblastic & not histiocytic.

*N.B:
it is important to note that several T, previously diagnosed as MFH, actually exhibit markers for cells of other origin (e.g., smooth muscle cells, adipocytes, & skeletal muscle cells) & are therefore more appropriately classified as leiomyosarcomas, liposarcomas, rhabdomyosarcomas) Such T behave like others of that same class.

*Nevertheless, detailed immunohistochemical analyses demonstrate that a significant number of such tumors actually derive from other cell types (e.g., muscle cells)
muscle cell تعطي علامات في ال immunostain على انها
*Consequently, the term fibrohistiocytic, especially in regard to the malignant variants, should be considered descriptive & not necessarily indicating specific cellular origin.

*Alternatively, some T designated as MFH are so poorly differentiated that they do not express any discernible (clear) precursor phenotype.

*The MFH exhibiting fibroblastic differentiation are usually large (5-20 cm), gray-white, not encapsulated infiltrative masses, that often appear deceptively circumscribed.

*MFH usually arise in the musculature of the proximal extremities or in the retroperitoneum.
*Most of MFH are extremely aggressive, recur unless widely excised, & have a metastatic rate of up to 50%.

SMOOTH MUSCLE TUMORS

1. Leiomyoma	2. Leiomyosarcoma
Benign T of smooth muscle	comprise 10% to 20% of soft tissue sarcomas
well-circumscribed but not encapsulated, can arise from smooth muscle cells anywhere in the body	They commonly present as firm, painless masses; retroperitoneal T can be large & bulky& cause abdominal symptoms
most commonly in the uterus (the commonest benign T in females)	They occur in adults, more commonly females Common sites are skin, deep soft tissues of the extremities retroperitoneum
	H, they show spindle cells with rounded end (cigar-shaped) nuclei arranged in interweaving fascicles.
	Treatment depends on the size, location, & grade of T

- Superficial or cutaneous leiomyosarcomas are usually small & have a good prognosis,
- Retroperitoneal tumors are larger, cannot be entirely excised, & fatal by both local extension & metastases.

SYNOVIAL SARCOMA

- the cell of origin is unclear & is most certainly not a synoviocyte, less than 10% of synovial sarcomas are intra-articular and 90% extra articular reflecting a non-joint origin!
- Account for 10% of all soft tissue sarcomas.
- Typically occurring in individuals in their 20s to 40s.

- Most develop in deep soft tissues around the large joints of the extremities (juxta-articular), with 60% to 70% occurring around the knee {Remember OS & GCT of Bone!)
- Commonly metastasize to the lung, bone, & regional LN.

- Most synovial sarcomas show a characteristic t(X;18)
- Aggressive treatment with limb-sparing surgery and chemotherapy gives a 5-year survival rate of 25% to 62%.
- H: synovial sacromas may be biphasic or monophasic

Biphasic synovial sarcoma	**Monophasic synovial sarcoma**
Easley diagnosed	difficult to diagnose
exhibits differentiation of tumor cells into both: (1) epithelial-like cells, cuboidal to columnar & form glands or grow in solid cords or aggregates with NO BASEMENT MEMBRANE between them the (2) spindle cells arranging in densely cellular fascicles that surround the epithelial cells.	composed of spindled cells only (which are easily mistaken for fibrosarcomas or malignant peripheral nerve sheath T) or, rarely, epithelial cells only *Immunohistochemistry is helpful, because the T cells are positive for keratin & epithelial membrane antigen (EMA) differentiating them from most other sarcomas