Pathology of Soft Tissue Neoplasms

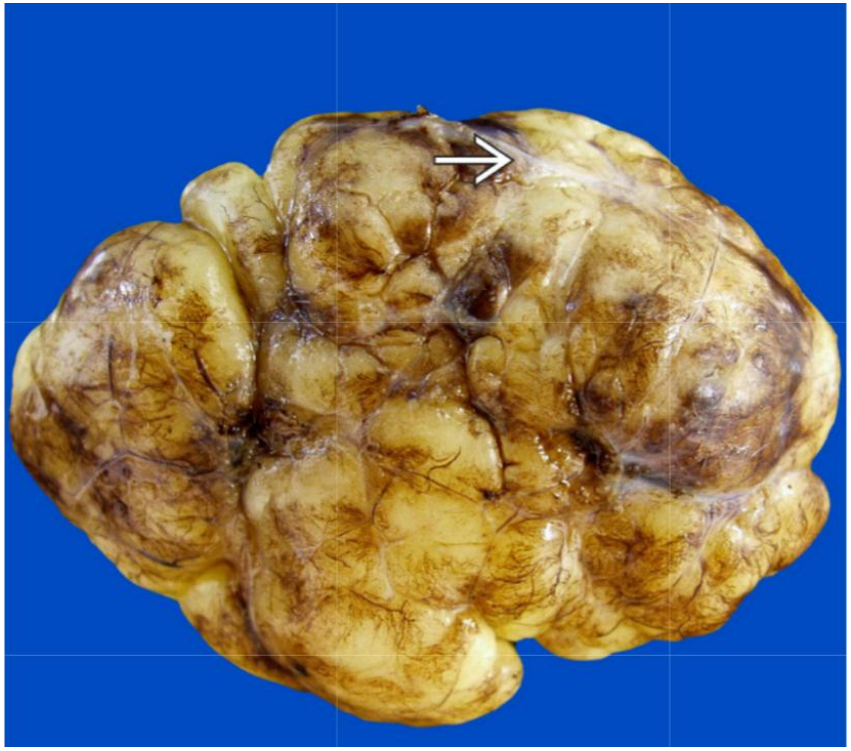
By Konstantinos Linos M.D.

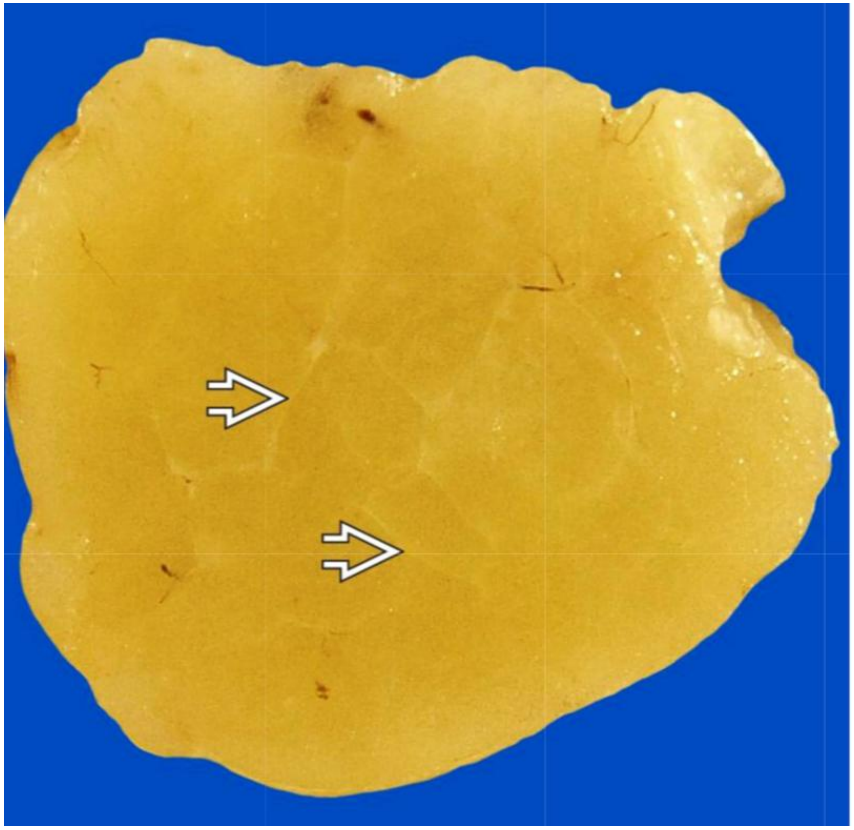
Tumors of Adipose Tissue

LIPOMA

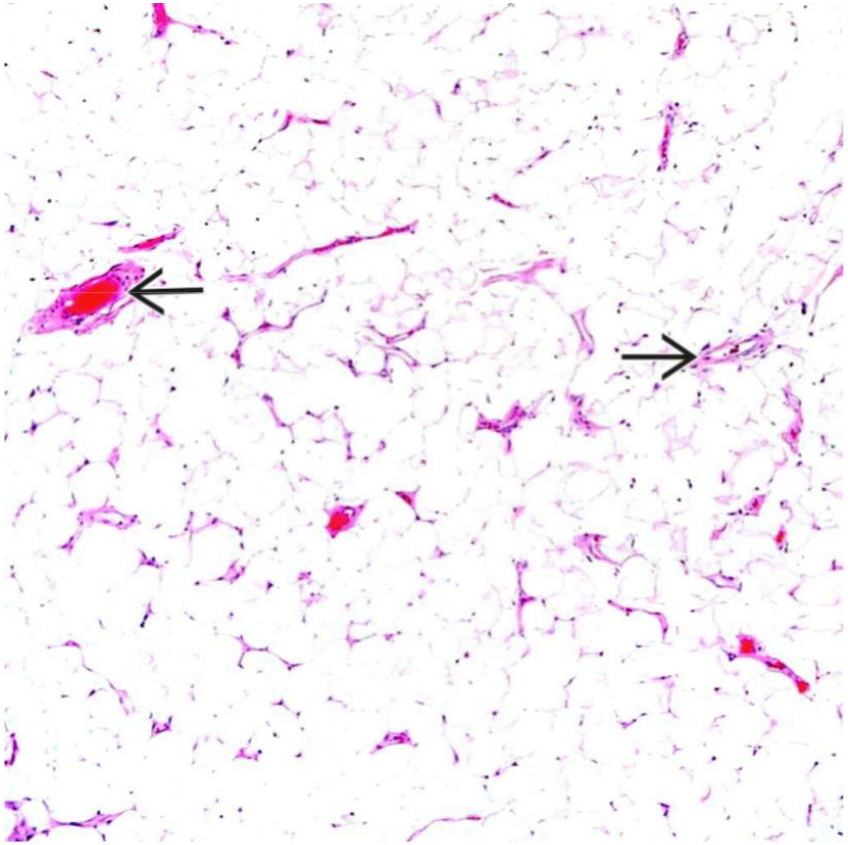
- Benign neoplasm of mature adipocytes (white fat)
- Most common soft tissue overall
- Superficial lipomas most common in upper back, shoulder, neck and abdomen
- Surgical excision curative
  - Intramuscular lipoma can recur (15% rate)
- Lipomatosis: Diffuse & regional overgrowth of mature adipose tissue

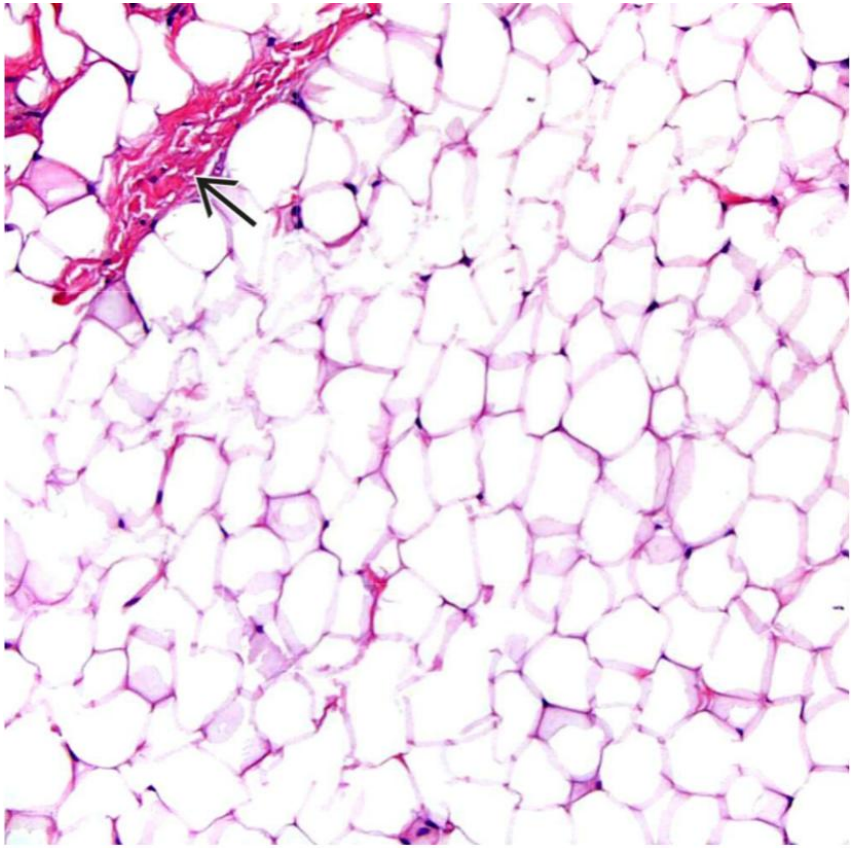
Macroscopic

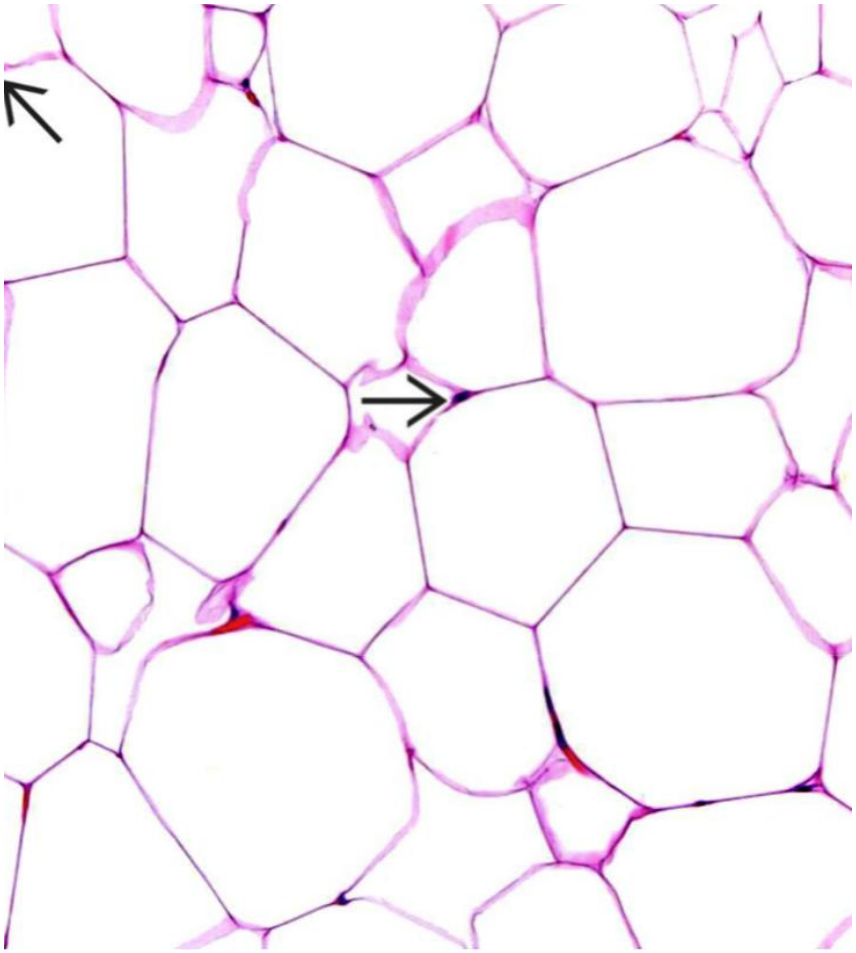


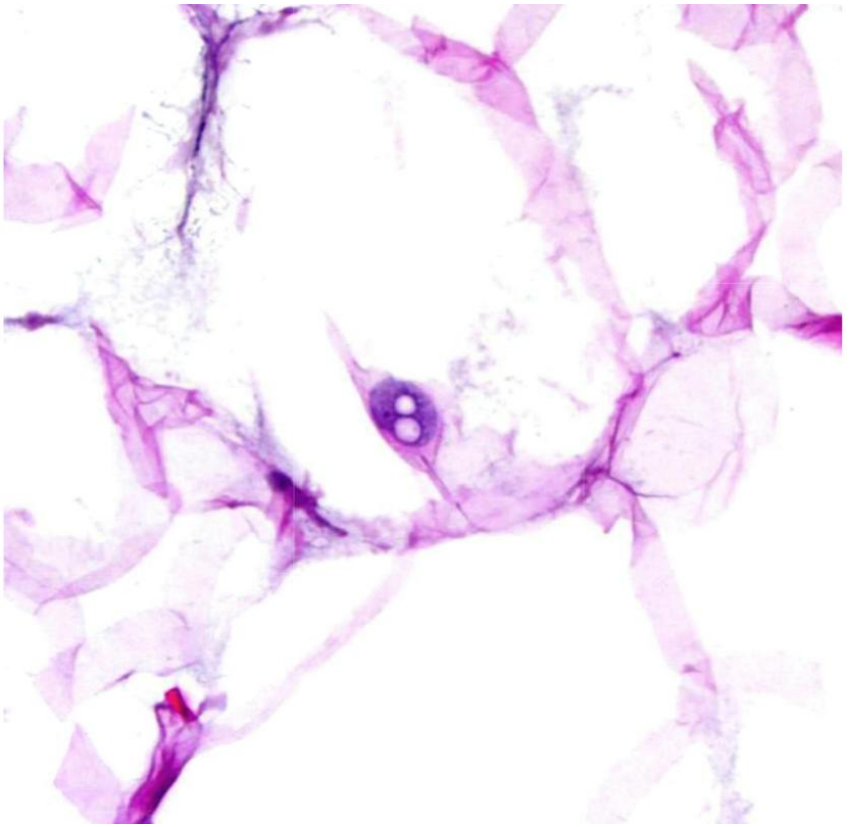


Microscopic

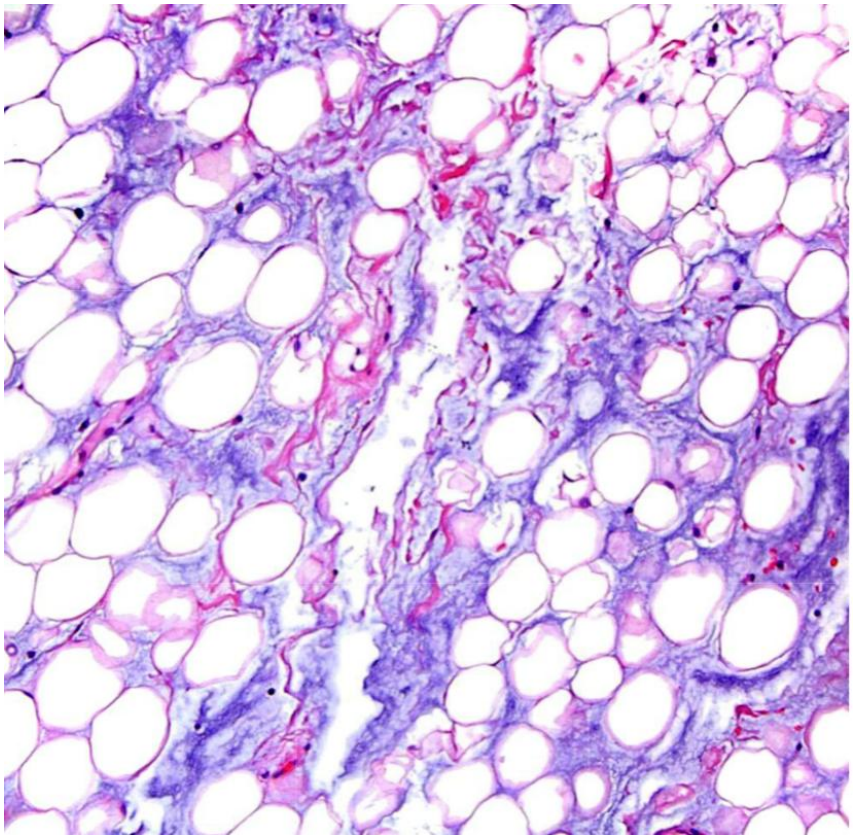




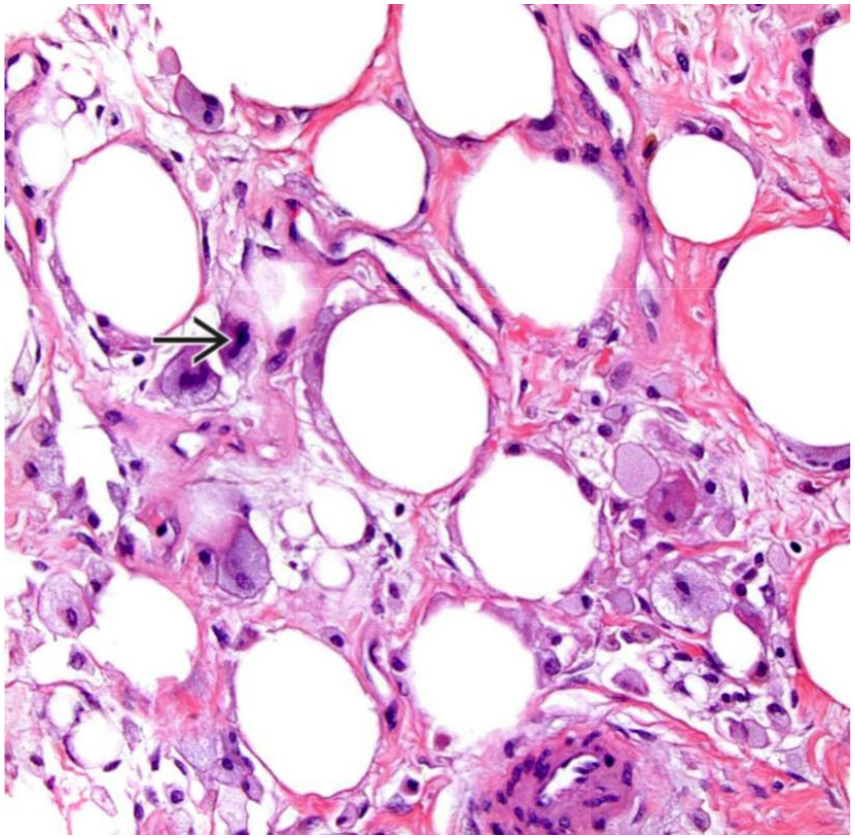




Myxoid changes



Fat necrosis with histiocytes



Ancillary tests

- Aberrations involving at 12q13-15 are most common

- No amplification of MDM2 gene

Differential diagnosis

- Atypical lipomatous tumor/well-differentiated liposarcoma
- Spindle cell lipoma
- Myxoid liposarcoma
- Hibernoma
- Lipomatosis of nerve

Angiolipoma

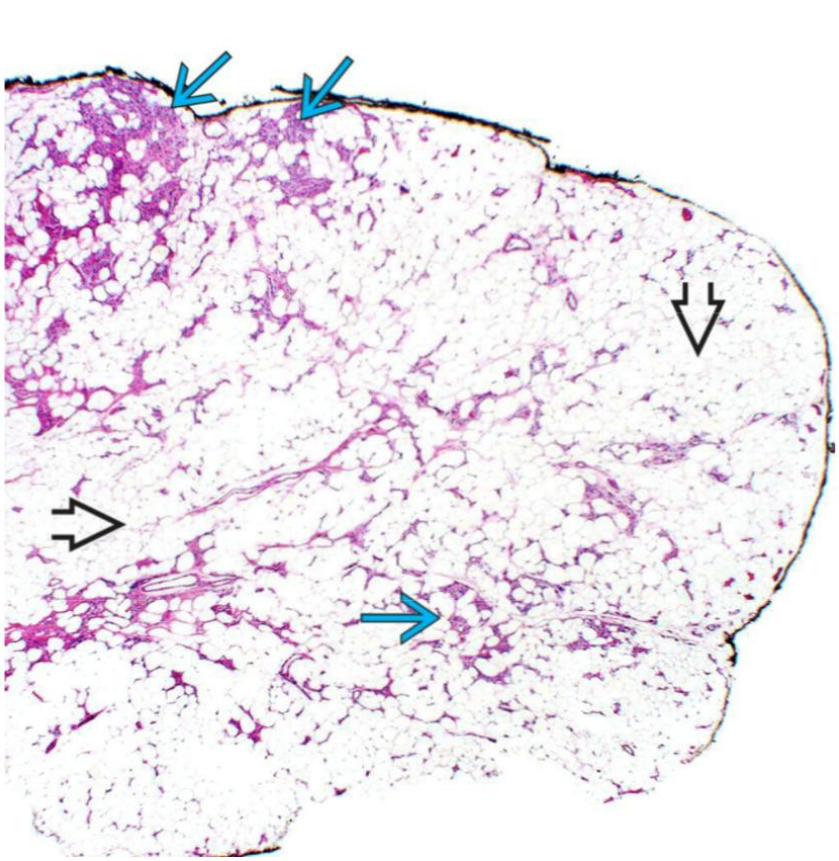
- Benign tumor consisting of **mature adipocytes** and thin-walled **blood vessels** with intraluminal **fibrin thrombi**

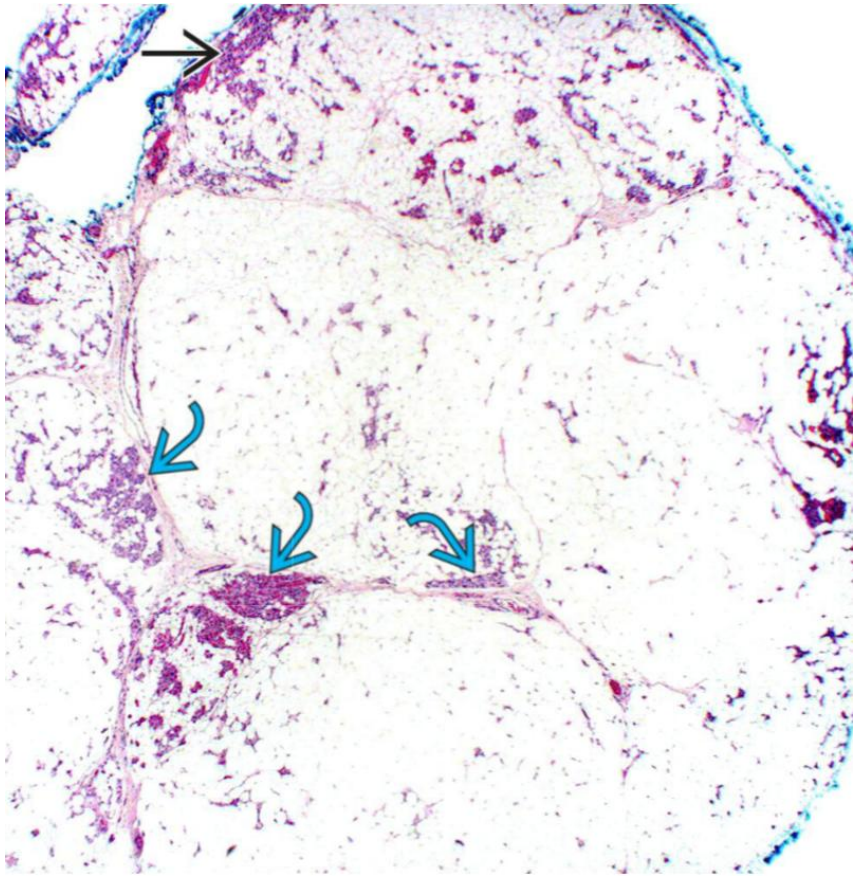
- Most are sporadic; rare familial cases

Clinical issues

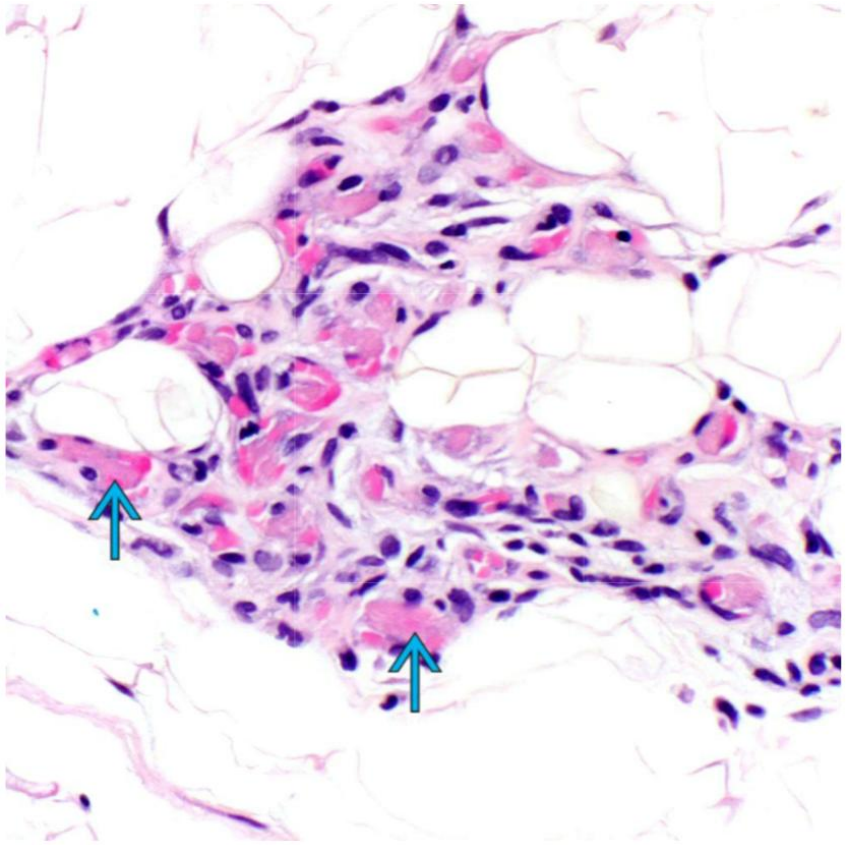
- Commonly in young adults
  - Male predominance
- Forearm, trunk, and upper arm most common sites
- Painful tender subcutaneous nodules
  - Often multiple
- Treatment: Simple surgical excision
- Excellent prognosis
  - Local recurrence very rare
  - No risk of malignant transformation

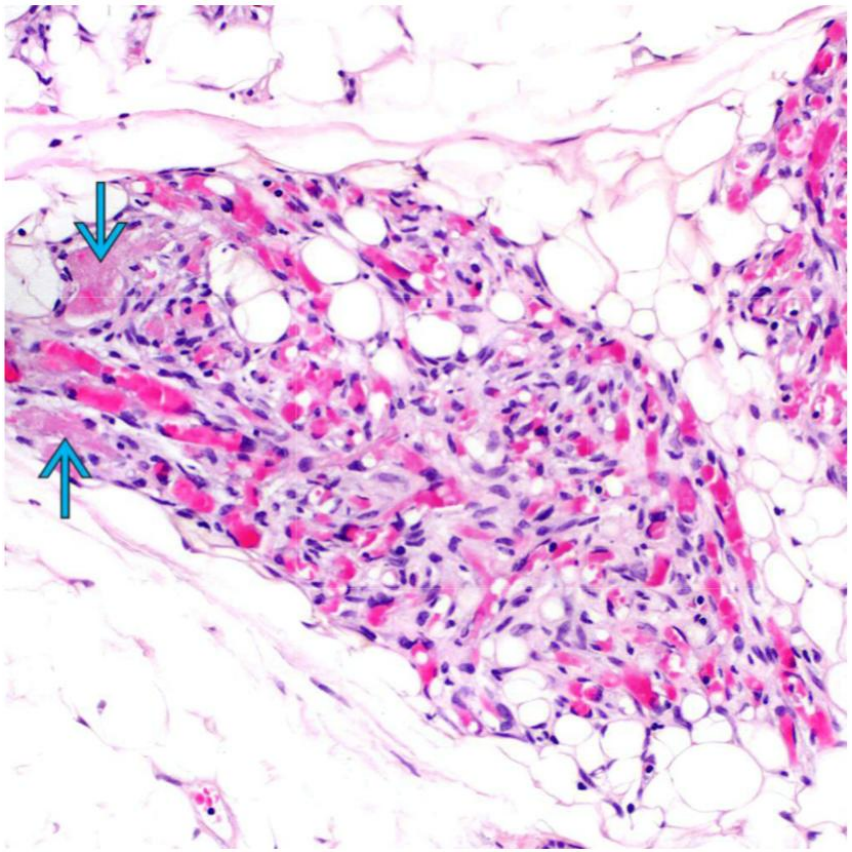
Microscopic



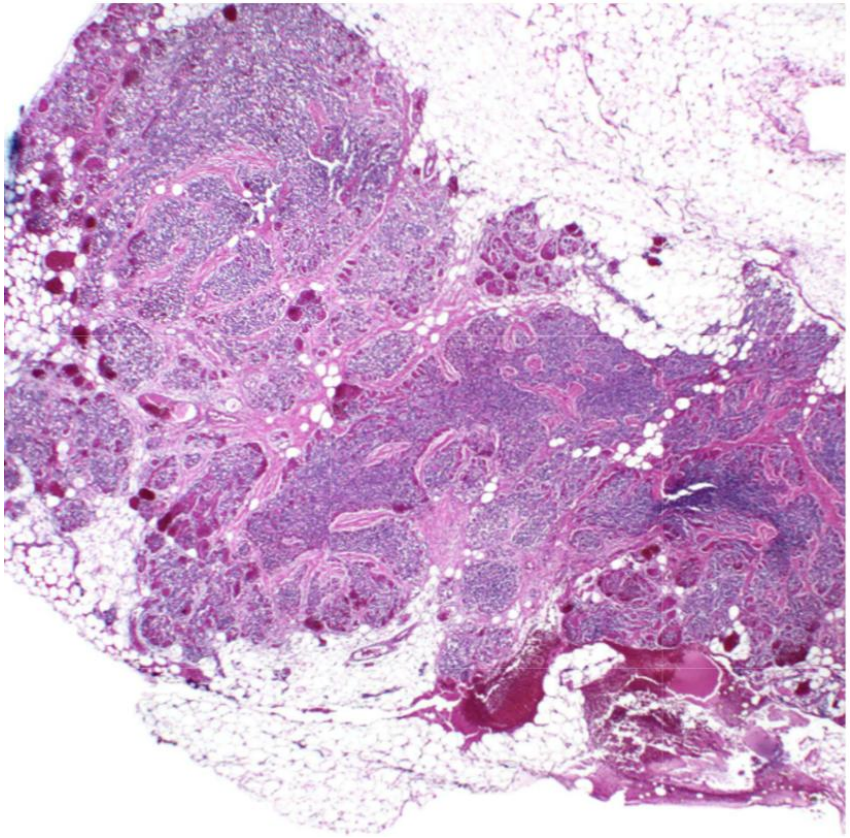


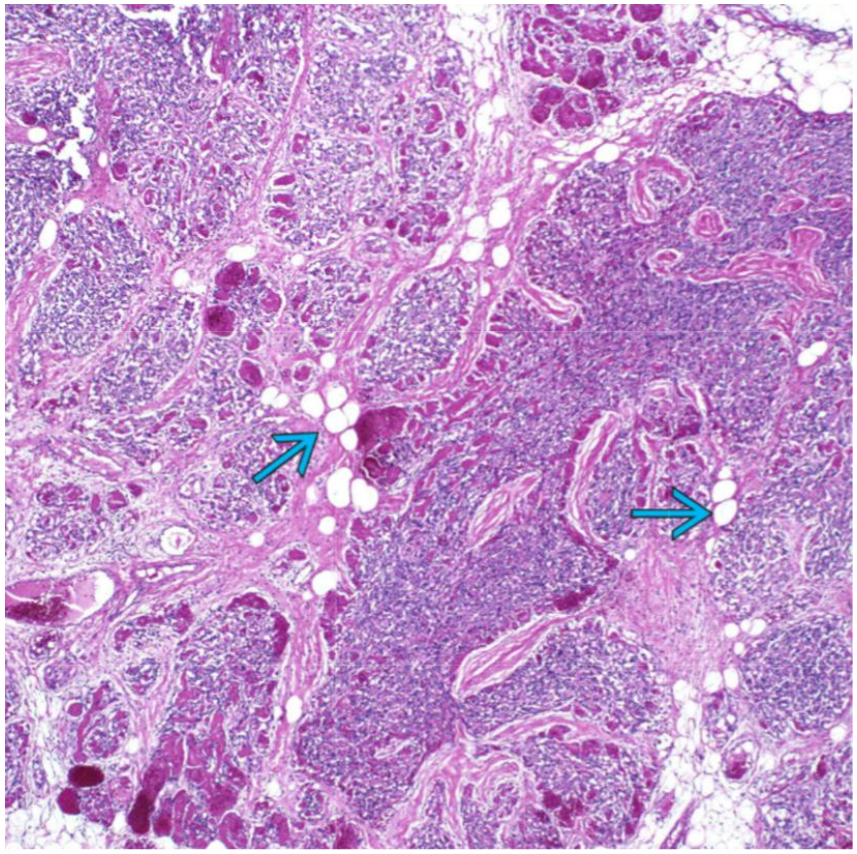
Fibrin thrombi





Cellular angiolipoma





Differential diagnosis

- Lipoma
- Intramuscular hemangioma
- Kaposi sarcoma
- Spindle cell hemangioma
- Angiomyolipoma

Spindle cell/Pleomorphic lipoma

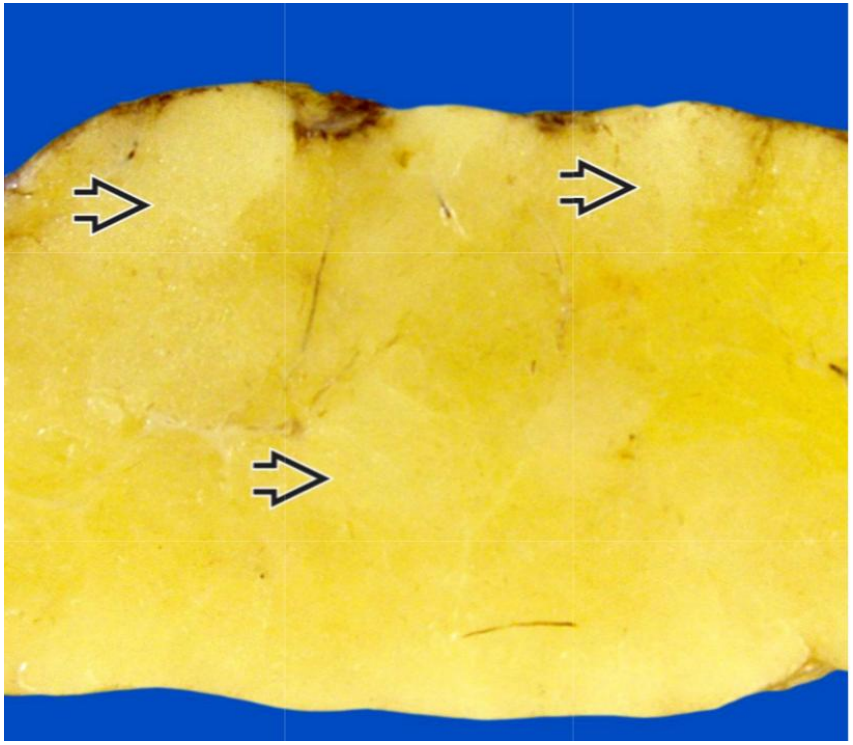
- Benign adipocytic tumor with variable admixture
  - spindle cells
  - “ropey” collagen
  - mature adipose tissue,
  - multinucleate tumor giant cells

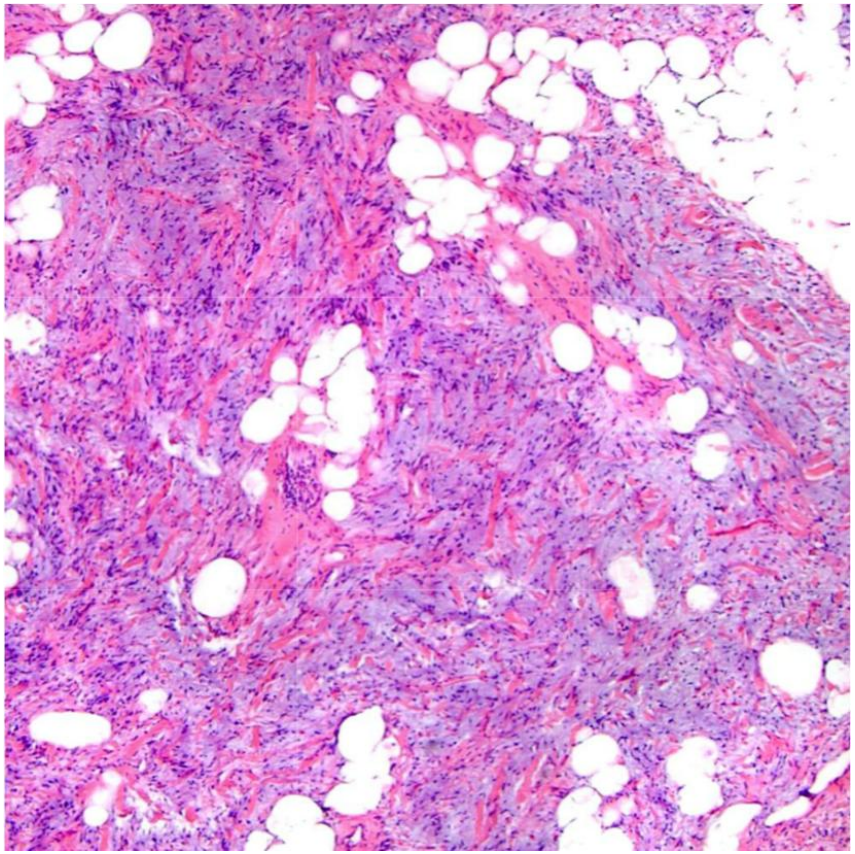
- Spindle cell lipoma (SCL) and pleomorphic lipoma (PL) are morphologic variations of same neoplasm

Clinical issues

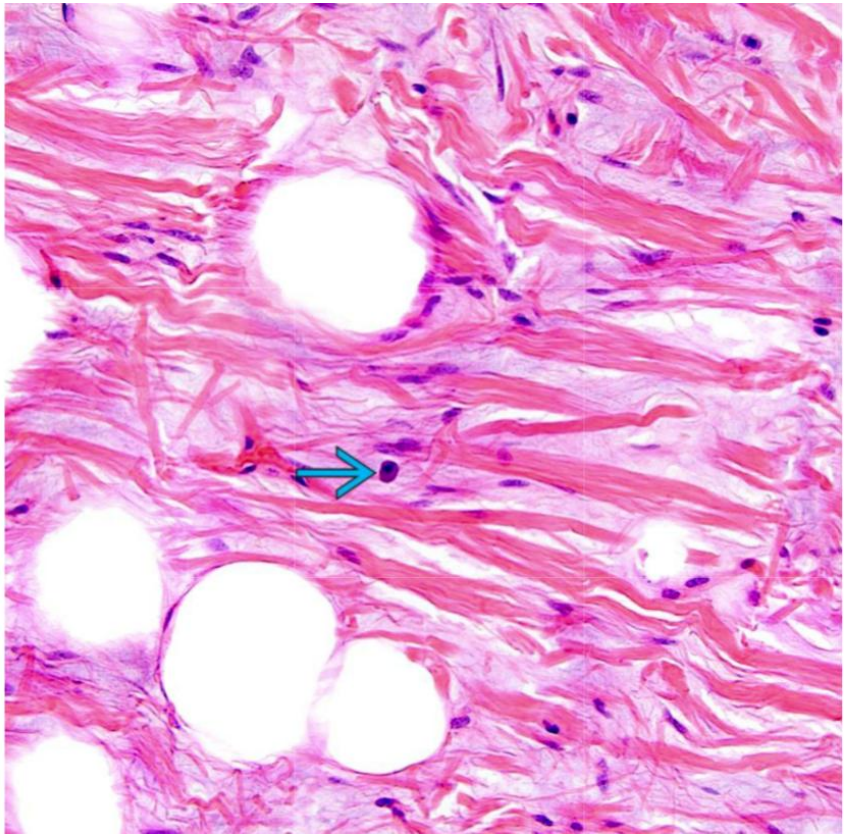
- Most common in older (> 50 years) men
- Typically arise in shoulder, posterior neck, or back
- Benign; conservative surgical excision only

Macroscopic and Microscopic

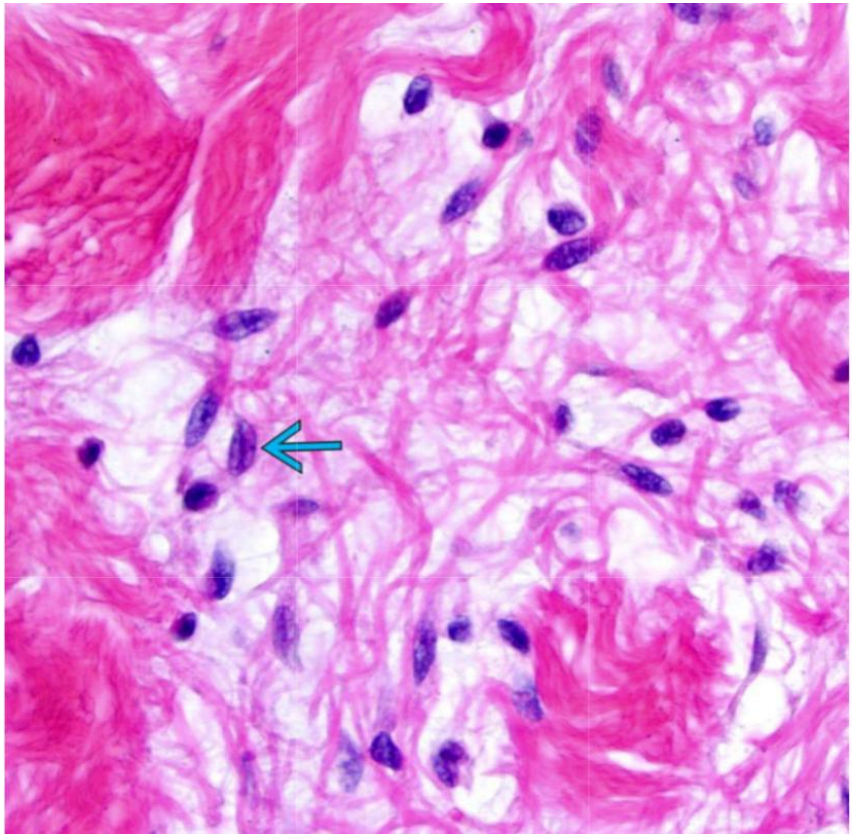




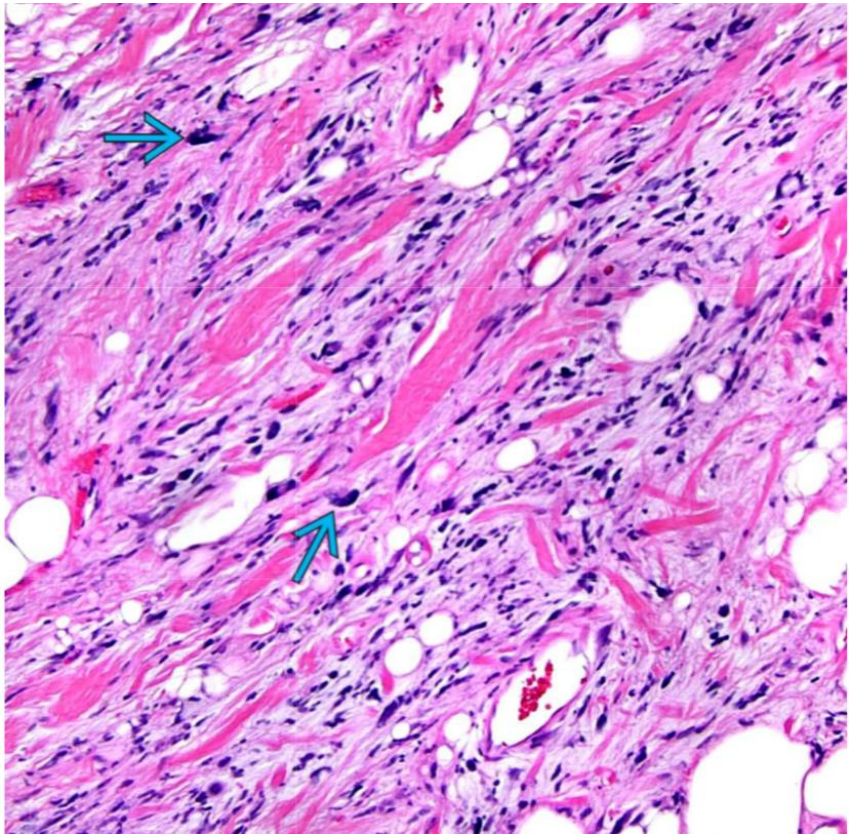
Ropey collagen and mast cells



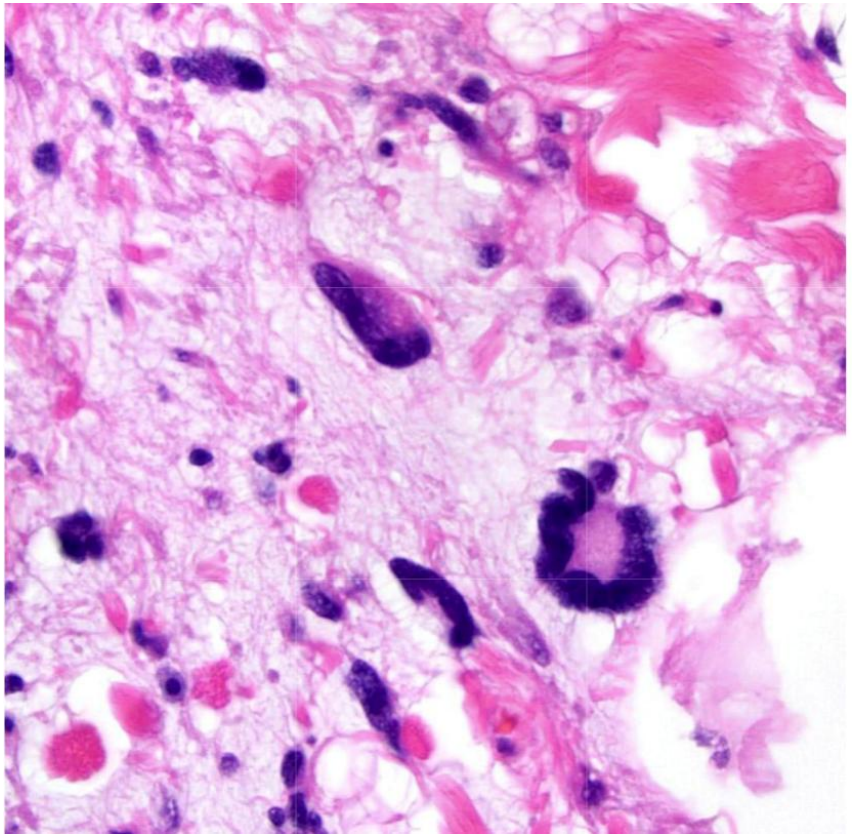
Bipolar, bland spindle cells



Pleomorphic cells with degenerate atypia



“Floret cells”

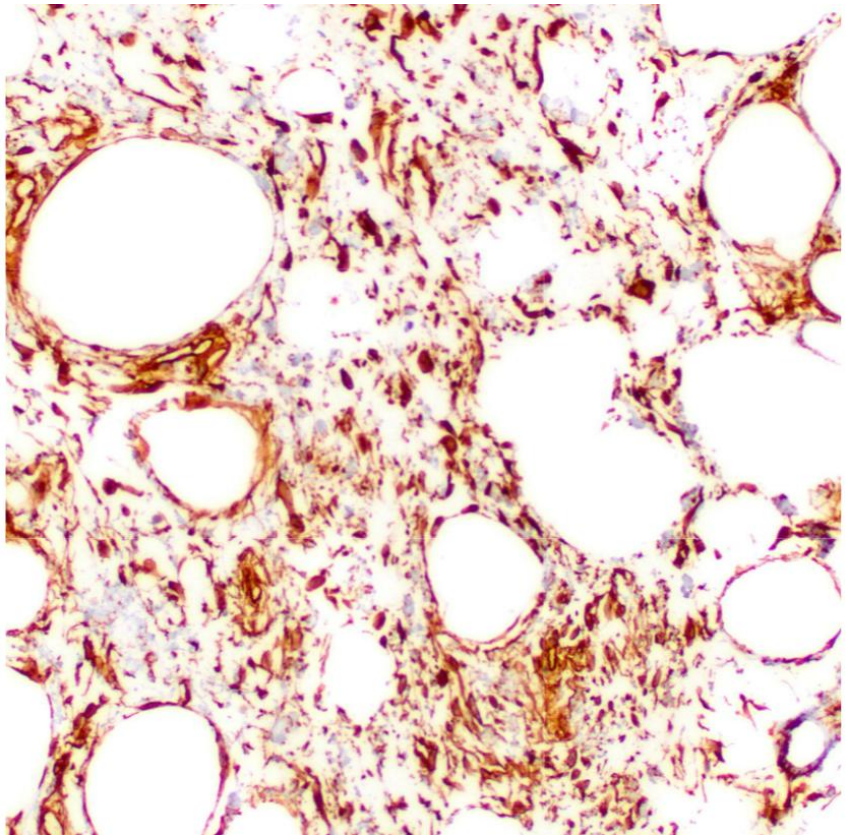


Ancillary tests

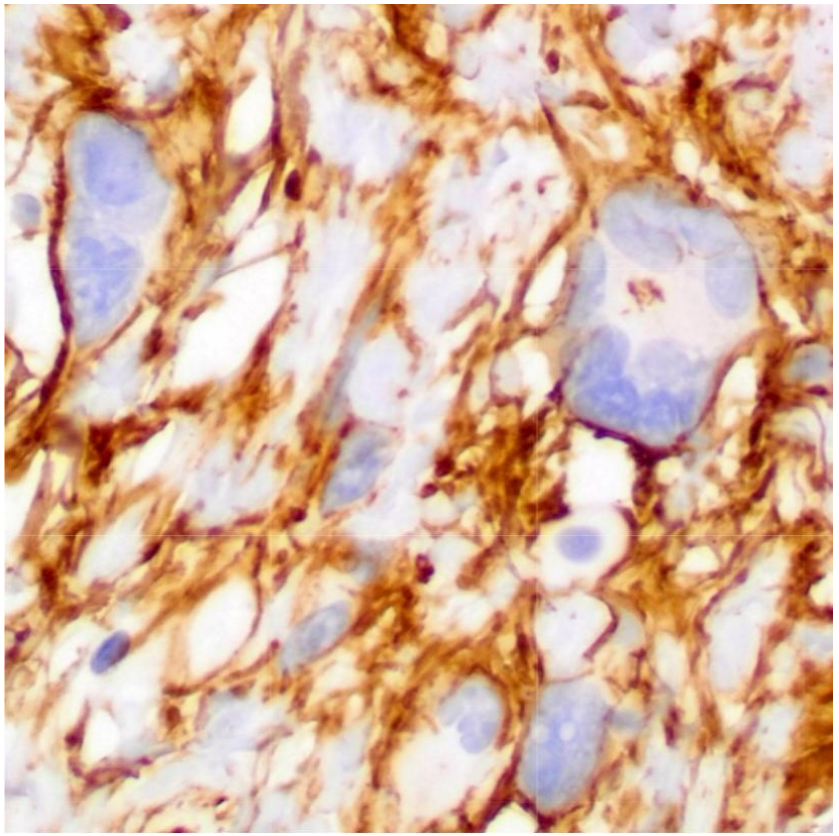
- CD34(+); loss of nuclear Rb expression
- Molecular: Deletion of RB1 (13q14)

Microscopic

CD34



CD34 and “floret cells”



Differential Diagnosis

- Atypical lipomatous tumor
- Neurofibroma
- Myxoid liposarcoma
- Solitary fibrous tumor

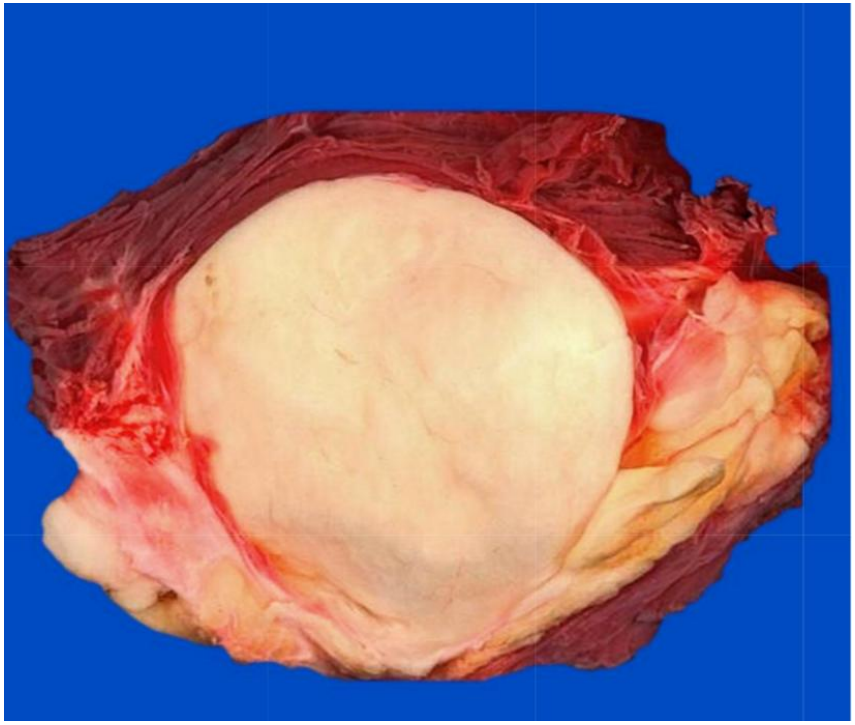
Atypical Lipomatous Tumor/Well Differentiated Liposarcoma

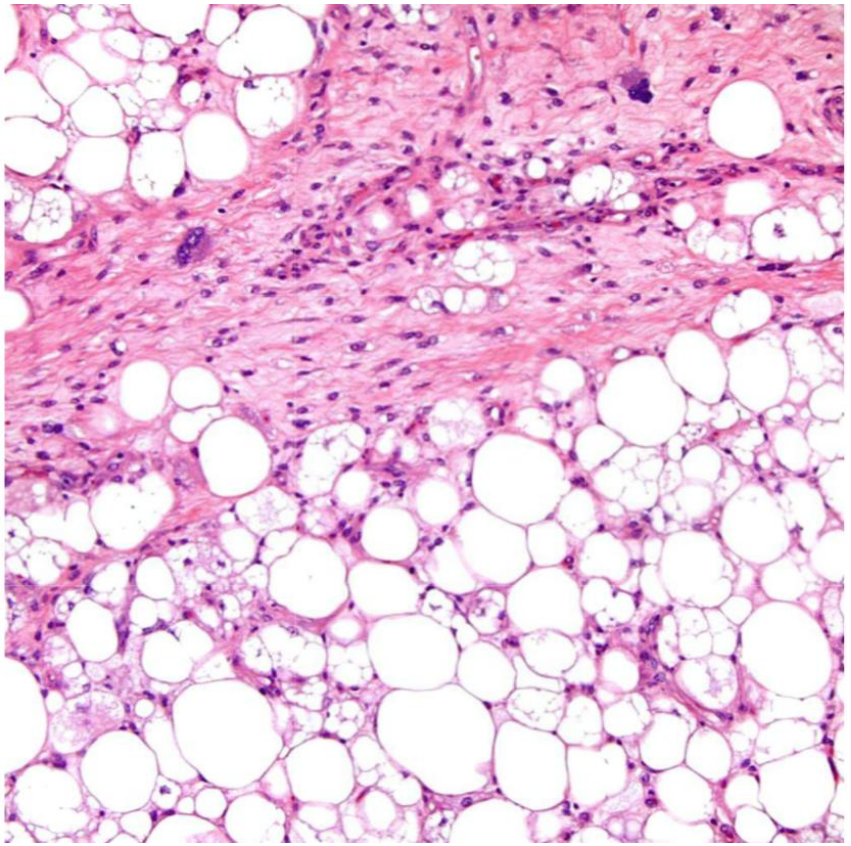
- Locally aggressive mesenchymal neoplasm
  - atypical adipocytes and with least focal nuclear atypia in adipocytes &/or stromal cells

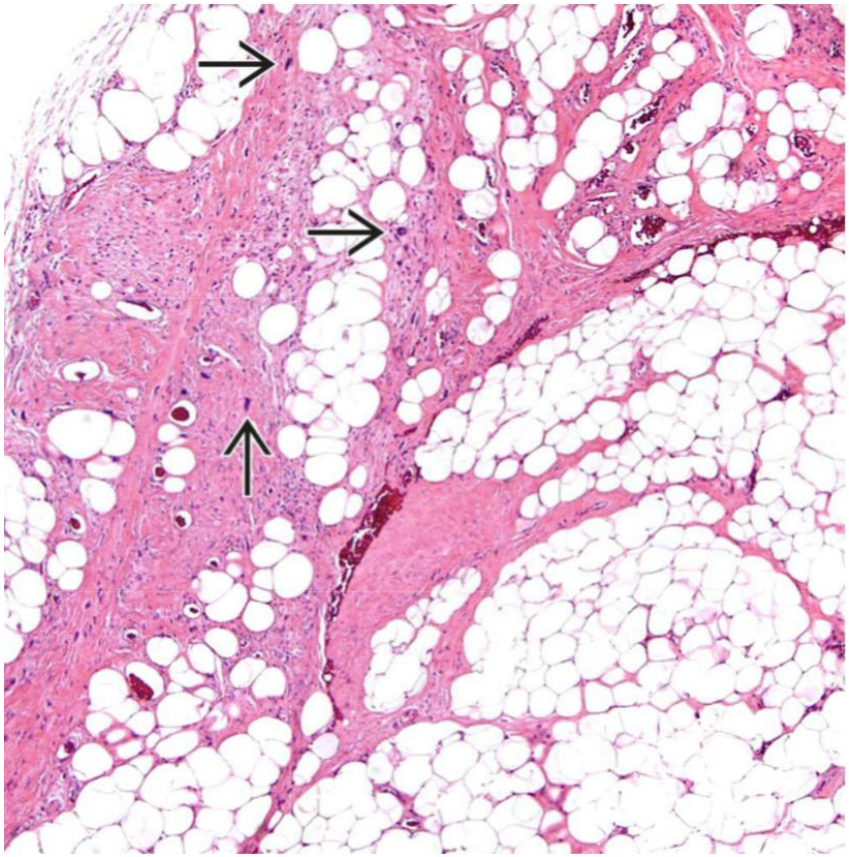
Clinical Issues

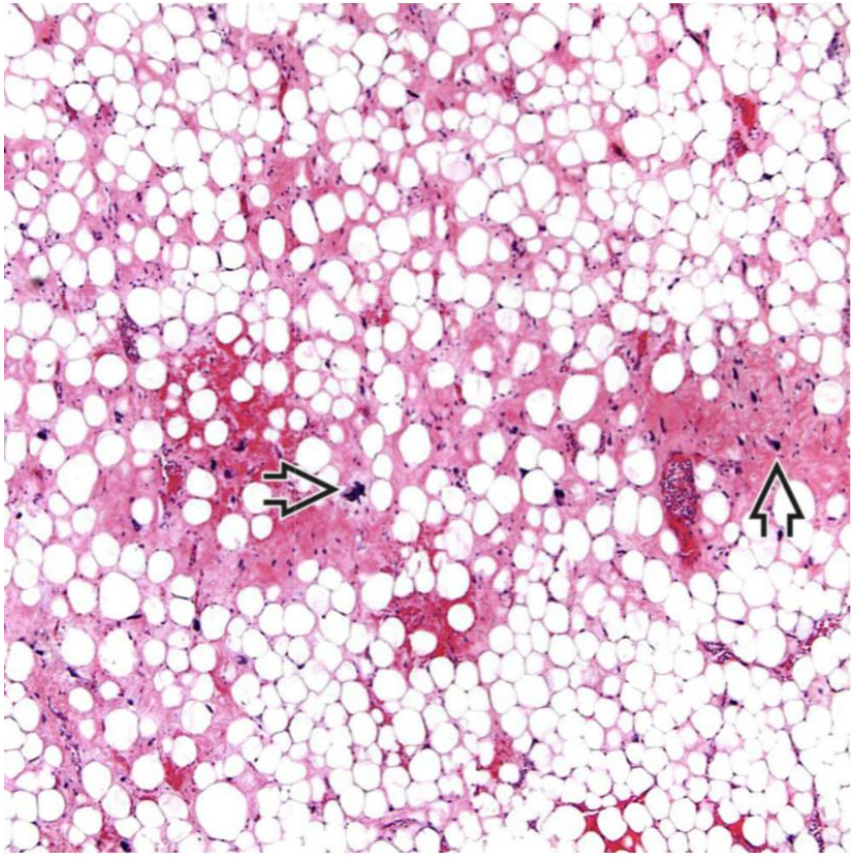
- Most common form of liposarcoma (40-45% of cases)
- Most occur in middle-aged to elderly adults
- Extremities, retroperitoneum, abdominal cavity, paratesticular region, mediastinum
- Treatment: Complete surgical excision with negative margins
- Anatomic site is most important prognostic factor
  - Low risk of recurrence and dedifferentiation in extremities
  - More significant risk of recurrence/dedifferentiation in body cavities
  - No metastatic potential

Macroscopic and Microscopic

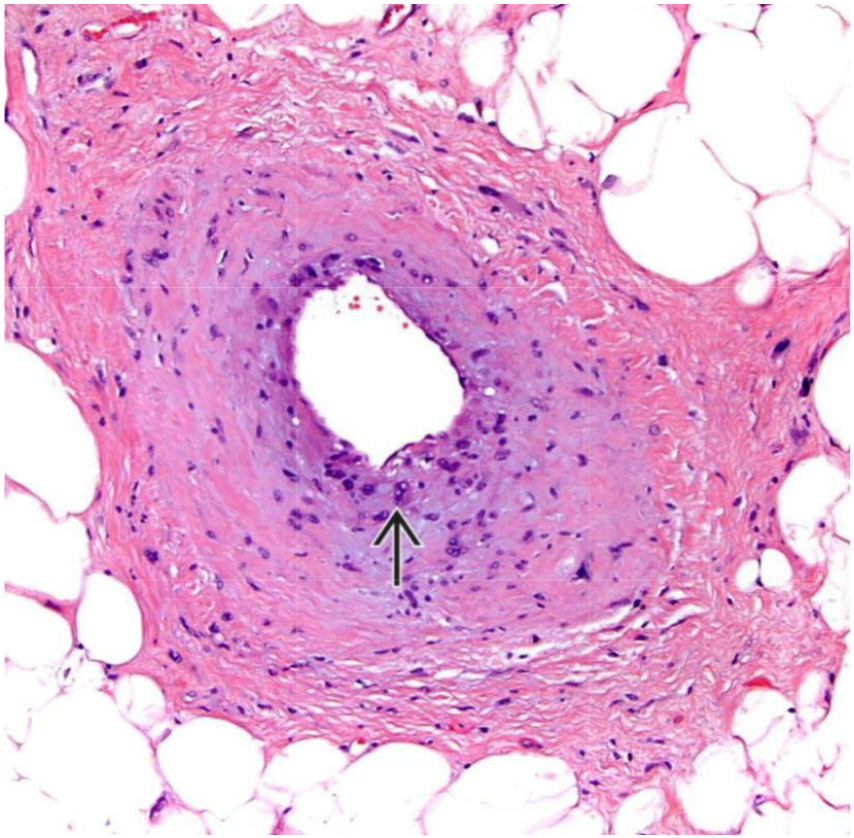




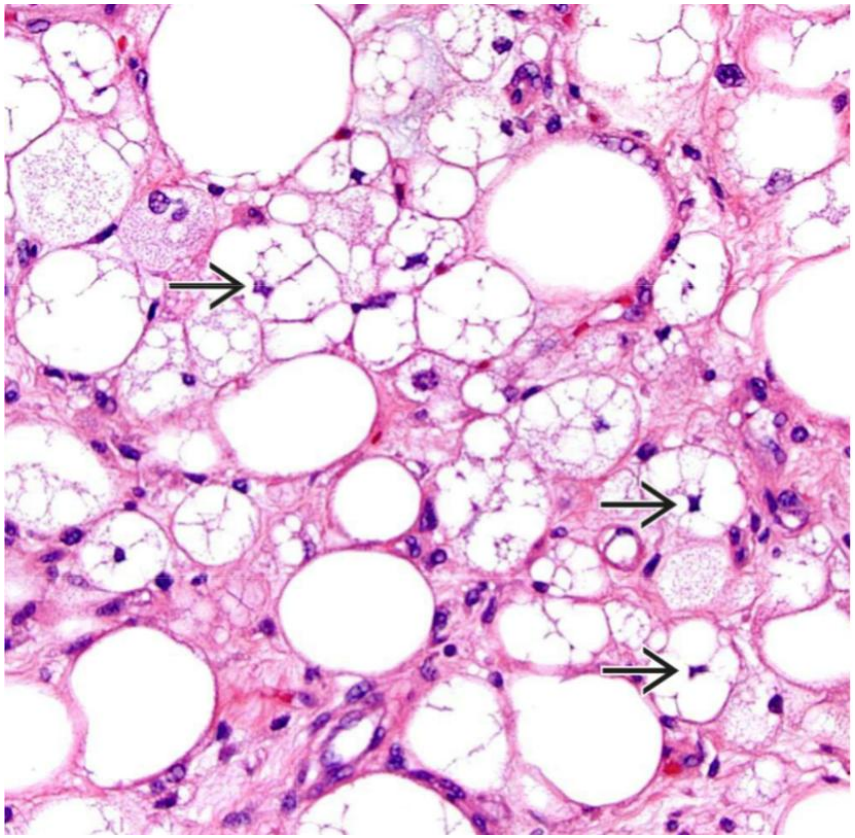




Atypical cells in vessel wall



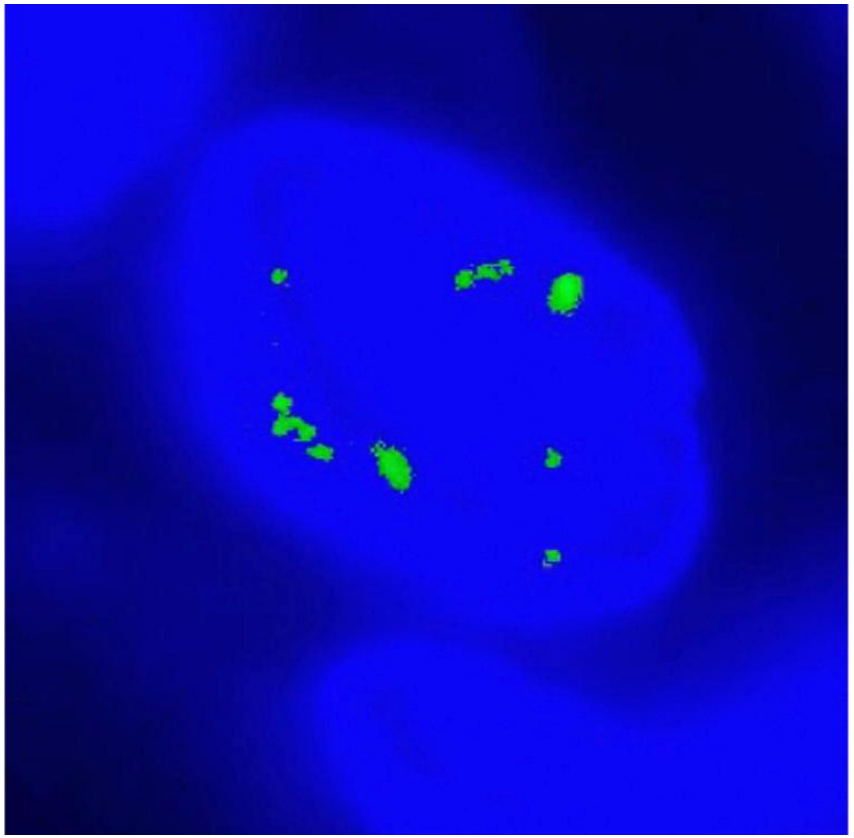
Lipoblasts



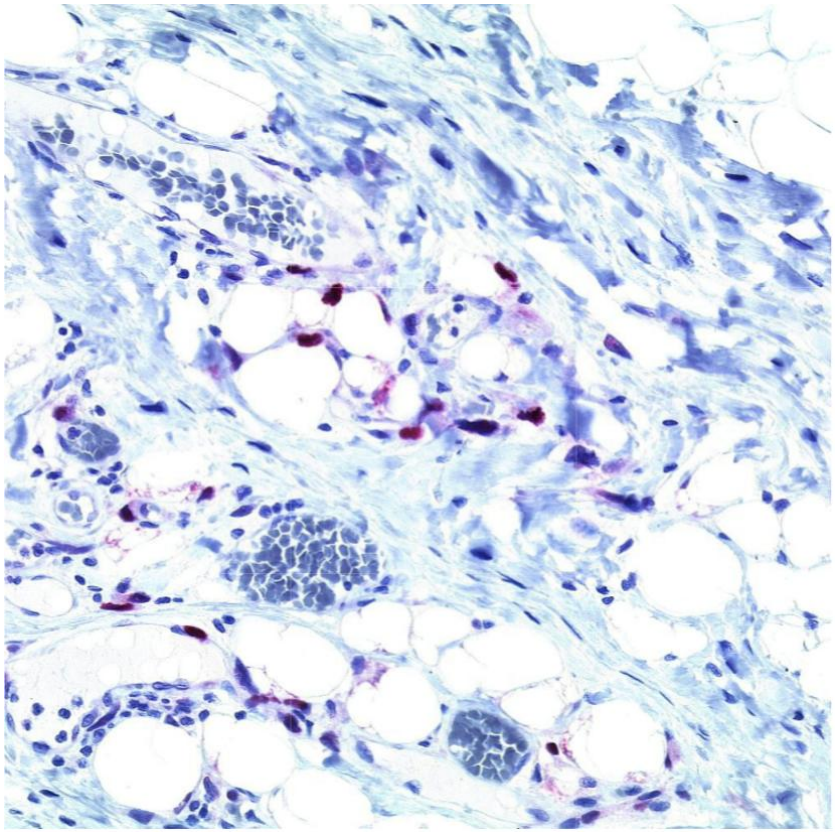
Ancillary Tests

- Overexpression of nuclear MDM2 and CDK4 by IHC
- Molecular: **MDM2 amplification**
- Supernumerary ring and giant marker chromosomes

FISH with *MDM2* amplification



IHC for *MDM2*



Differential Diagnosis

- Lipoma
- Pleomorphic lipoma
- Dedifferentiated liposarcoma
- Massive localized lymphedema

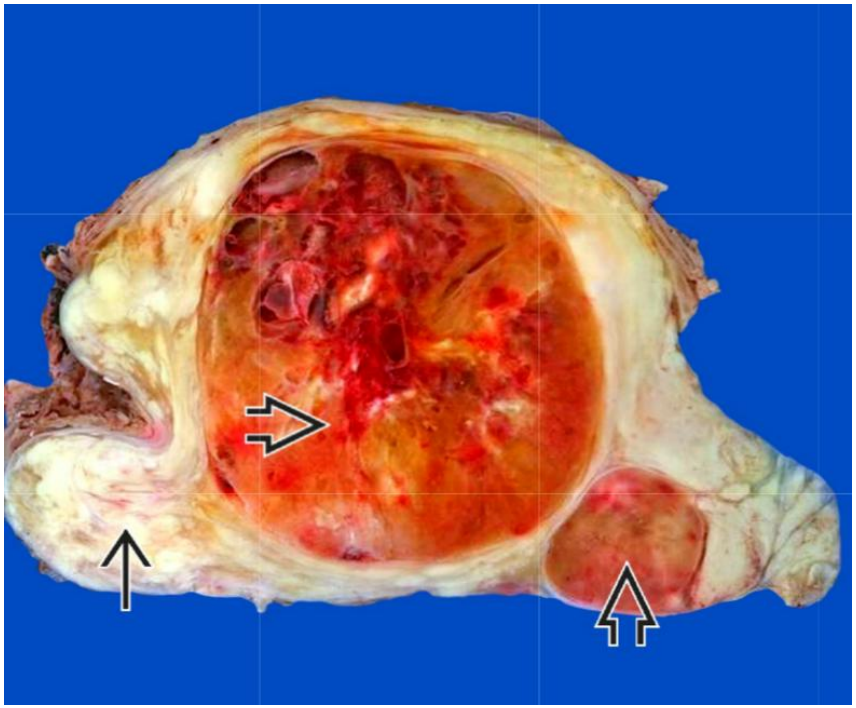
Dedifferentiated Liposarcoma

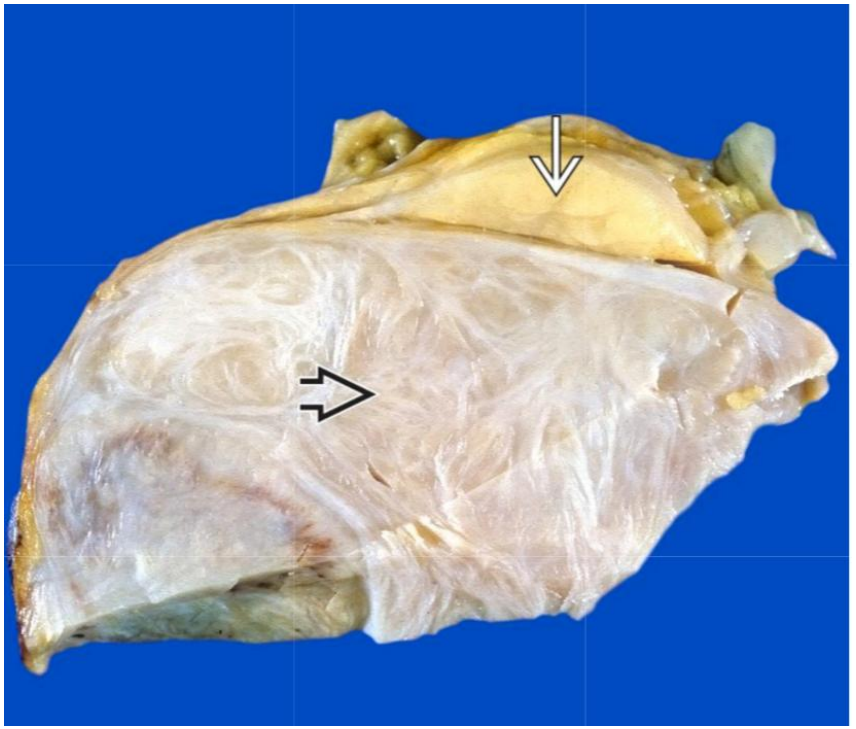
- Malignant, generally **nonlipogenic sarcoma** of variable histologic grade
- Often arising in association with identifiable component of atypical lipomatous tumor (ALT)/well-differentiated liposarcoma (WDLPS)

Clinical Issues

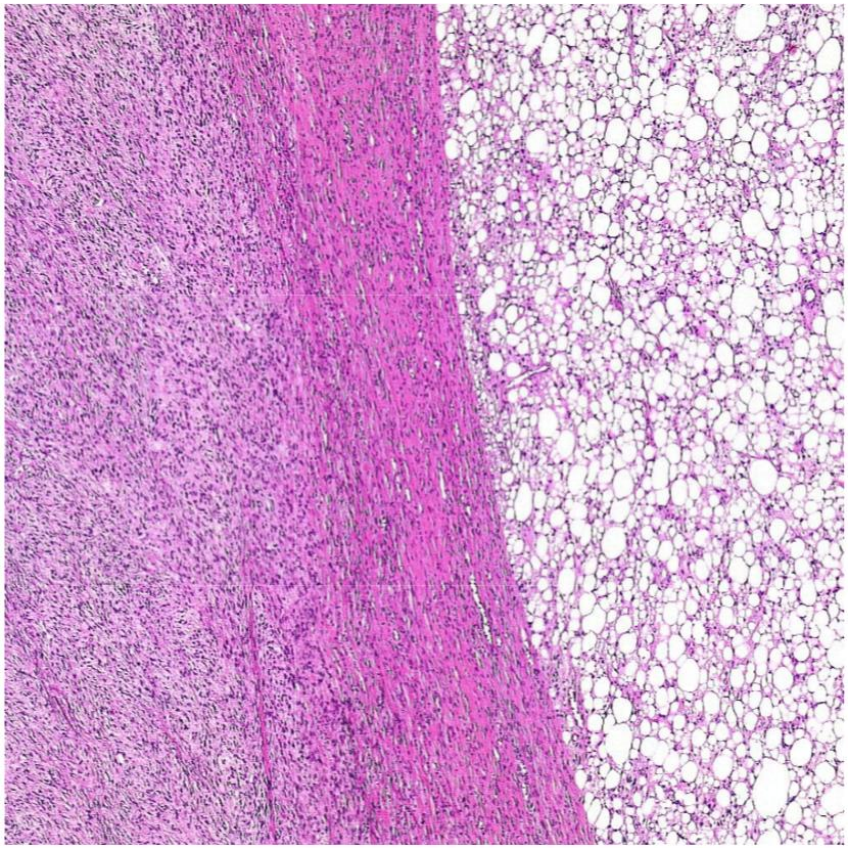
- Dedifferentiation occurs in up to 10% of ALT/WDLPS
- Vast majority (90%) arise de novo
- Middle-aged to elderly adults
- Most common in retroperitoneum/abdominal cavity
  - Also spermatic cord, trunk, extremities, head/neck
- Treatment: Complete surgical resection with negative margins
  - Anatomic location is most important prognostic factor
  - Local recurrence in ~ 40% of cases
  - Distant metastases observed in 15-20% of cases

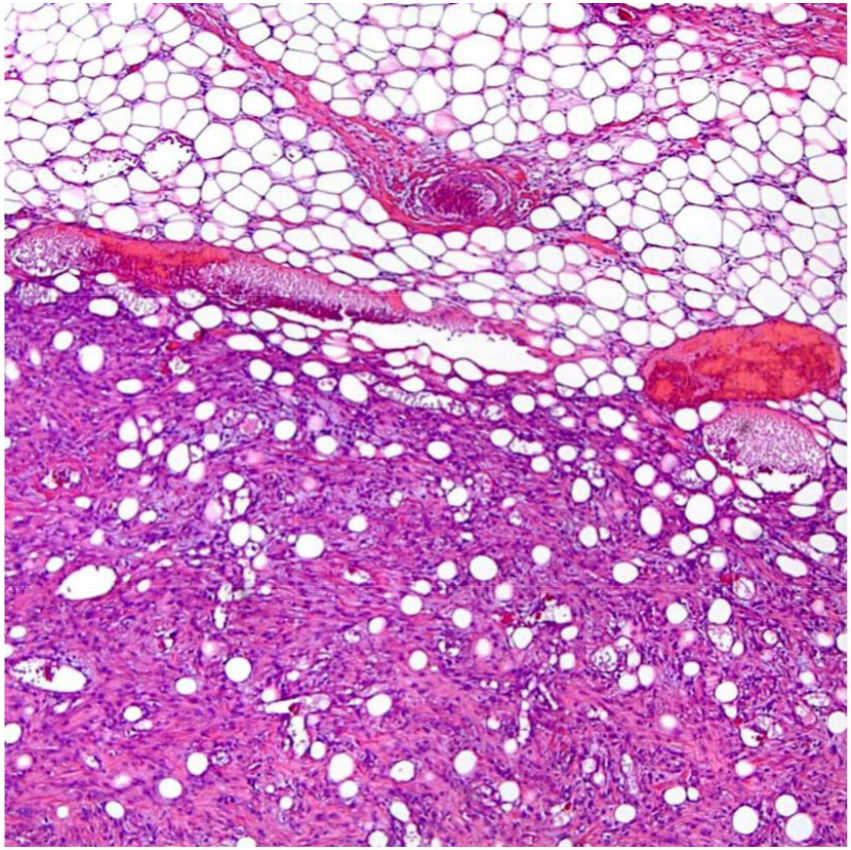
Macroscopic

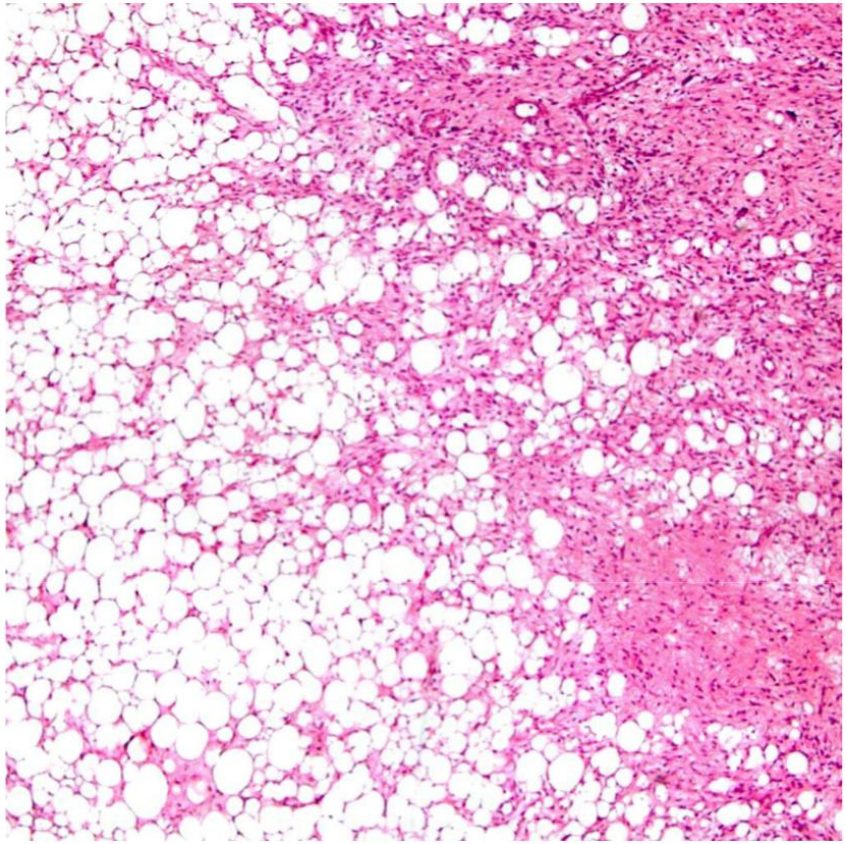


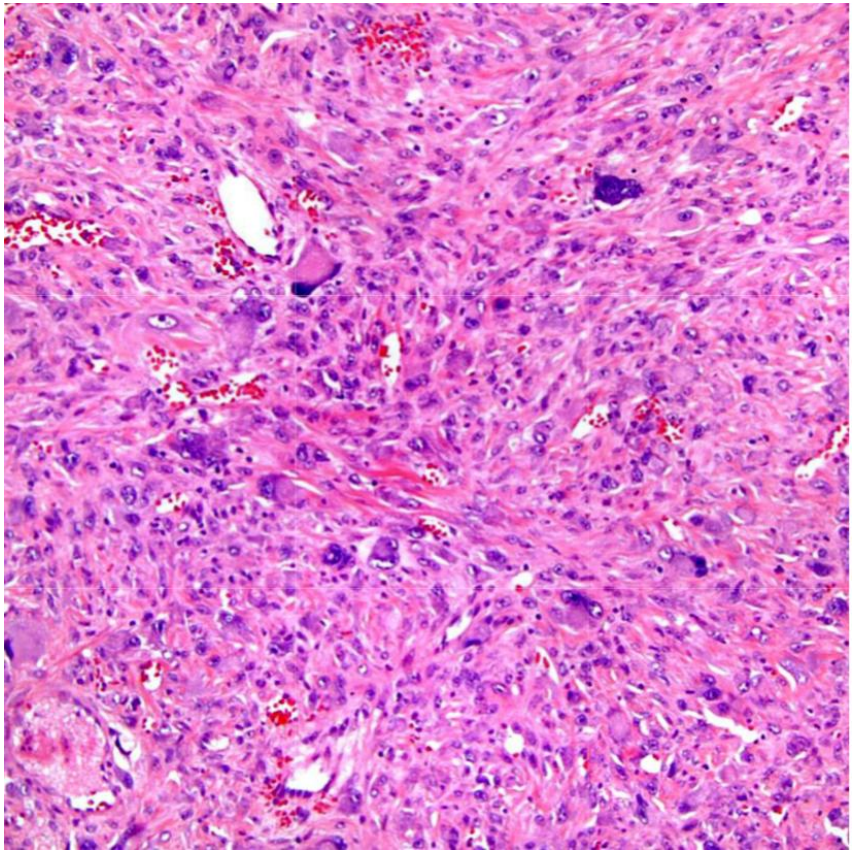


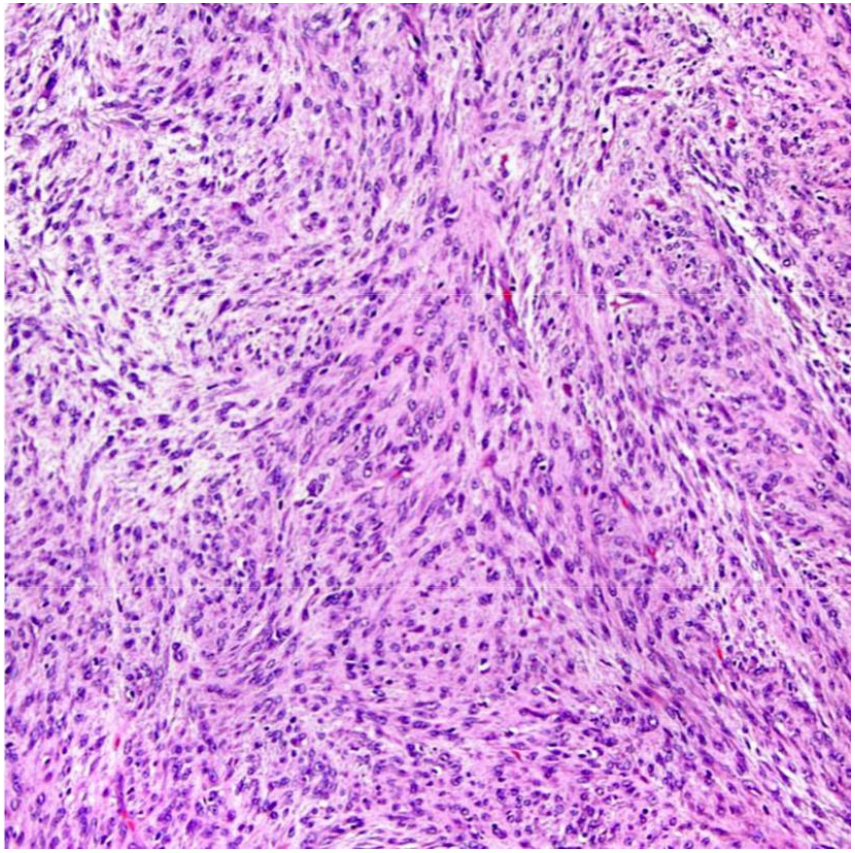
Microscopic

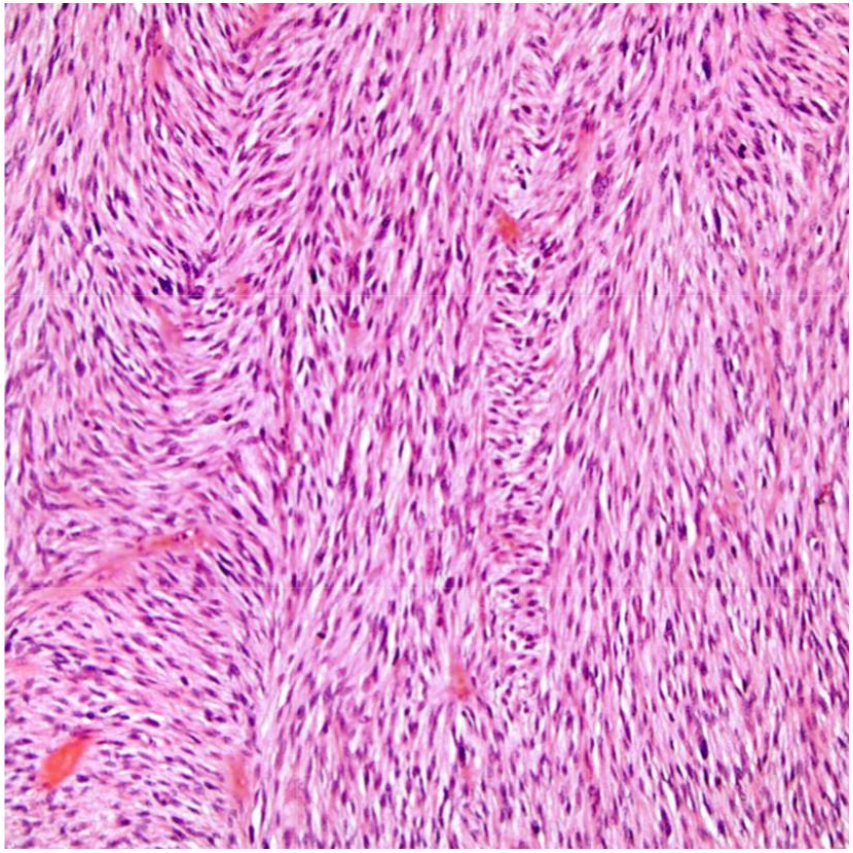








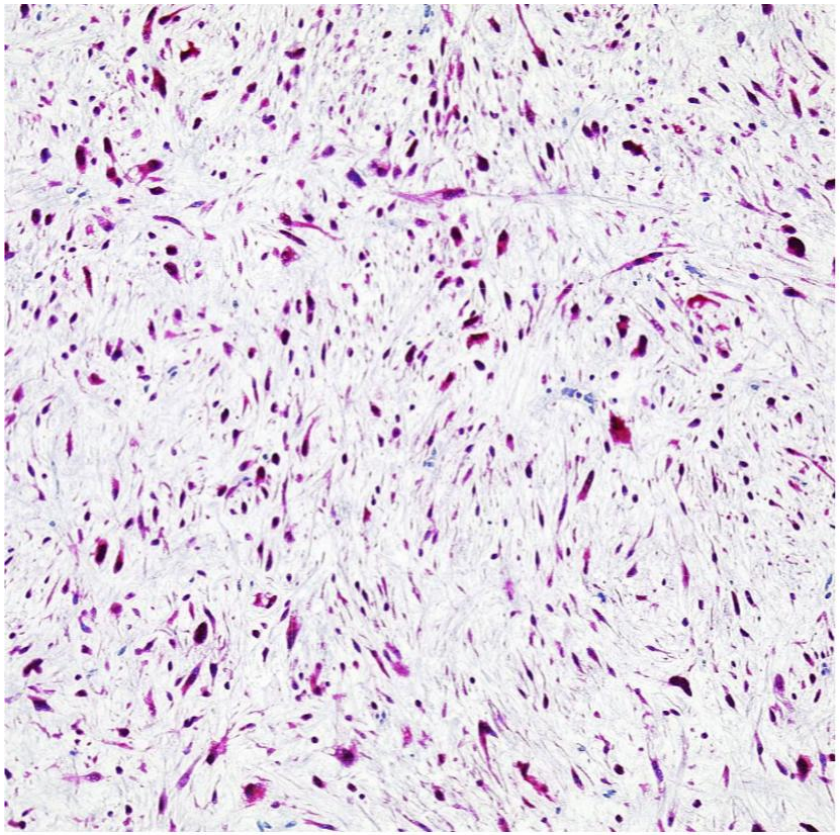




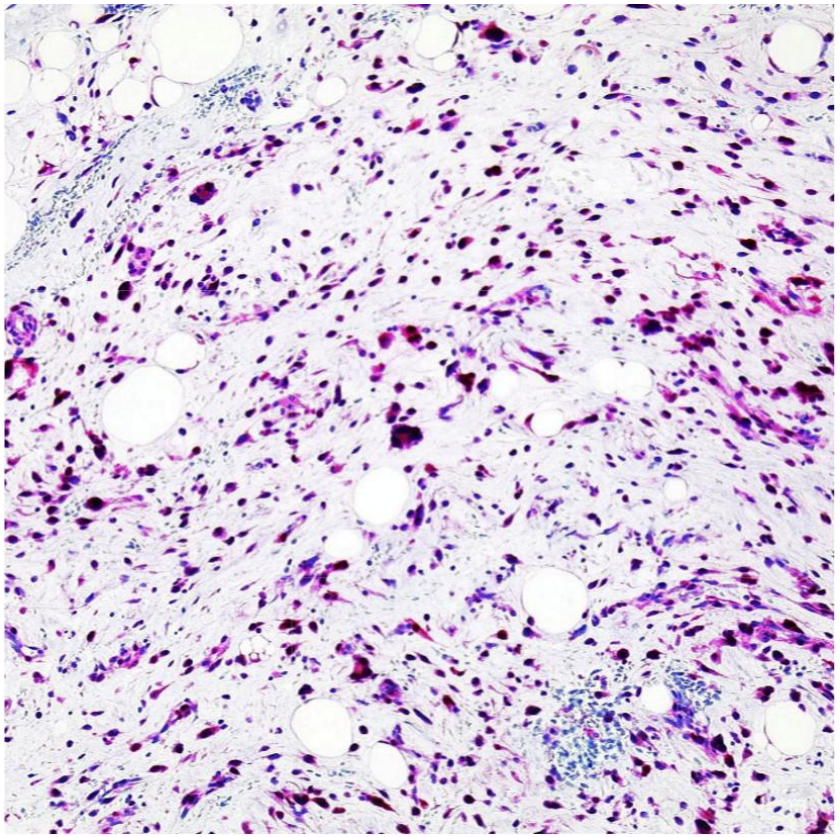
Ancillary Tests

- Diffuse nuclear MDM2(+) and CDK4(+)
- Molecular: Overexpression of MDM2

IHC for CDK4



IHC for MDM2



Differential Diagnosis

- Undifferentiated pleomorphic sarcoma
- Myxofibrosarcoma
- Pleomorphic liposarcoma

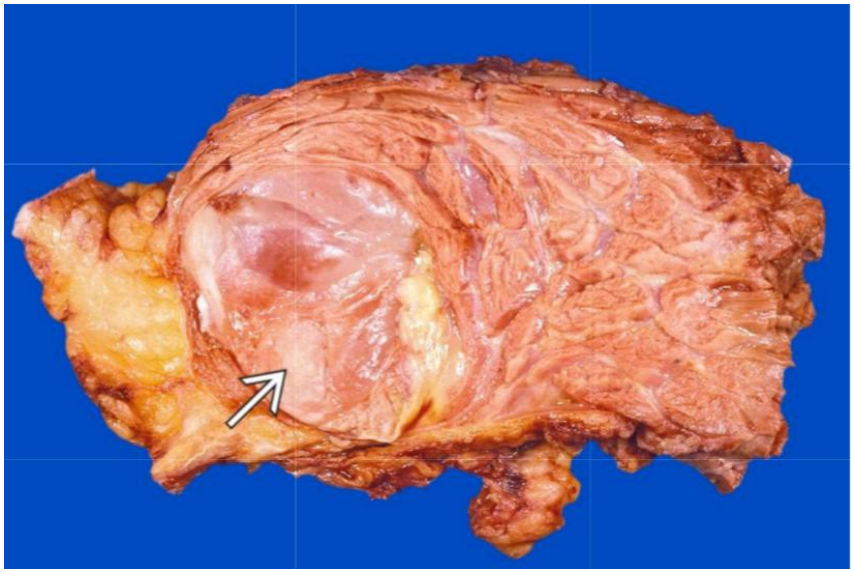
Myxoid Liposarcoma

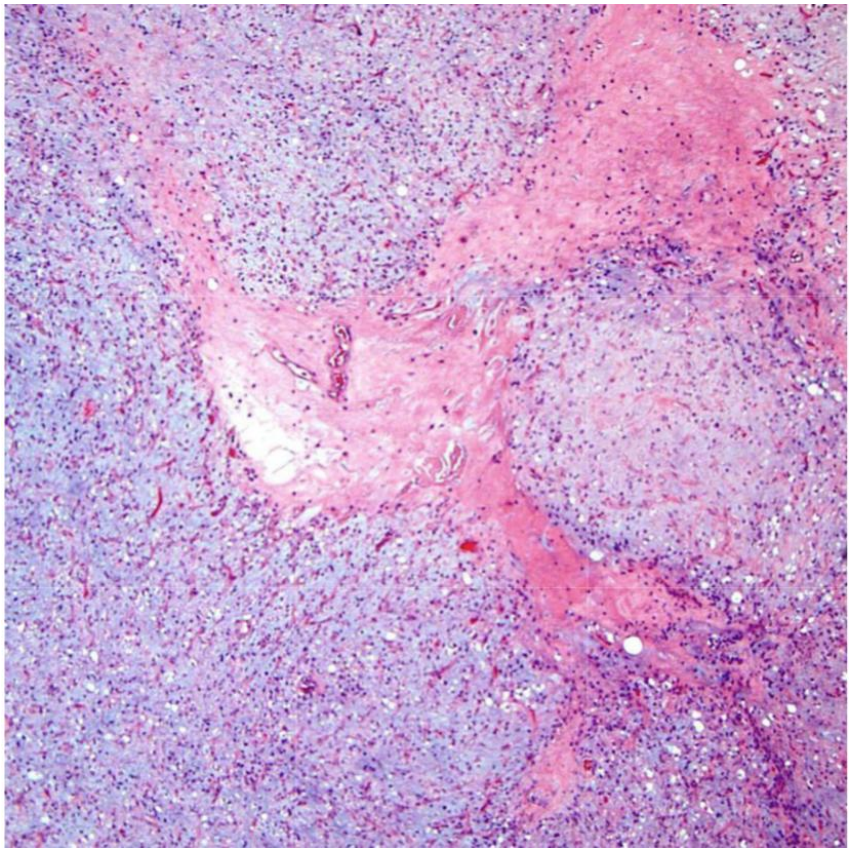
- Malignant neoplasm composed of **primitive nonlipogenic mesenchymal cells** and **variable number of lipoblasts**
- Prominent myxoid stroma with characteristic branching capillary vasculature

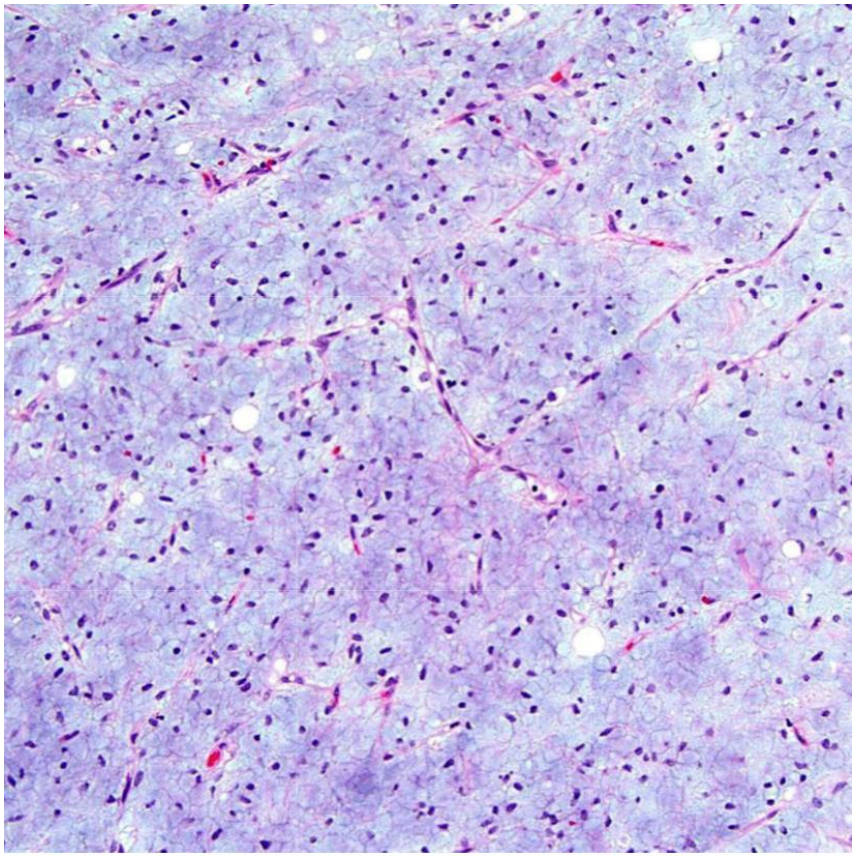
Clinical

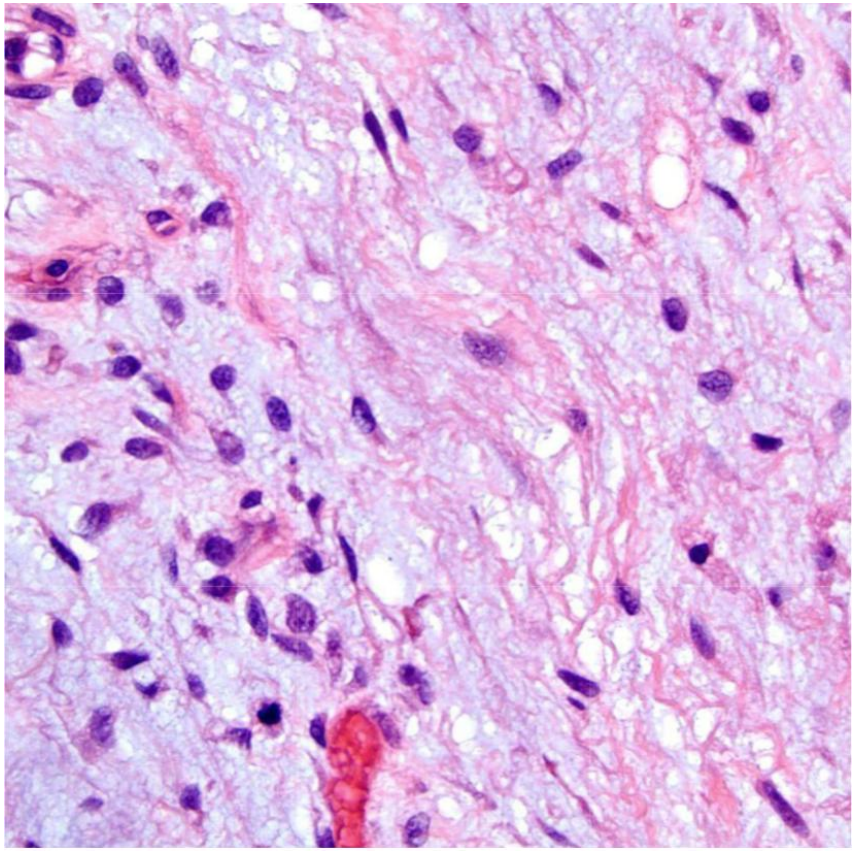
- Accounts for ~ 30-35% of all liposarcomas
- Most occur in young to middle-aged adults
- Usually arise in deep soft tissue of the extremities
- Treatment: Complete surgical resection with negative margins
- Local recurrence in ~ 30% of cases
- Metastatic risk varies by histologic grade (< 10% up to 60%)
- Presence of hypercellular (round cell) areas is most important histologic predictor of outcome

Macroscopic and Microscopic

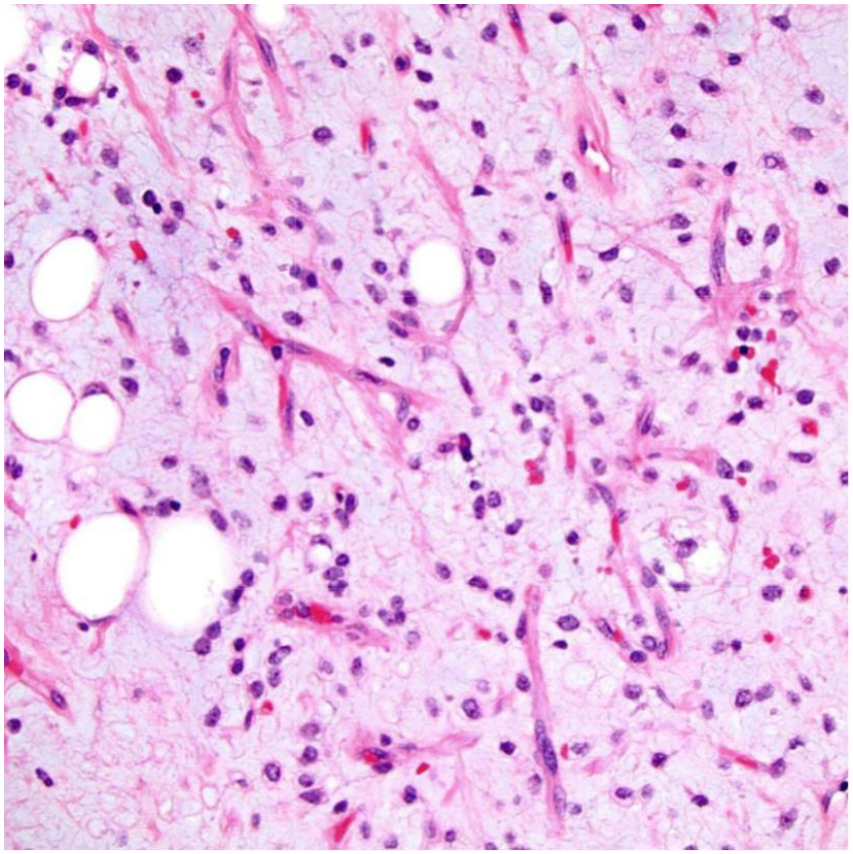


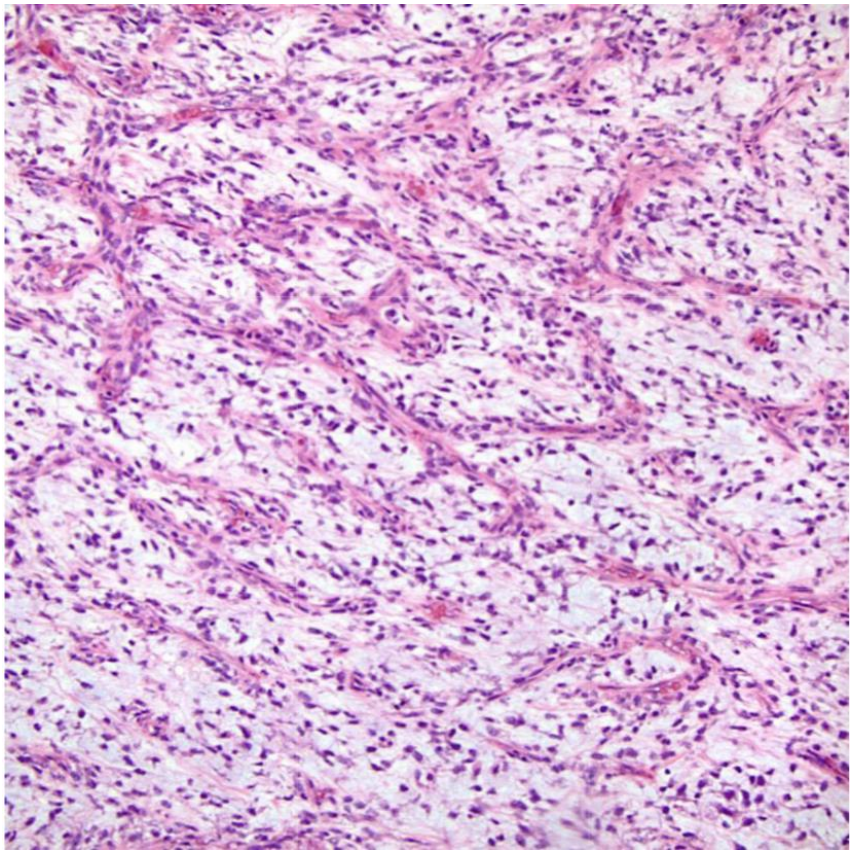


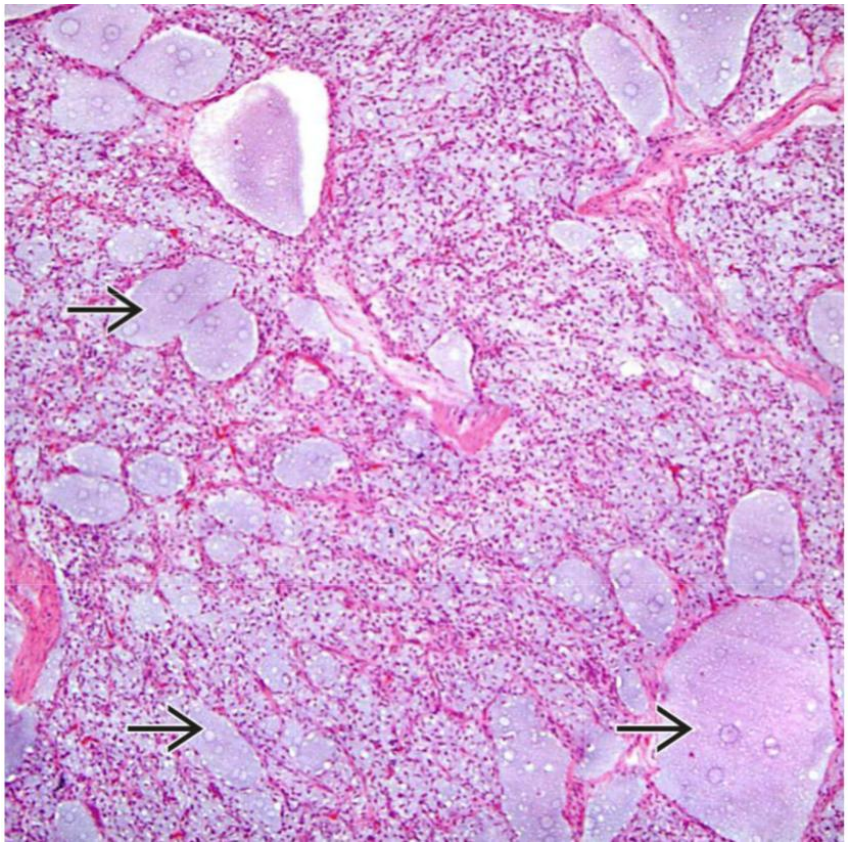


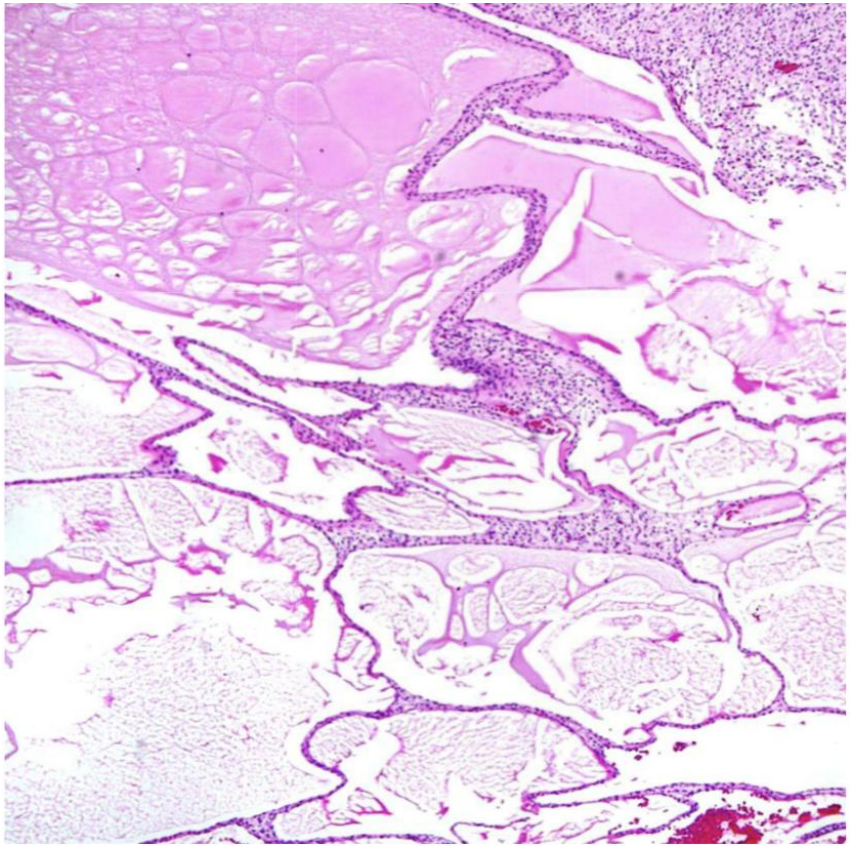


Microscopic









Ancillary Tests and Differential Diagnosis

- Molecular: Characteristic t(12;16)(q13;p11)

- Atypical lipomatous tumor/well-differentiated liposarcoma
- Myxofibrosarcoma
- Intramuscular myxoma
- Low-grade fibromyxoid sarcoma

Fibroblastic/Myofibroblastic Lesions

Nodulat Fasciitis

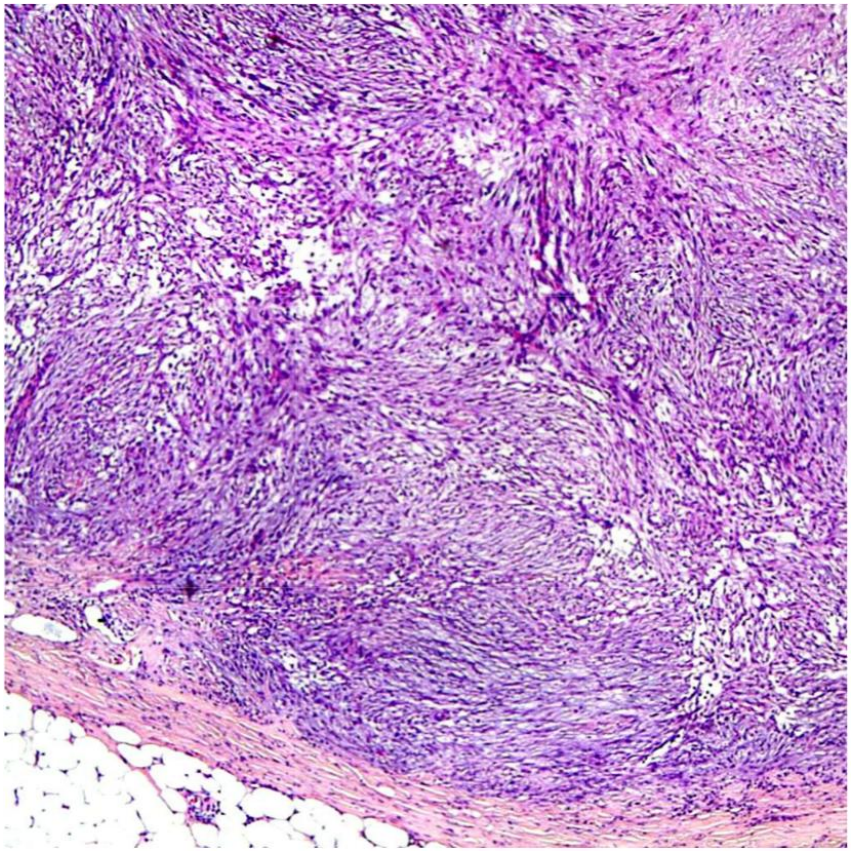
- Self-limited, benign fibroblastic/myofibroblastic neoplasm
- Characterized in most cases by **USP6 – MYH9** gene fusion

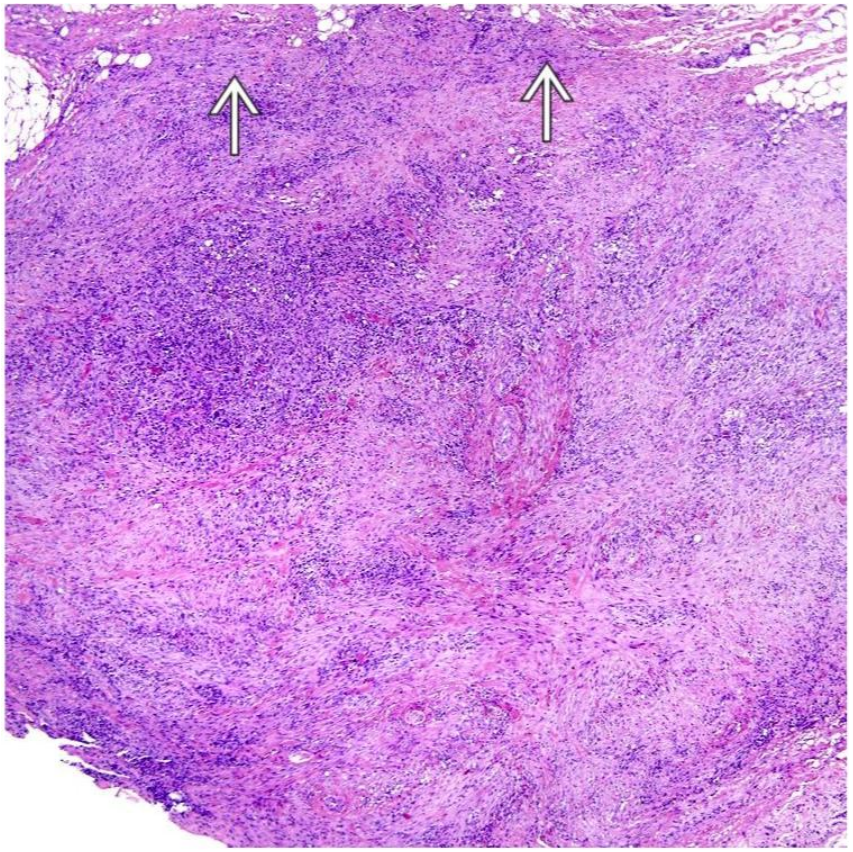
- Variants: Intravascular fasciitis, cranial fasciitis

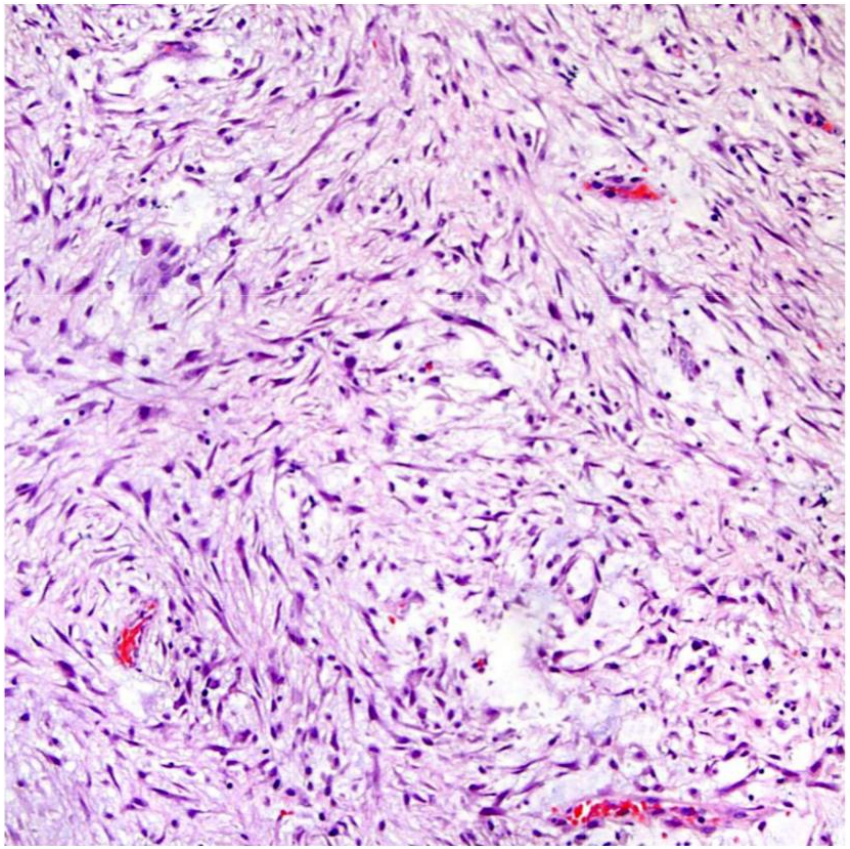
Clinical Issues

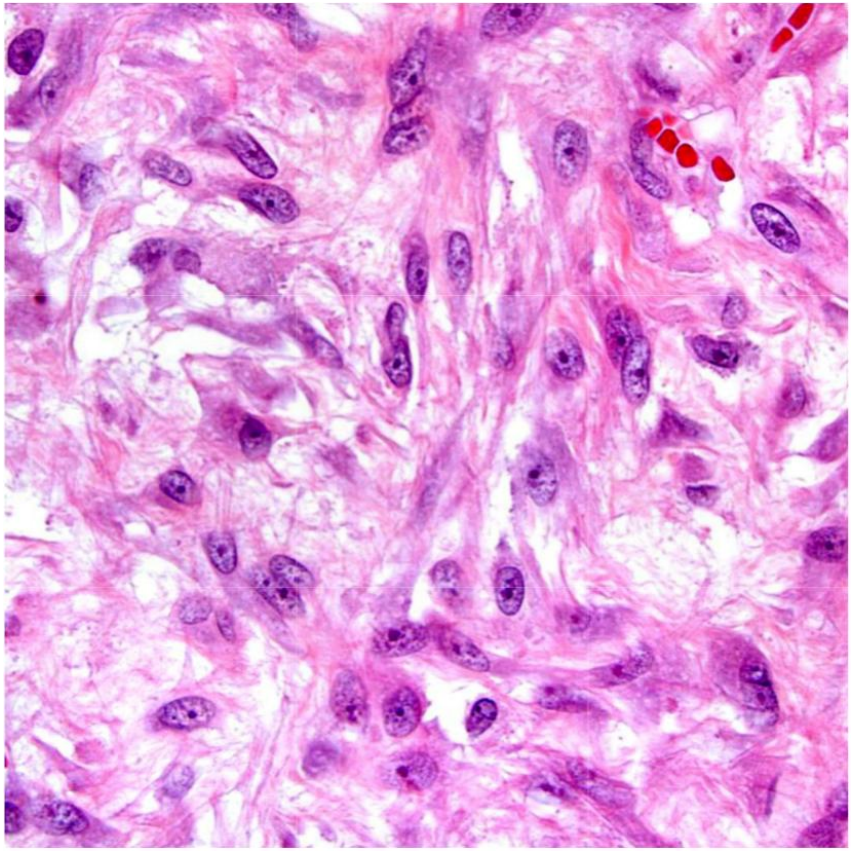
- Wide range (most common: 20-40 years)
- Most common in **extremities** (particularly forearm), trunk, and head and neck
- Usually in subcutaneous tissue
- Small tumor with **rapid growth characteristic**
- Treatment: Conservative surgical excision
- Excellent prognosis; local recurrence very rare

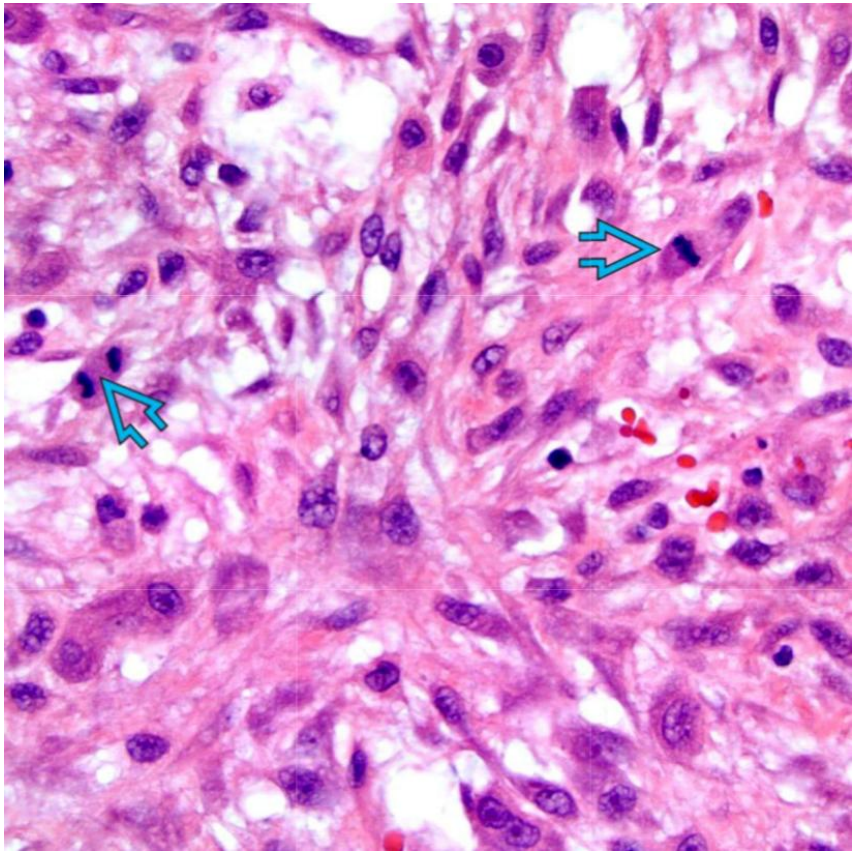
Microscopic

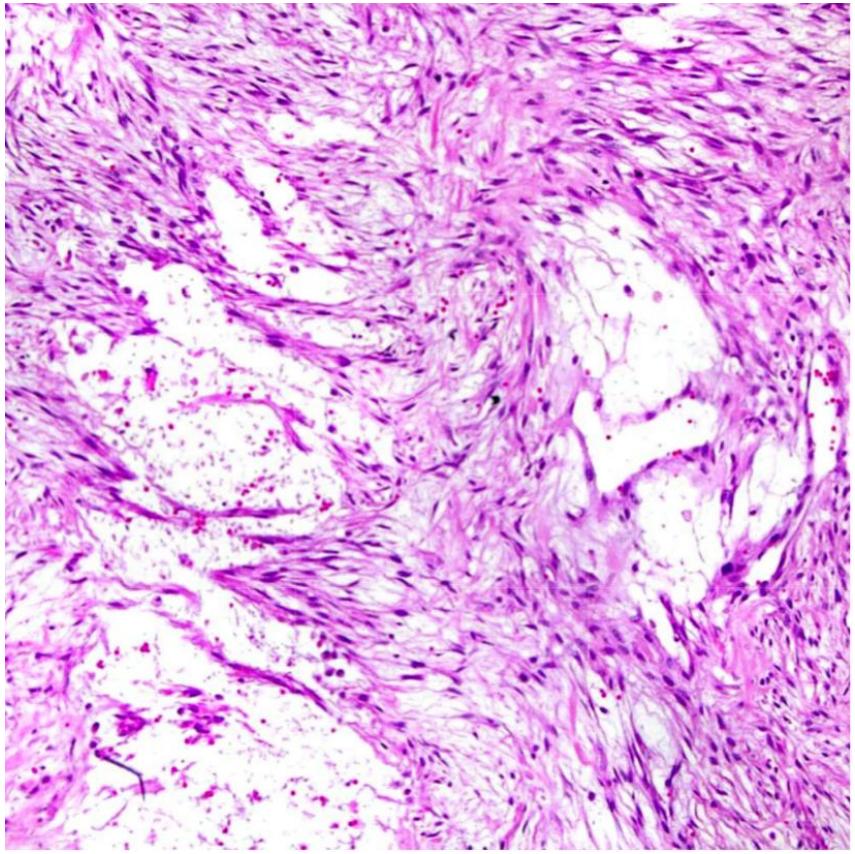












Ancillary Tests and Differential diagnosis

- Molecular: USP6 gene rearrangement in most cases
  - USP6-MYH9 fusion most common

- Desmoid fibromatosis
- Inflammatory myofibroblastic tumor
- Leiomyosarcoma
- Pseudosarcomatous myofibroblastic proliferation

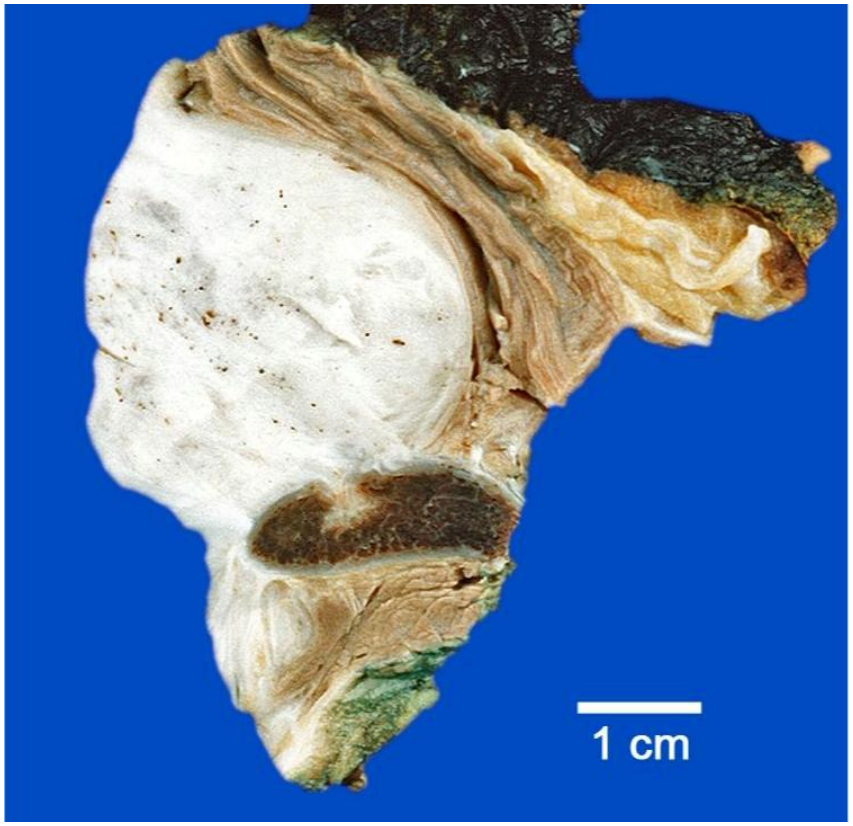
Desmoid-type Fibromatosis

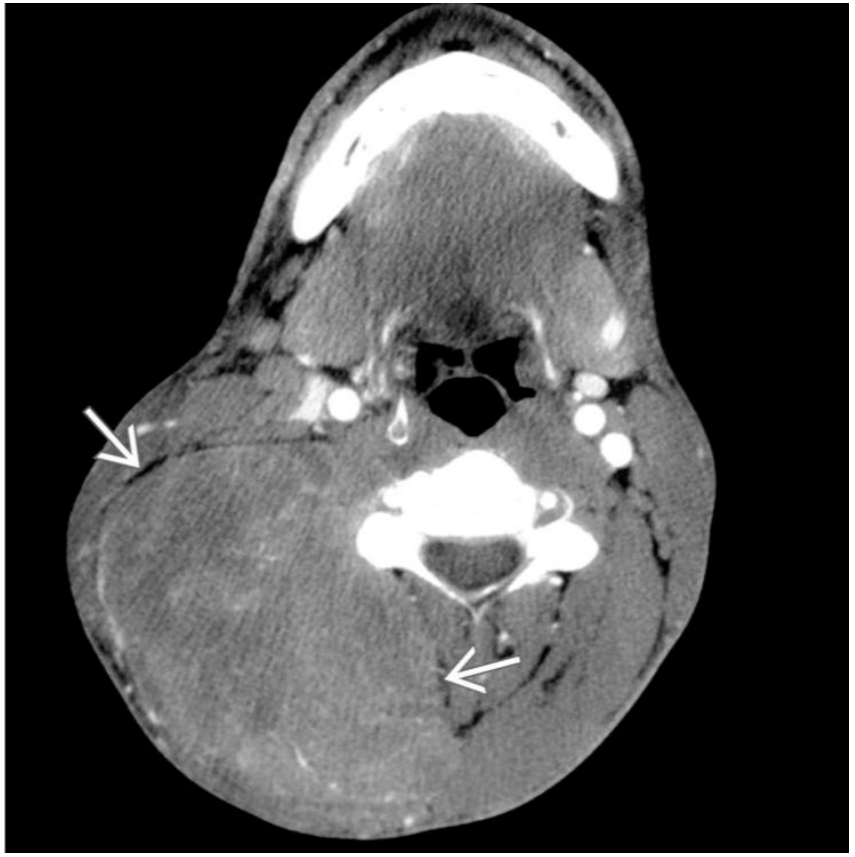
- **Intermediate (locally aggressive)**, but nonmetastasizing myofibroblastic neoplasm that is characterized by infiltrative growth and a tendency toward local recurrence

Clinical Issues

- Most are sporadic; 10% familial
- Wide age range (most common in young to middle-aged adults)
- Abdominal wall tumors common in pregnant women
- Extraabdominal and intraabdominal tumors
- Mesenteric tumors can be associated with **FAP/Gardner syndrome**
- Usually large, painless, slow-growing mass
- Treatment: Surgical excision with preservation of function, radiation, or nonsurgical medical therapy
- Benign; does not metastasize
- **Significant rate of local recurrence**

Macroscopic and Imaging





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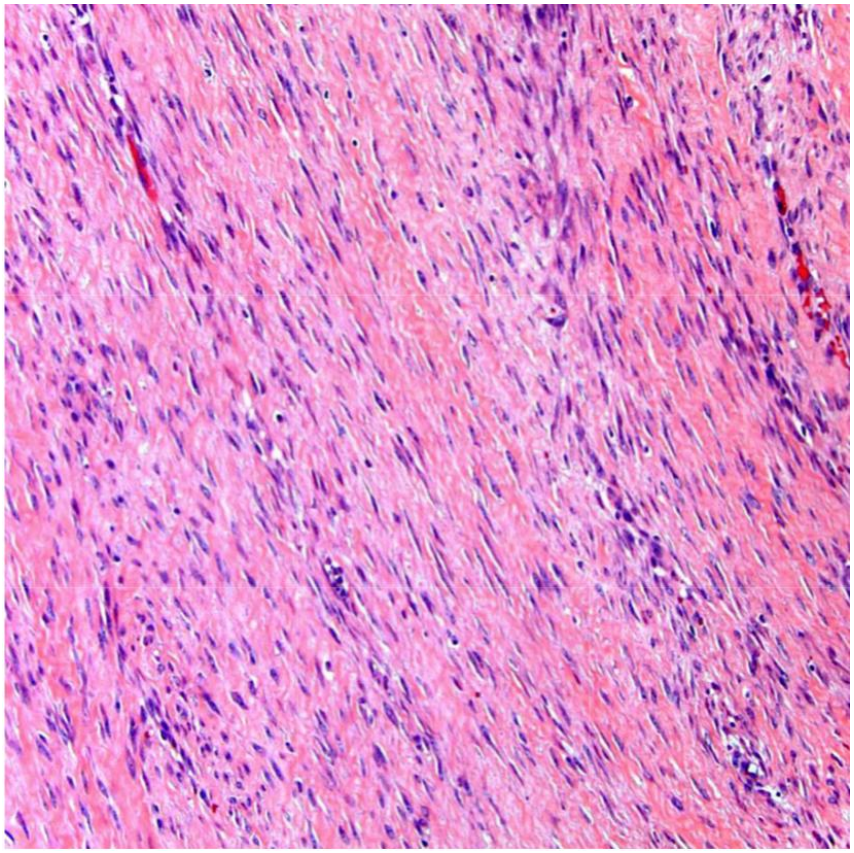
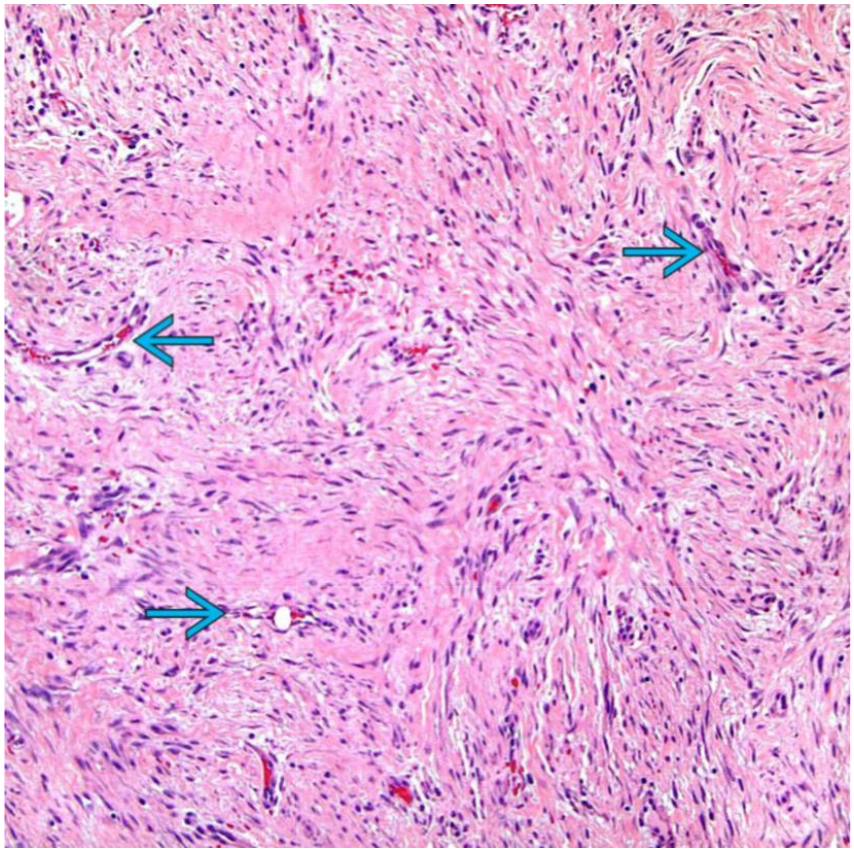
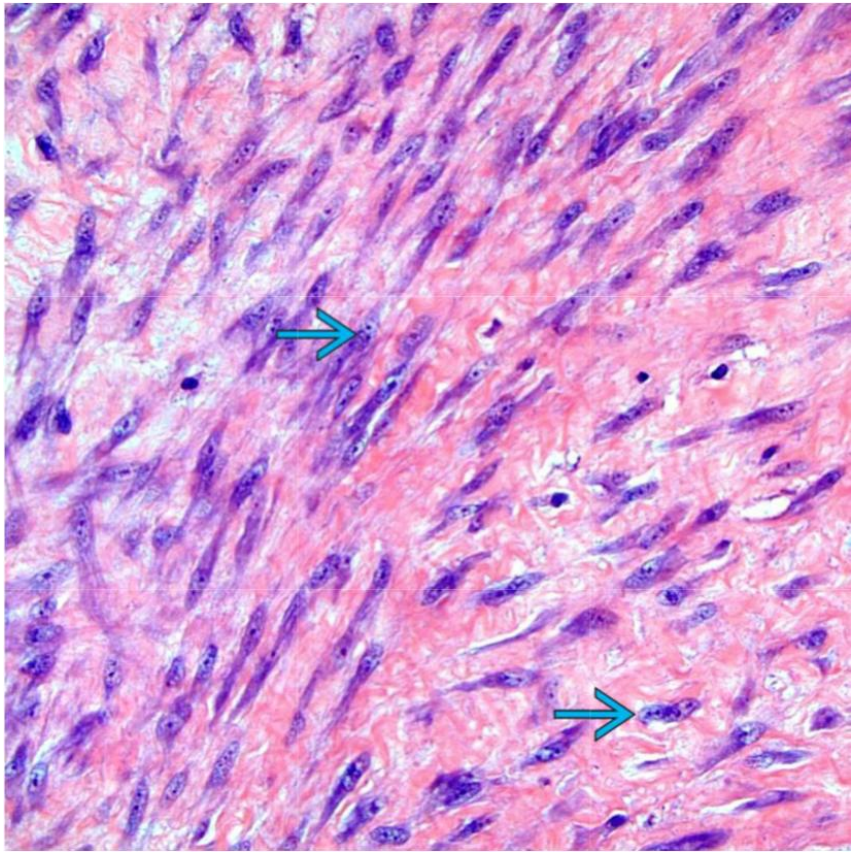
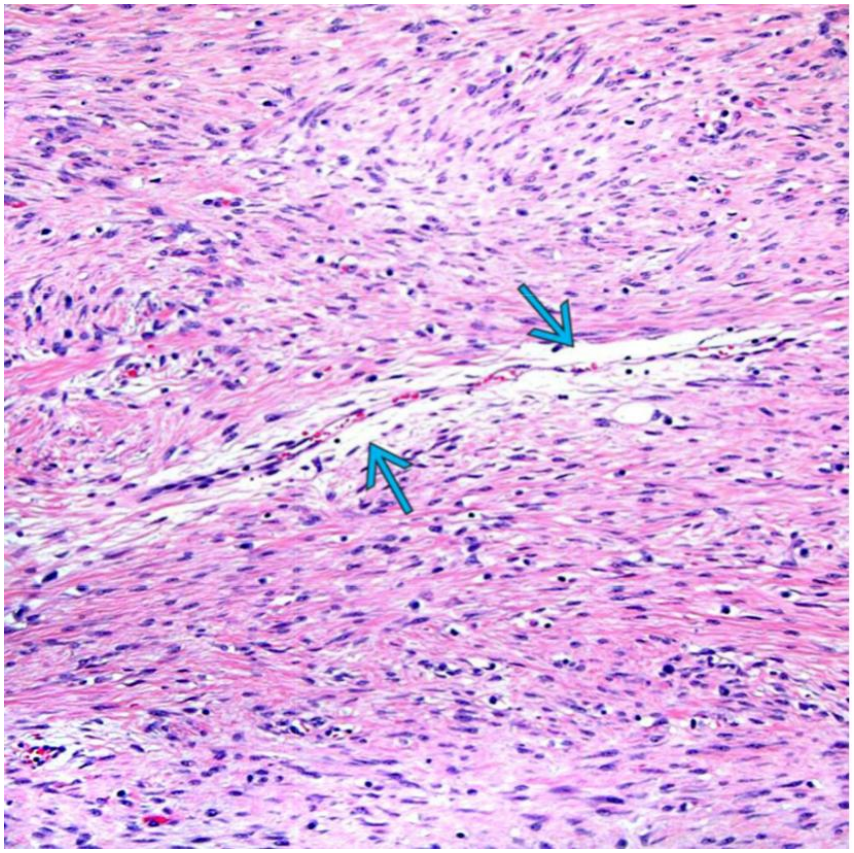
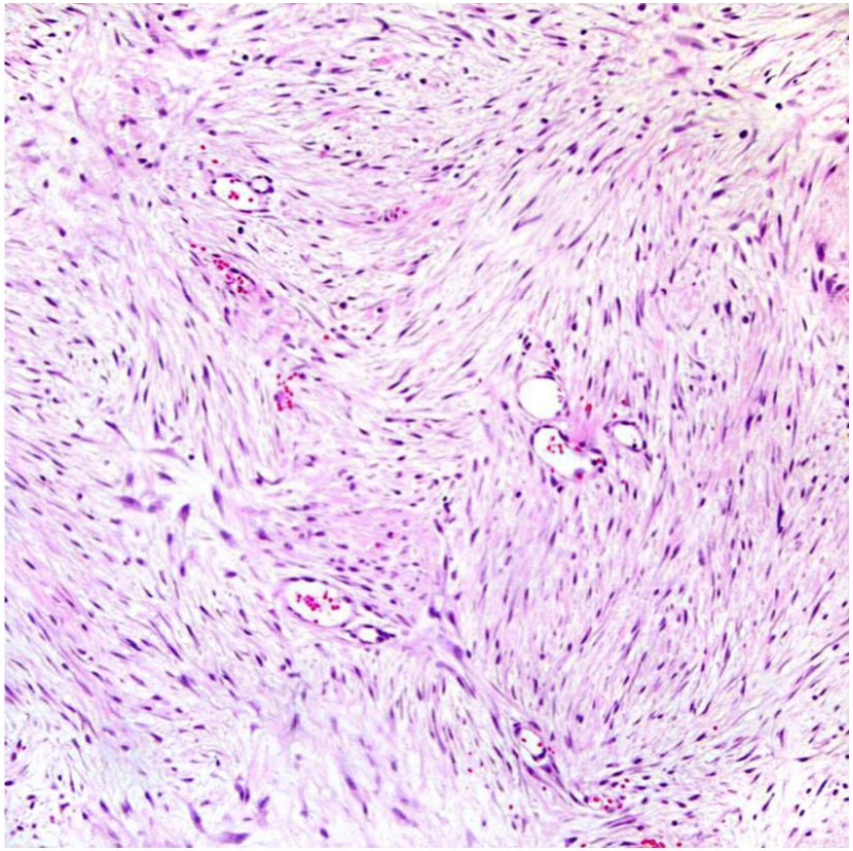
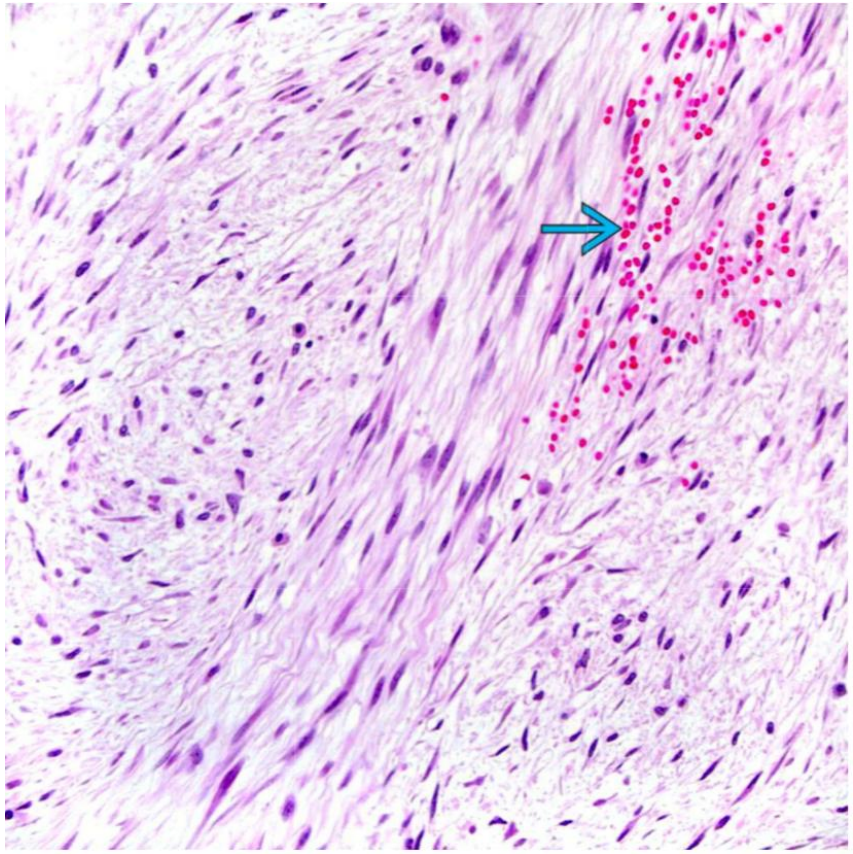








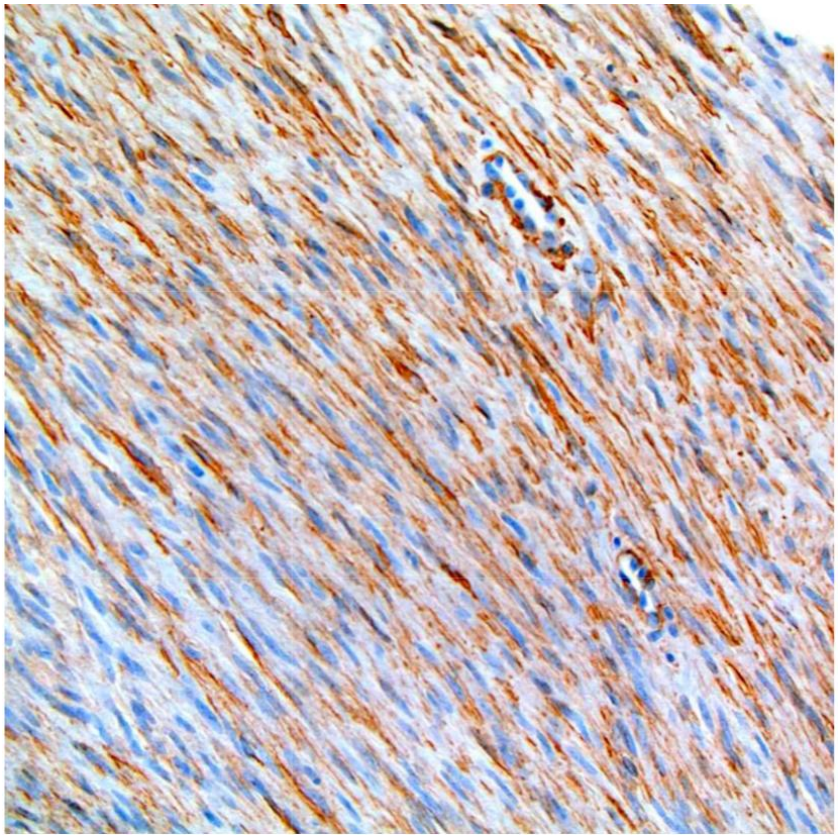




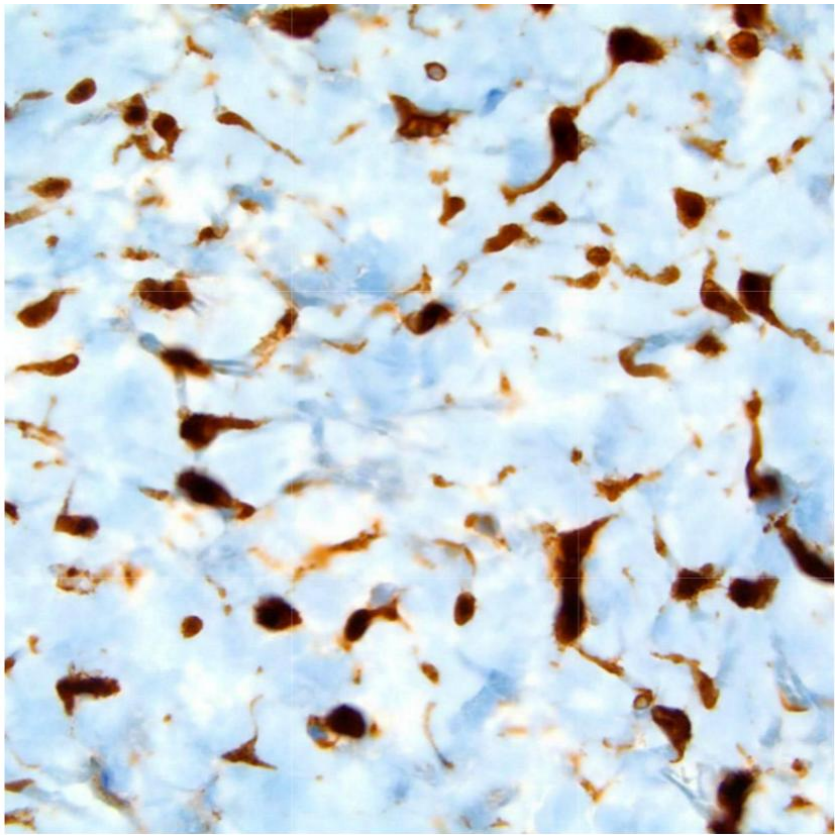
Ancillary Tests

- **Nuclear β-catenin (+)** in ~ 70% of cases
- SMA(+), MSA(+), focal desmin (+), S100 protein (-), CD117(-)

IHC for SMA



IHC for b-catenin



Differential Diagnosis

- Low-grade myofibroblastic sarcoma
- Gastrointestinal stromal tumor (spindle cell type)
- Fibrous scar
- Nodular fasciitis
- Sclerosing mesenteritis/idiopathic retroperitoneal fibrosis

Dermatofibrosaroma Protuberans (DFSP)

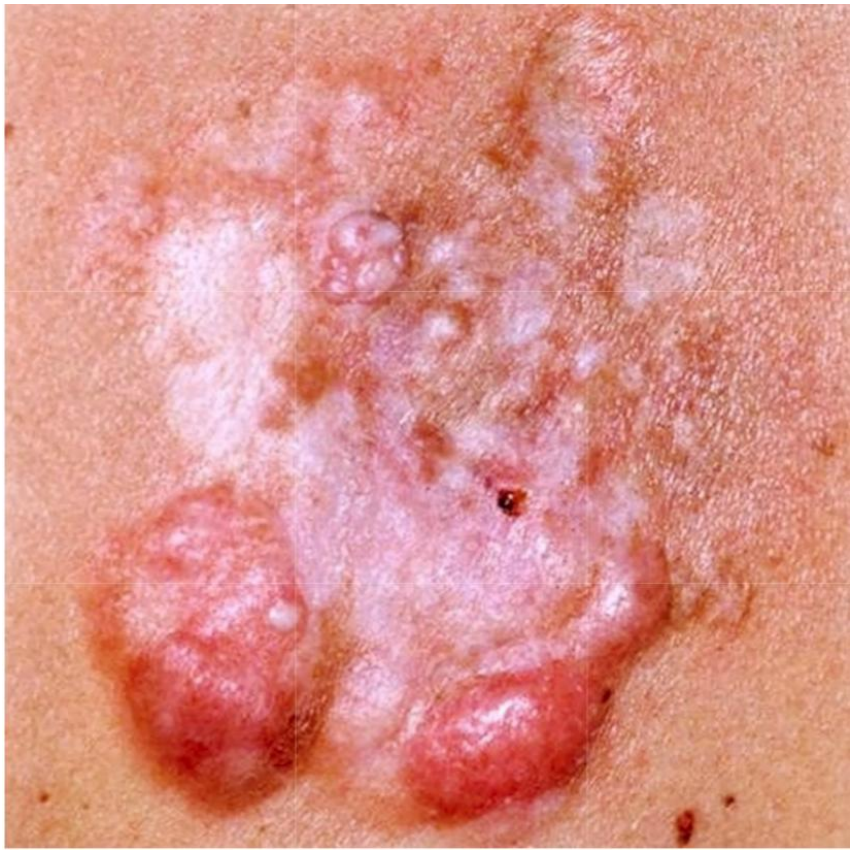
- Locally aggressive, low-grade, superficial fibroblastic sarcoma characterized by a **COL1A1 – PDGFB gene fusion**

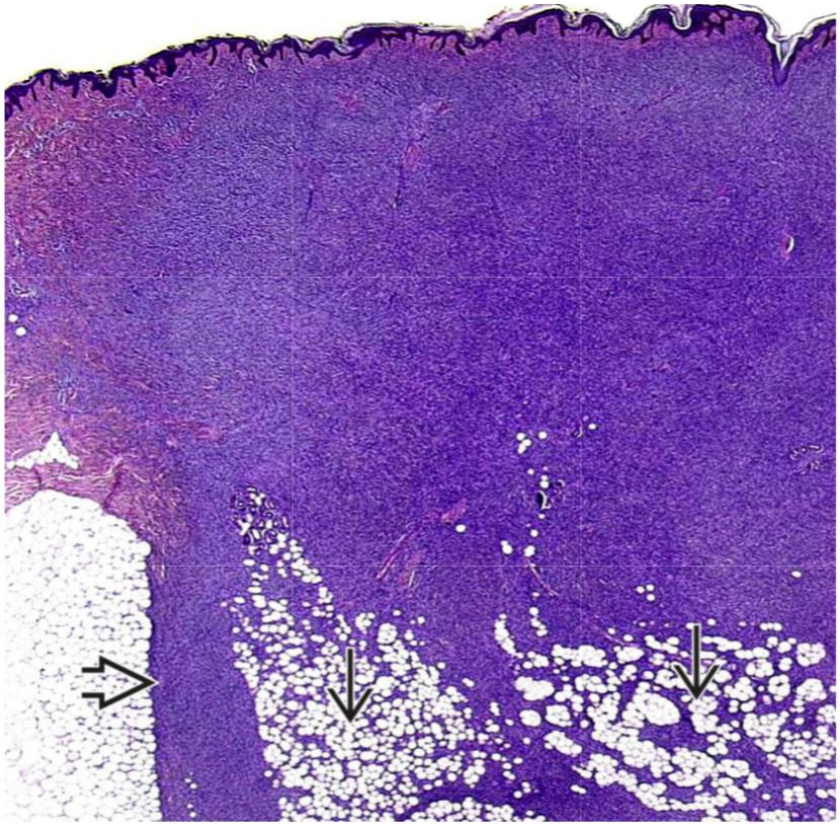
- May show progression to higher grade neoplasm with increased metastatic risk (fibrosarcomatous DFSP)

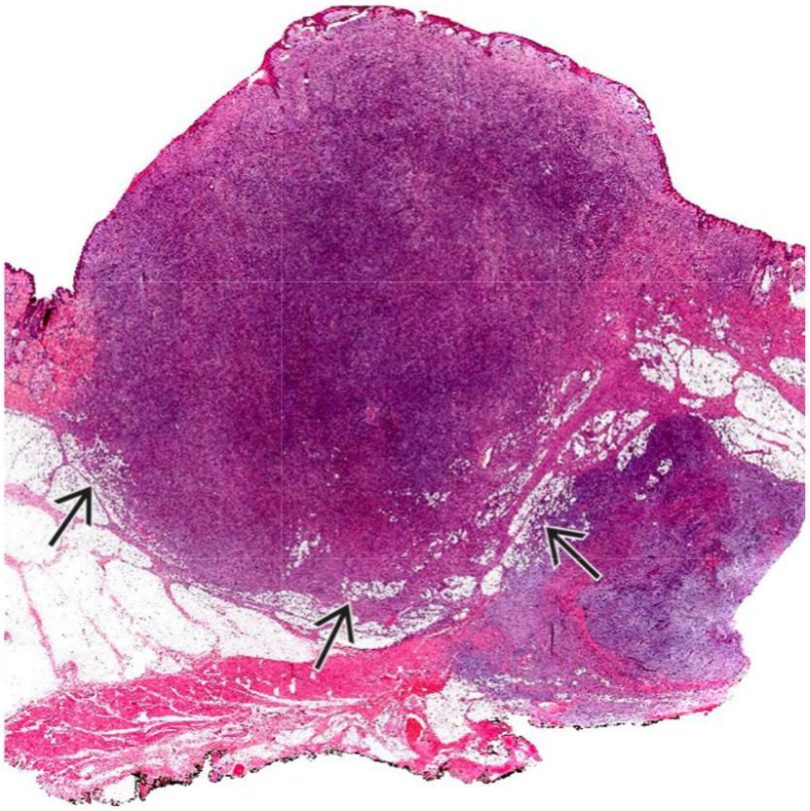
Clinical Issues

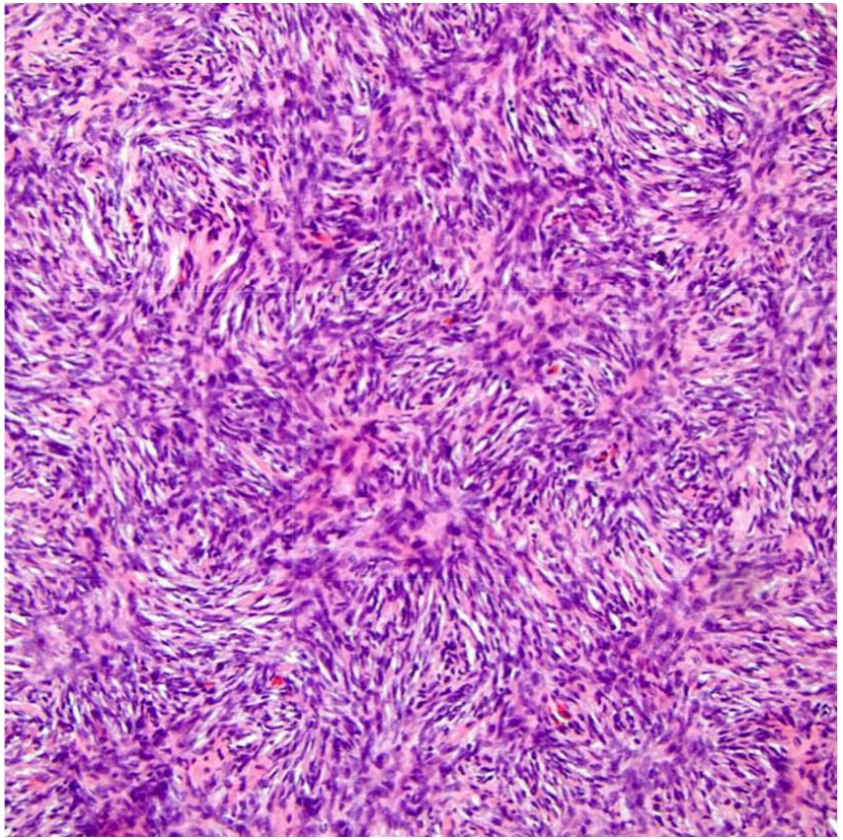
- Young to middle-aged adults
- Most common in trunk and proximal extremities
- Persistent, slow-growing, plaque-like or protuberant nodular/multinodular cutaneous mass
- Treatment: Complete surgical excision with widely negative (2-3 cm) margins
- Local recurrences common (up to 50% of cases)
- Metastases extremely rare (< 0.5%)
- 10-15% risk in tumors with fibrosarcomatous changes

Macroscopic and Microscopic

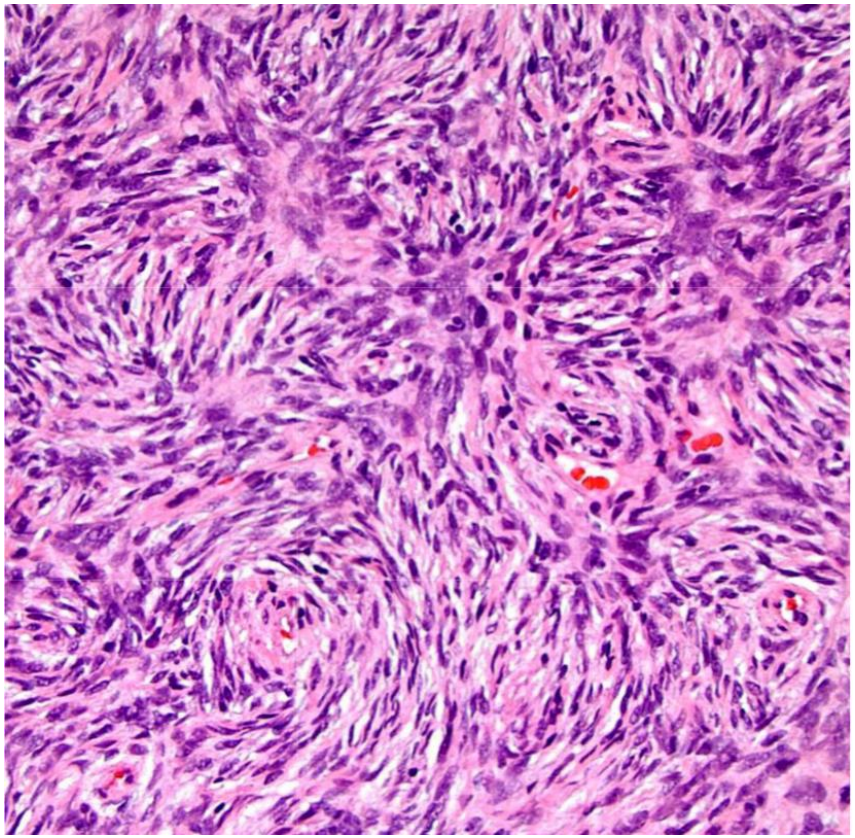




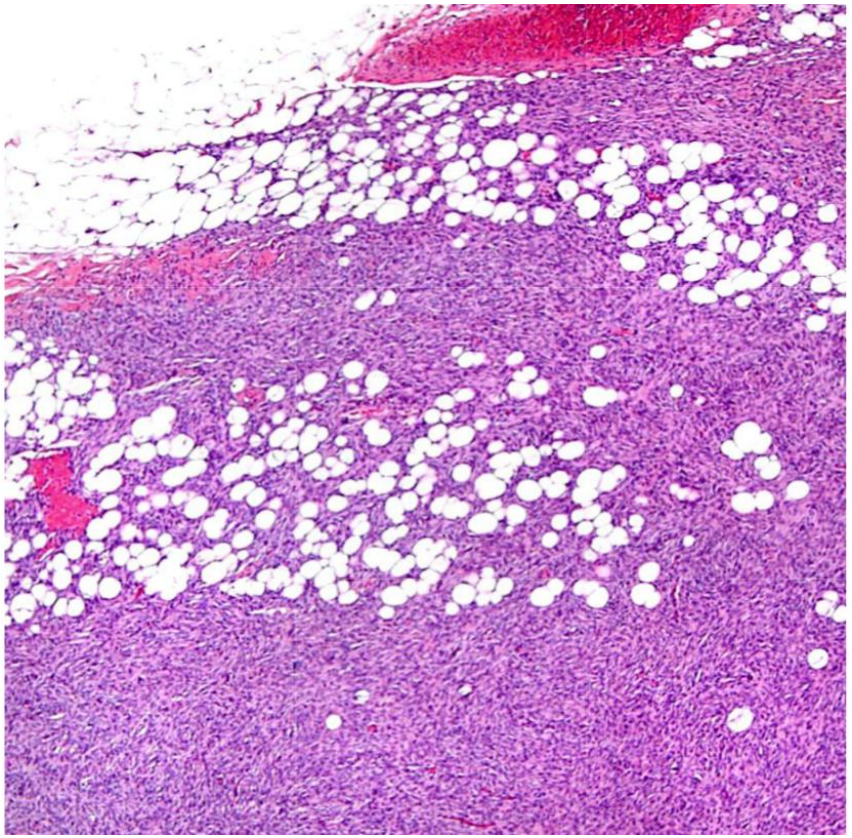


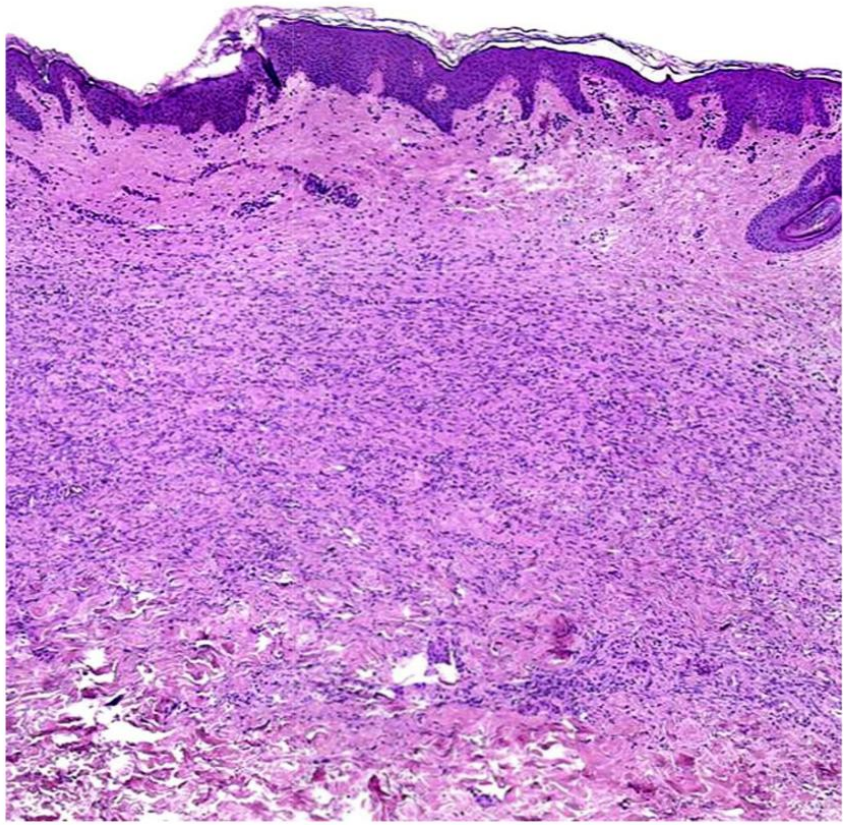


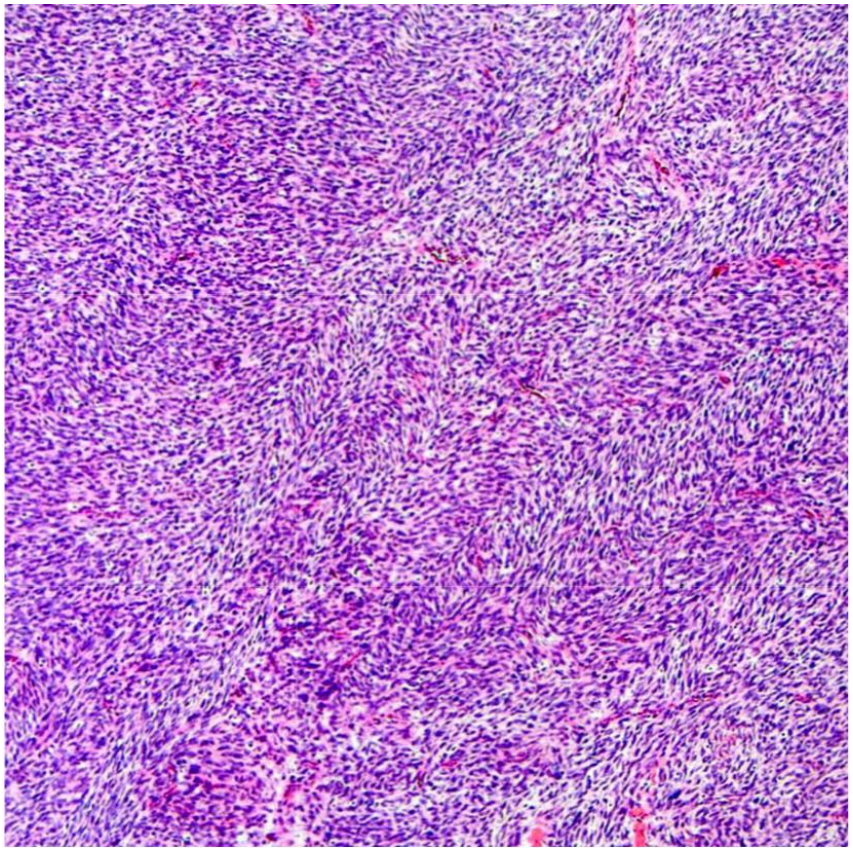
Storiform growth pattern



Infiltration in a honeycomb fashion







Ancillary Tests

- Diffuse CD34(+)

- Molecular: Characteristic t(17;22)(q22;q13) leading to **COL1A1 – PDGFB** fusion product

Differential Diagnosis

- Dermatofibroma (fibrous histiocytoma)
- Diffuse neurofibroma
- Perineurioma
- Dermatomyofibroma

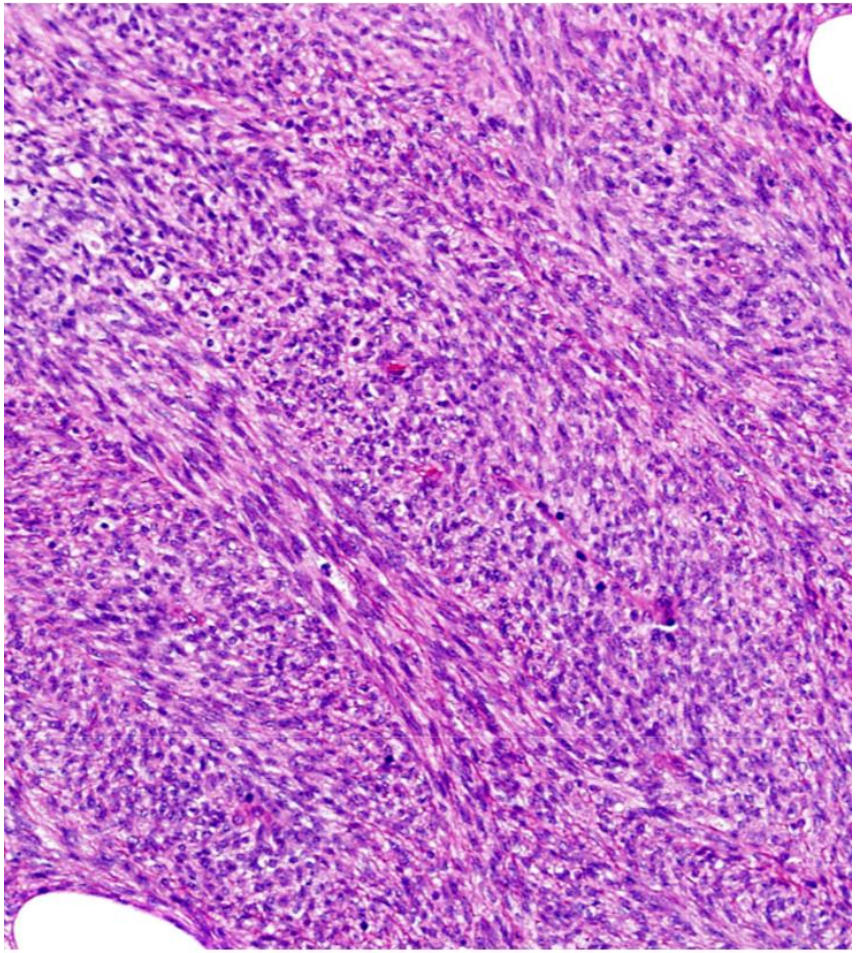
Adult-type Fibrosarcoma

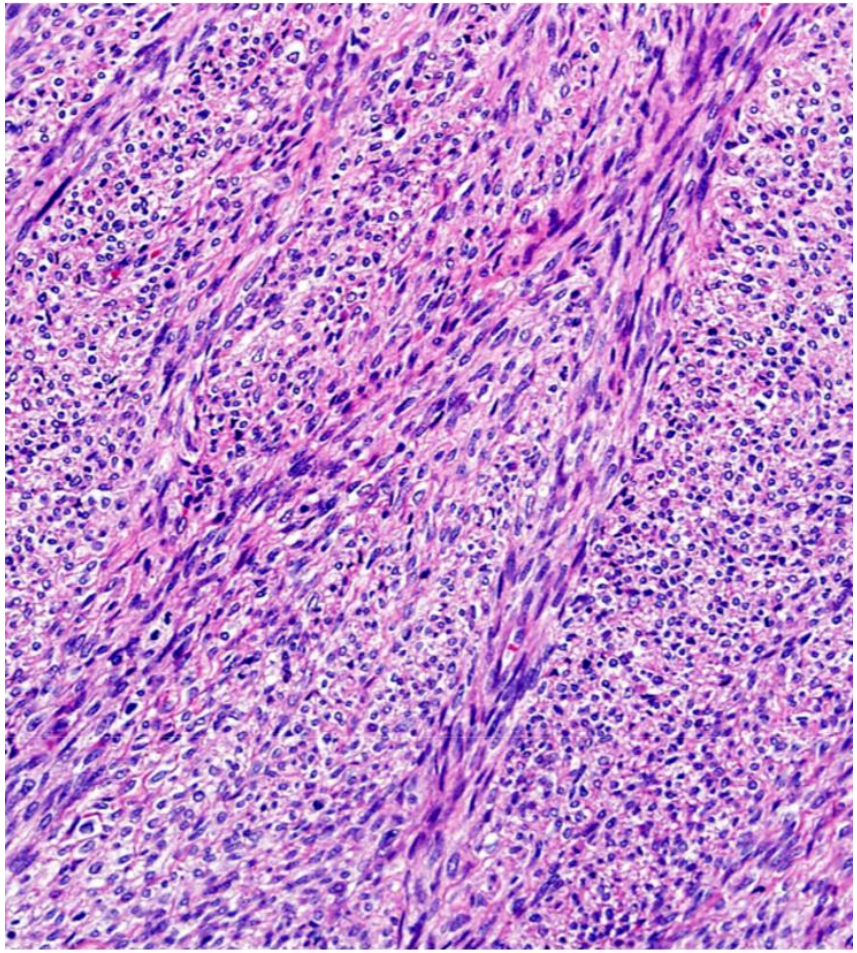
- Sarcoma composed of spindle cells resembling fibroblasts
- Most tumors classified as fibrosarcoma in older literature now reclassified as other entities
- **Must lack features of well-defined fibrosarcoma subtypes and other entities**
- **Diagnosis of exclusion**
- Lacks significant nuclear pleomorphism
- Tumors with marked pleomorphism classified as undifferentiated pleomorphic sarcoma

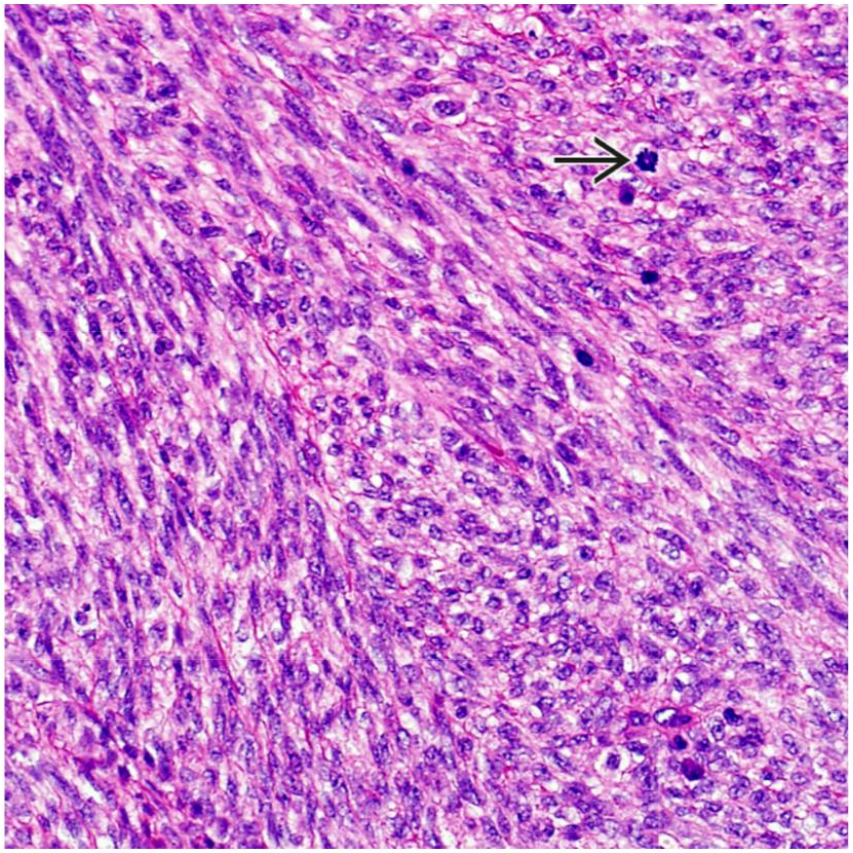
Clinical Issues

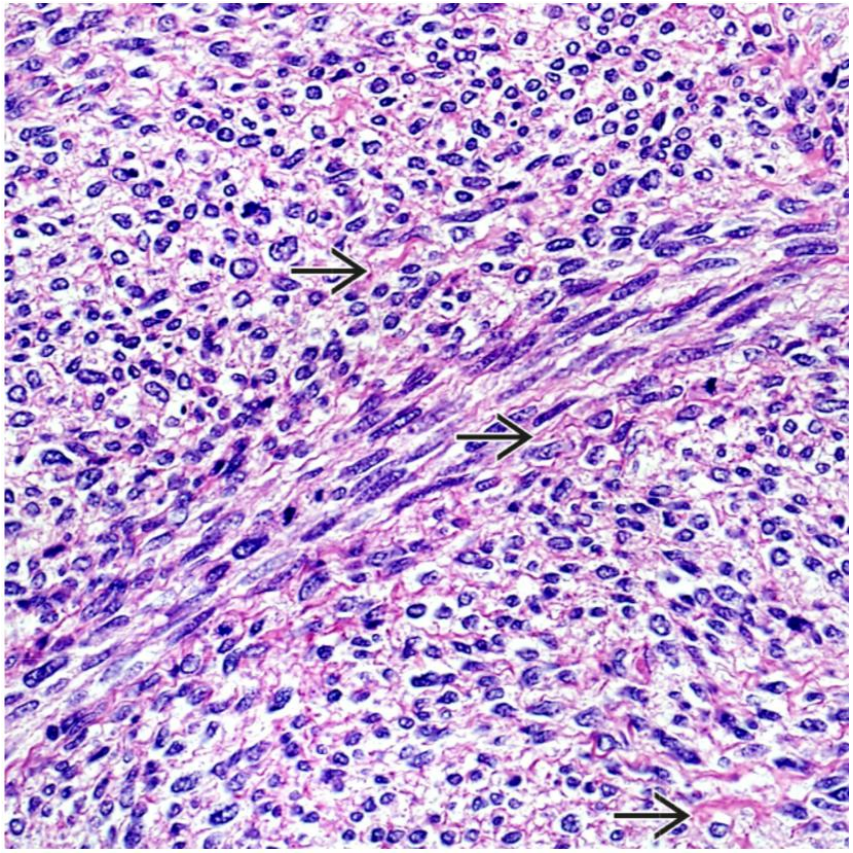
- Vanishingly rare if strictly defined
- Most arise in deep soft tissues of extremities in adults
- Treatment: Wide surgical resection
- Limited prognostic data using modern strict diagnostic criteria
- 50% overall mortality

Herringbone pattern









Differential Diagnosis

- Undifferentiated pleomorphic sarcoma
- Synovial sarcoma
- Malignant peripheral nerve sheath tumor
- Fibrosarcomatous dermatofibrosarcoma protuberans
- Desmoid fibromatosis
- Cellular dermatofibroma
- Low-grade myofibroblastic sarcoma
- Leiomyosarcoma

Fibrohistiocytic Tumors

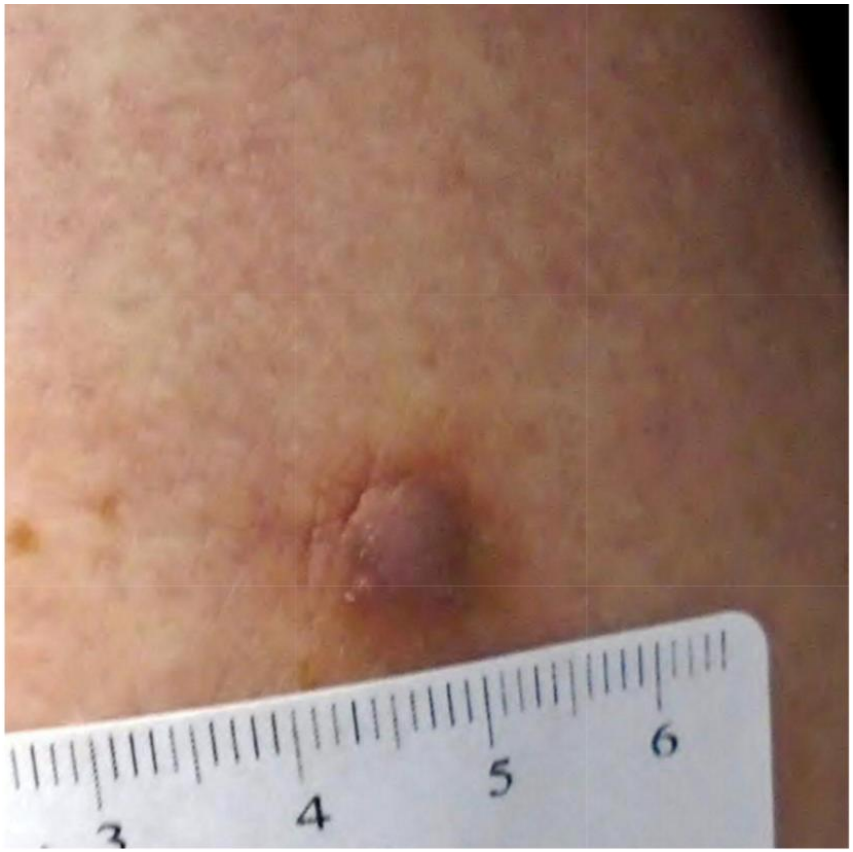
Dermatofibroma/Benign Fibrous Histiocytoma

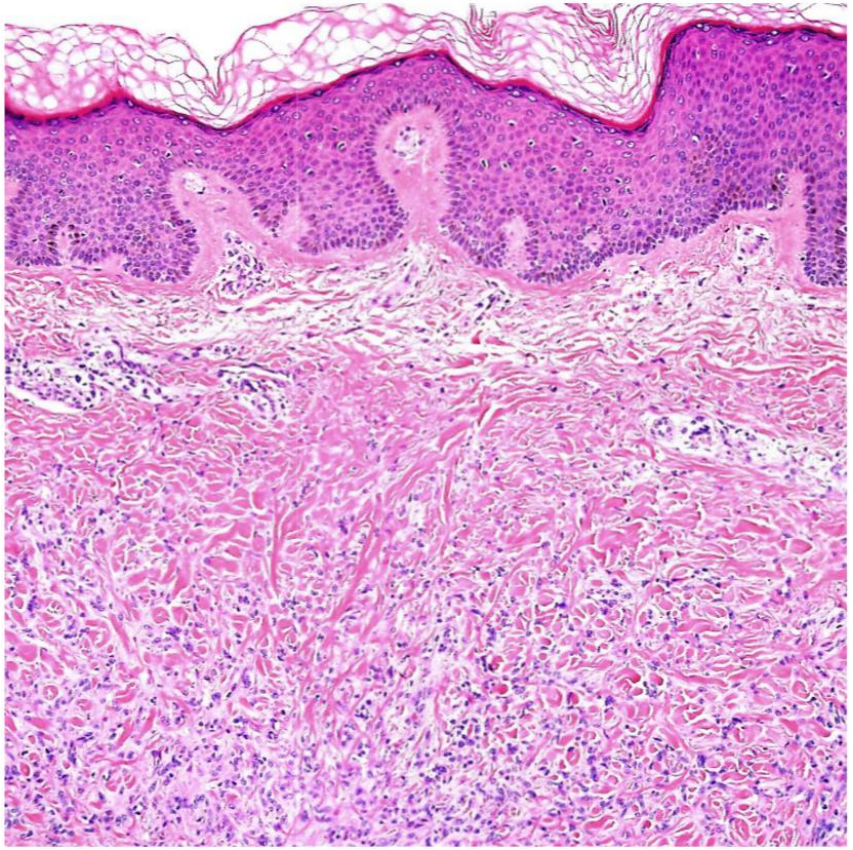
- Benign, limited proliferation of histiocytic and fibroblastic cells in dermis
- Terms dermatofibroma (DF) and fibrous histiocytoma (FH) are interchangeable
- Evidence supports both neoplastic and reactive pathogenesis
- Tumor may be preceded by local trauma, including insect bite, in some cases

Clinical Issues

- Affects all ages, but most common in young adults
- Typically occur on distal extremities, but may present at any cutaneous site
- Firm, isolated, flesh-colored subcutaneous papule or nodule
- Excellent prognosis in vast majority of cases
- Metastasis and death in very rare cases of cellular and atypical DF

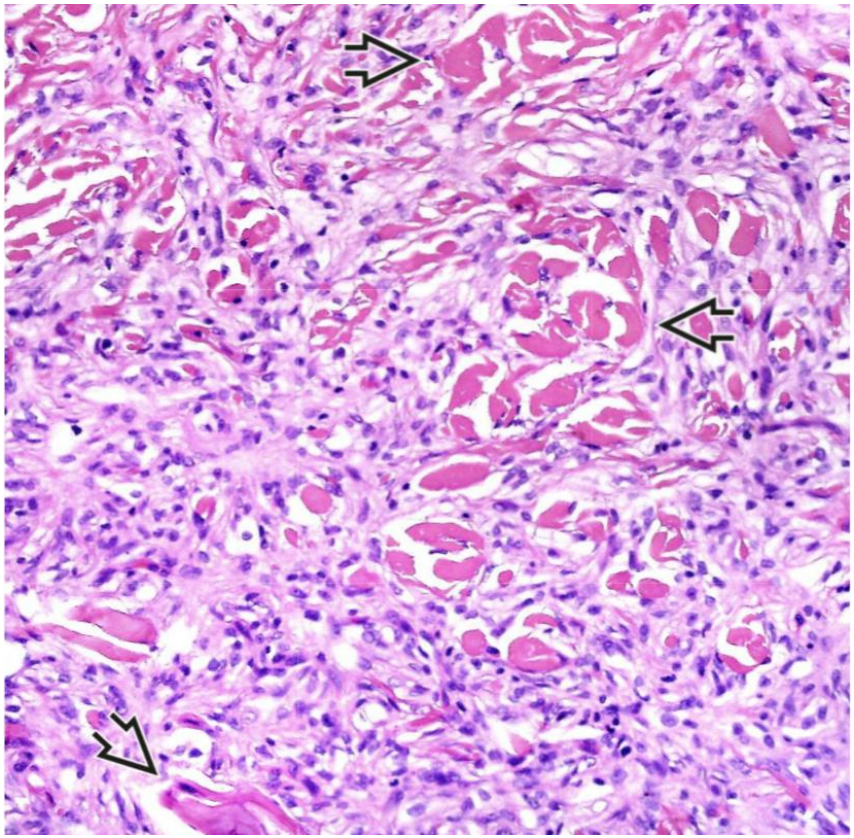
Macroscopic and Microscopic



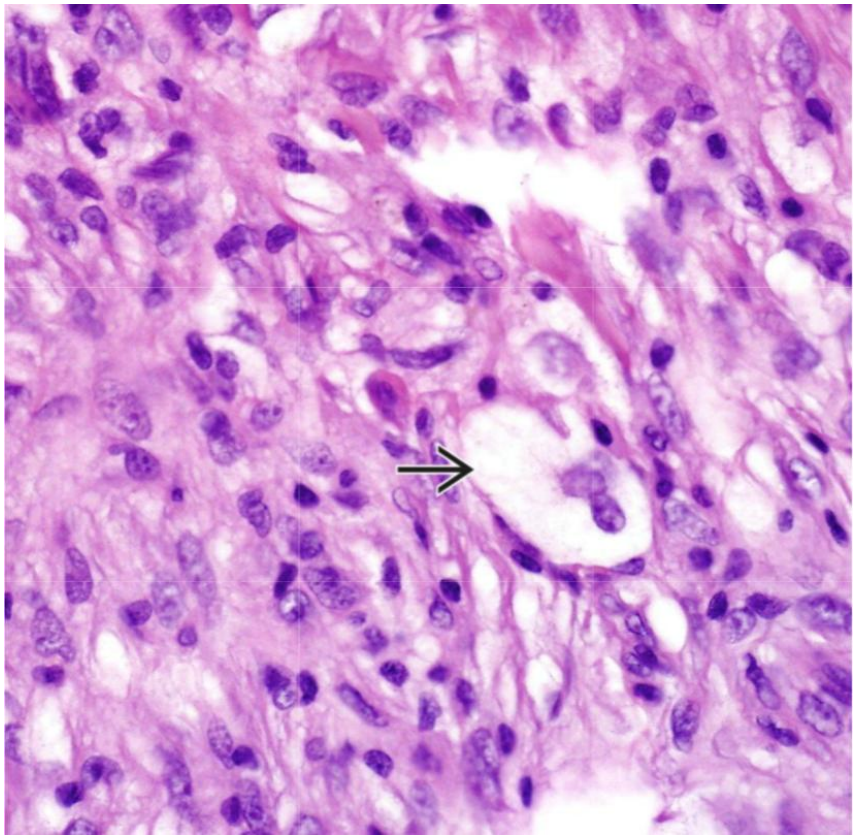


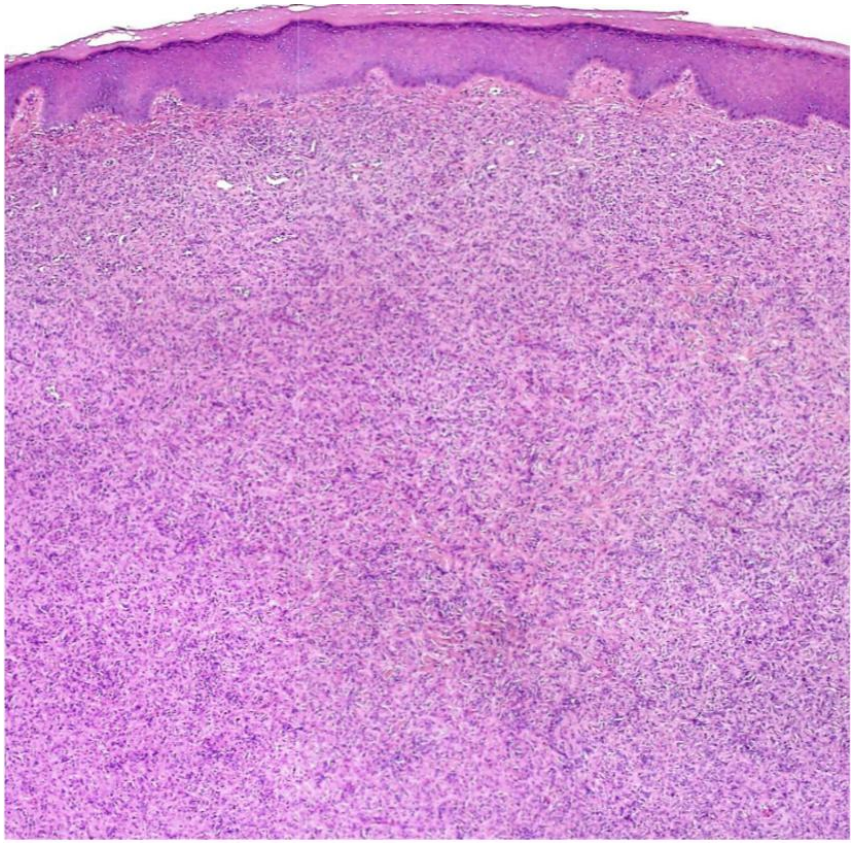
Microscopic

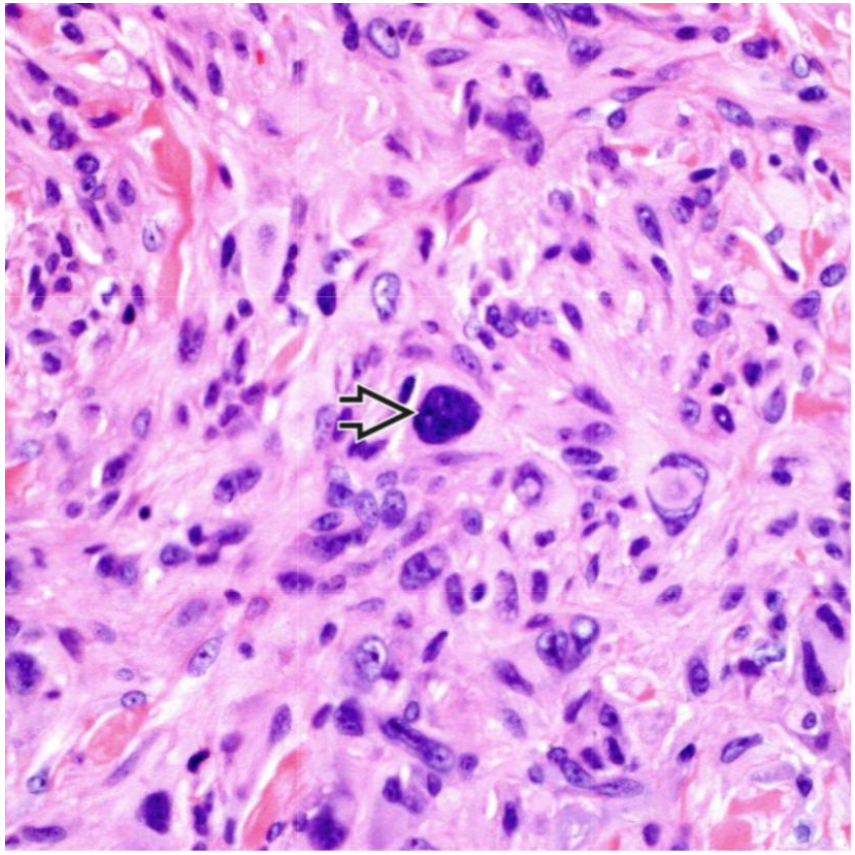
Entrapment of collagen fibers



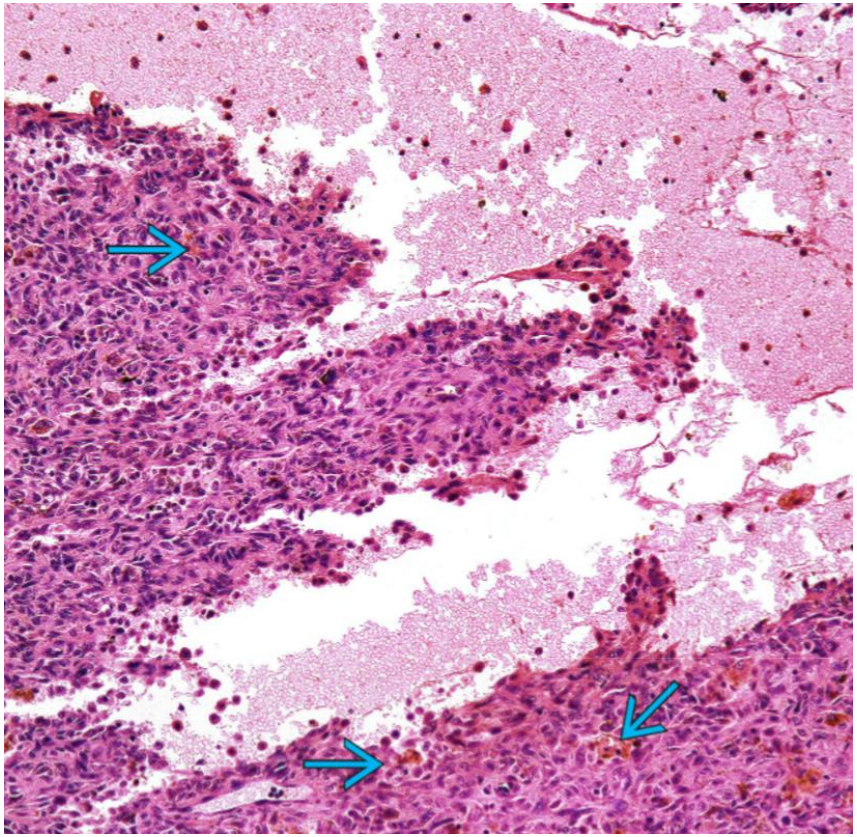
Lipidized cells



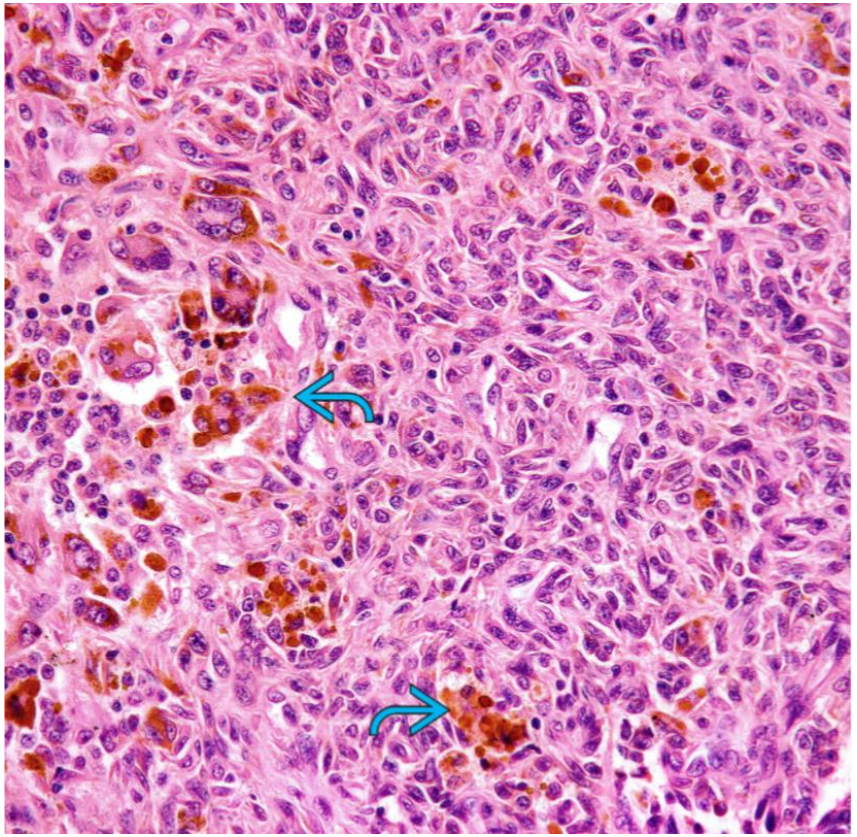




Aneurysmal type



Hemosiderin



Differential Diagnosis

- Dermatofibrosarcoma protuberans
- Atypical fibroxanthoma (AFX)
- Basal cell carcinoma
- Angiosarcoma
- Kaposi Sarcoma

Smooth Muscle Tumors

Superficial Leiomyoma

- Benign dermal smooth muscle neoplasm
- Pilar type (piloleiomyoma) arises from arrector pili
- Genital type arises from specialized genital smooth muscle

Etiology/Pathogenesis

- **Hereditary leiomyomatosis and renal cell cancer syndrome (HLRCC)**
  - Multiple leiomyomas of skin and uterus
  - Subset develop renal cell carcinoma (RCC)
  - Often aggressive types
  - Mutations in fumarate hydratase (FH) gene (autosomal dominant)

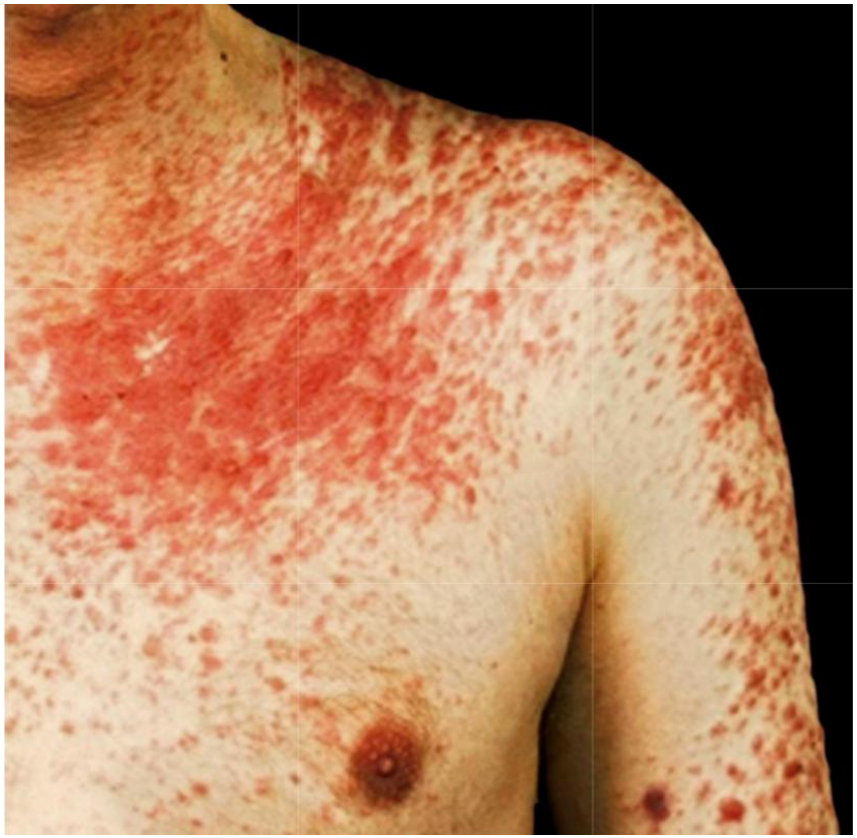
Clinical Issues

- Pilar leiomyoma: Multiple painful pink/brown papules/nodules, most < 2 cm

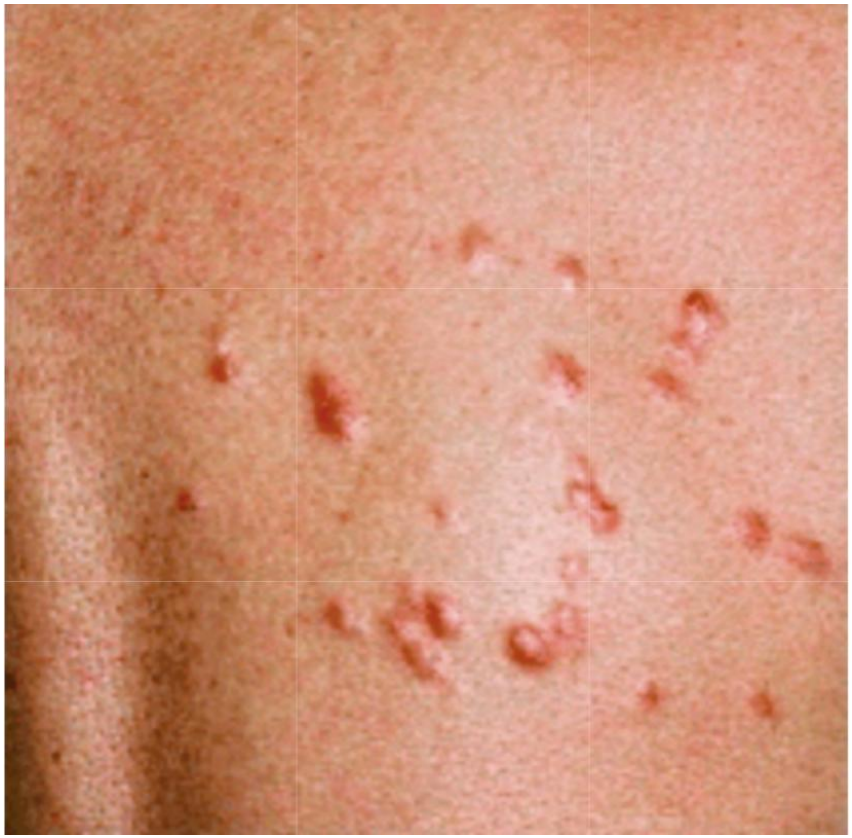
- Genital leiomyoma: Solitary painless nodule on scrotum, penis, vulva, or nipple of adults

Clinical

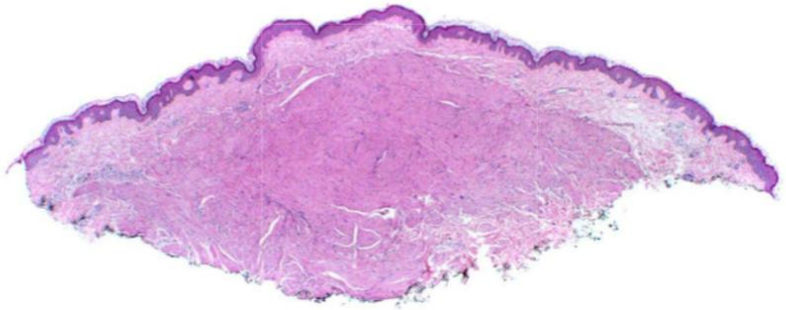
Cutaneous leiomyoma & HLRCC

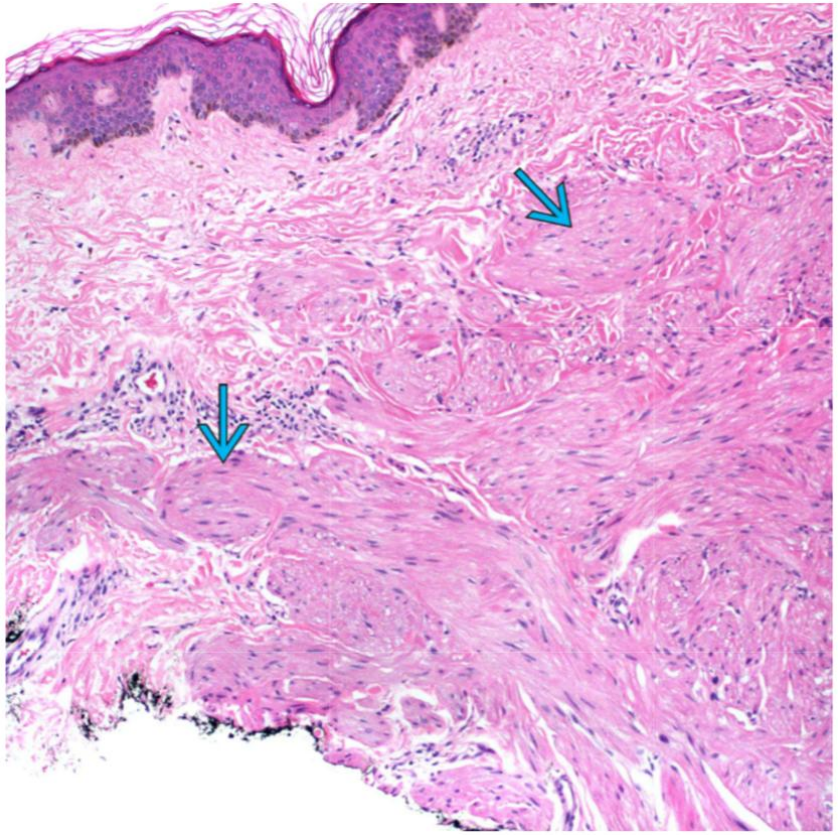


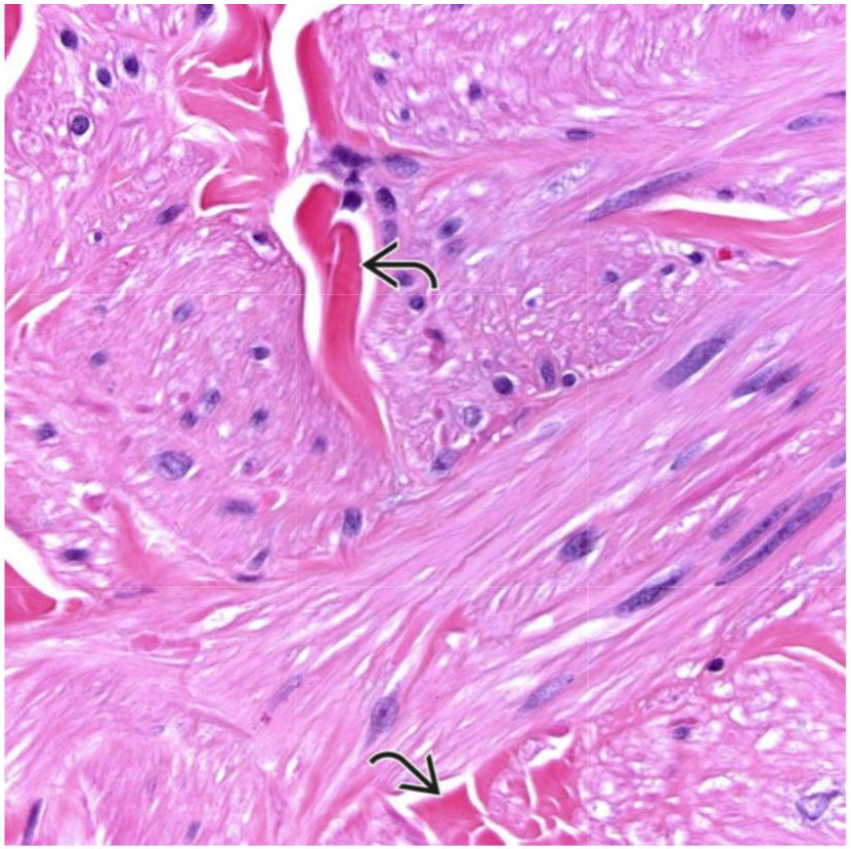
Multiple Pilar leiomyomas

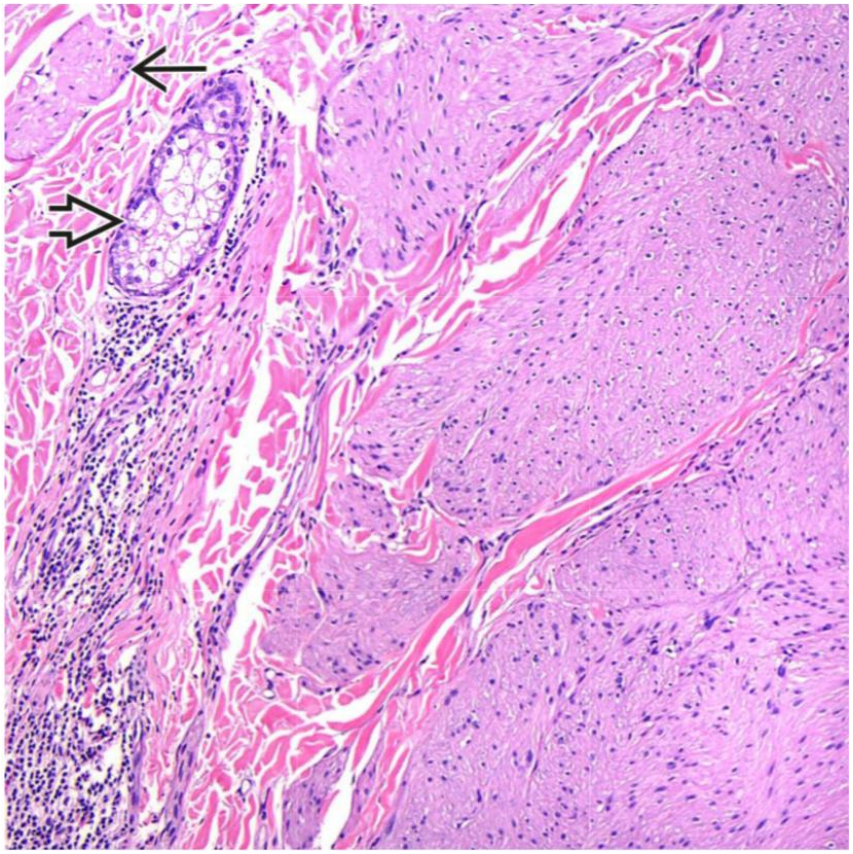


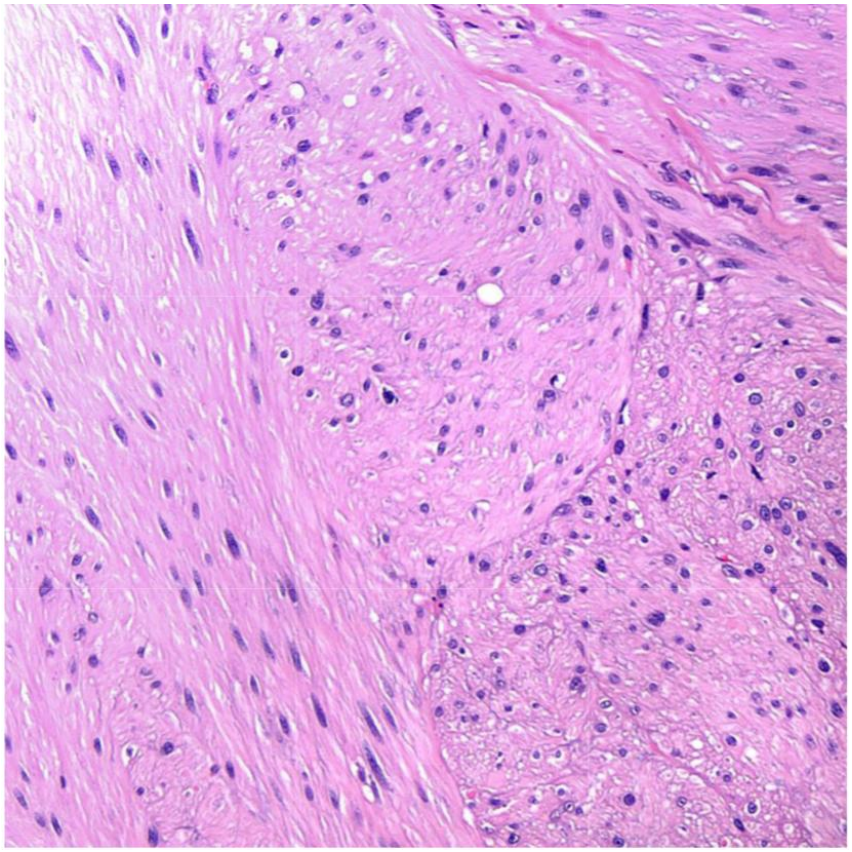
Microscopic

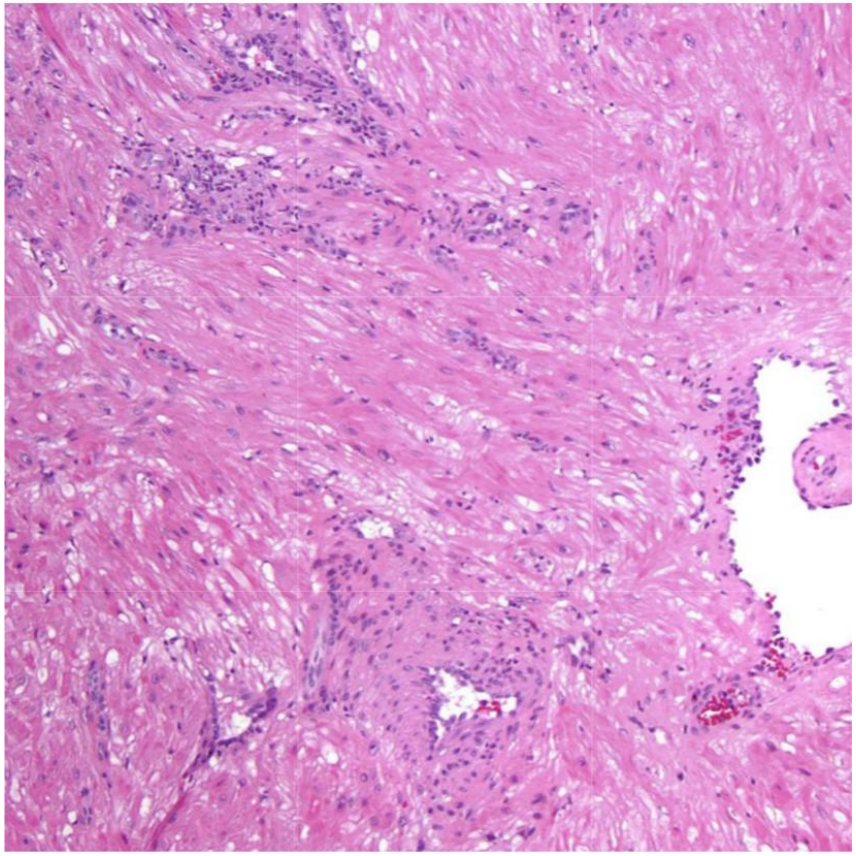












Differential Diagnosis

- Superficial leiomyosarcoma
- Congenital smooth muscle hamartoma
- Angioleiomyoma
- Dermatomyofibroma

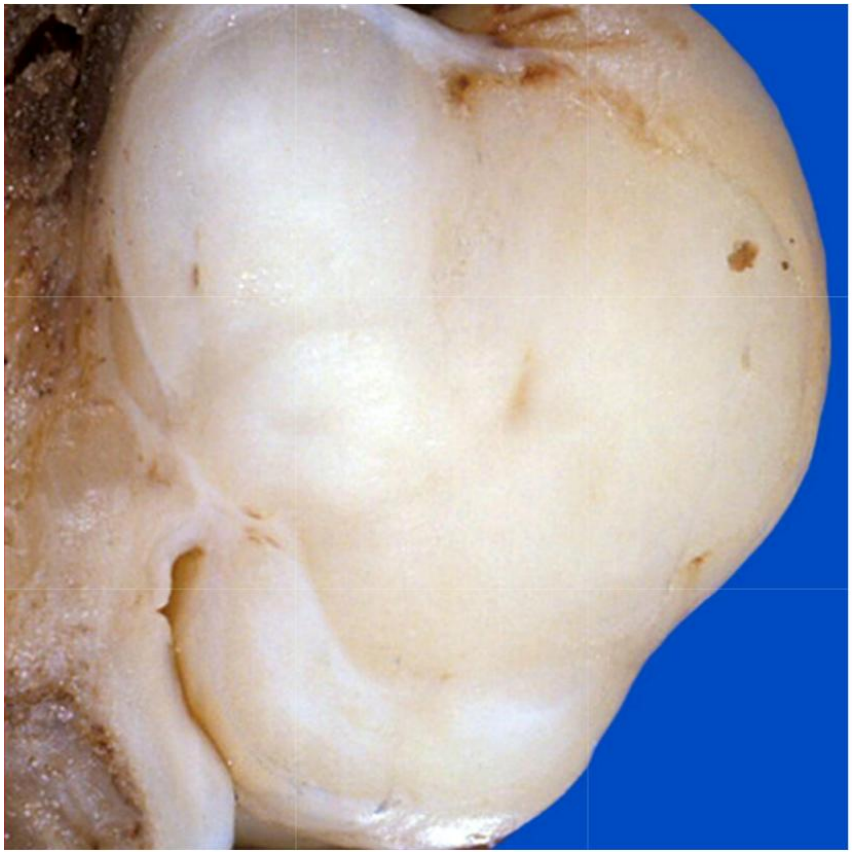
Leiomyosarcoma

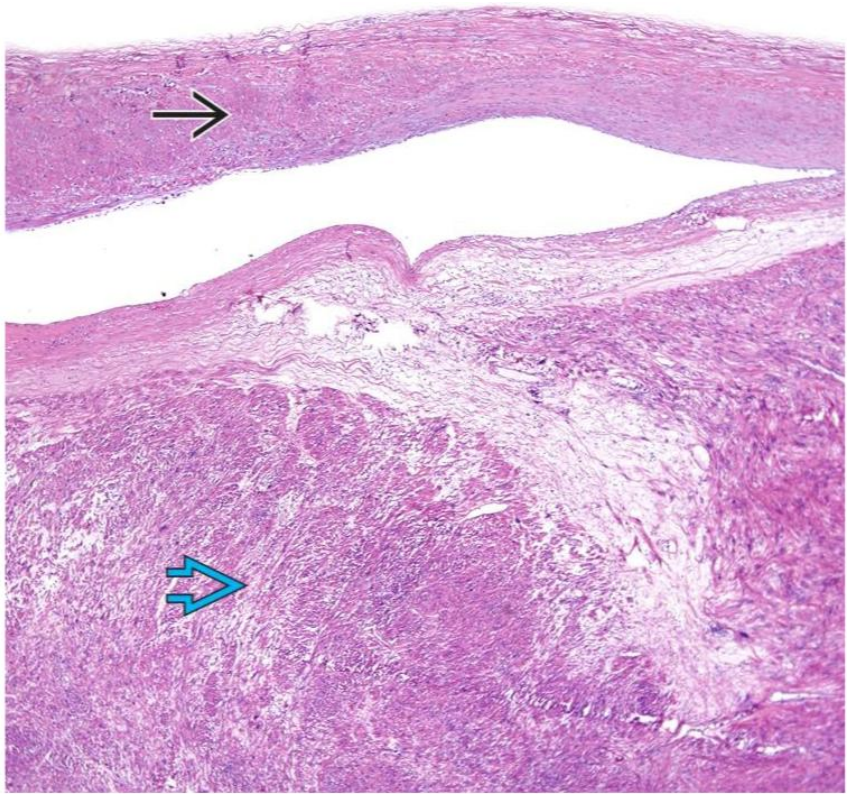
- Malignant neoplasm composed of cells exhibiting true smooth muscle differentiation

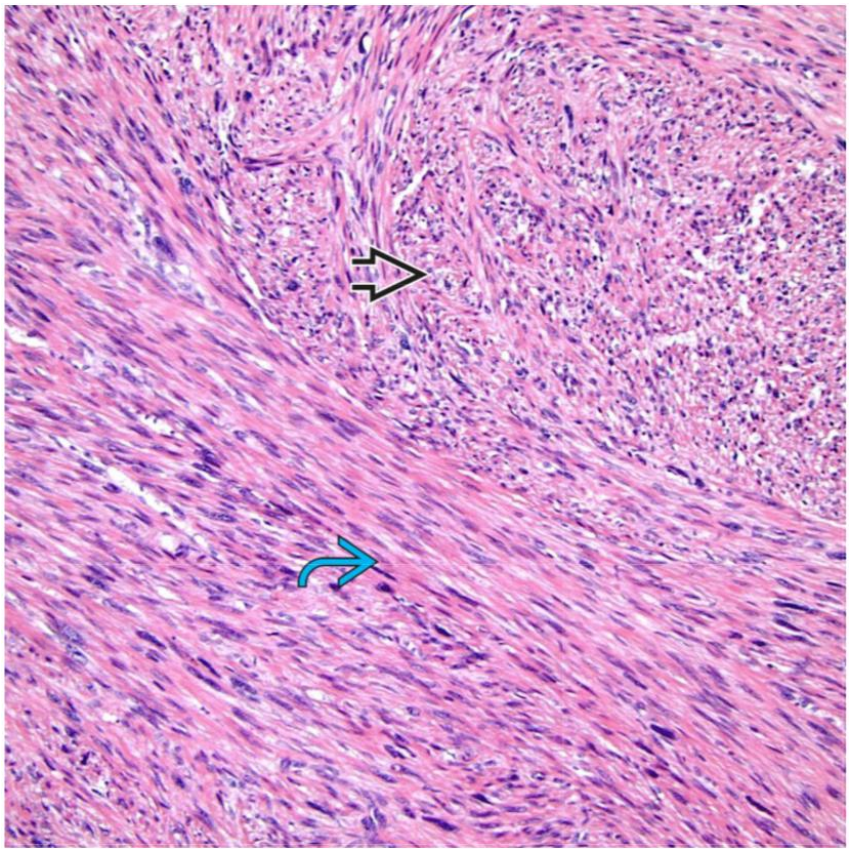
Clinical Issues

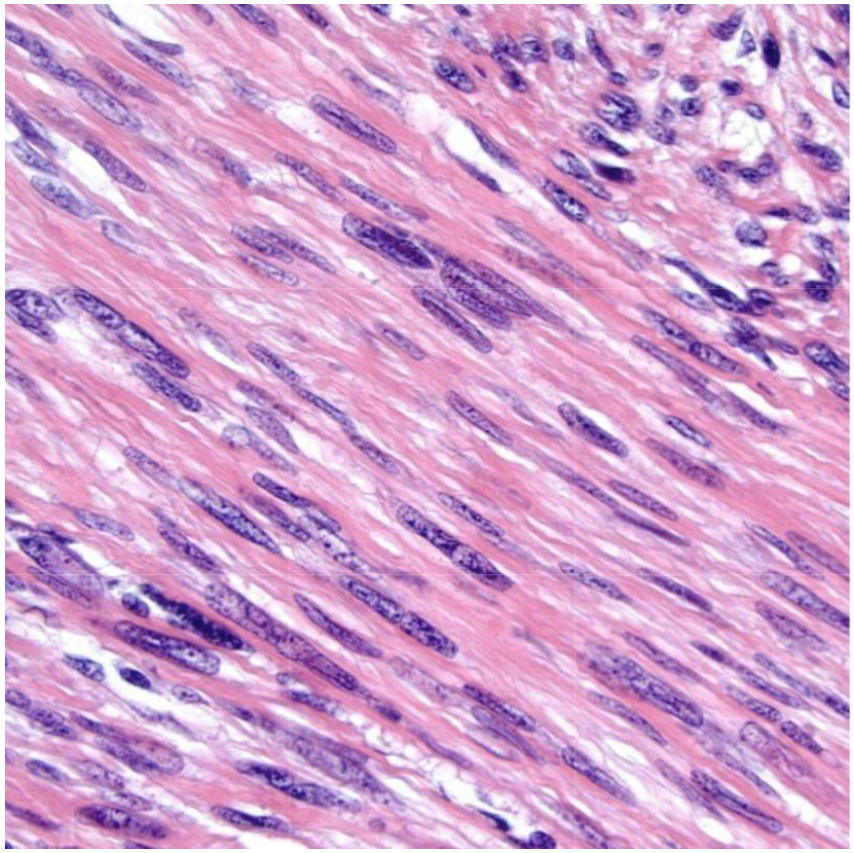
- Most common in middle-aged to older adults
- Female predilection in retroperitoneum/pelvis
  - **Retroperitoneum** most common site
  - Also inferior vena cava, extremities, head/neck
  - Vena caval tumors may cause Budd-Chiari syndrome
- Treatment: Complete surgical resection
- **Overall poor prognosis**
  - Local recurrence and metastasis common
  - Retroperitoneal tumors have worst prognosis
- **Lung** is most common site of metastasis
- Can also metastasize to skin, lymph nodes, bone, and other soft tissue sites

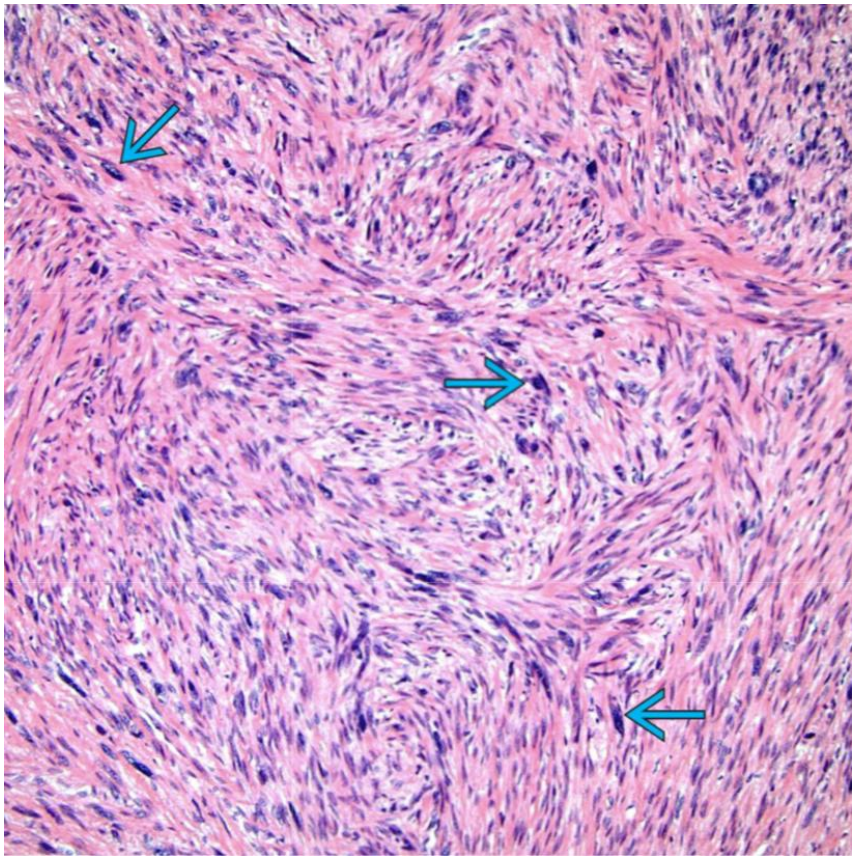
Clinical and Microscopic

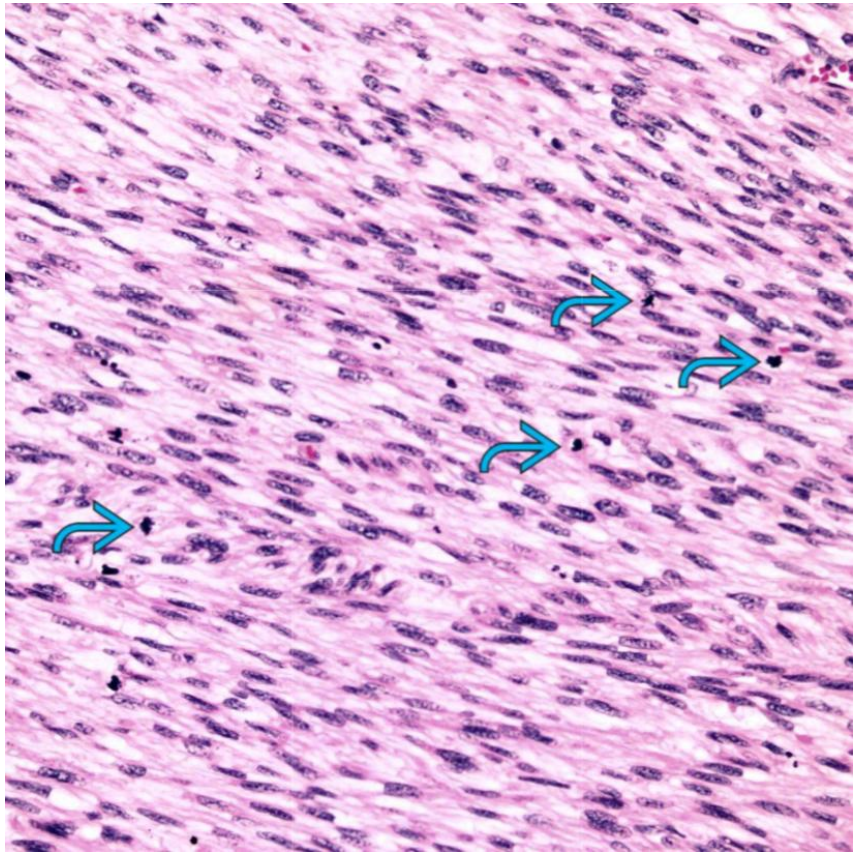


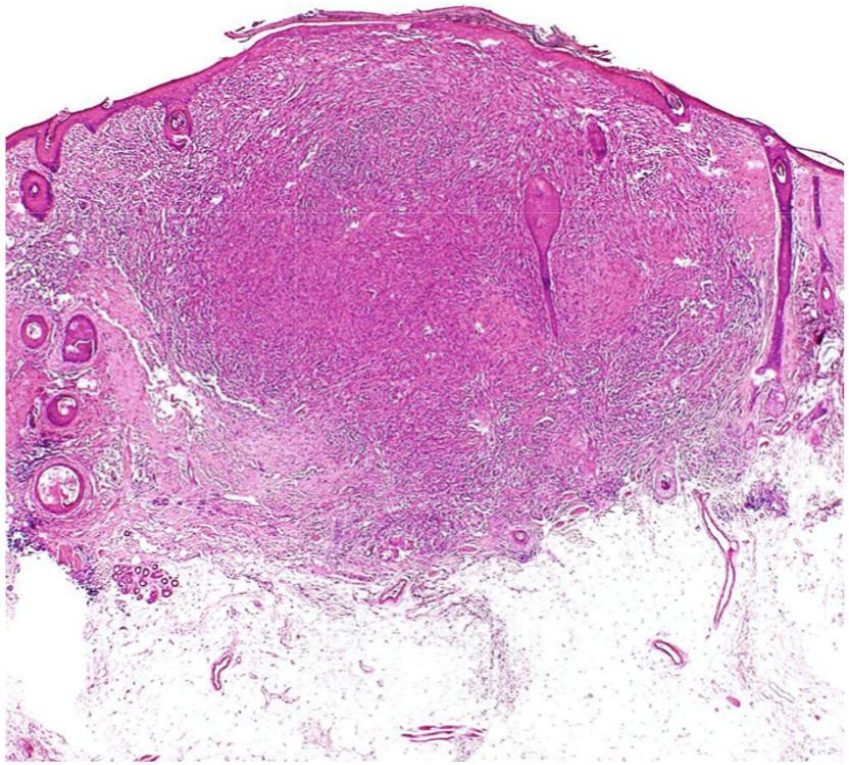


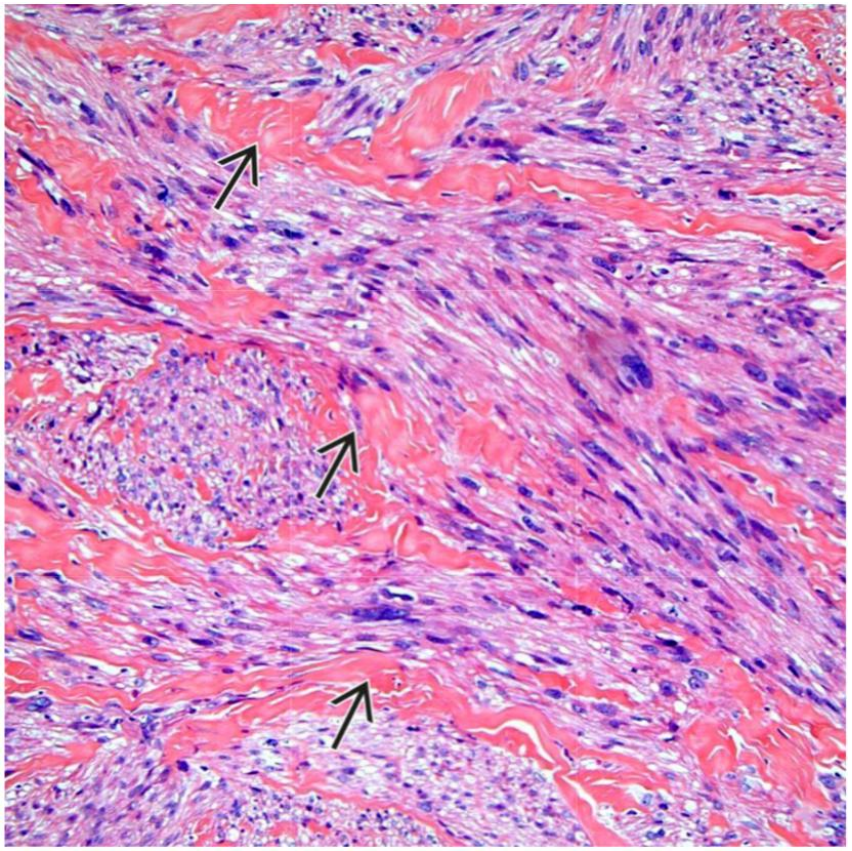






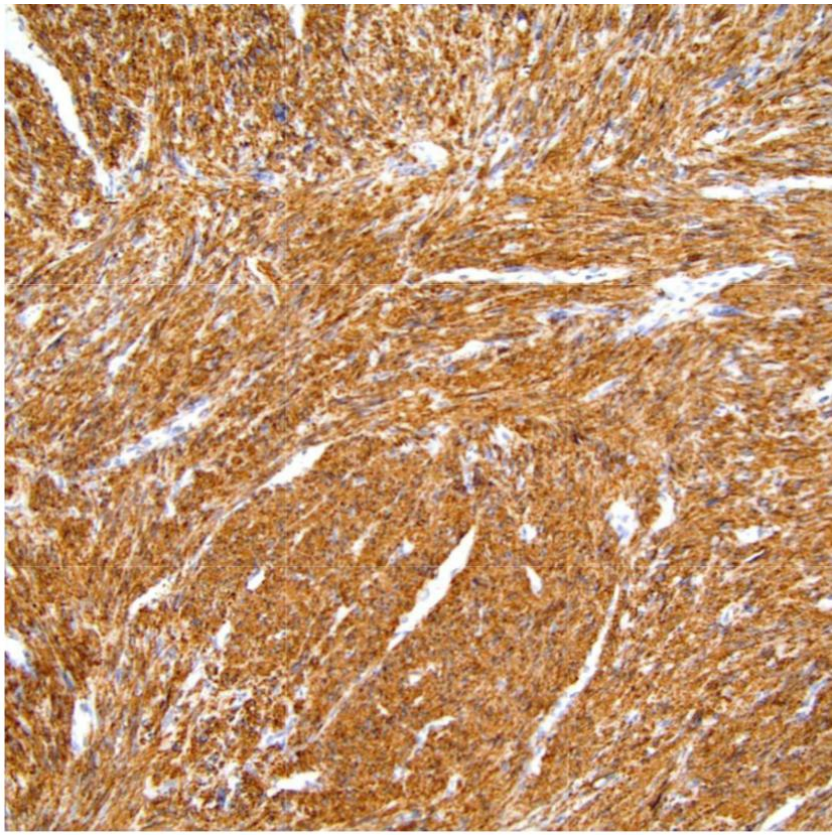




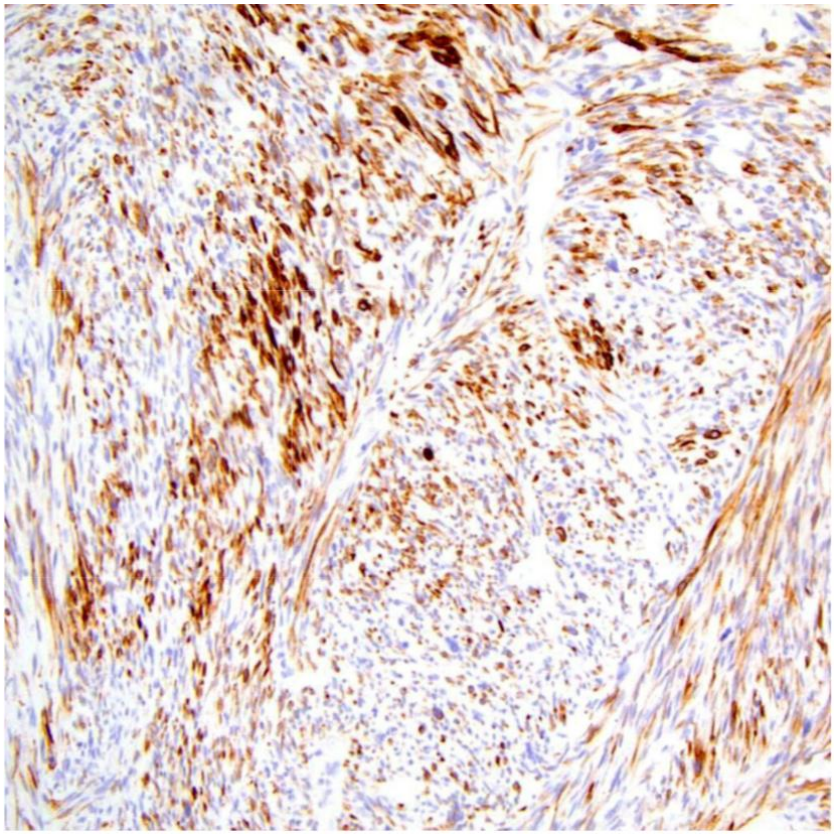


Ancillary Tests

IHC for Smooth Muscle Actin



IHC for desmin



Differential Diagnosis

- Leiomyoma
- PEComa
- Desmoid fibromatosis
- Malignant peripheral nerve sheath tumor
- Undifferentiated pleomorphic sarcoma

Tumors of Skeletal Muscle

Embryonal Rhabdomyosarcoma

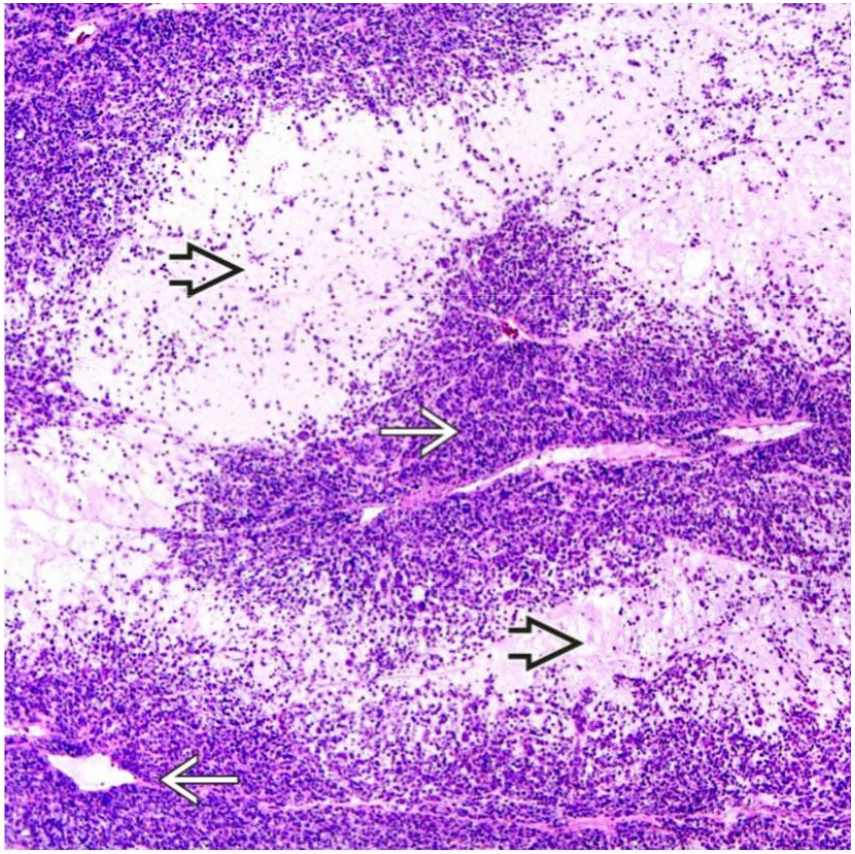
- Malignant primitive mesenchymal neoplasm that shows variable differentiation toward embryonic skeletal muscle

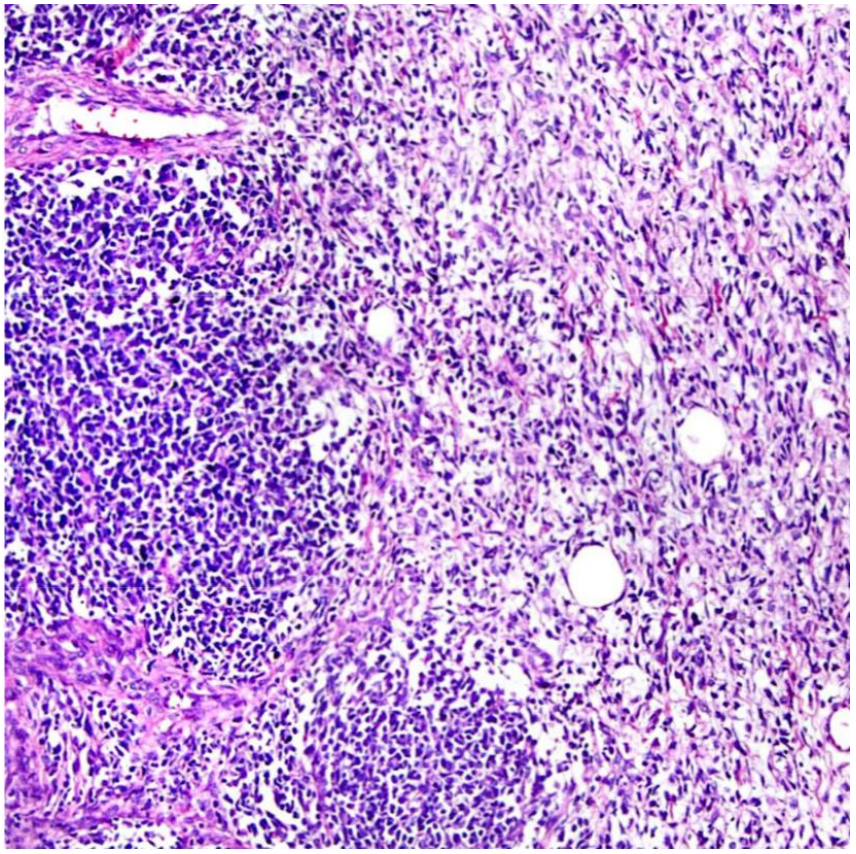
- May originate in epithelial-lined viscera (botryoid type)

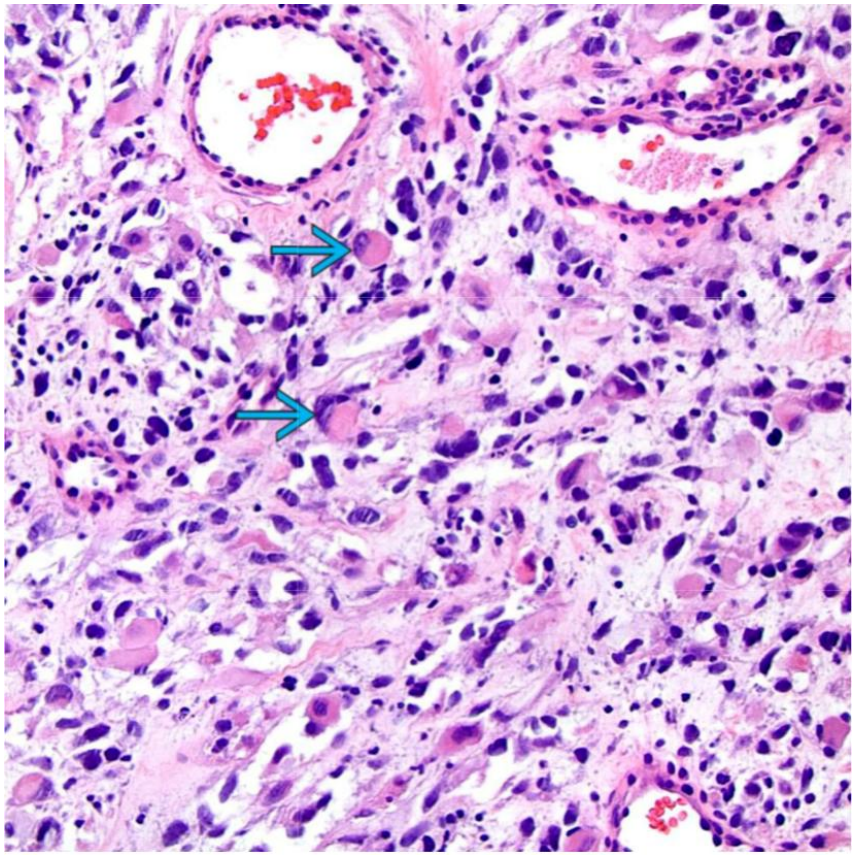
Clinical Issues

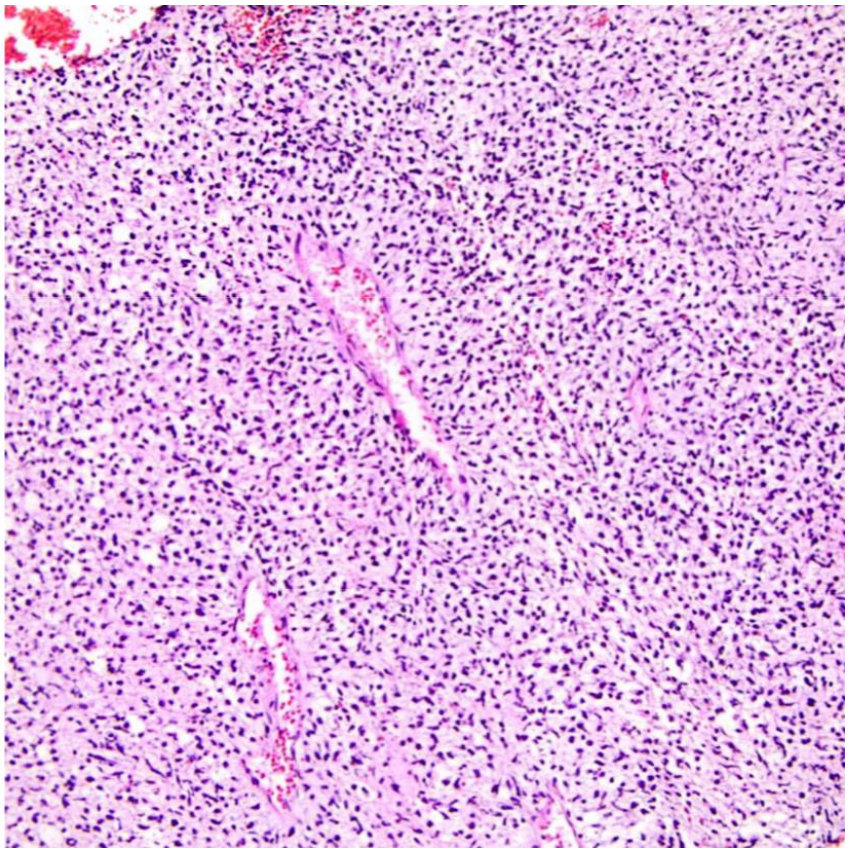
- Embryonal rhabdomyosarcoma (ERMS) is **most common subtype (60-70%)**
- Most occur in 1st decade of life
- Most arise in head/neck region or genitourinary system
- Suddenly enlarging mass
- Botryoid-type ERMS arises as polypoid growth in mucosal sites (e.g., vagina, bladder)
- Treatment: Multimodality therapy
- Main prognostic parameters are histologic type, disease stage, age, and site
  - ERMS has significantly better prognosis than alveolar rhabdomyosarcoma (ARMS)

Microscopic

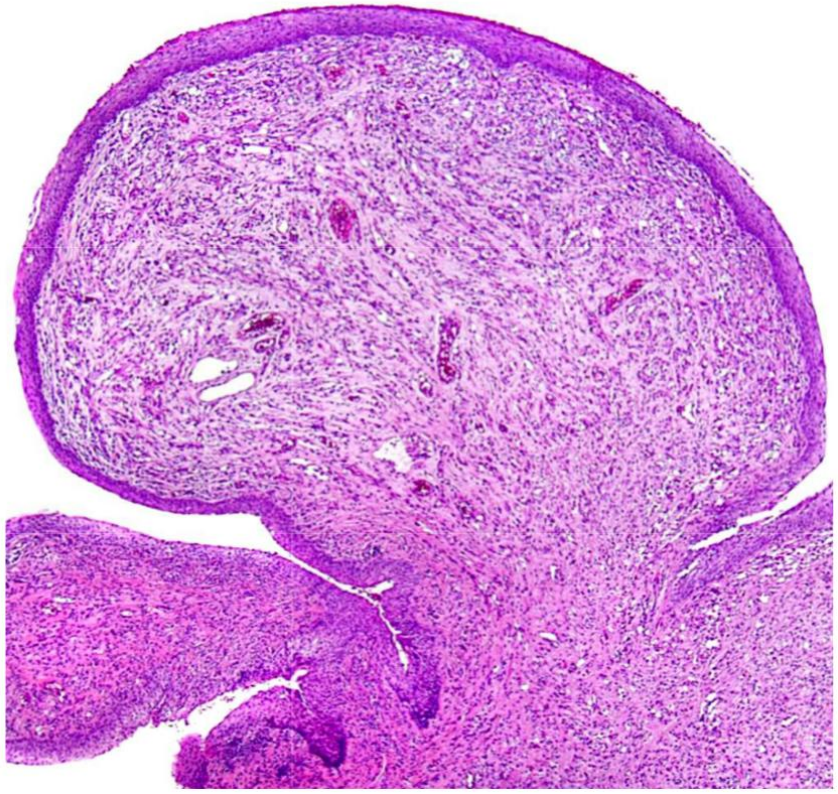




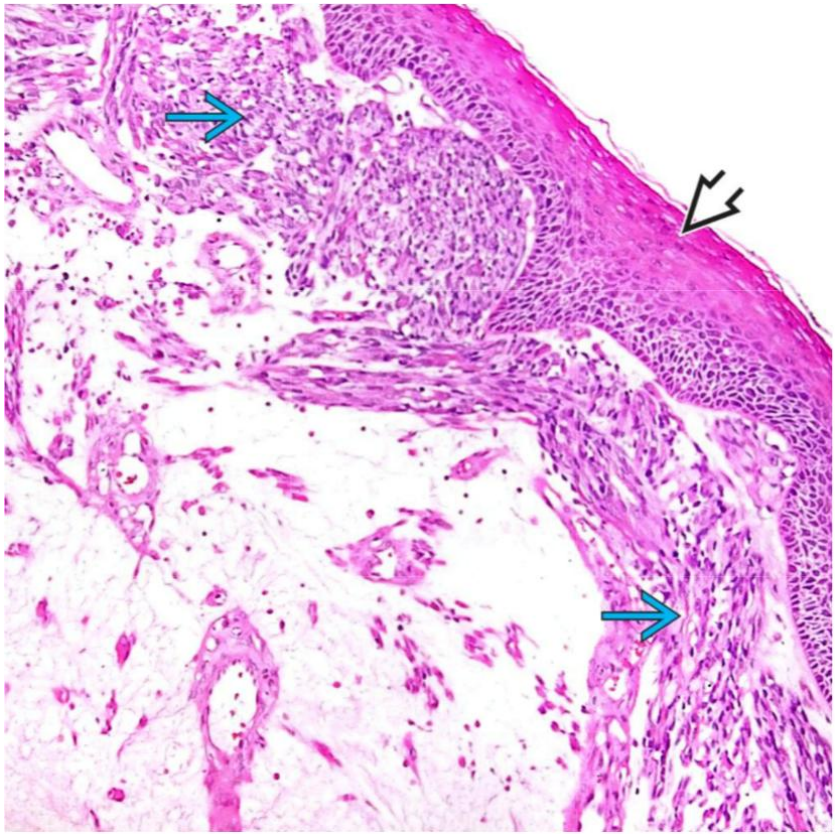




Botryoid-type



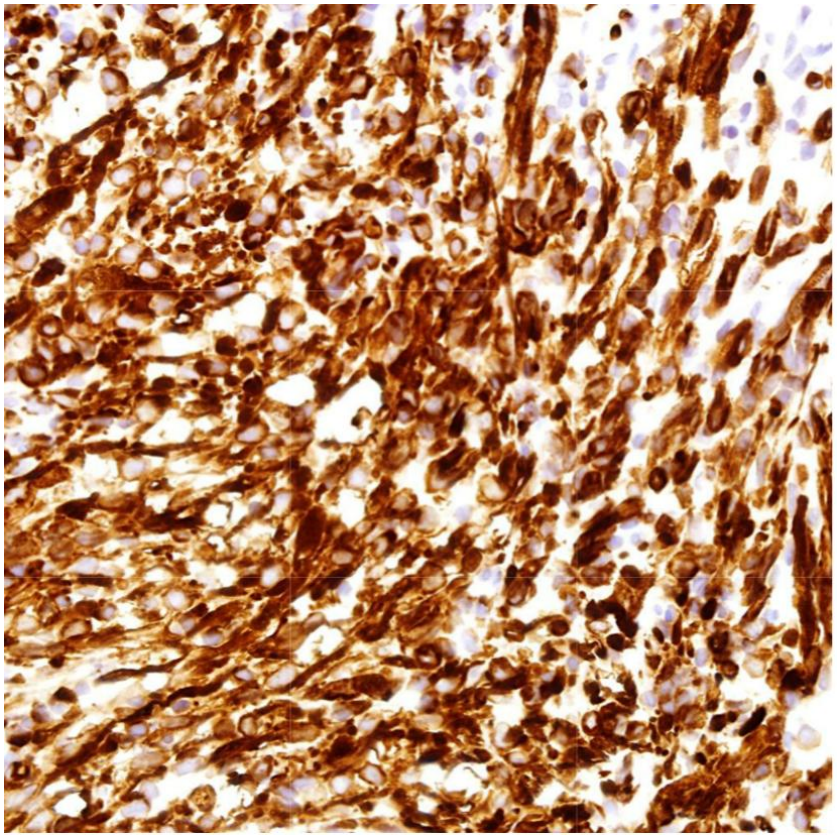
Cambium Layer



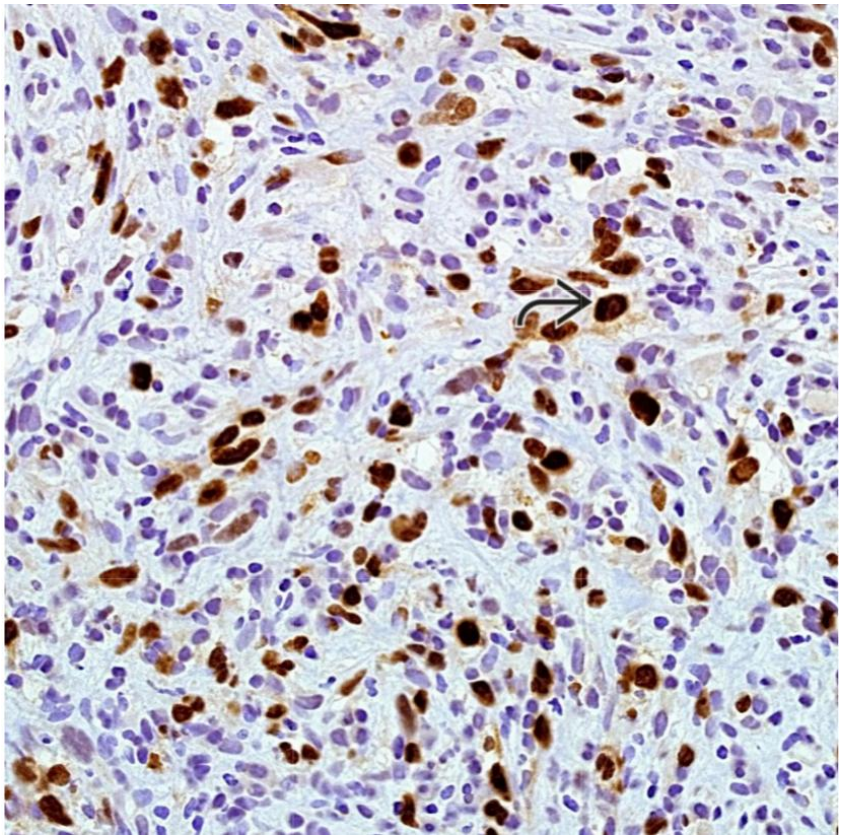
Ancillary tests

- Diffuse desmin (+)
- Nuclear myogenin (+) and MYOD1(+)
- Molecular: Absence of FOXO1 translocations

IHC for Desmin



IHC for myogenin



Differential Diagnosis

- Rhabdomyoma
- Alveolar rhabdomyosarcoma
- Malignant peripheral nerve sheath tumor (MPNST) with rhabdomyoblastic differentiation
- Neuroblastoma

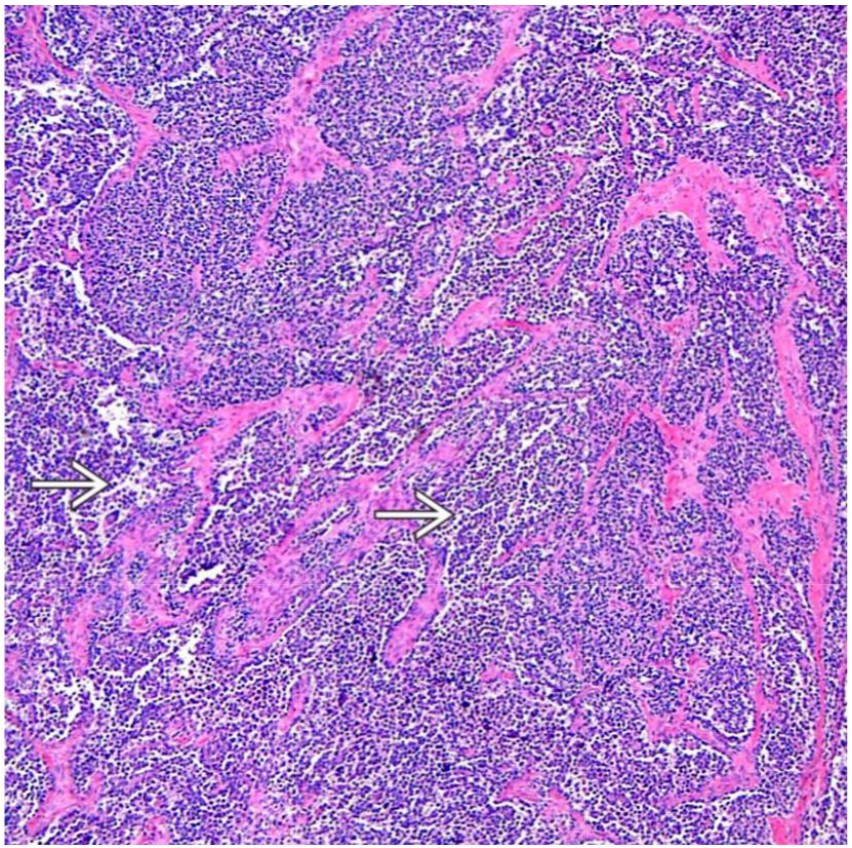
Alveolar Rhabdomyosarcoma

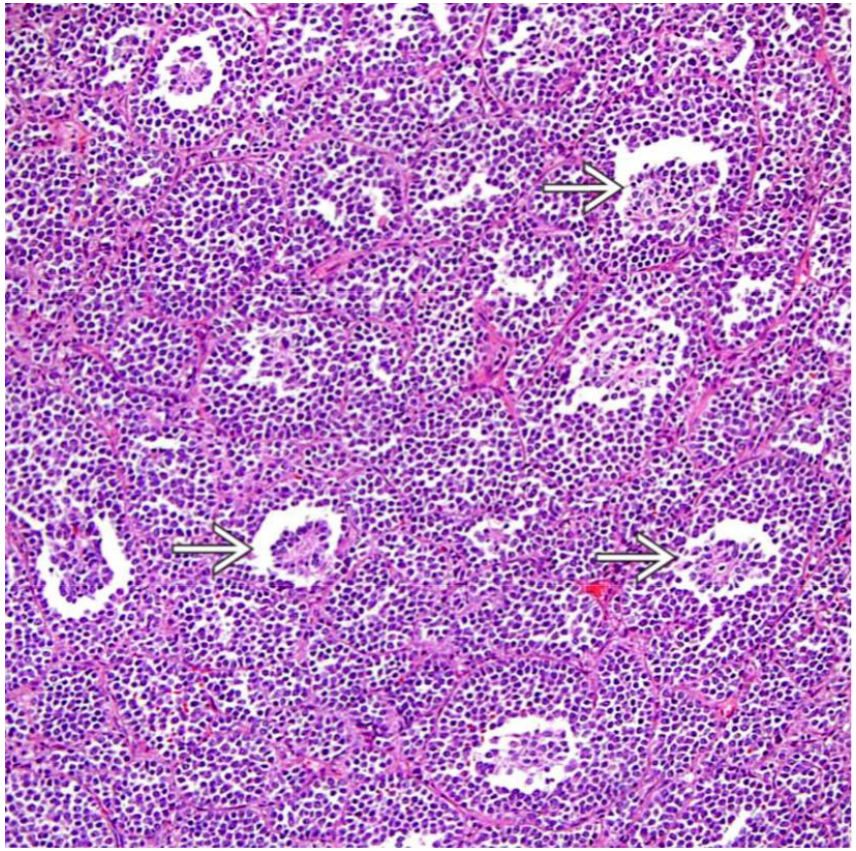
- Cellular, malignant neoplasm composed of primitive round cells with evidence of skeletal muscle differentiation

Clinical Issues

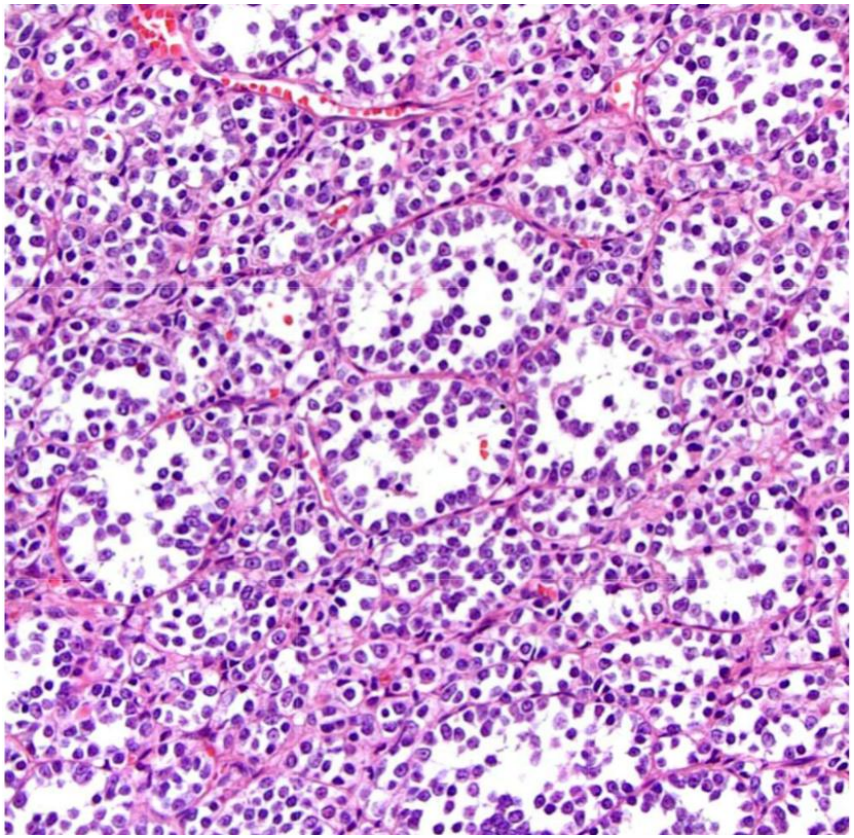
- Most common between 10-25 years of age
- Most frequent in deep soft tissues of extremities
- Often high stage at presentation
- Treatment: Multimodality approach
- Fully malignant, high-grade sarcoma
- Overall worse prognosis than embryonal rhabdomyosarcoma (ERMS)
  - Recent evidence suggests that prognosis may be related to fusion status

Microscopic

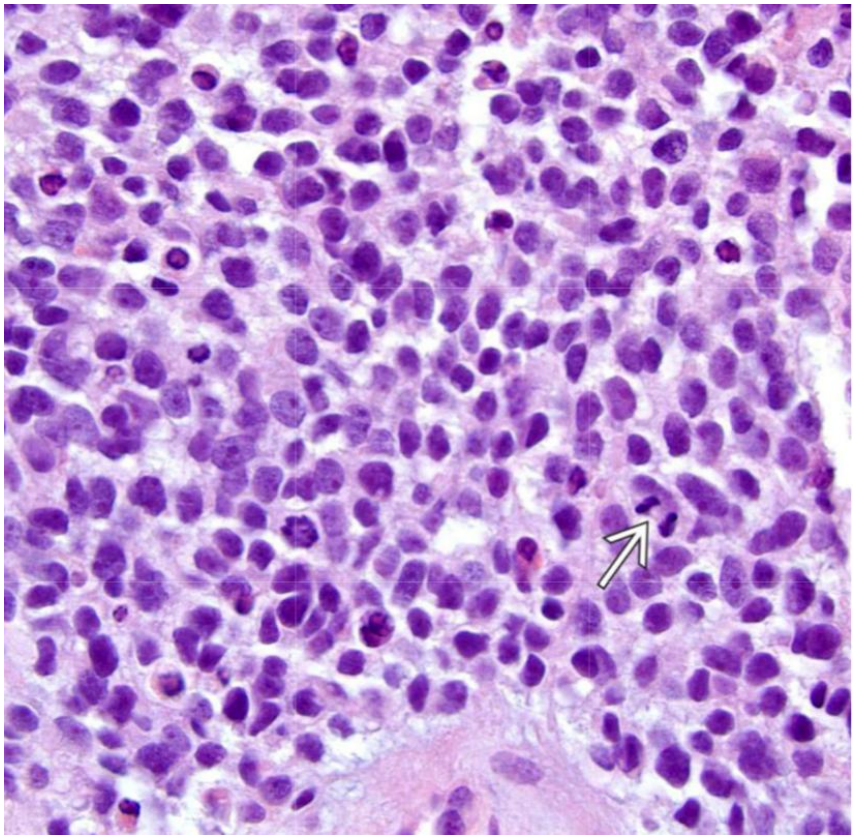




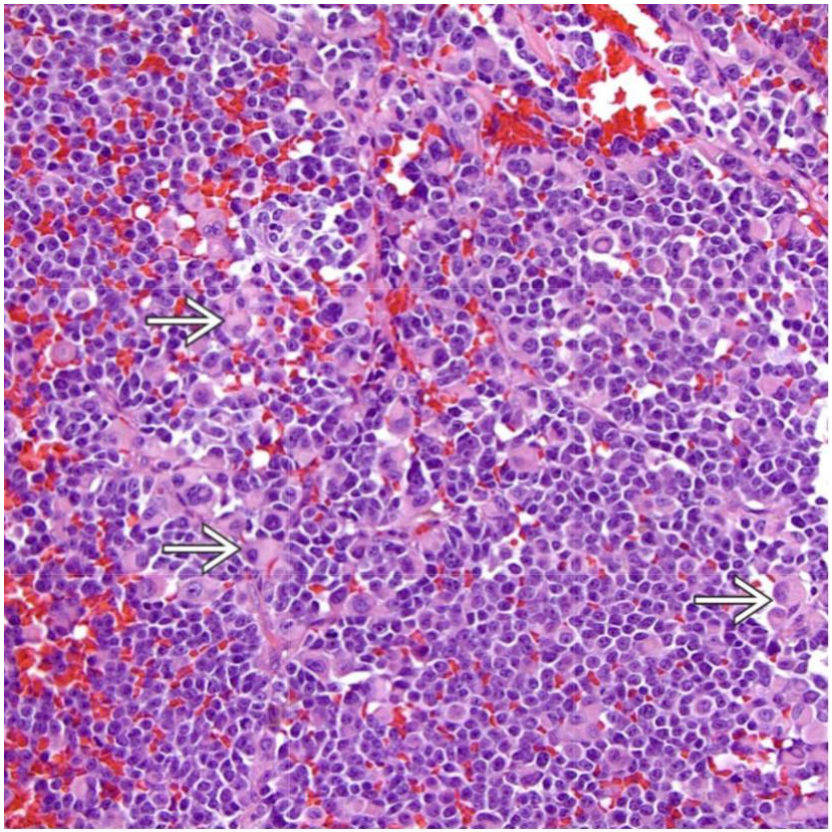
Pseudoalveolar pattern



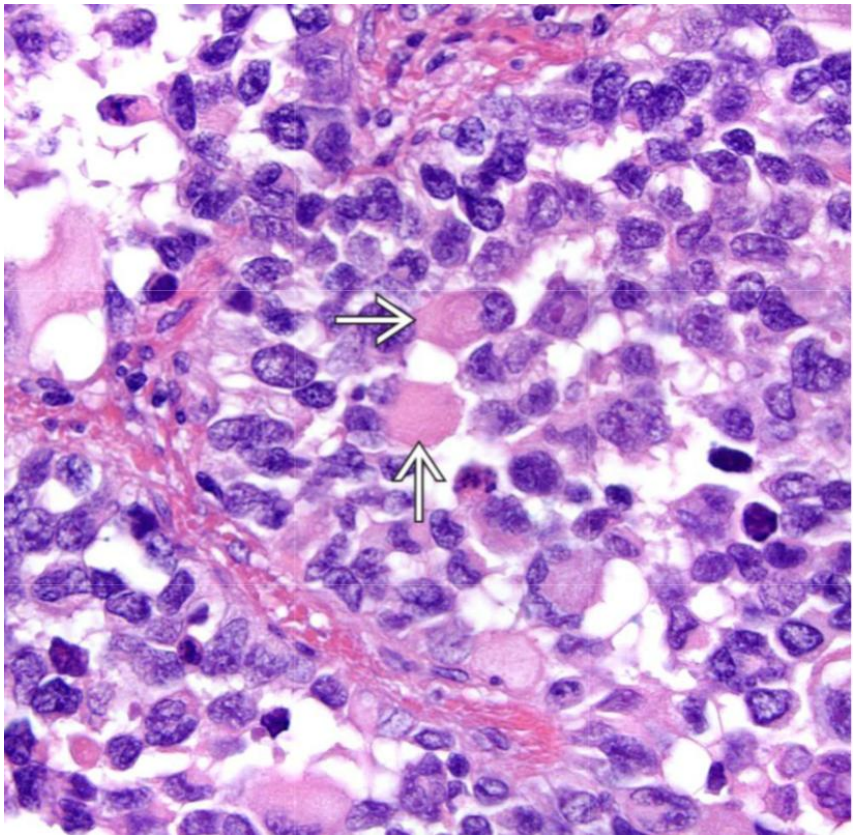
Cytologic features



Rhabdomyoblasts



Rhabdomyoblasts



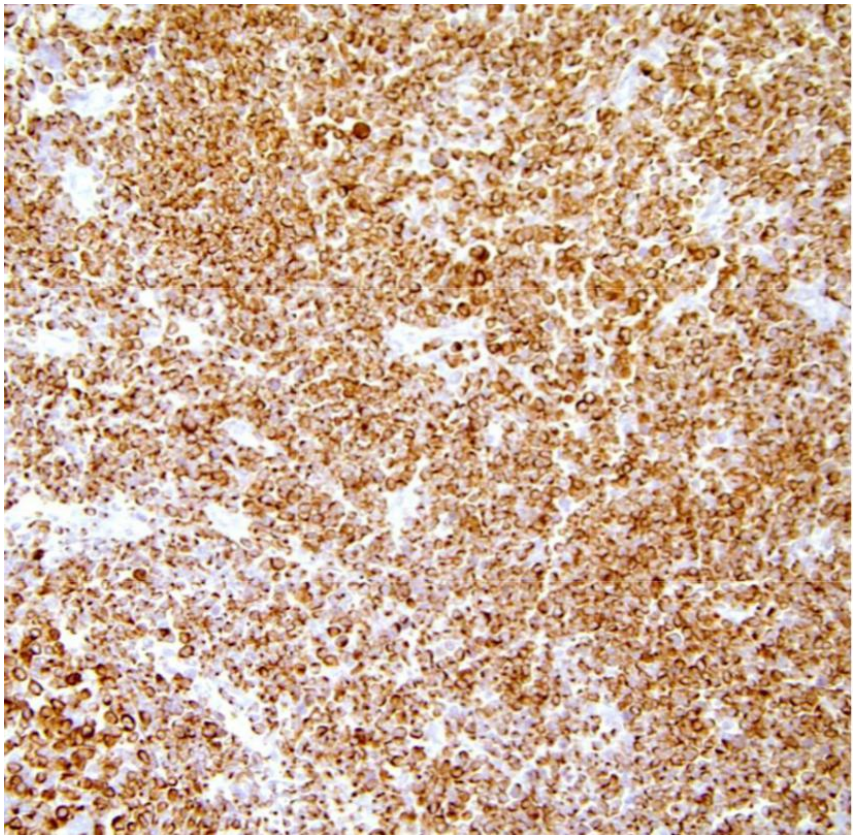
Ancillary Tests

- Usually diffuse desmin(+), myogenin (+) and MyoD1(+)

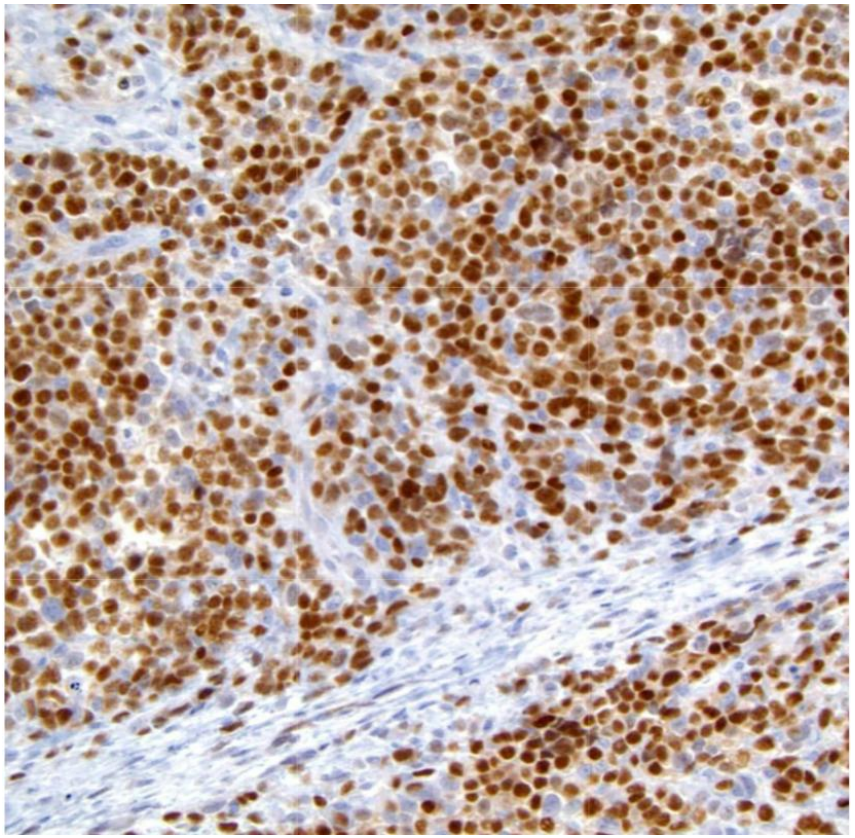
- Molecular: 2 characteristic recurrent chromosomal translocations (80% of cases)
  - t(2;13)(PAX3-FOXO1) or t(1;13)(PAX7-FOXO1)

Ancillary tests

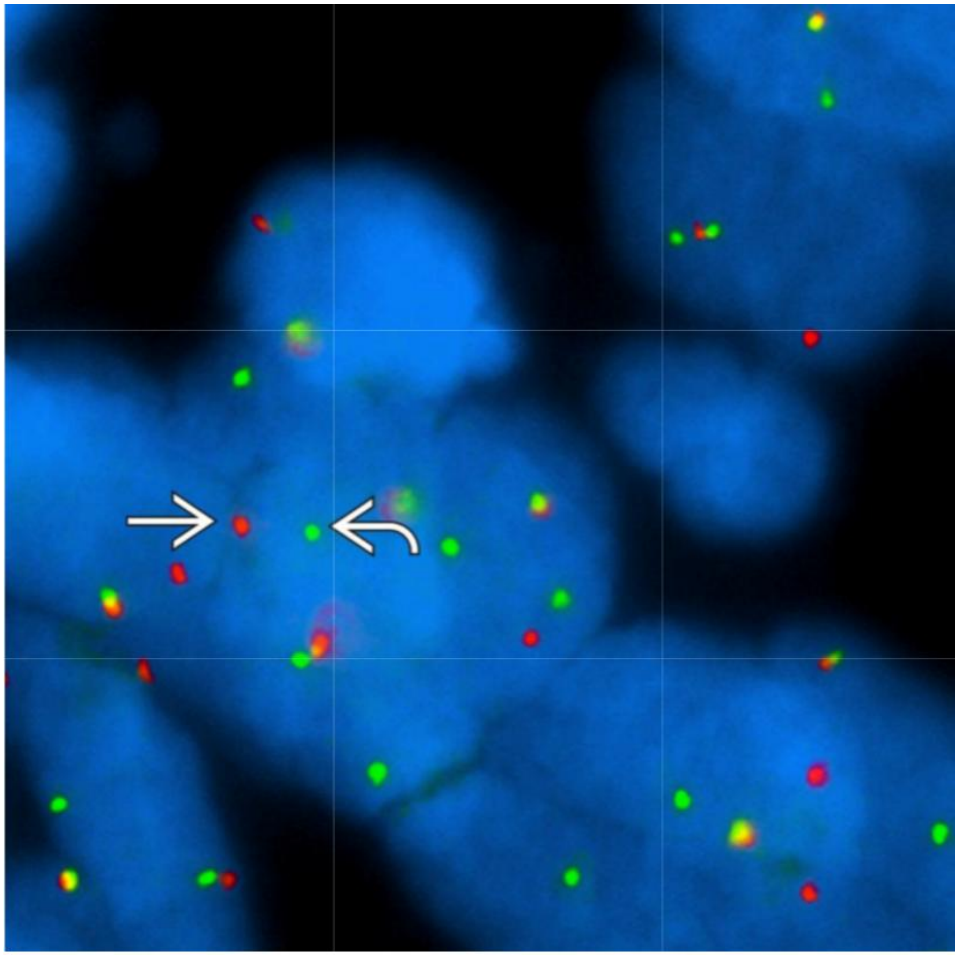
IHC for desmin



IHC for myogenin



FISH for FOX01



Differential Diagnosis

- Embryonal rhabdomyosarcoma
- Sclerosing rhabdomyosarcoma
- Various small round blue cell tumors

Vascular Tumors

Lobular Capillary Hemangioma

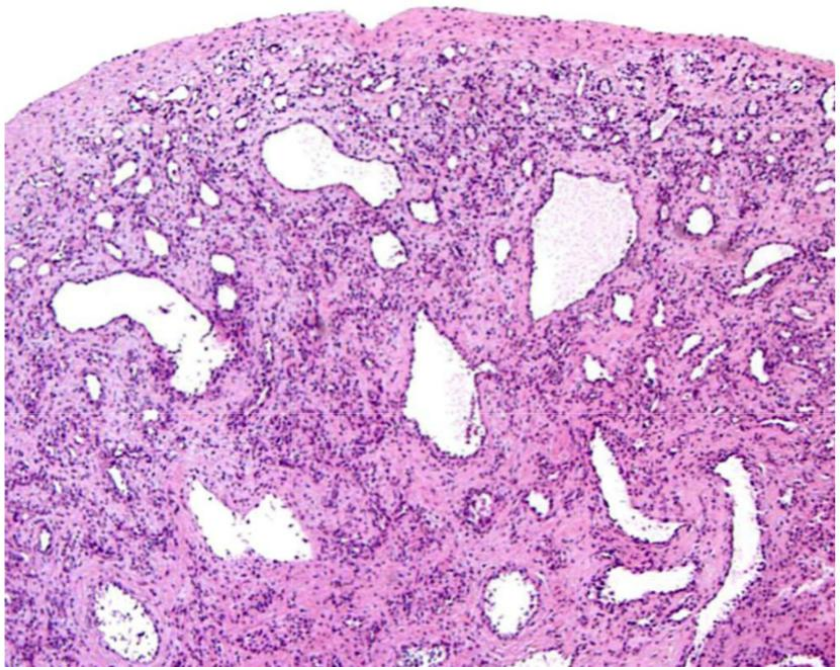
- Clinically distinctive benign vascular lesion characterized by vague lobules of capillary channels arranged around larger “feeder” vessels

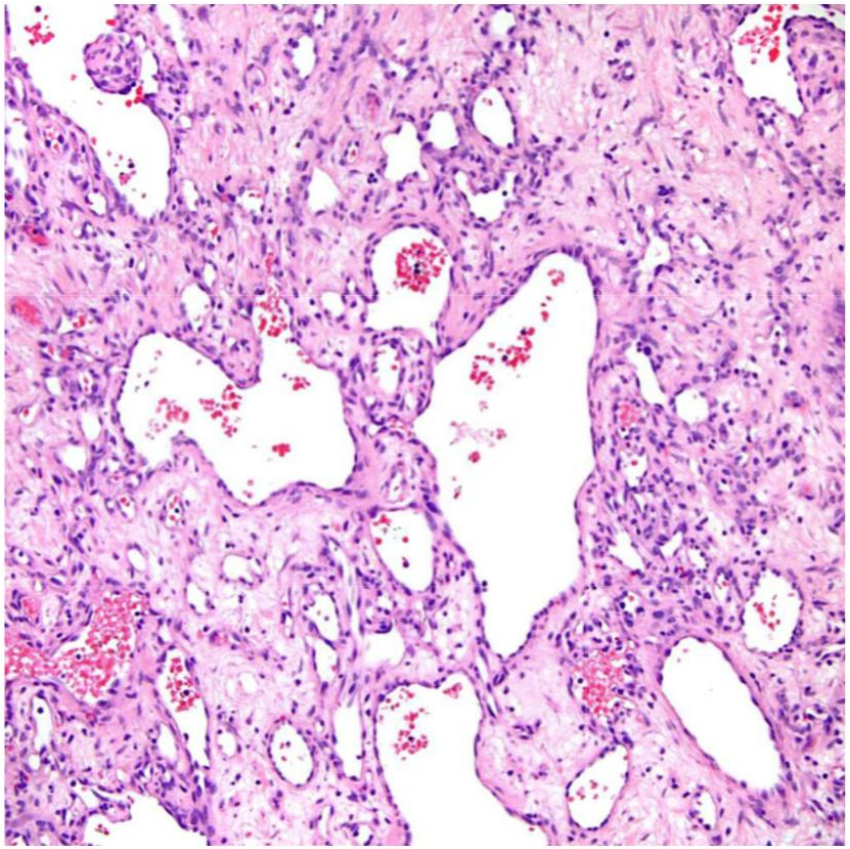
- Synonym: **Pyogenic granuloma**

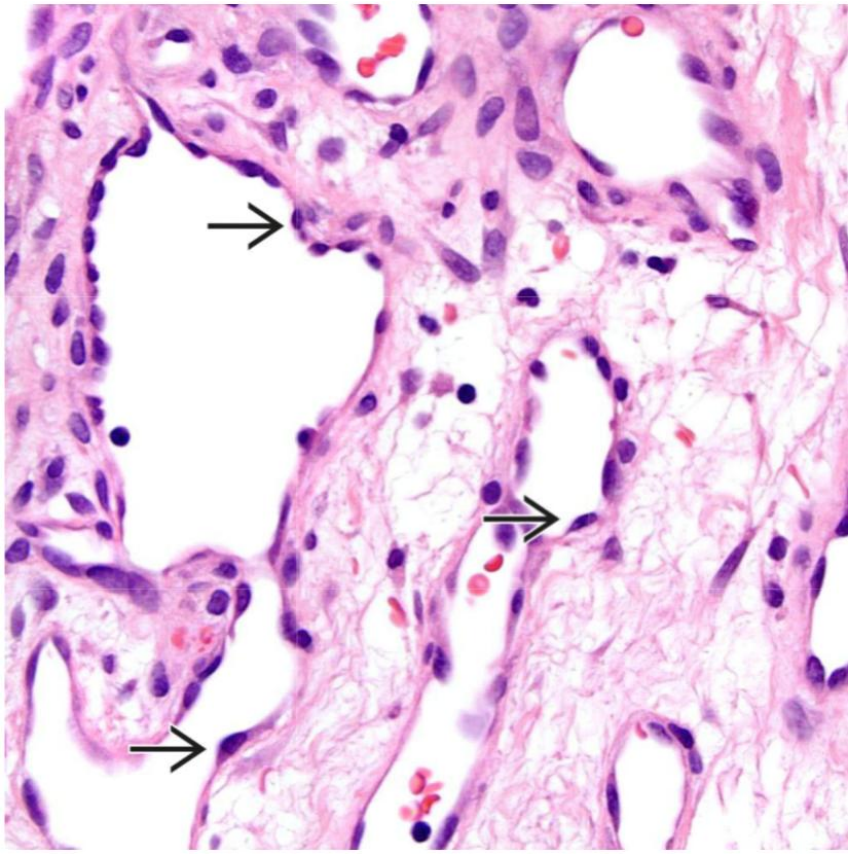
Clinical issues

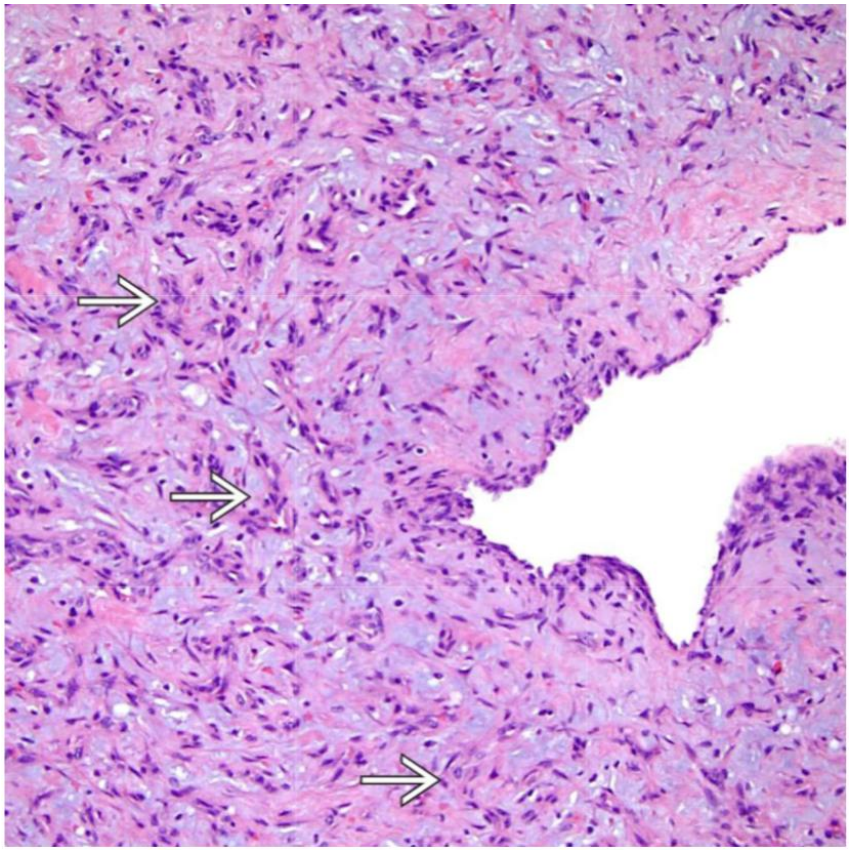
- Wide age range (common in children and young adults)
- Occurs in superficial skin and mucosal sites
  - Head and neck most common (particularly lip, gingiva, nasal cavity)
- Small (< 2.5 cm), red-purple, rapidly growing exophytic nodule
  - Overlying mucosal surface often atrophic or ulcerated
- May occur during pregnancy (granuloma gravidarum)
- Treatment: Simple excision
- Benign
  - Local recurrence is rare

Microscopic









Differential Diagnosis

- Bacillary angiomatosis
- Angiofibroma of soft tissue
- Angiosarcoma

Angiosarcoma

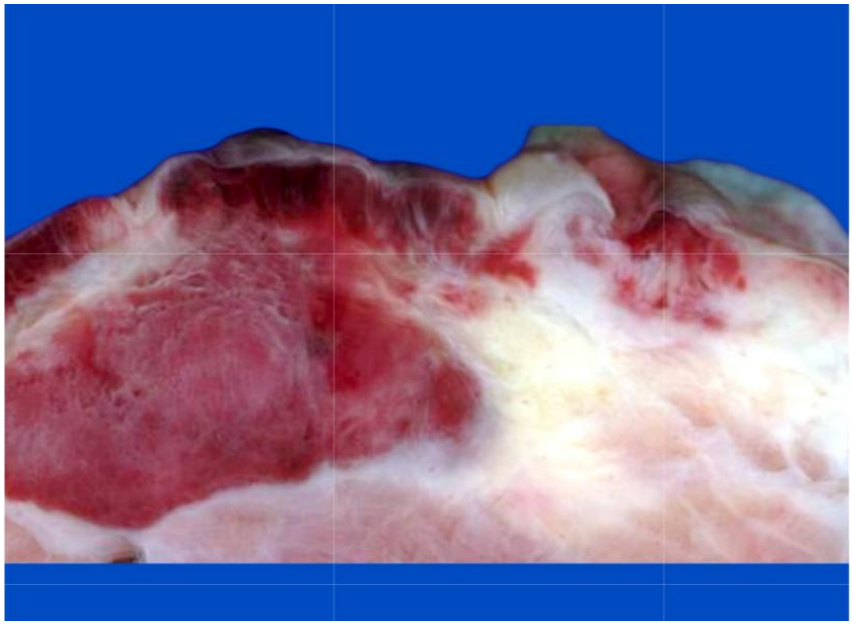
- Malignant neoplasm showing morphologic &/or immunophenotypic evidence of vascular/endothelial differentiation

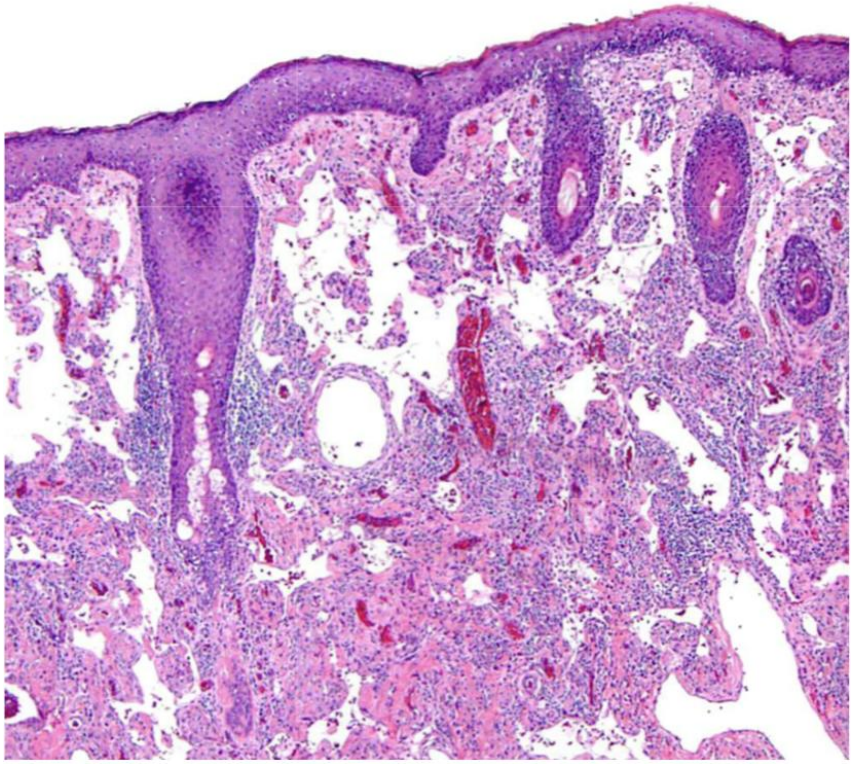
- Subsets associated with prior radiotherapy, chronic lymphedema, exposure to certain chemicals, certain syndromes

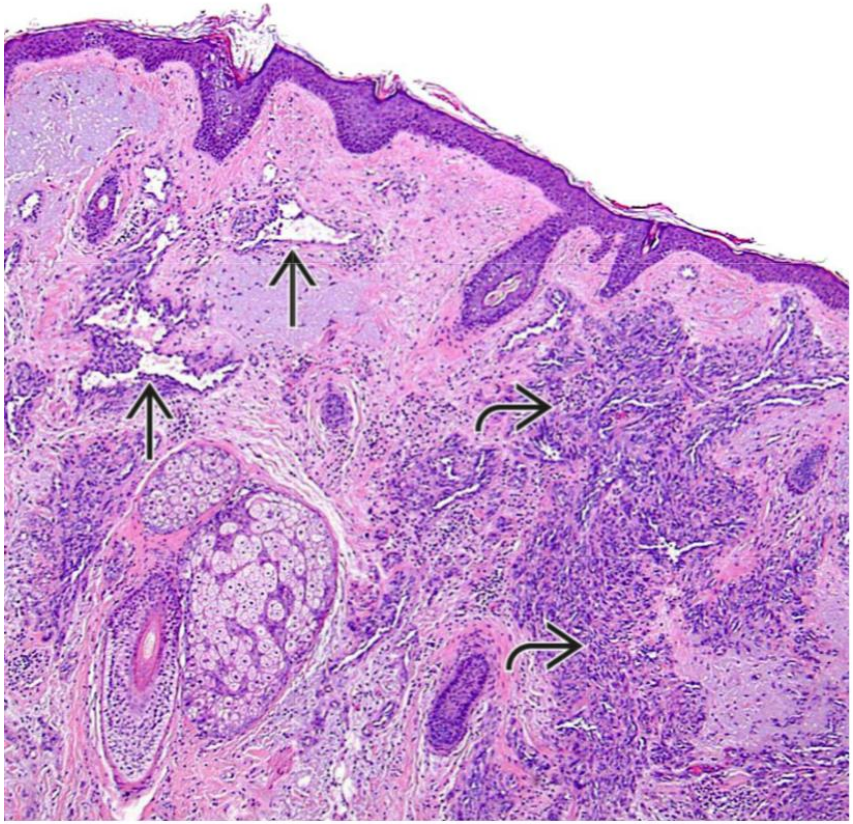
Clinical Issues

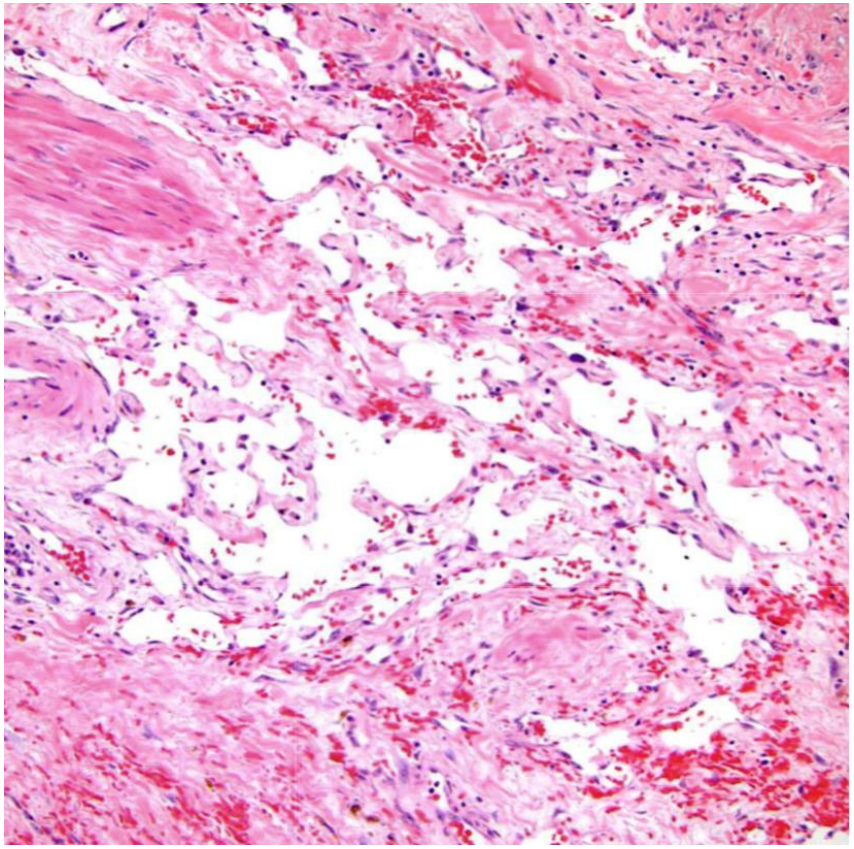
- Wide age range overall (more common in adults)
- Cutaneous scalp/face in elderly, cutaneous breast with history of radiotherapy or chronic lymphedema, parenchymal breast in young women
- Deep soft tissue forms most common in lower extremity
- Treatment: Aggressive surgical resection with widely negative margins
- Overall poor prognosis (overall survival rate: 30%)

Macroscopic and Microscopic

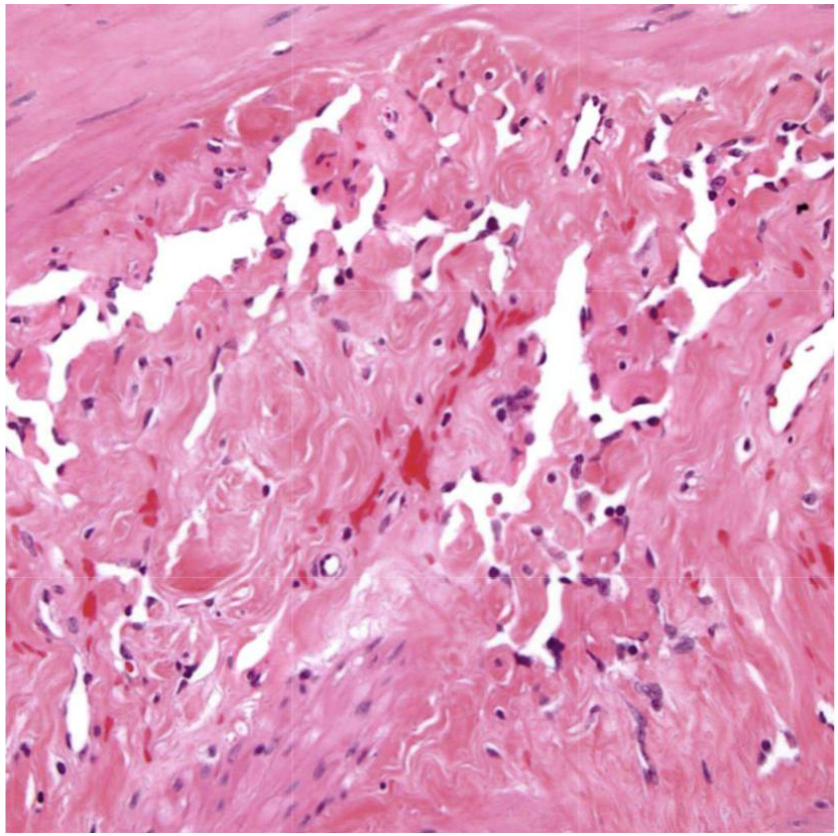




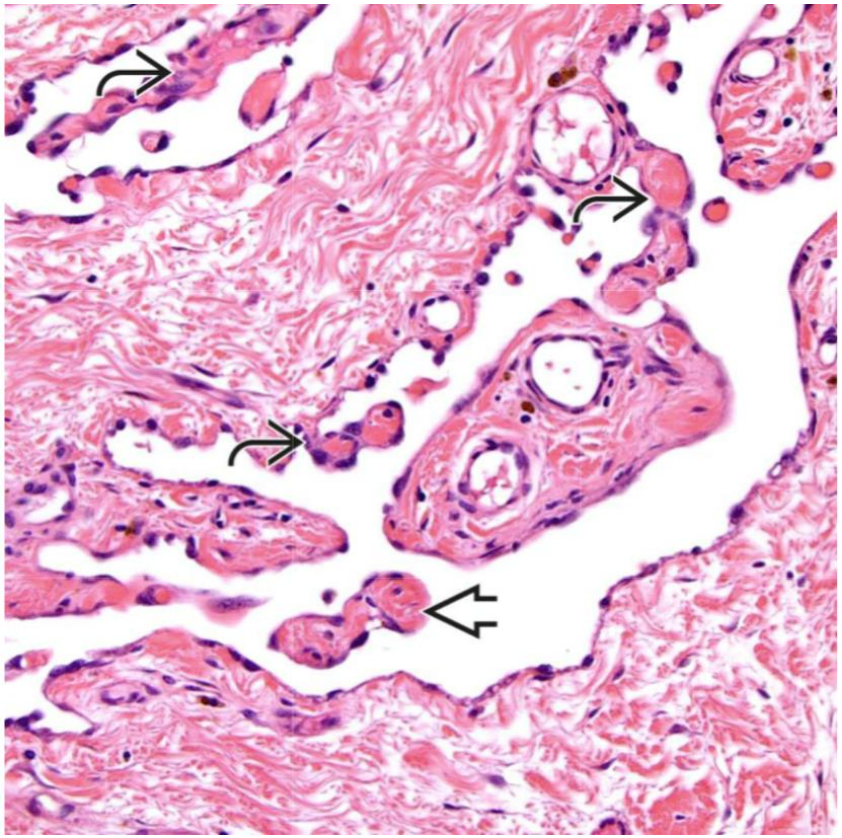




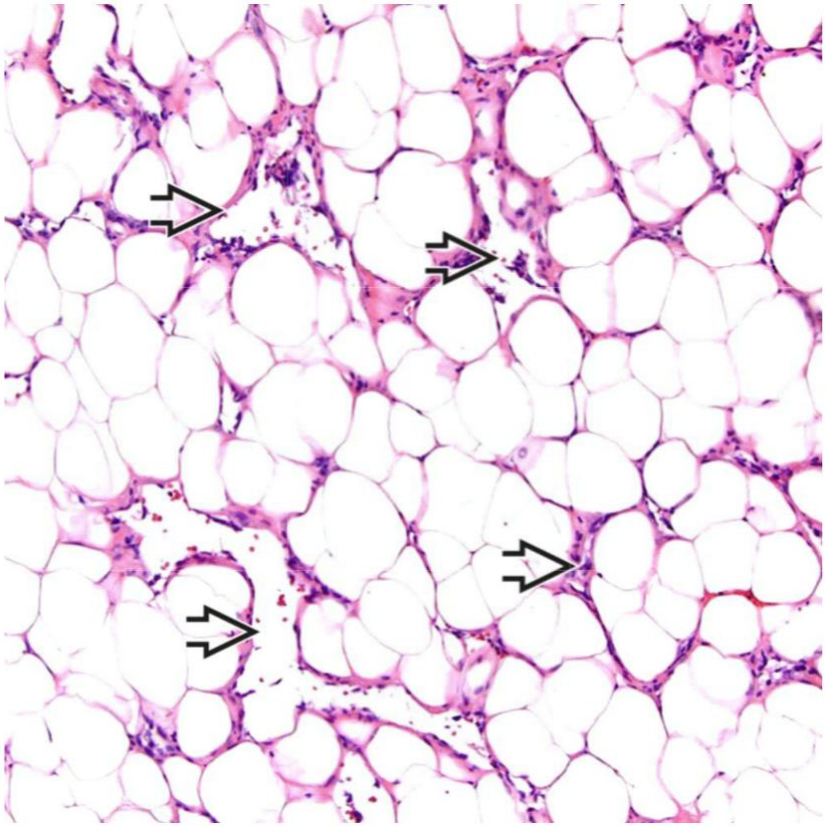
Subtle nuclear atypia



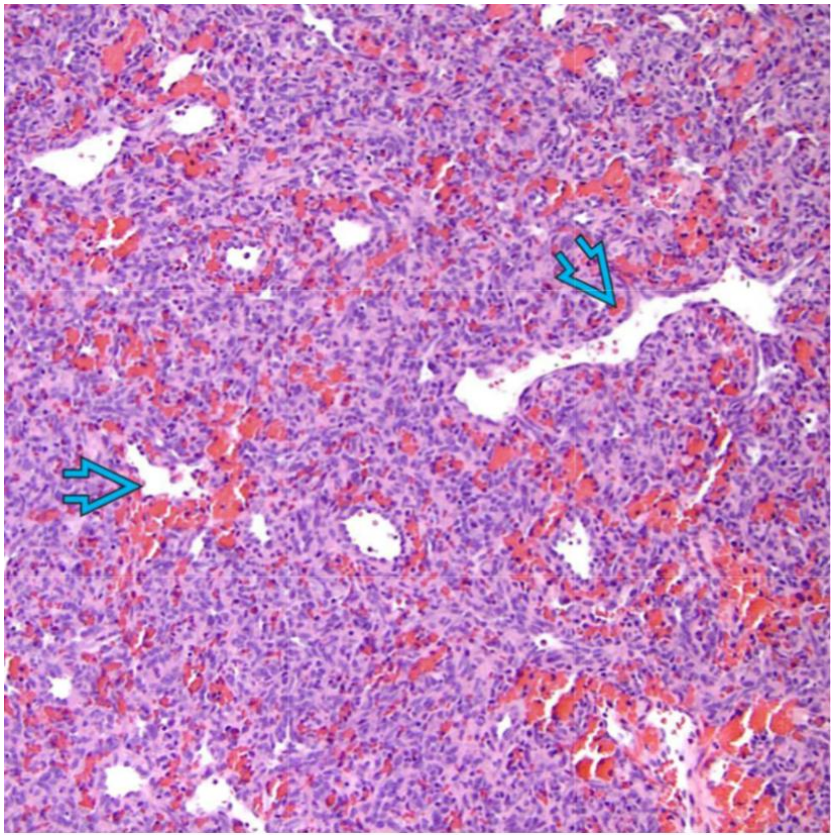
Papillary-like structures



Infiltration of adipose tissue



Solid growth



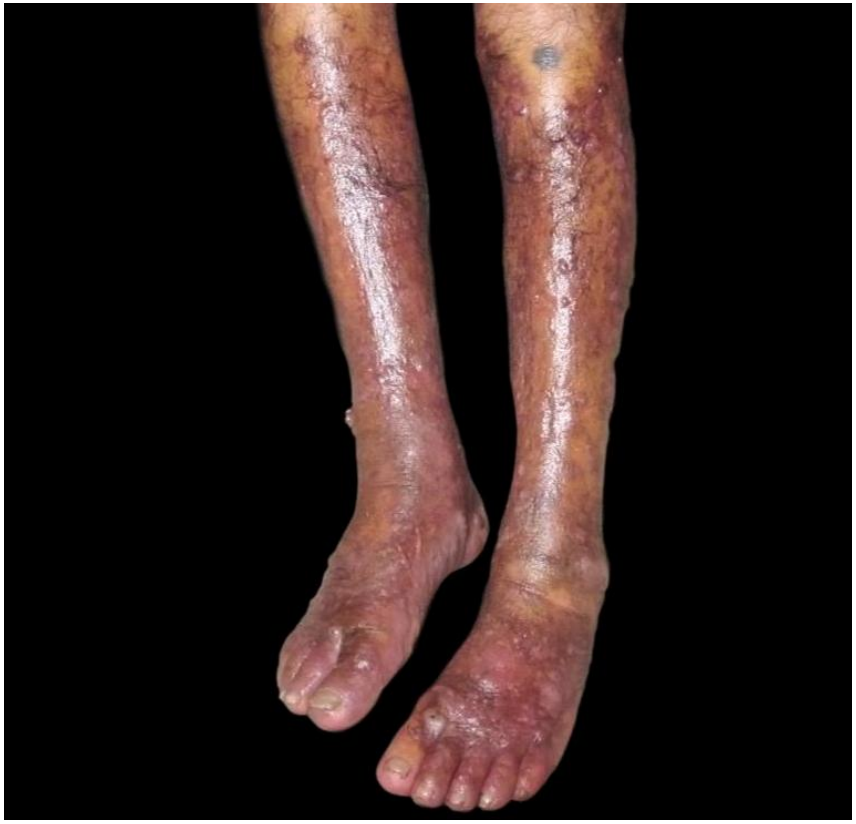
Differential Diagnosis

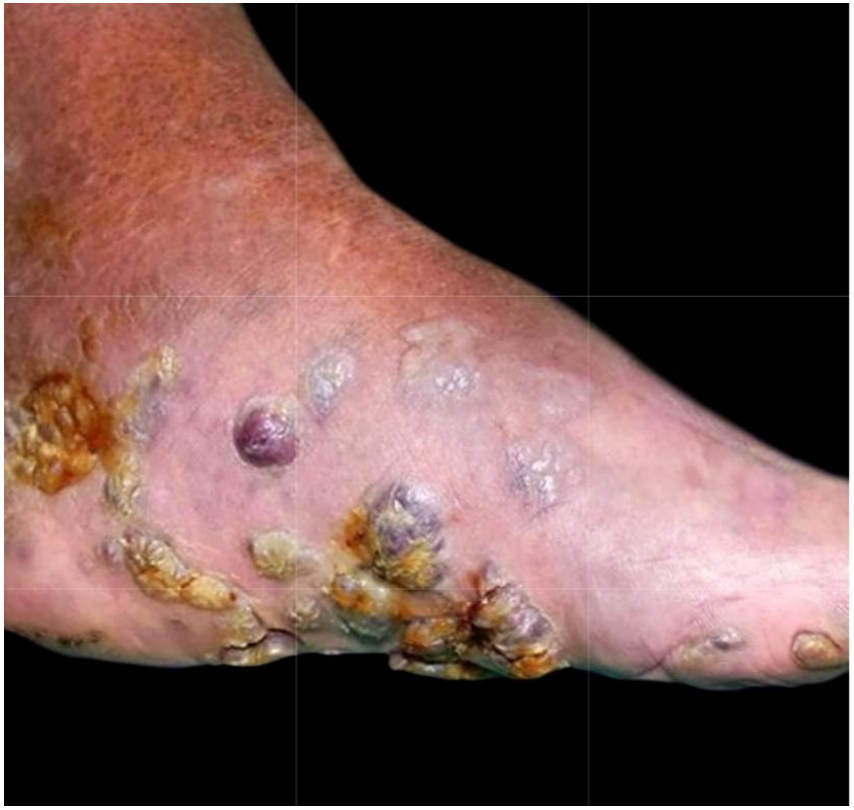
- Hemangioma
- Atypical vascular lesion
- Metastatic carcinoma

Kaposi Sarcoma

- Vascular neoplasm (usually low grade) caused by **HHV8**
- Sites: Skin (majority), mucosa, lymph nodes, organs
- Clinical variants
  - **Classic**: Lower legs/feet of elderly males; indolent
  - **African/endemic**: Children/adults in equatorial Africa
  - **Iatrogenic**: Immunosuppressed patients of any age
  - **AIDS-associated**: Aggressive (often disseminated)
- Many modalities for symptom control, but no cure

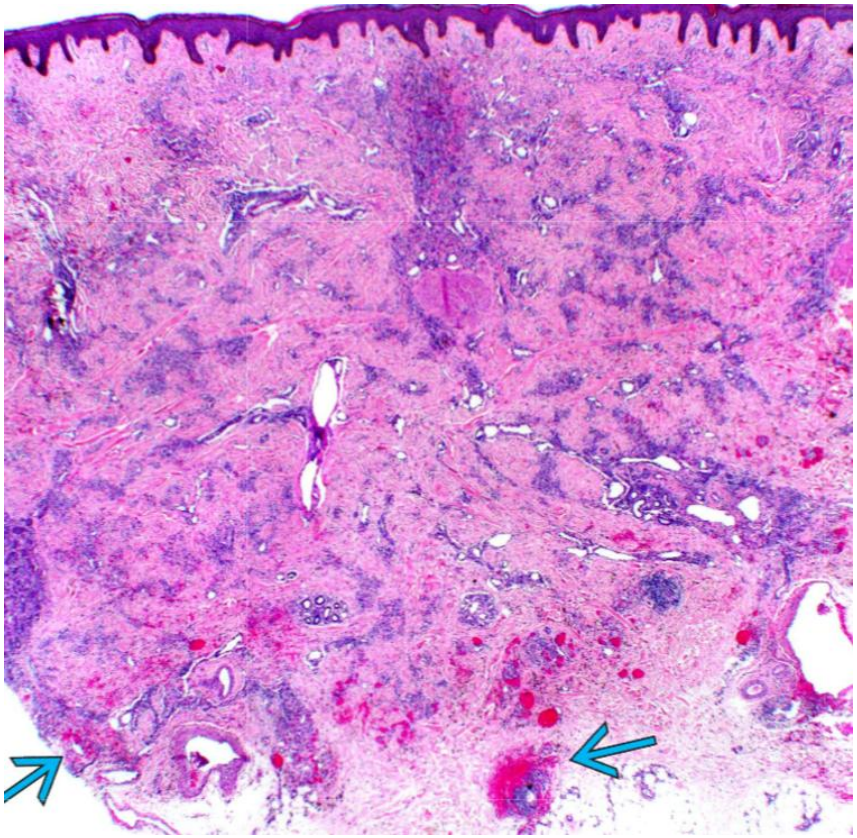
Clinical



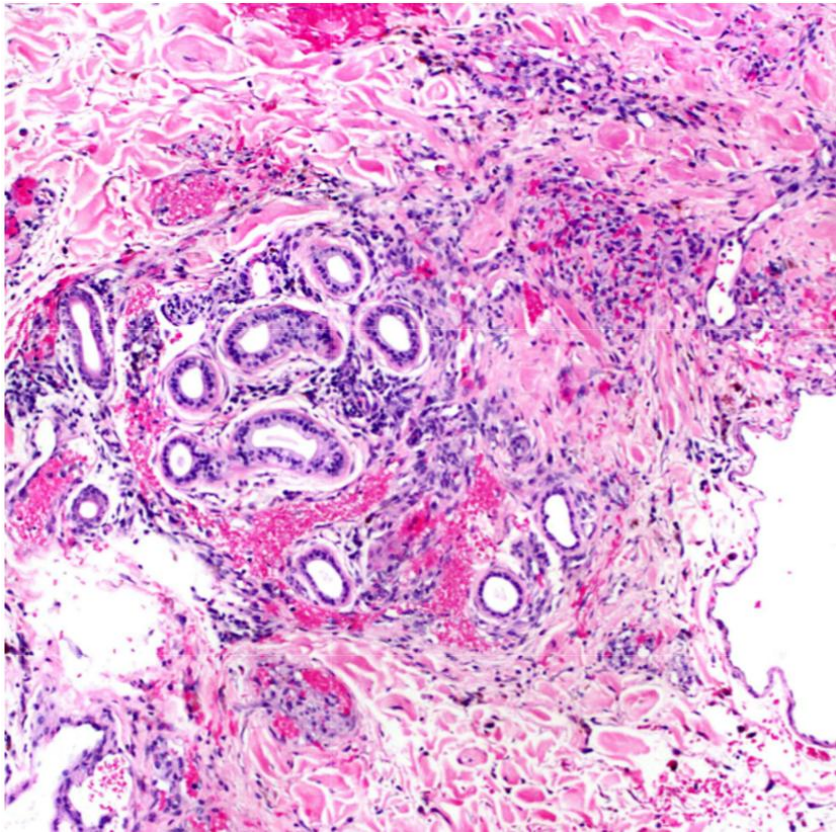


Microscopic

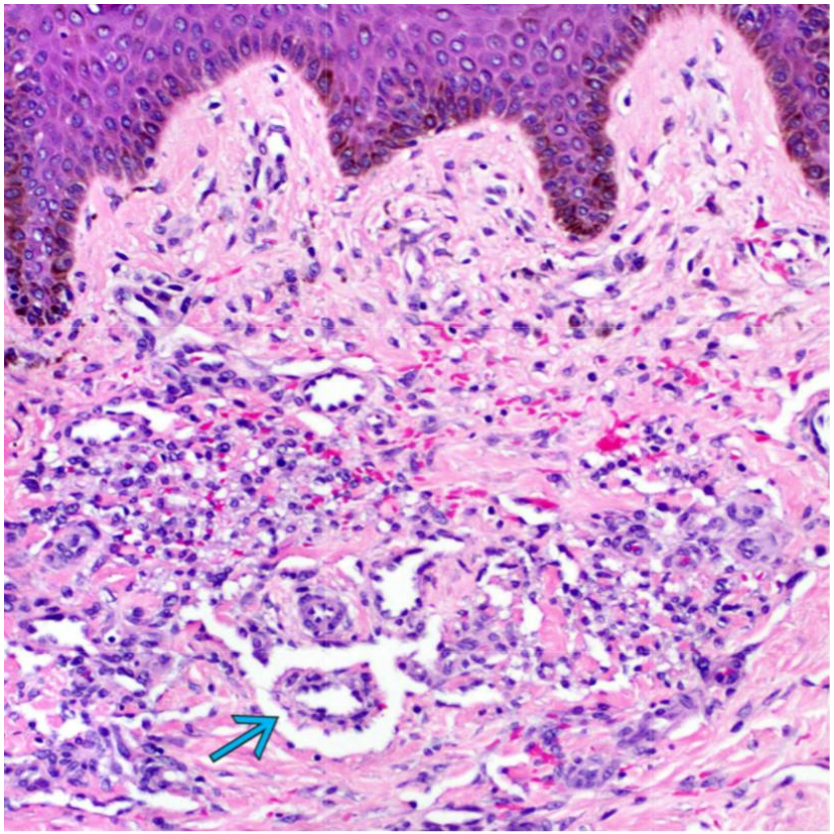
Infiltrating vascular channels



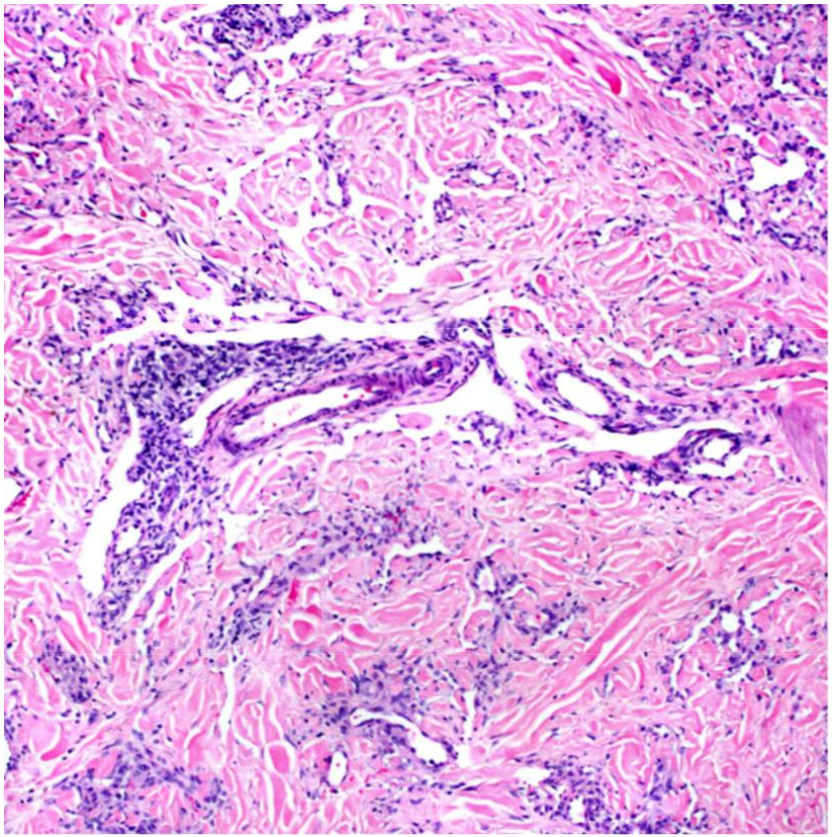
Infiltrative growth



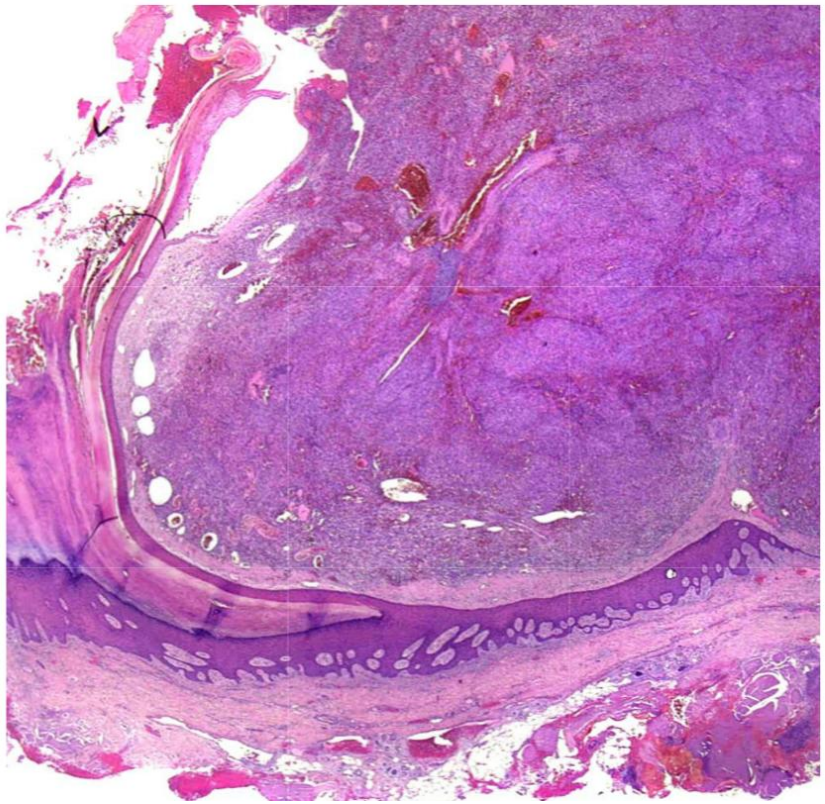
Early lesion/Increased number of vessels with promontory sign



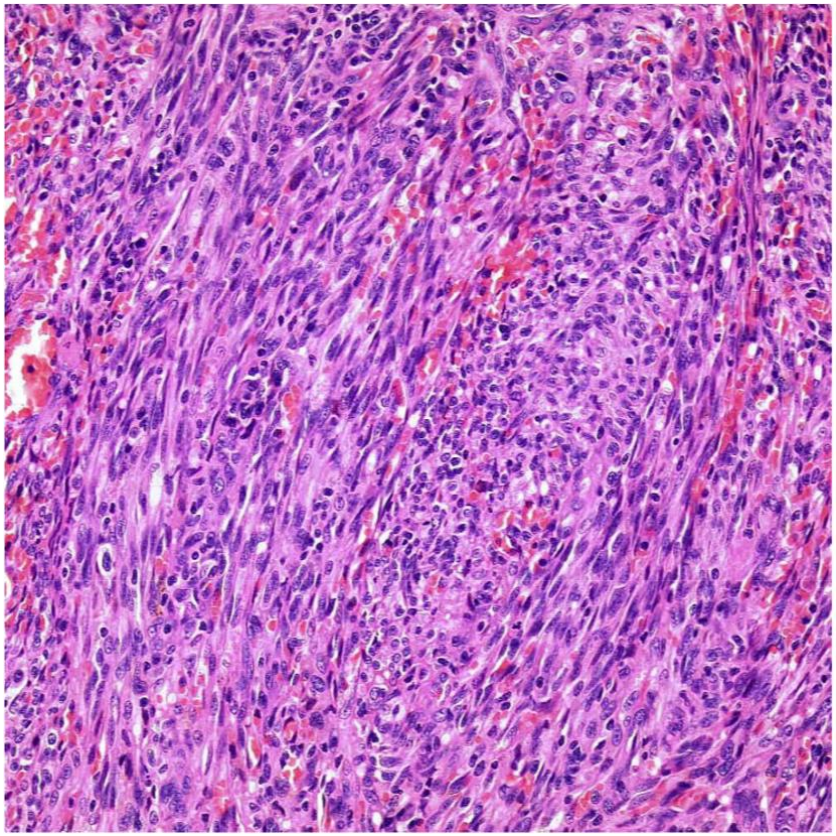
Inflammation



Tumor stage

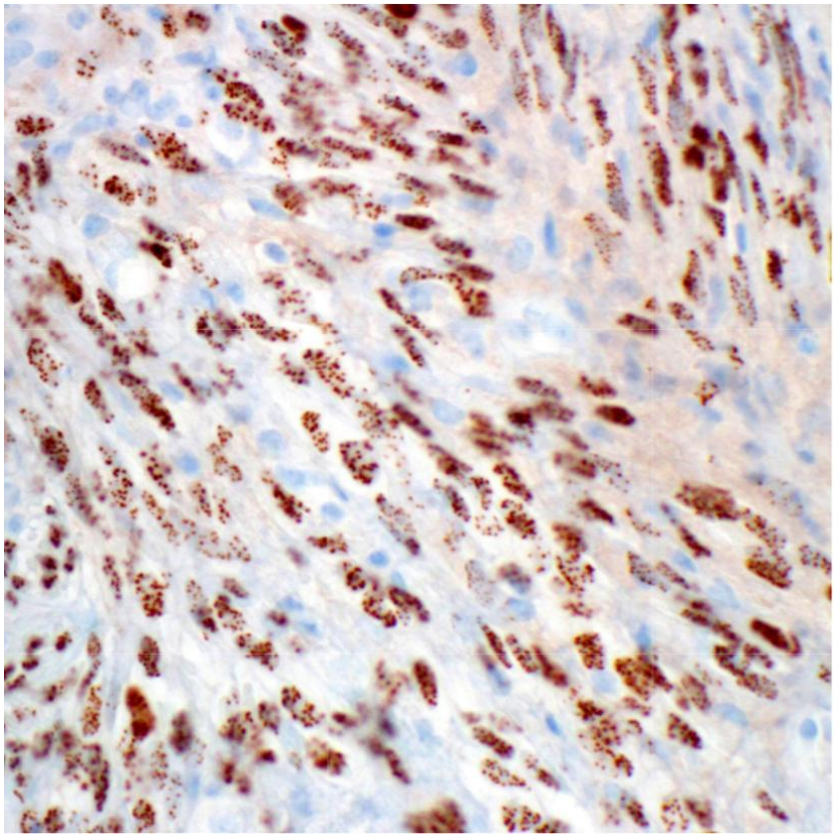


Cellular fascicle of spindle cells

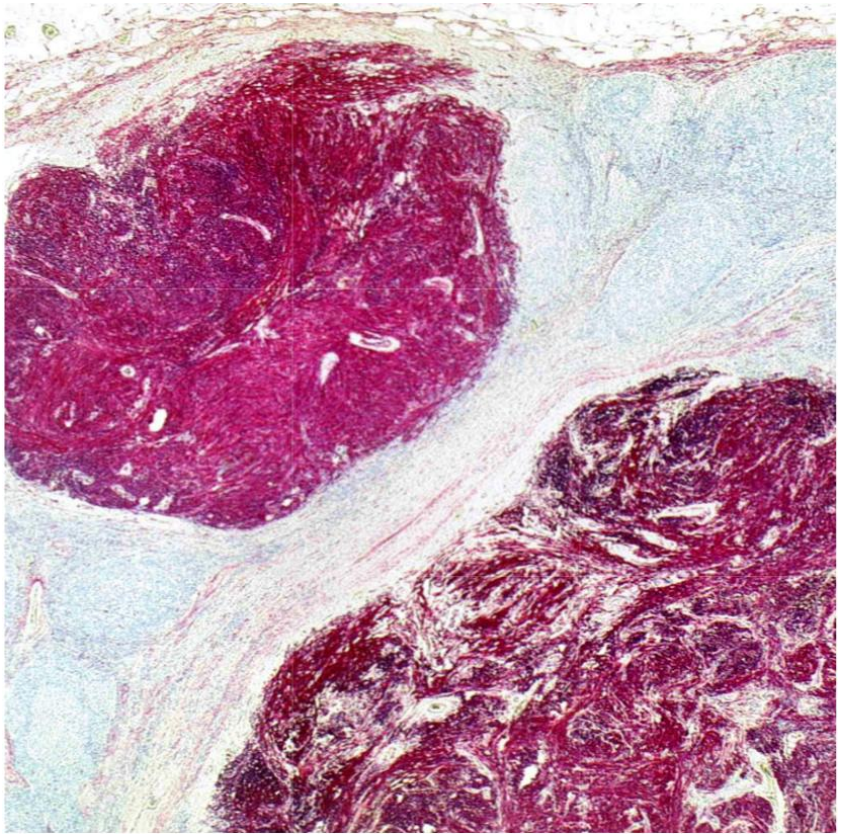


Ancillary tests

IHC for HHV8



IHC for CD34



Differential Diagnosis

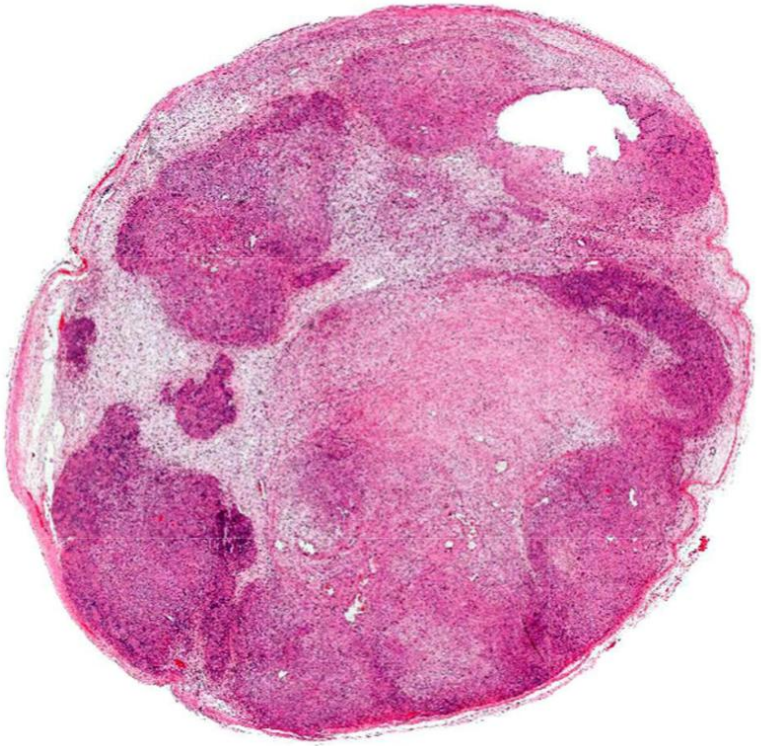
- Angiosarcoma
- Severe vascular stasis (acroangiodermatitis)
- Hobnail (targetoid hemosiderotic) hemangioma
- Microvenular hemangioma
- Spindle cell hemangioma
- Kaposiform hemangioendothelioma
- Acquired tufted angioma
- Progressive lymphangioma
- Cellular fibrous histiocytoma
- Leiomyosarcoma (cutaneous)

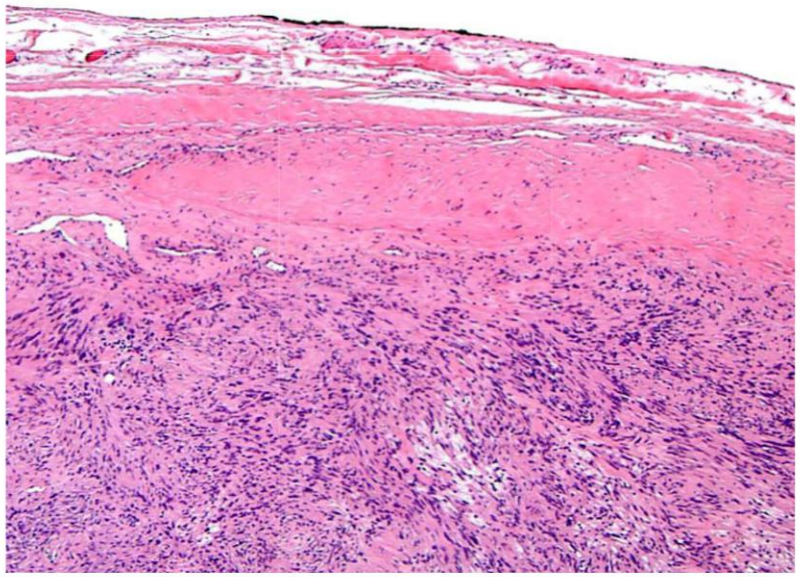
Peripheral Nerve Sheath Tumors

Schwannoma

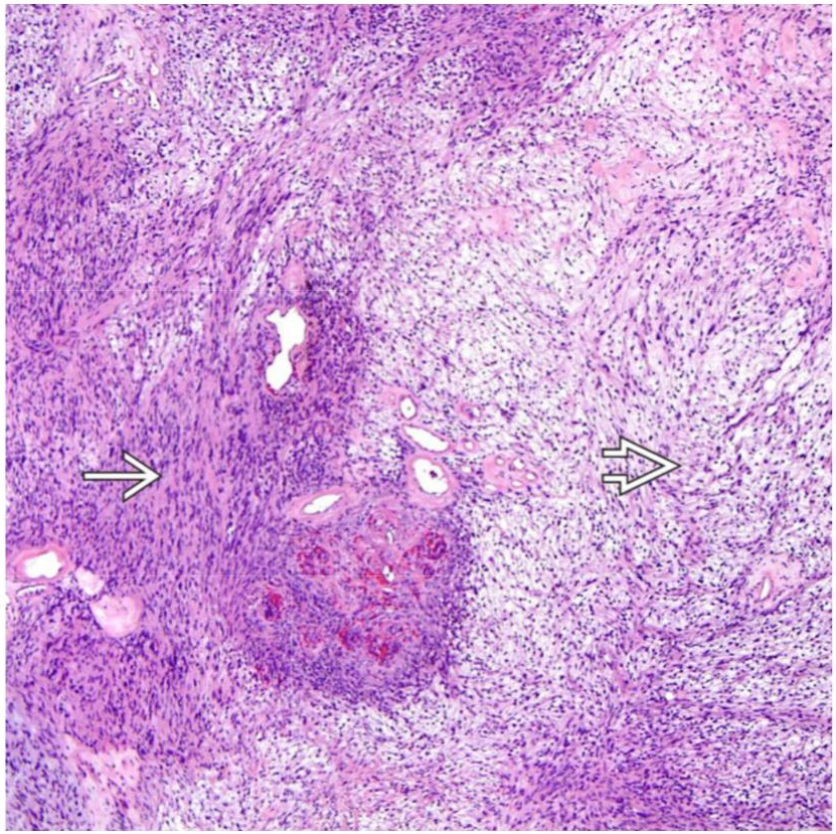
- Encapsulated, benign peripheral nerve sheath tumor composed predominantly of Schwann cells
- Any age
  - Most common: 20-50 years
- Most occur in superficial soft tissues of head/neck and upper or lower extremities
  - Also retroperitoneum, posterior mediastinum, and viscera (GI tract, kidney, etc.)
- Surgical excision is generally curative and recurrences are rare

Microscopic

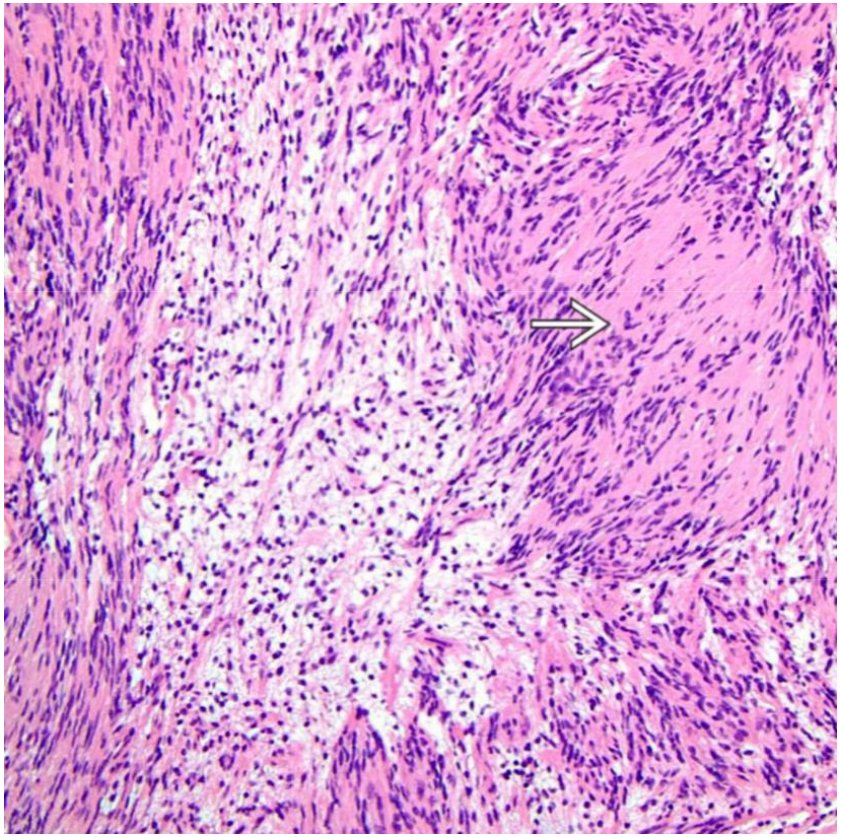




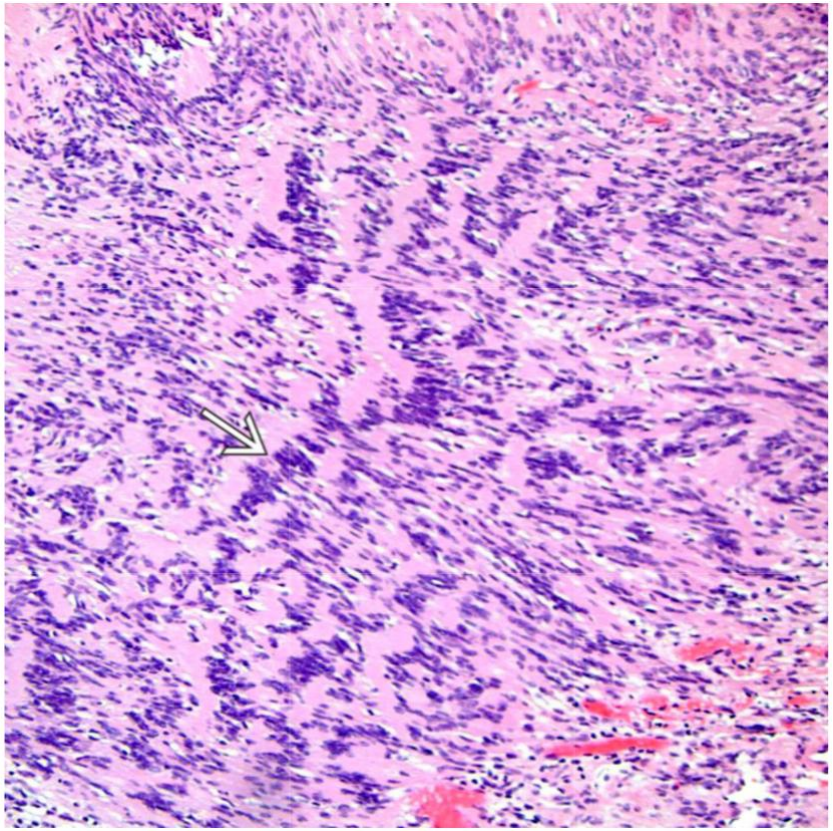
Alternating cellularity



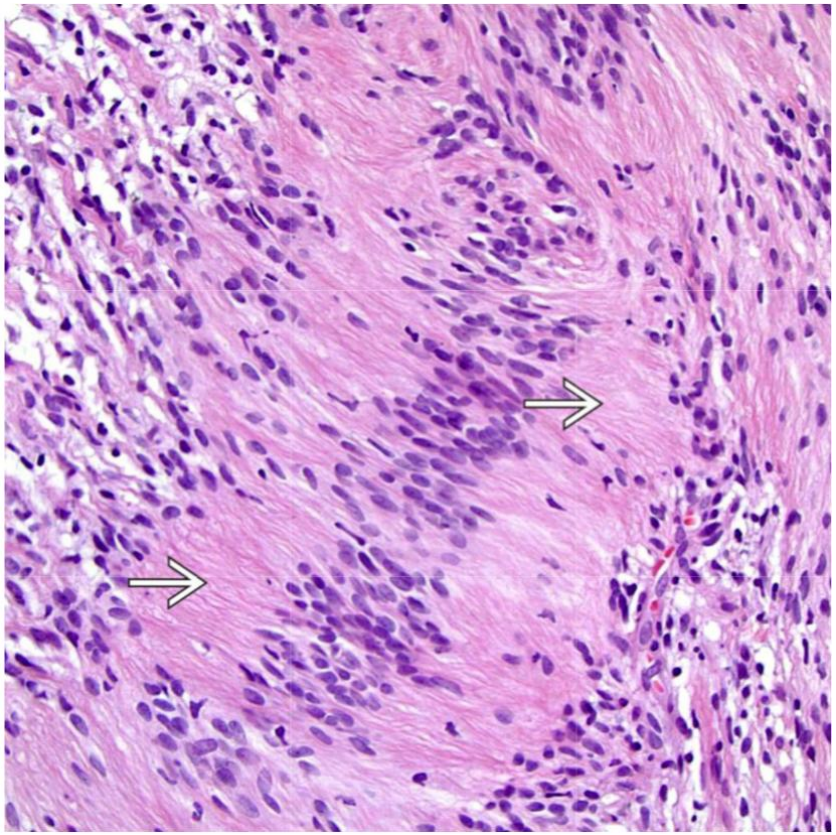
Antoni A and B zones

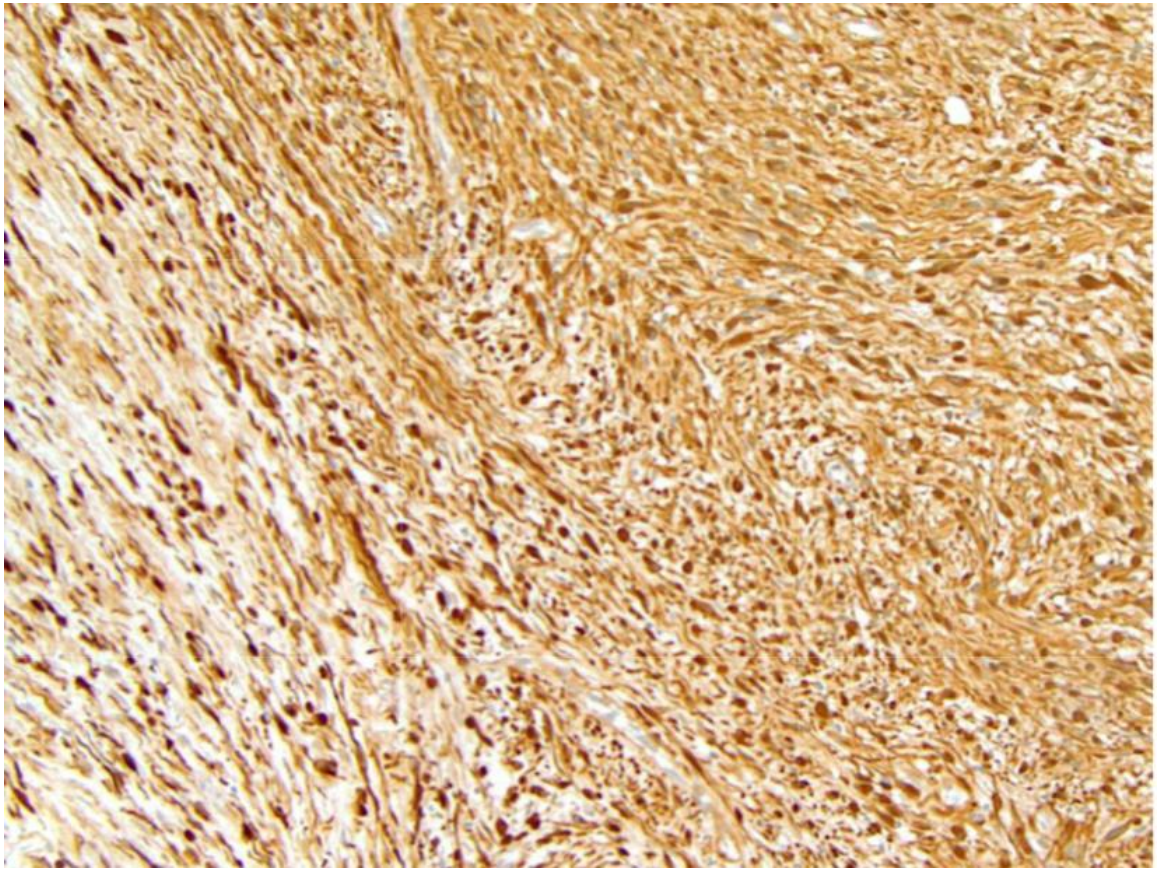


Nuclear palisading



Verocay body





Ancillary tests

S100-protein by IHC

Differential diagnosis

- Neurofibroma
- Malignant peripheral nerve sheath tumor
- Pleomorphic hyalinizing angiectatic tumor

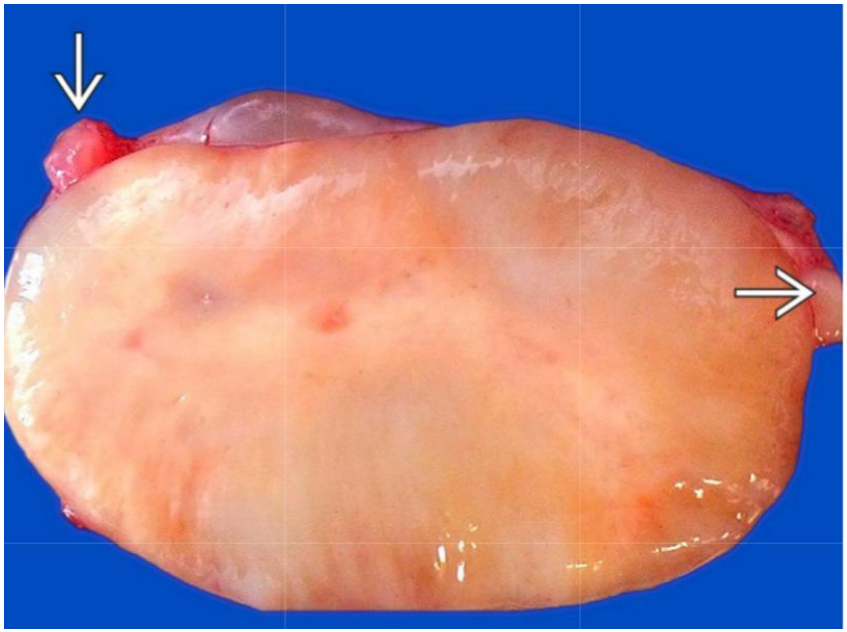
Neurofibroma

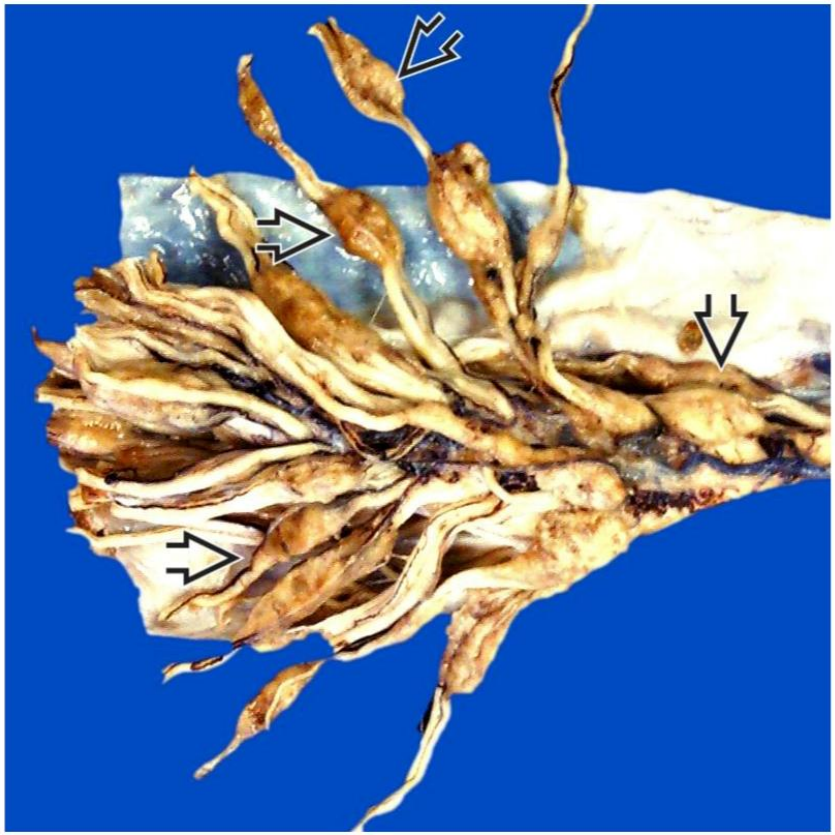
- Benign peripheral nerve sheath tumor composed of Schwann cells, fibroblasts, perineurial-like cells, and residual nerve axons within extracellular matrix

Clinical

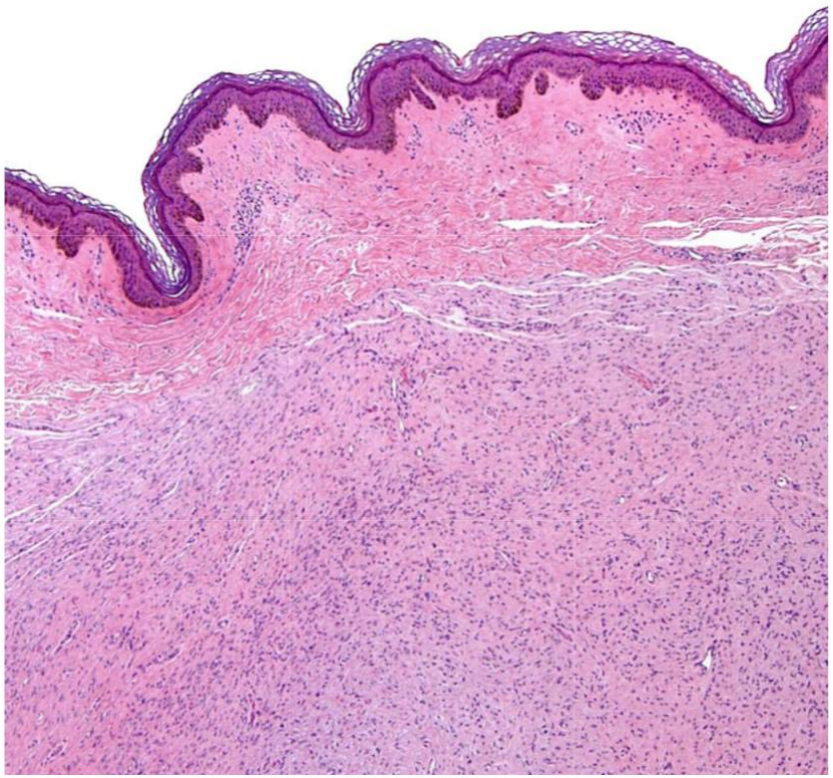
- Most common peripheral nerve sheath tumor
  - 3 main types: **Localized** (cutaneous or intraneural), **diffuse**, and **plexiform**
    - Plexiform type is essentially pathognomonic for neurofibromatosis type 1 (NF1)
- Wide age range
  - Diffuse and plexiform types most common in young
- Most (90%) of neurofibromas are sporadic
- Benign; very rare local recurrence
- **Malignant transformation** usually occurs in setting of NF1 (up to 10% of patients)

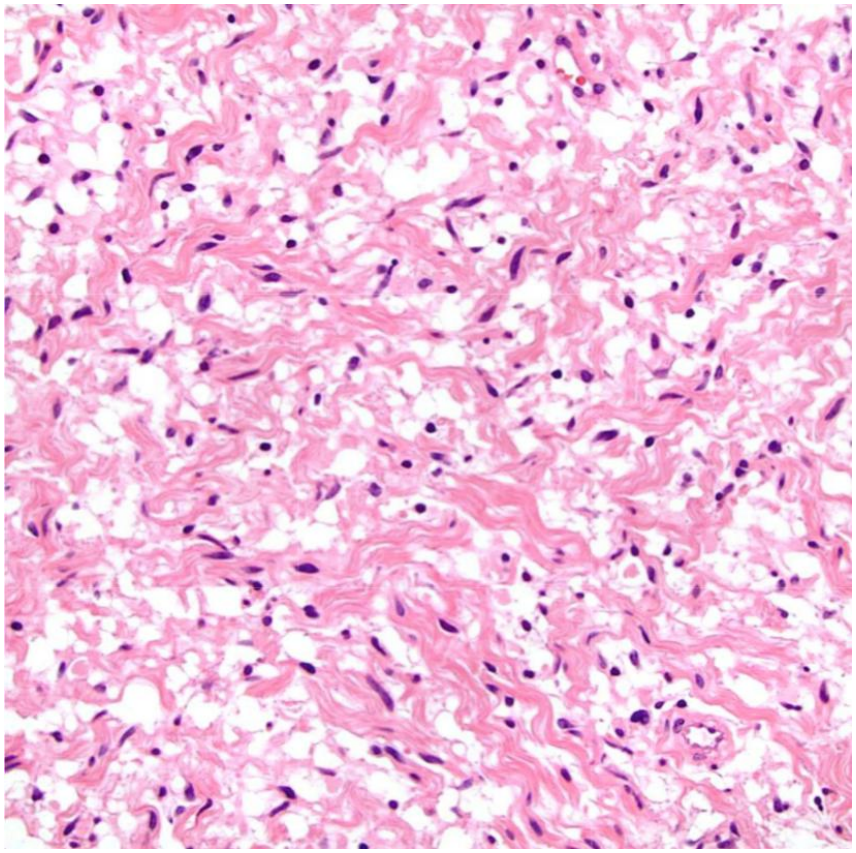
Macroscopic



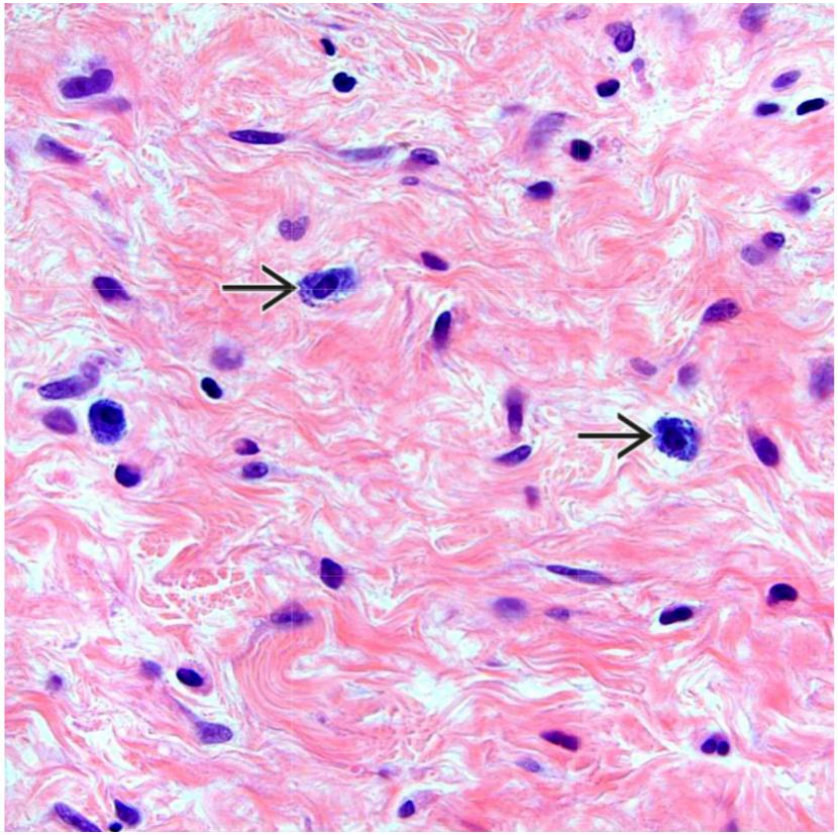


Microscopic

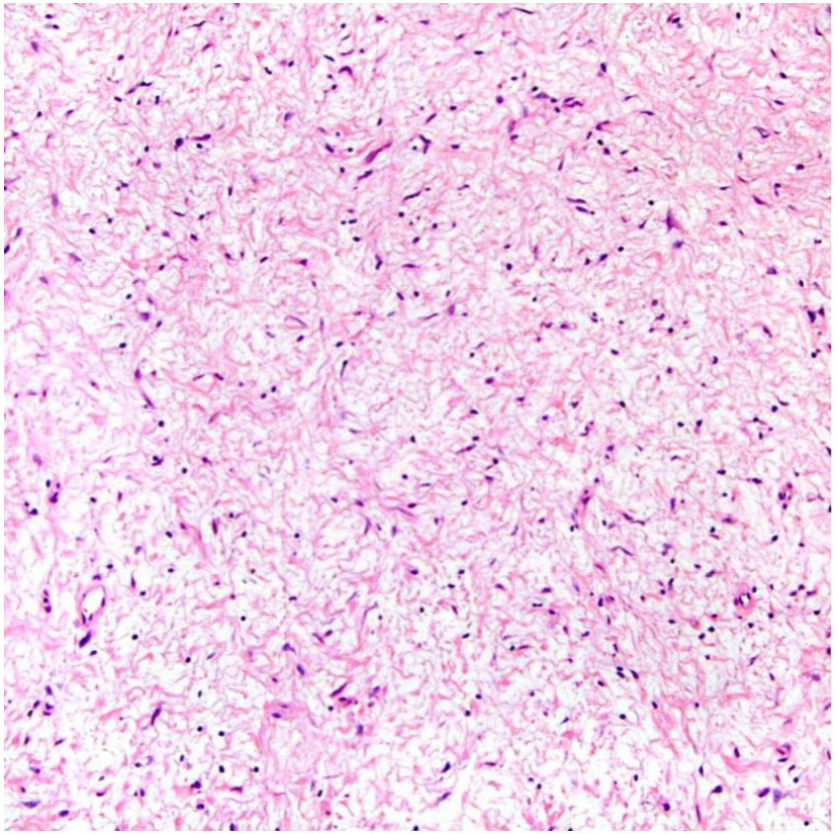




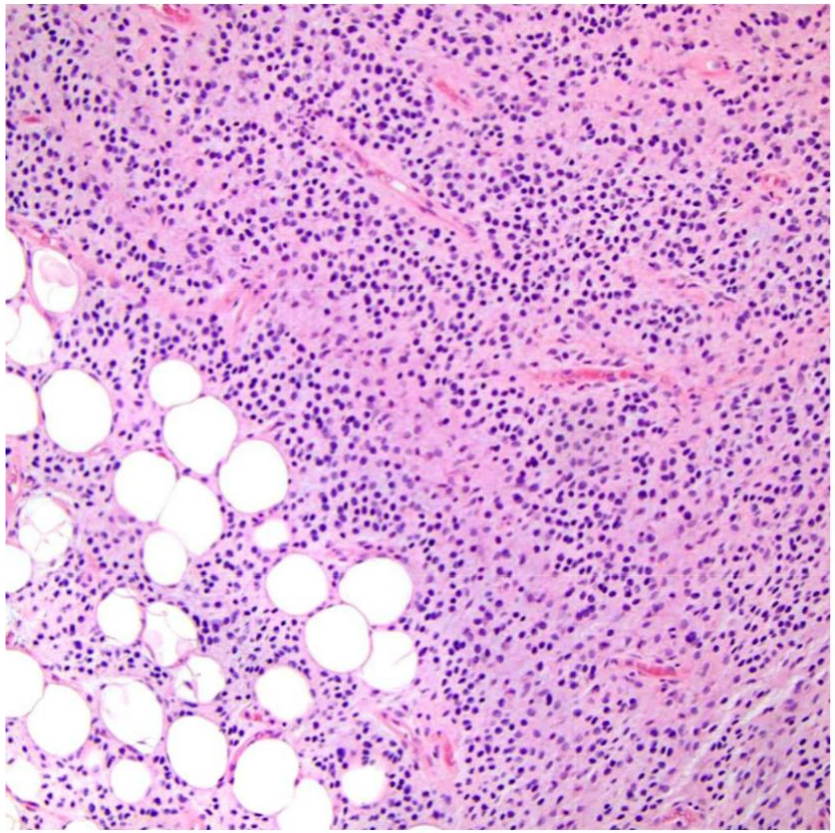
Mast cells



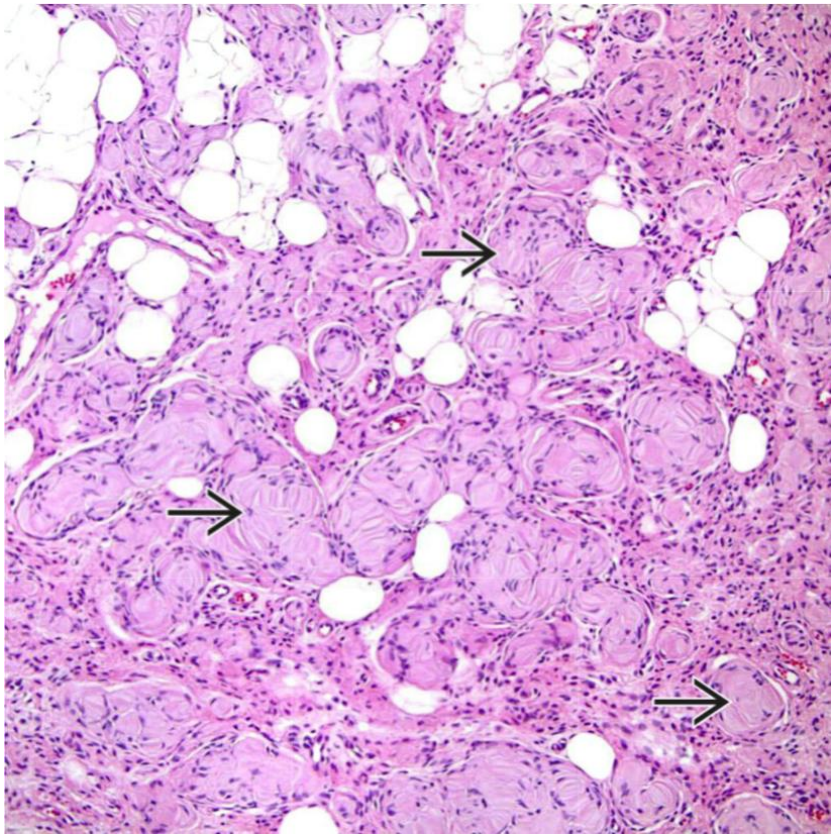
Hypocellularity



Rounded nuclei

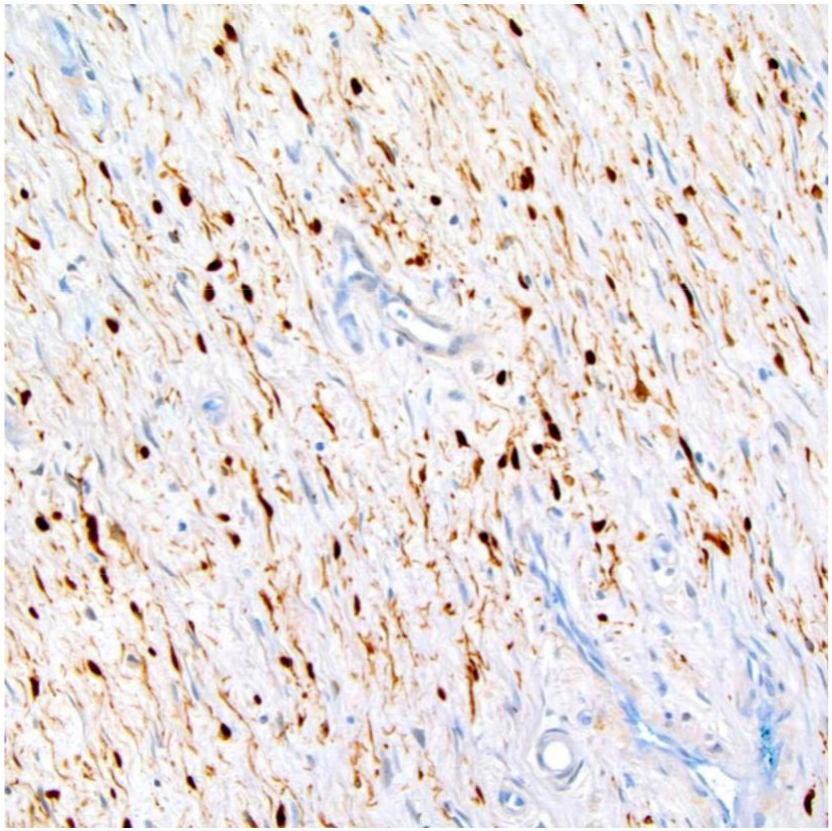


Wagner- Meissner Bodies

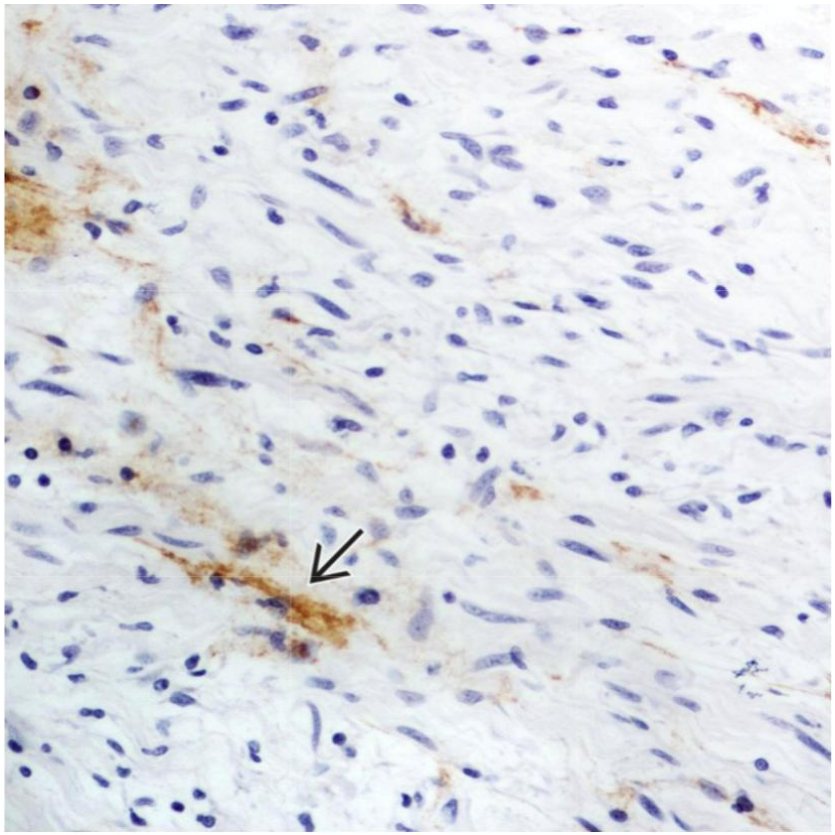


Ancillary tests

IHC for S100-protein



IHC for Epithelial membrane antigen (EMA)



Differential Diagnosis

- Malignant peripheral nerve sheath tumor
- Dermatofibrosarcoma protuberans
- Schwannoma
- Perineurioma

Malignant Peripheral Nerve Sheath Tumor (MPNST)

- Malignant neoplasm showing evidence of nerve sheath (mostly Schwannian) cellular differentiation

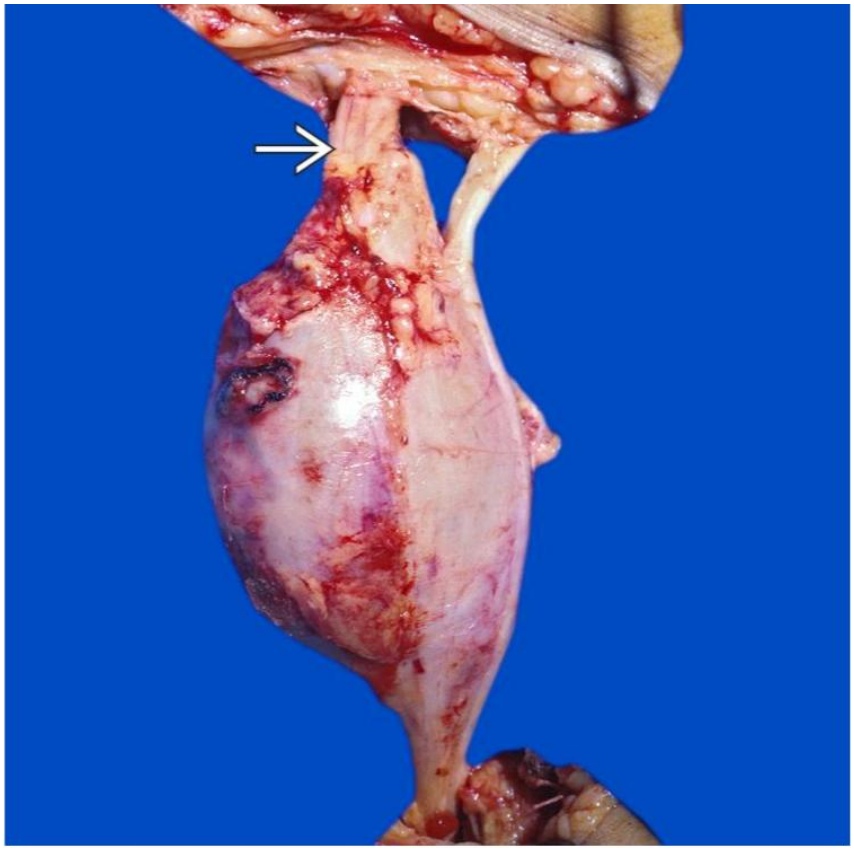
- May arise from peripheral nerve or preexisting benign nerve sheath tumor, or within context of NF1

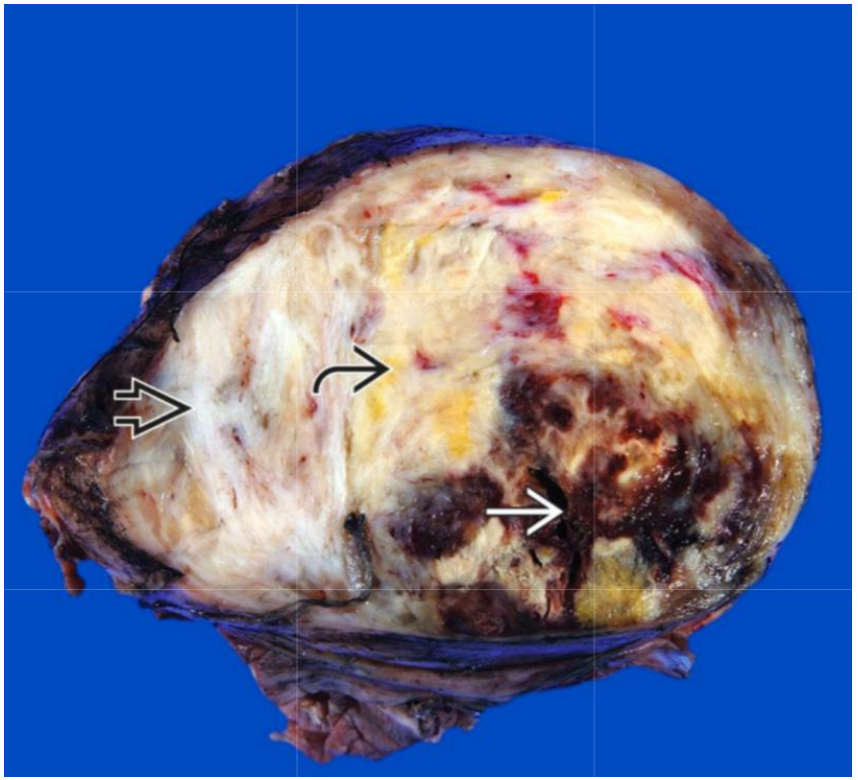
- 50% of cases associated with NF1

Clinical Issues

- Wide age range (most common 20-50 years)
- Extremities (often proximal), trunk, and head/neck
  - Most (70%) arise in major nerve trunks
- Treatment: Complete surgical resection
- Overall poor prognosis
  - Local recurrence in up to 40%
  - Metastasis: 30-60%

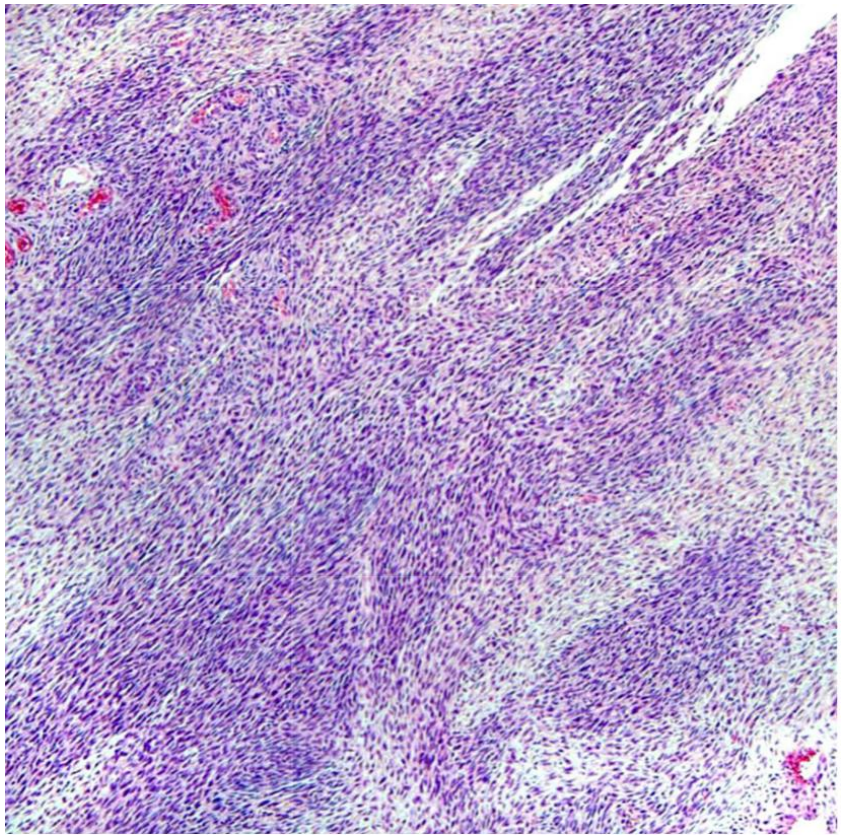
Macroscopic



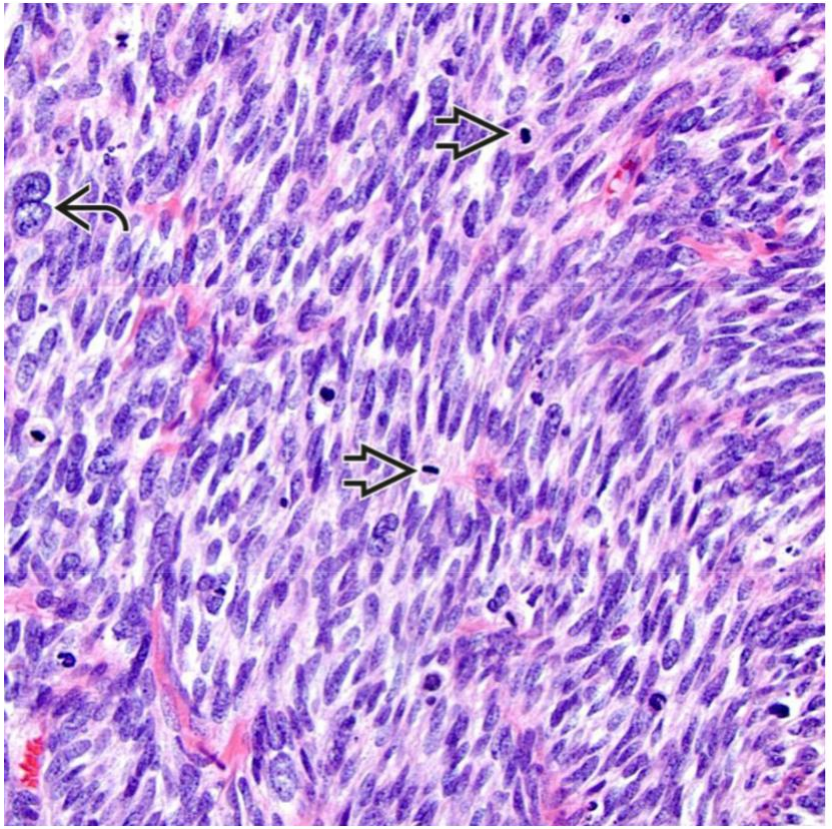


Microscopic

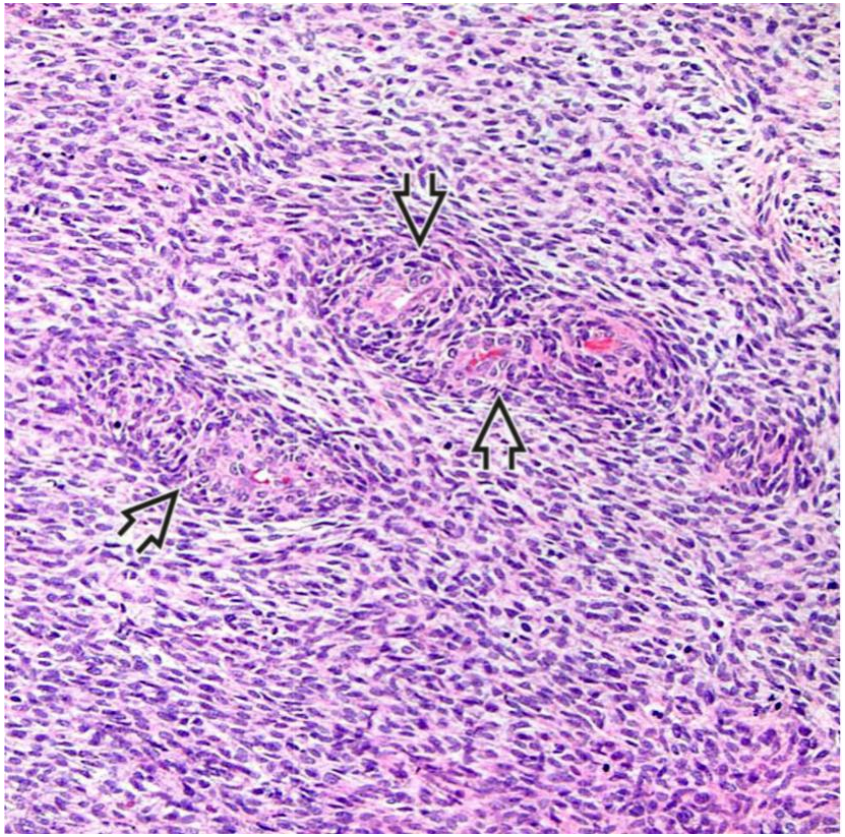
“Marbled” like pattern



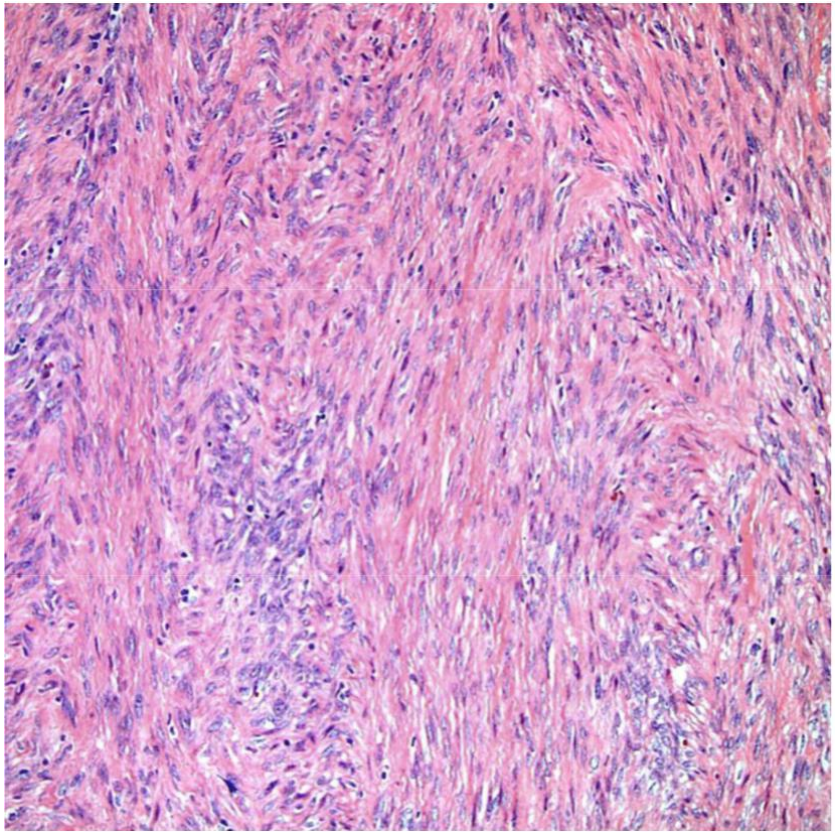
Nuclear atypia common



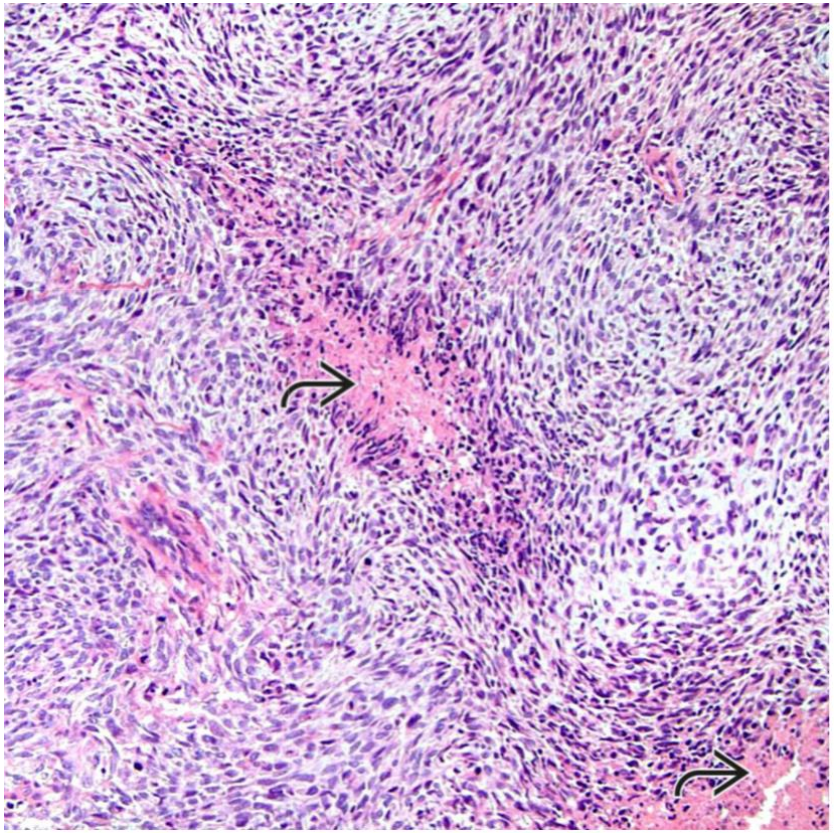
Perivascular accentuation



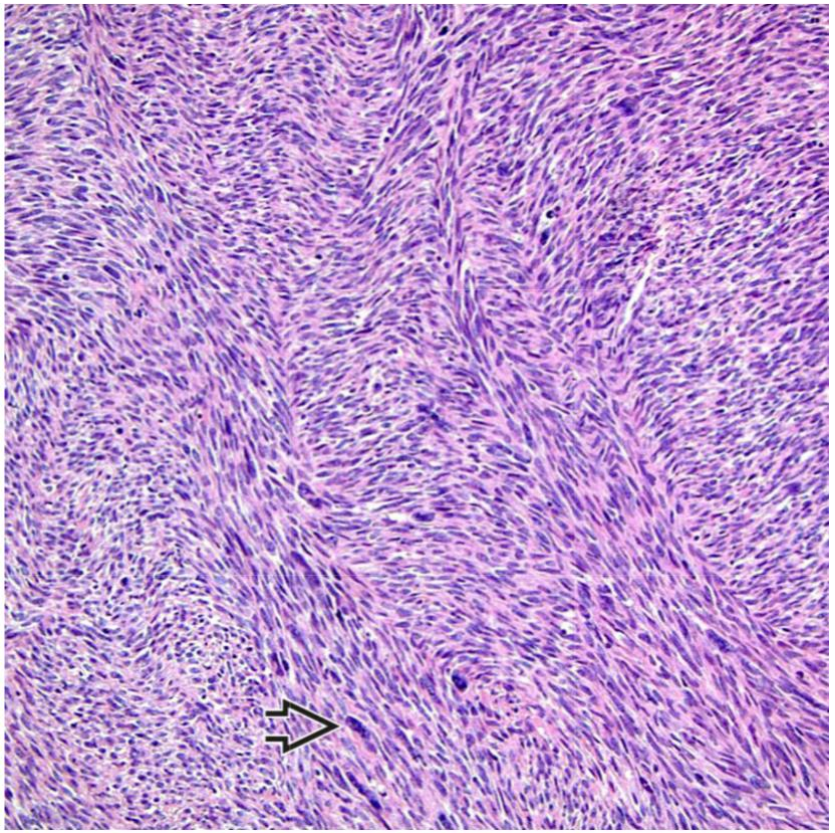
Collagenous stroma



Coagulative necrosis



Fascicular growth



Ancillary tests

- S100 protein (+) in up to 50%, characteristically focal

Differential Diagnosis

- Synovial sarcoma
- Cellular schwannoma
- Atypical neurofibroma

Tumors Of Uncertain Differentiation

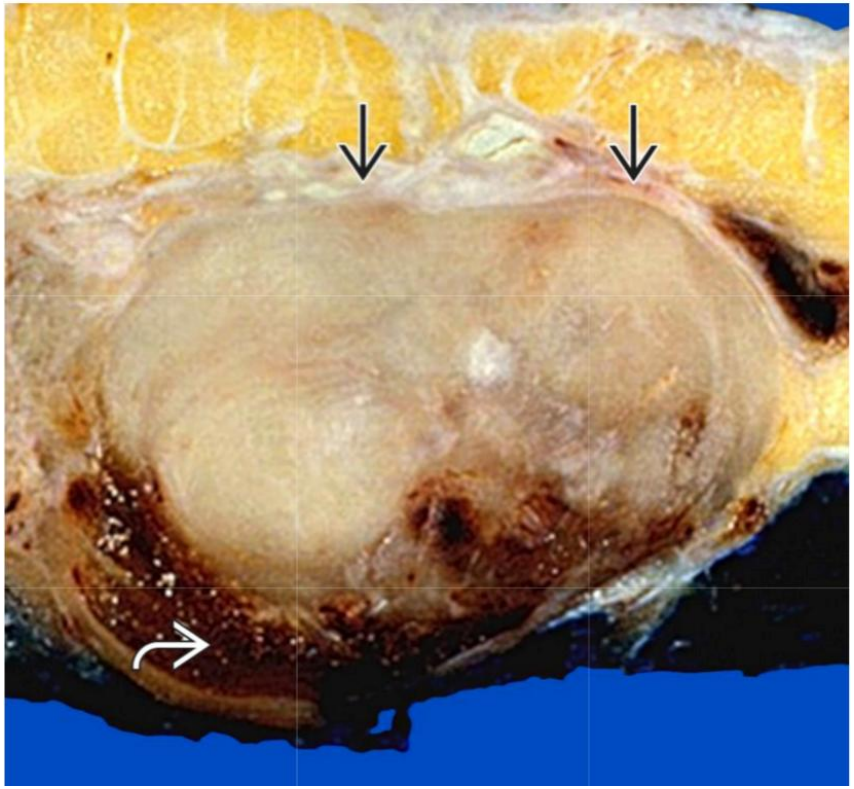
Synovial Sarcoma

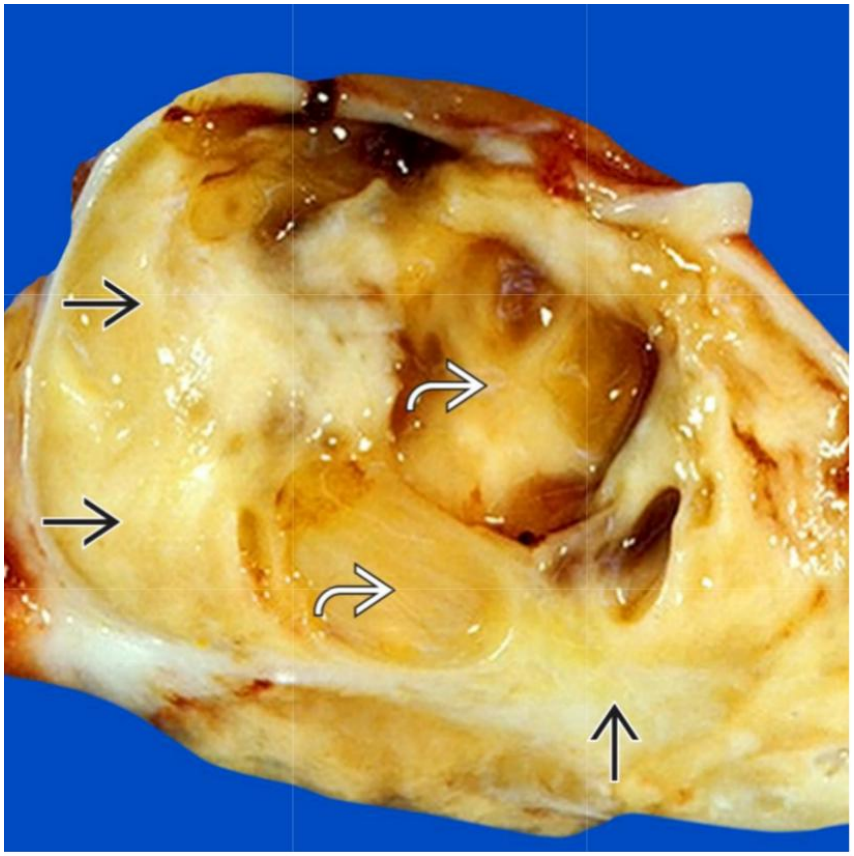
- Malignant mesenchymal spindle cell neoplasm with variable epithelial differentiation, including gland formation, and characterized by a specific chromosomal translocation **t(X;18)(p11;q11)**

Clinical issues

- Most common in **young adults**
- Most arise in deep soft tissues of the extremities
  - **Most common near joints** (particularly knee)
  - Also head/neck, trunk, many other sites
- Treatment: Complete surgical resection with negative margins
- Adjuvant therapy in some cases
- Local recurrence common
- Metastasis in up to 50% of cases
- Unfavorable prognostic factors
  - Size > 5 cm, age > 40 years, poorly differentiated histology

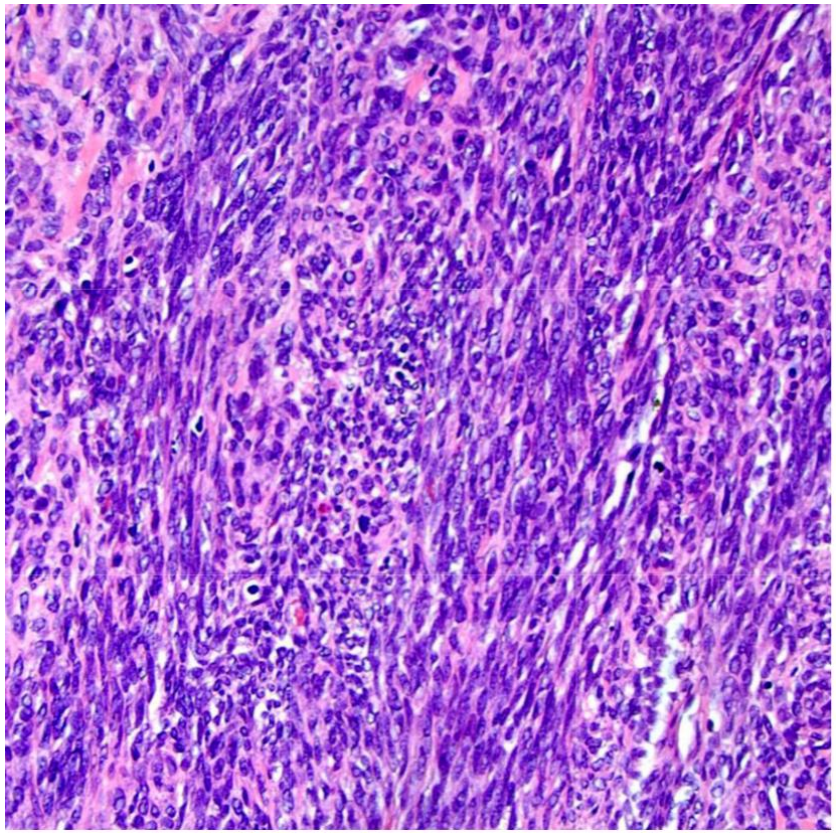
Macroscopic



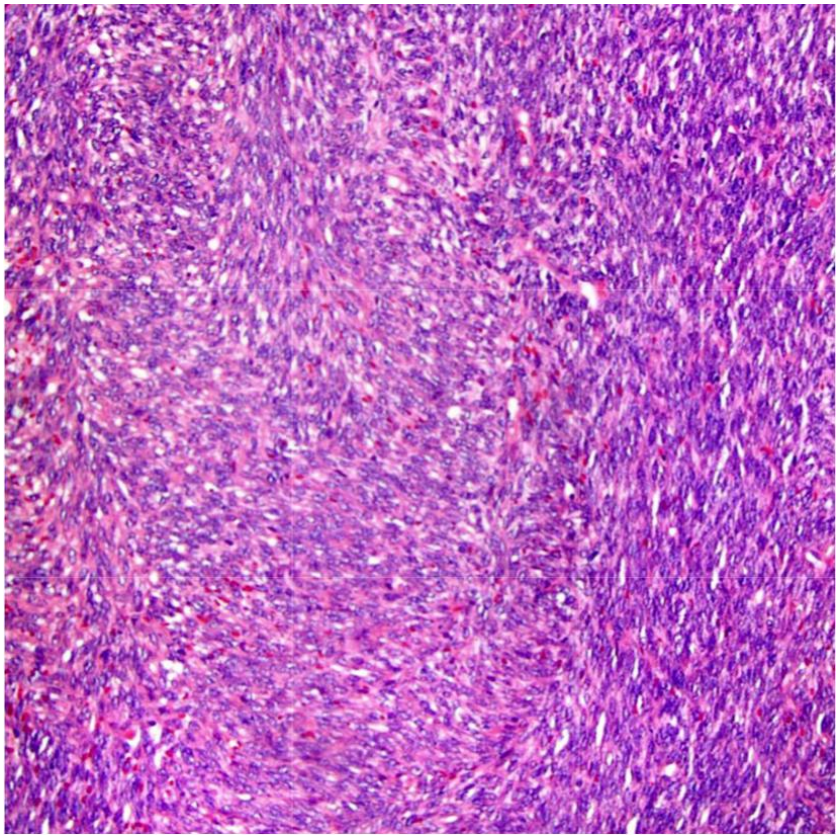


Microscopic

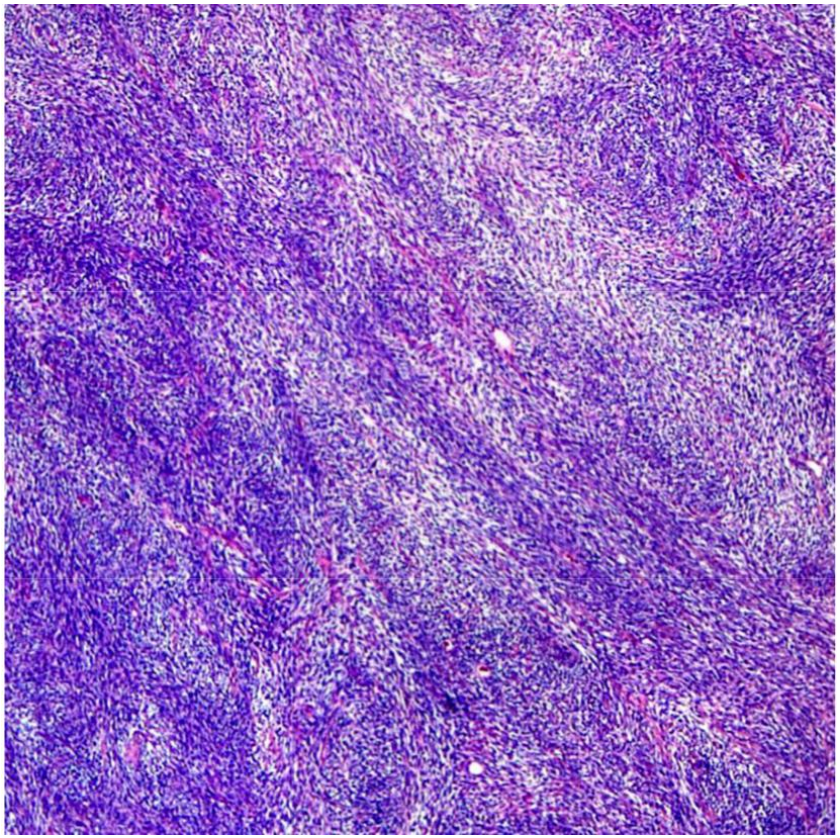
Monophasic morphology



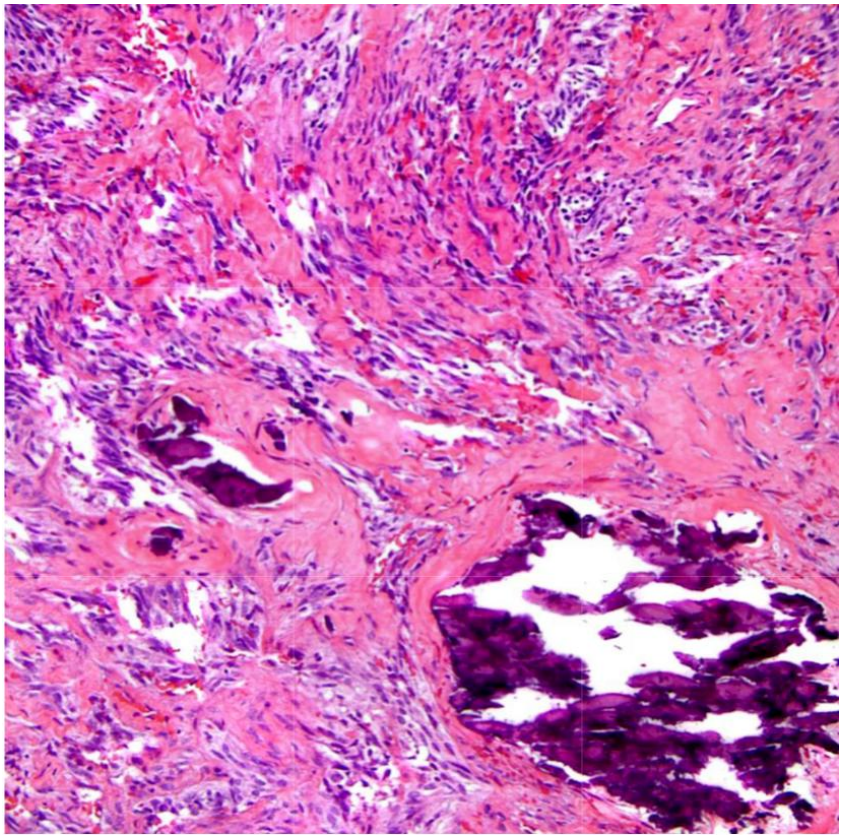
High cellularity



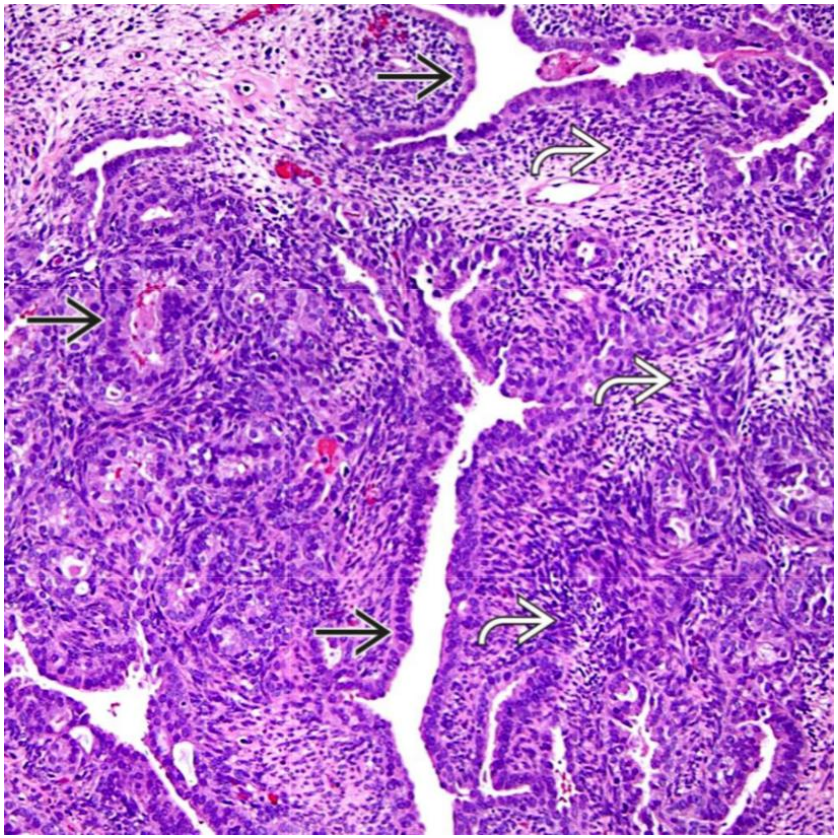
Variations in cellularity



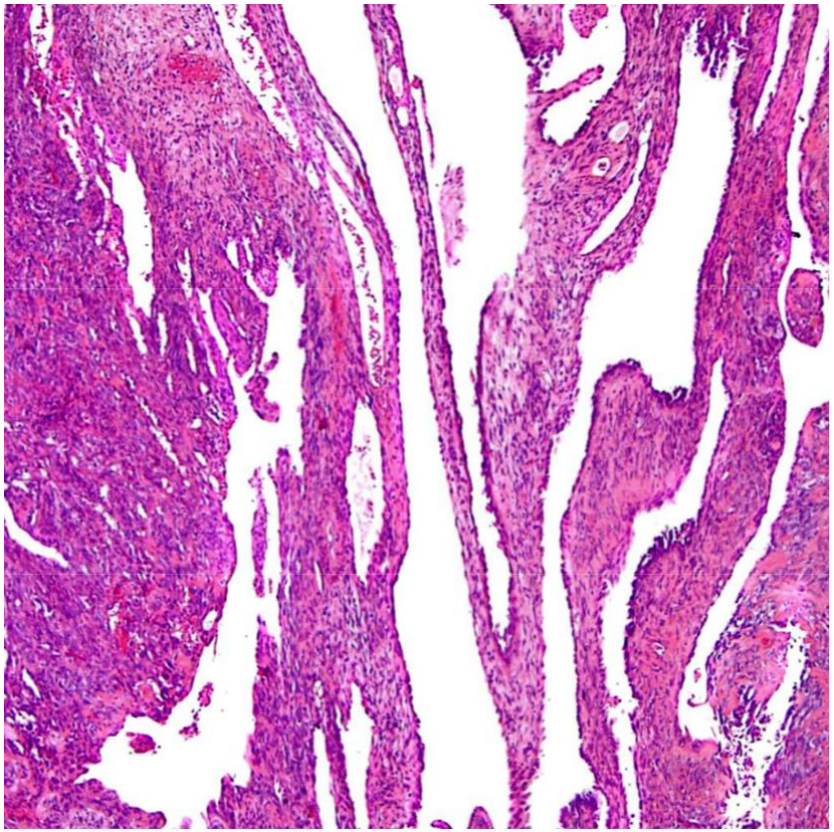
Prominent stromal collagen



Biphasic moprhology

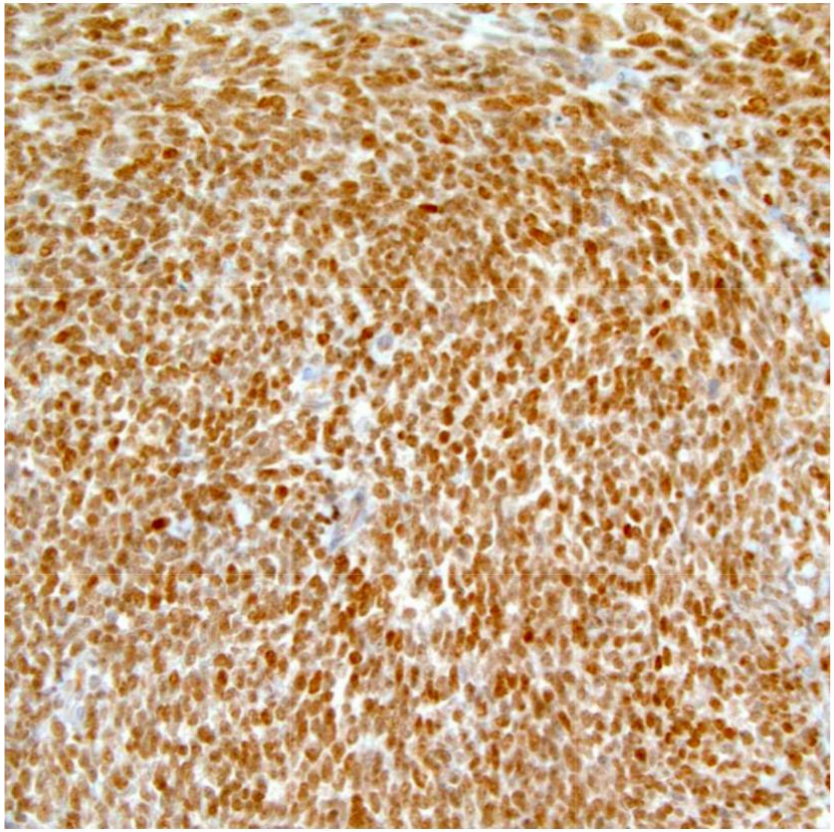


Cystic glands

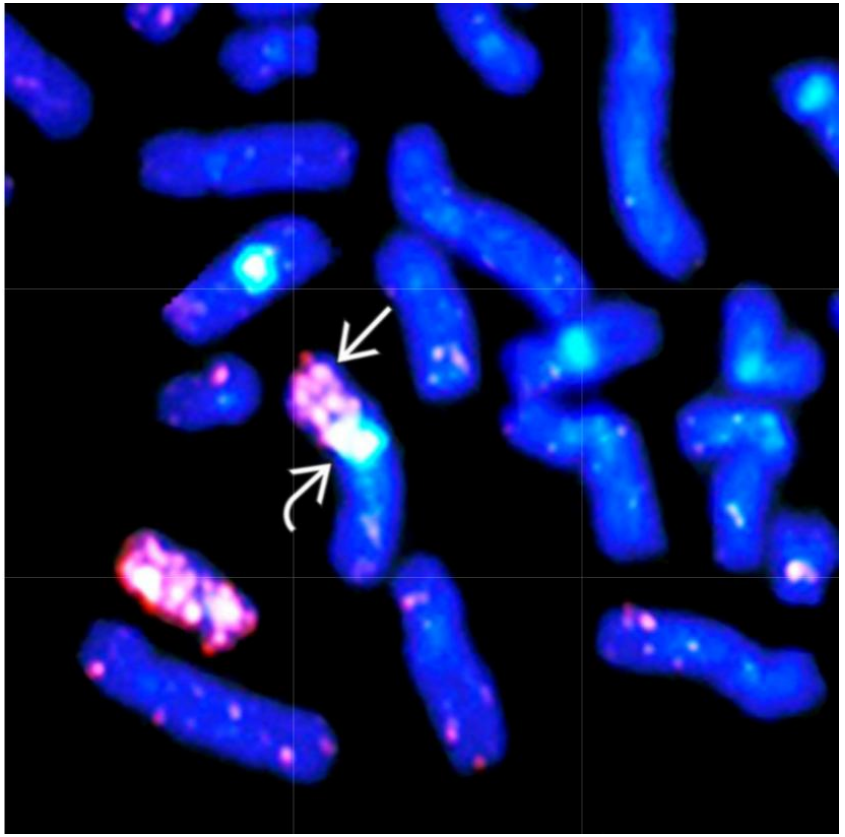


Ancillary tests

IHC for TLE1



FISH characteristic t(X;18)



Differential Diagnosis

- Malignant peripheral nerve sheath tumor
- Fibrosarcomatous dermatofibrosarcoma protuberans
- Solitary fibrous tumor

Extraskeletal Ewings Sarcoma

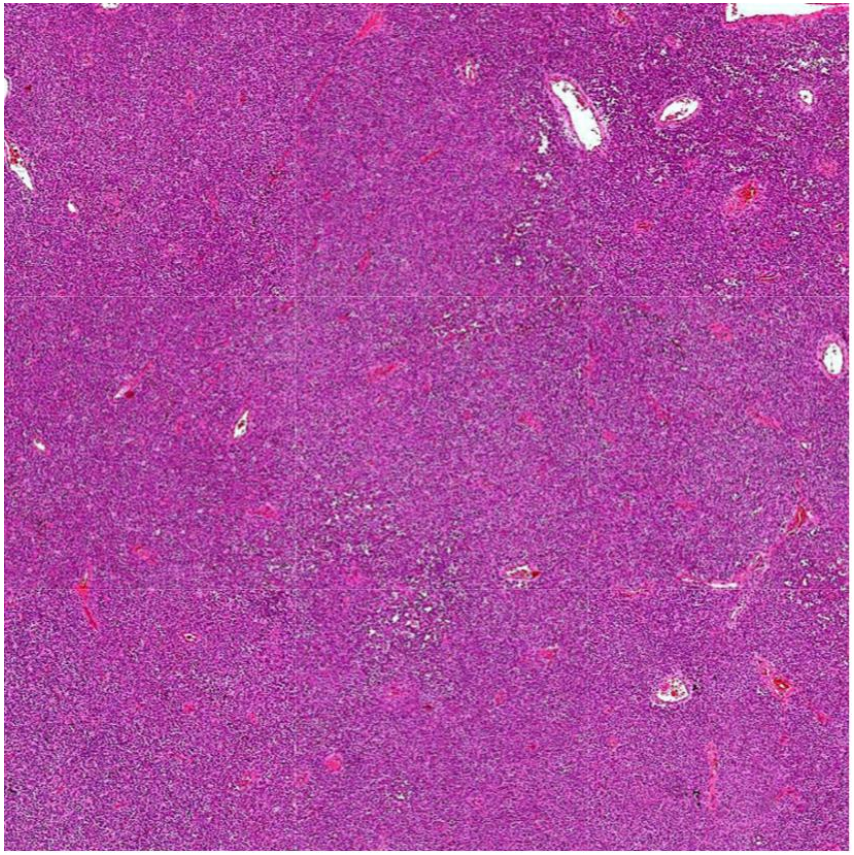
- Malignant small round blue cell neoplasm of bone and soft tissue characterized by specific **EWSR1 fusions**

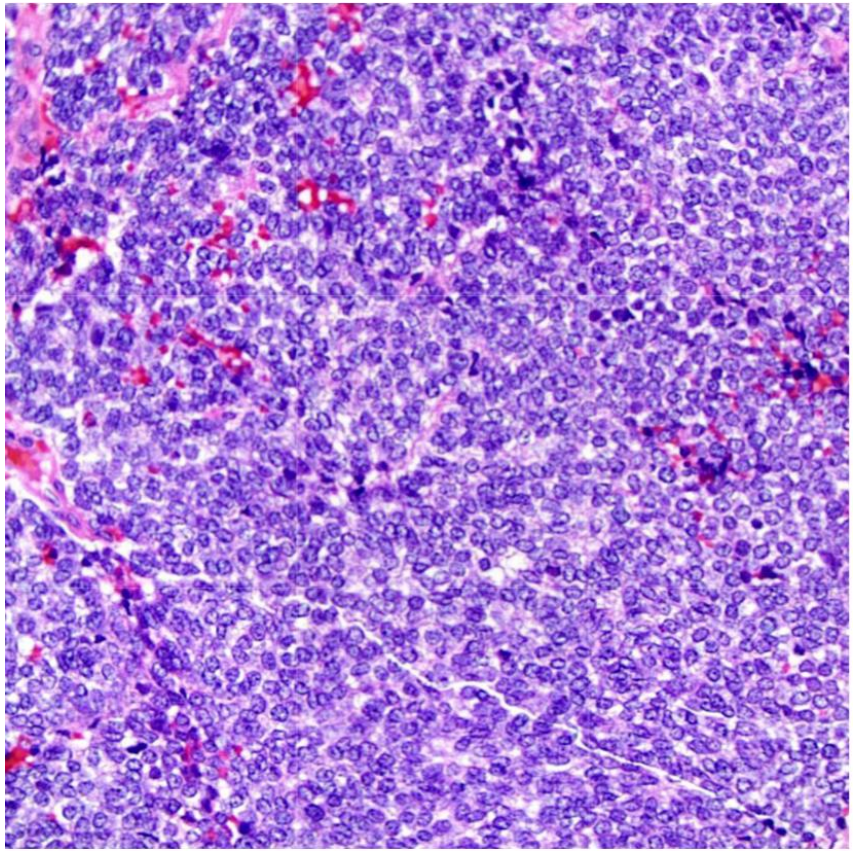
- Ewing sarcoma and primitive neuroectodermal tumor (PNET) represent continuous morphologic spectrum

Clinical Issues

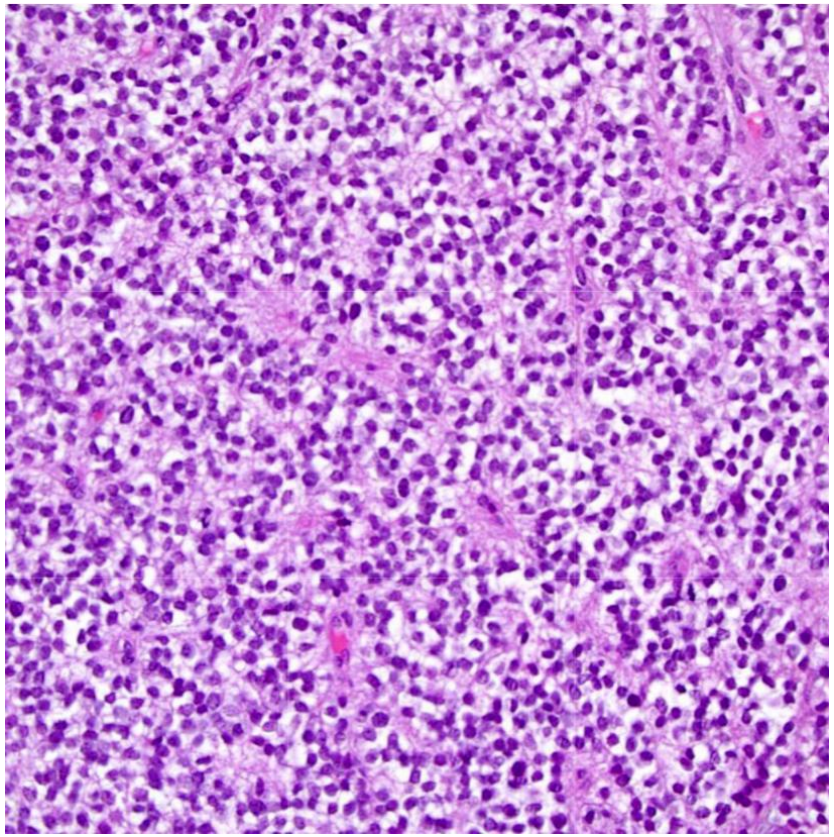
- Children, adolescents, and young adults
- Aggressive with propensity for early metastases
- 10-year survival
  - Localized disease at presentation: 67%
  - Metastatic disease at presentation: 28%

Microscopic

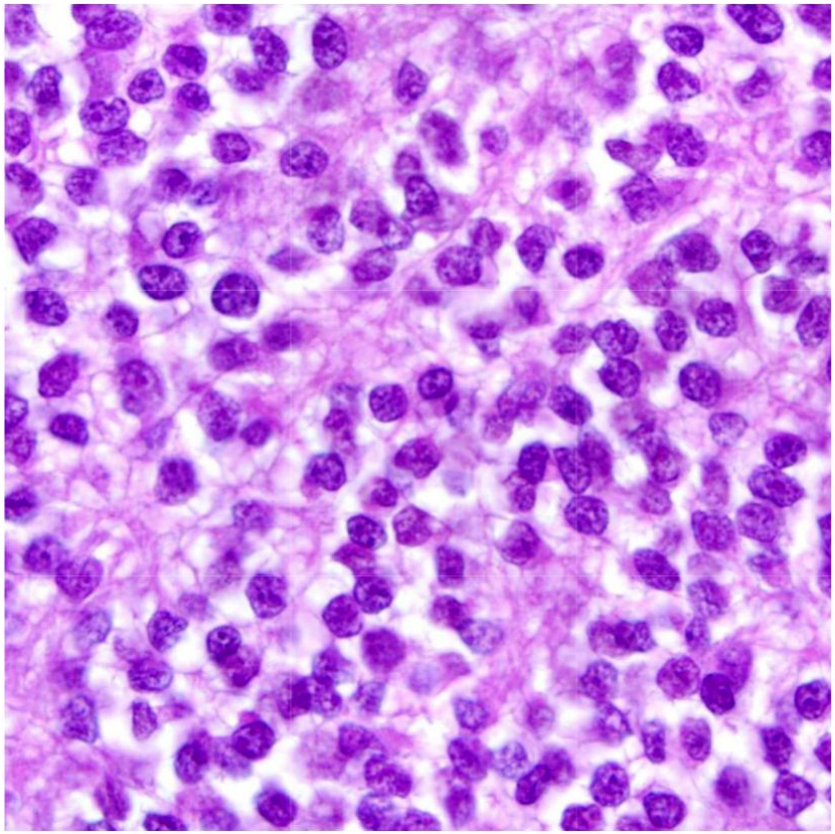




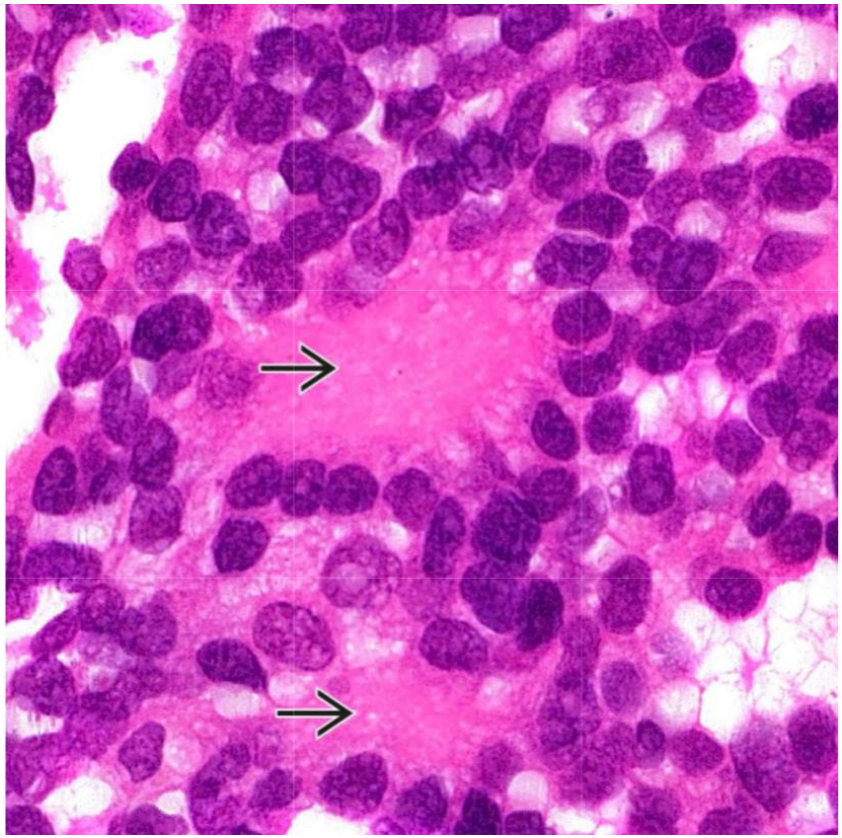
Clear cell cytoplasm common



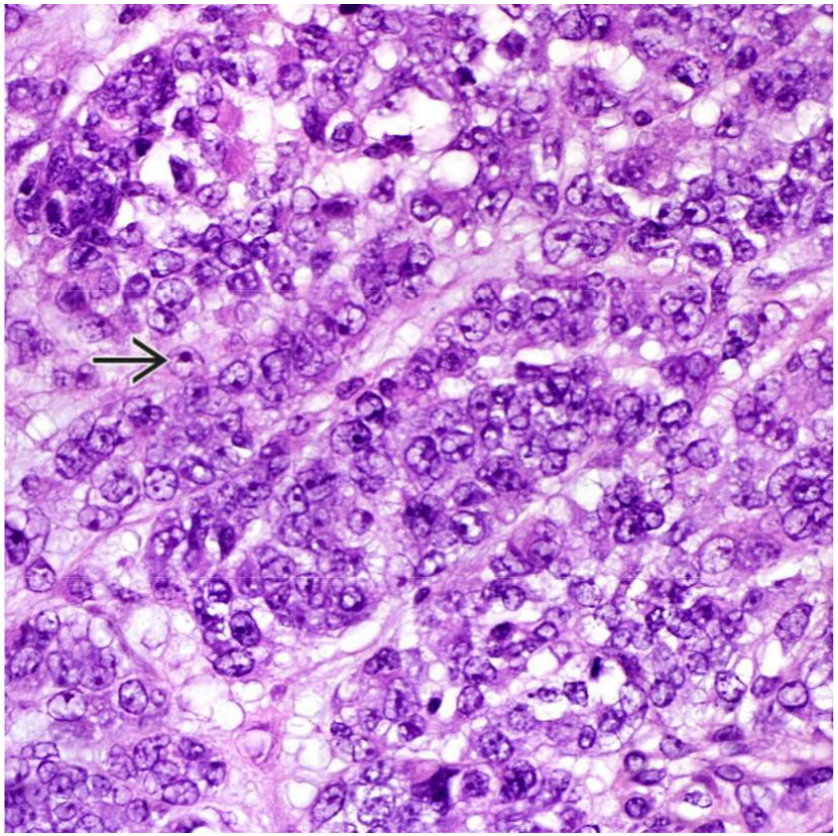
Monotonous



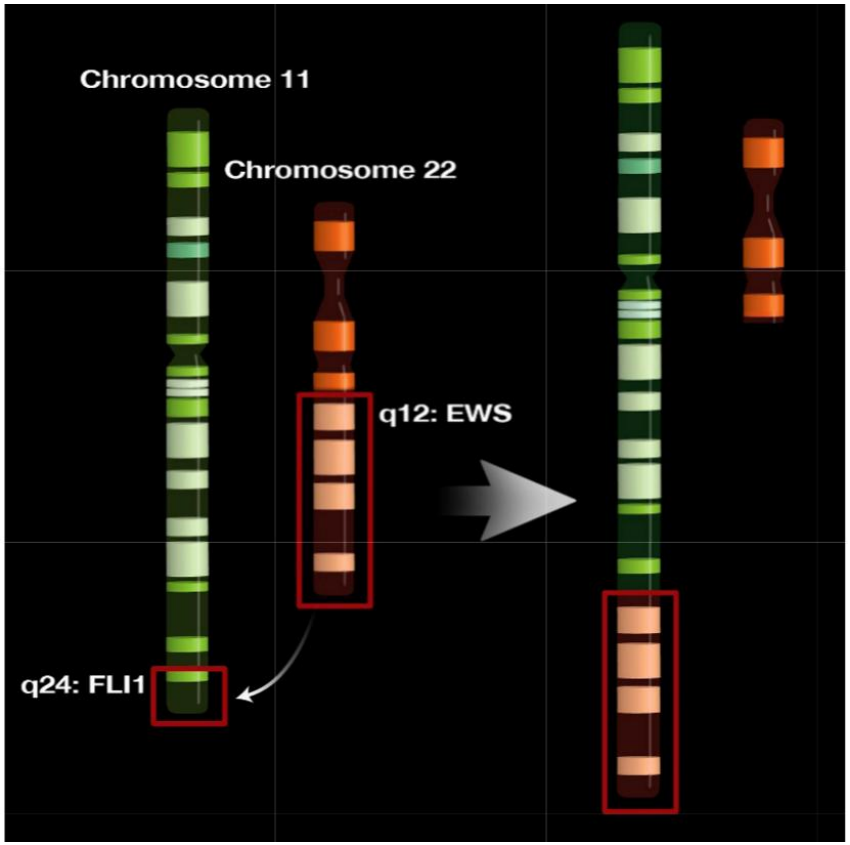
True rosette formation

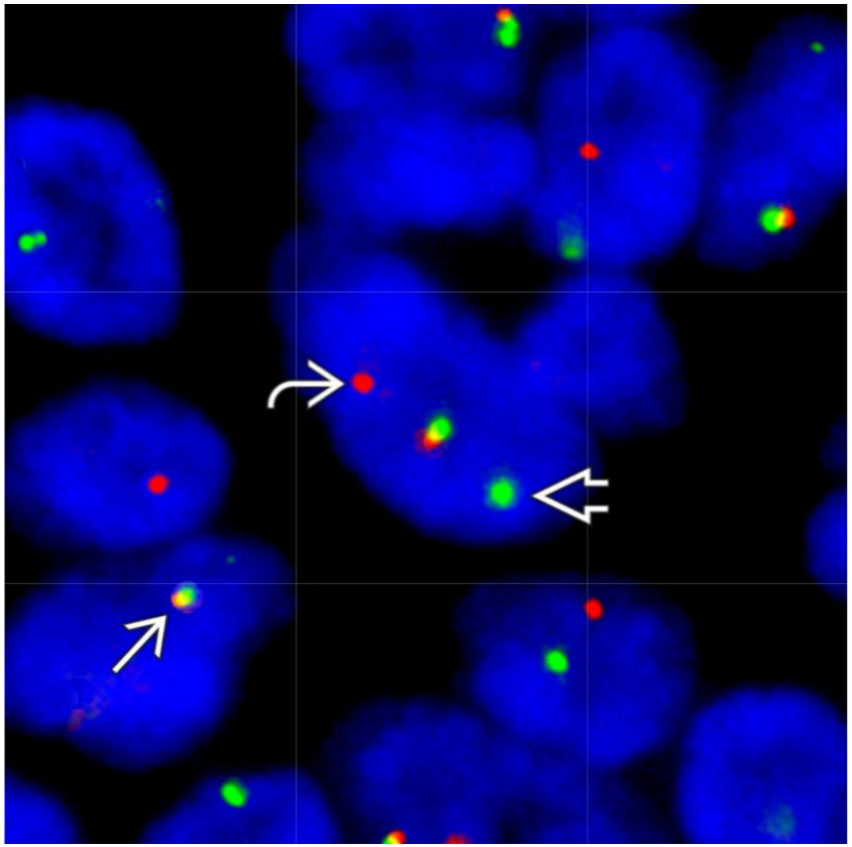


Large cell atypical variant



Ancillary tests





Differential Diagnosis

- Alveolar rhabdomyosarcoma
- Poorly differentiated synovial sarcoma
- Desmoplastic small round cell tumor
- Neuroblastoma
- Small cell carcinoma
- Extraskeletal mesenchymal chondrosarcoma
- Lymphoma

Undifferentiated/Unclassified Sarcomas

Undifferentiated Pleomorphic Sarcoma

- High-grade sarcoma composed of pleomorphic spindle and polygonal cells and showing **no other identifiable line of differentiation**

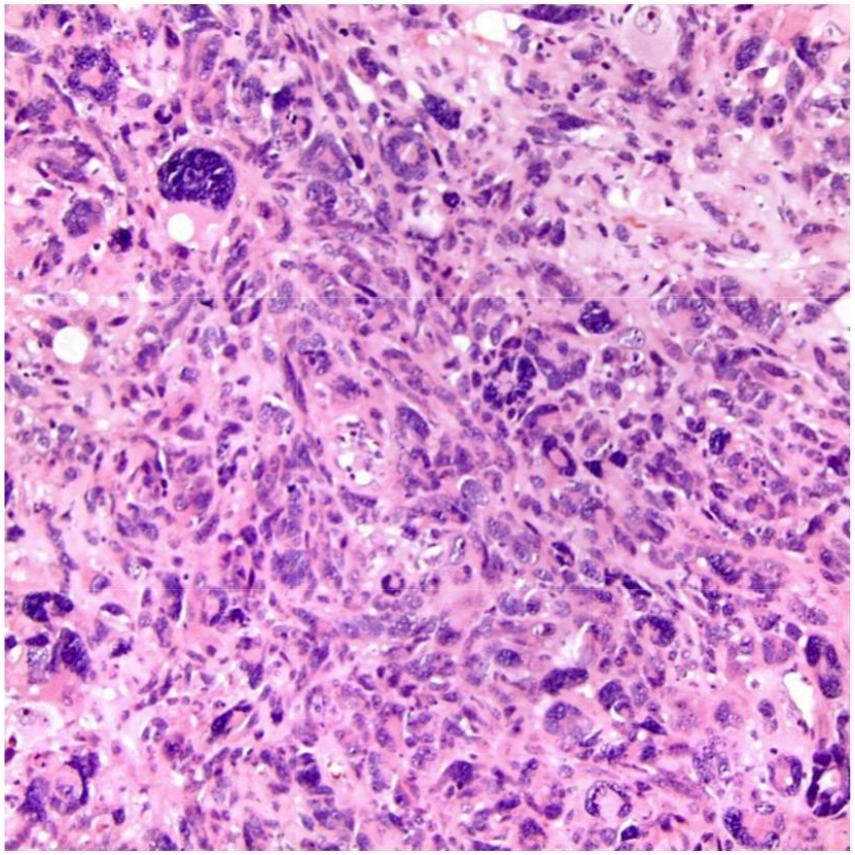
- Essentially a diagnosis of exclusion

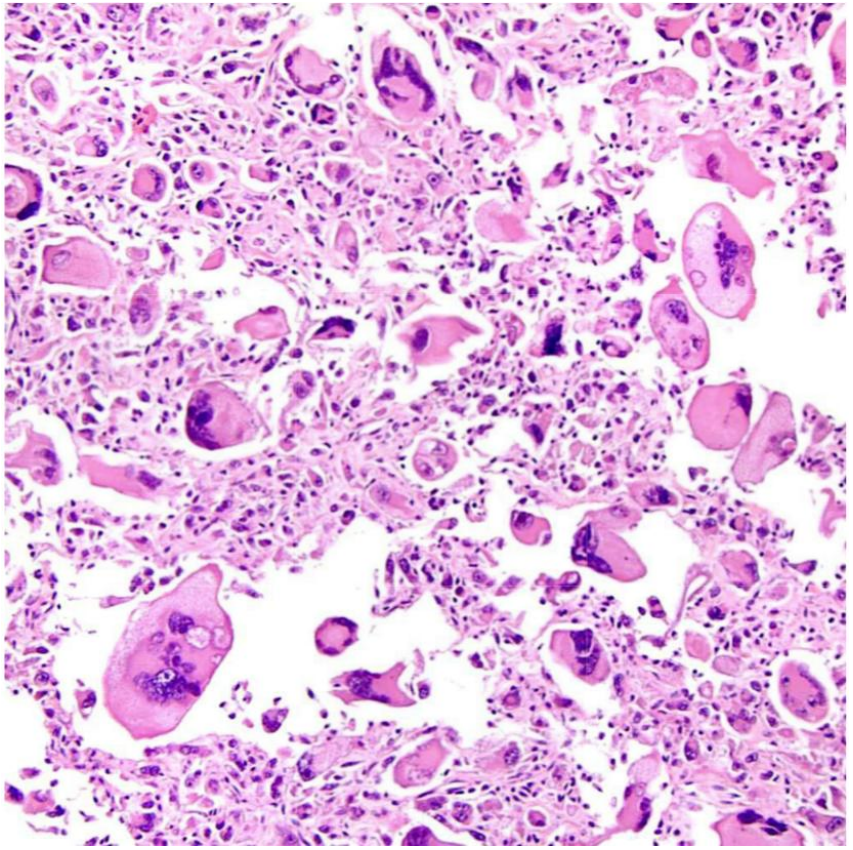
- Synonym: Malignant fibrous histiocytoma

Clinical

- Usually older and elderly adults (50-70 years)
- Most arise in deep soft tissues of extremities (thigh common)
- Treatment: Complete surgical resection with margins
- Fully malignant; usually high grade
  - Local recurrence in up to 30%; distant metastasis in up to 50%

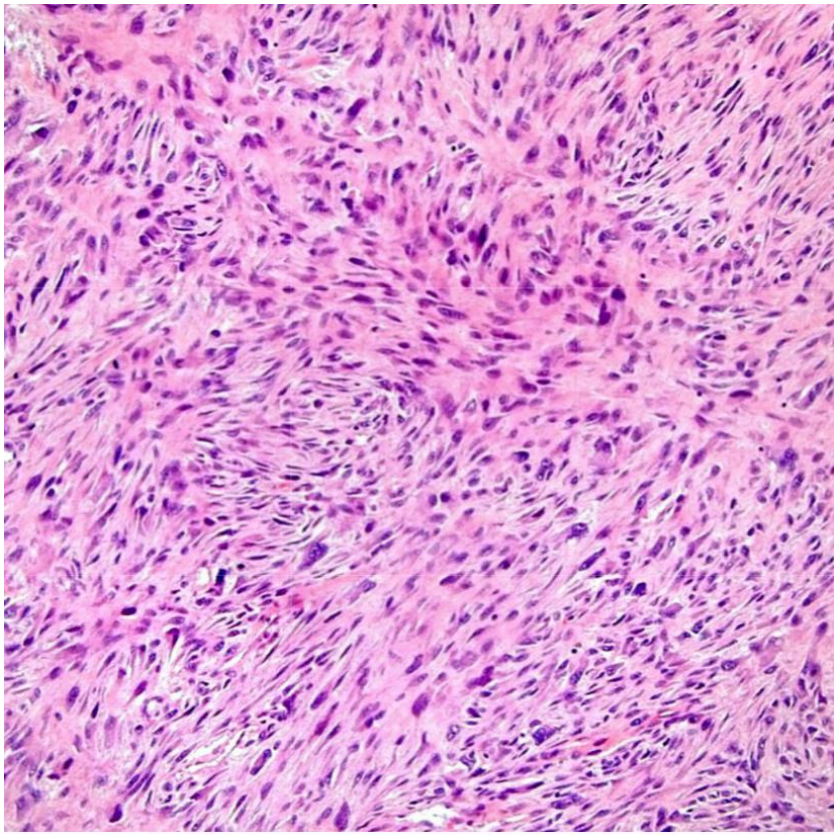
Microscopic



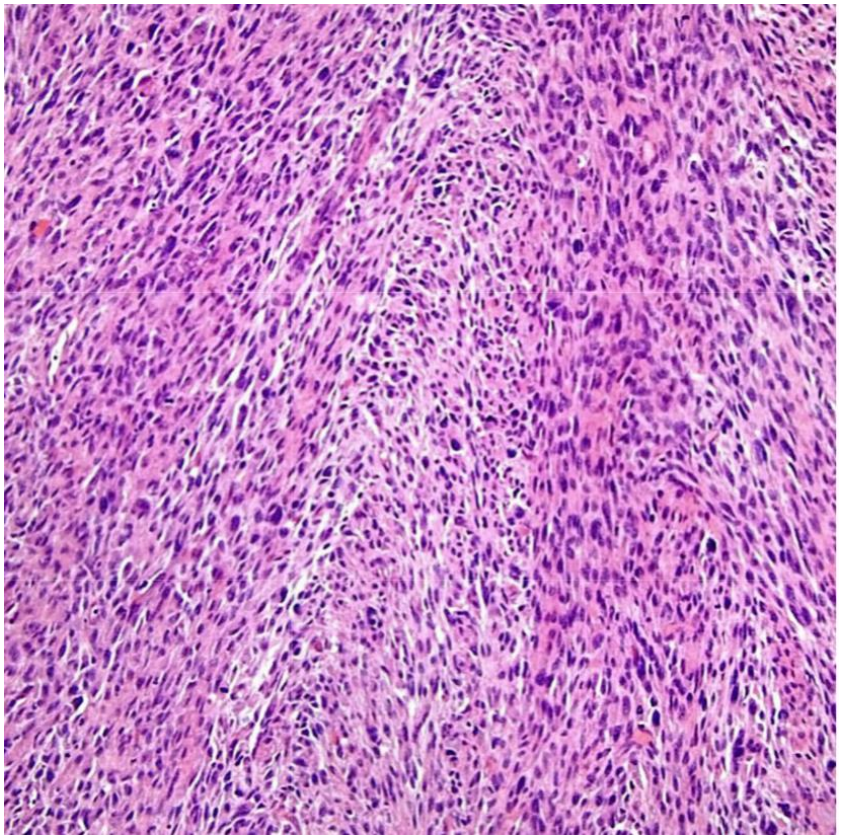


Microscopic

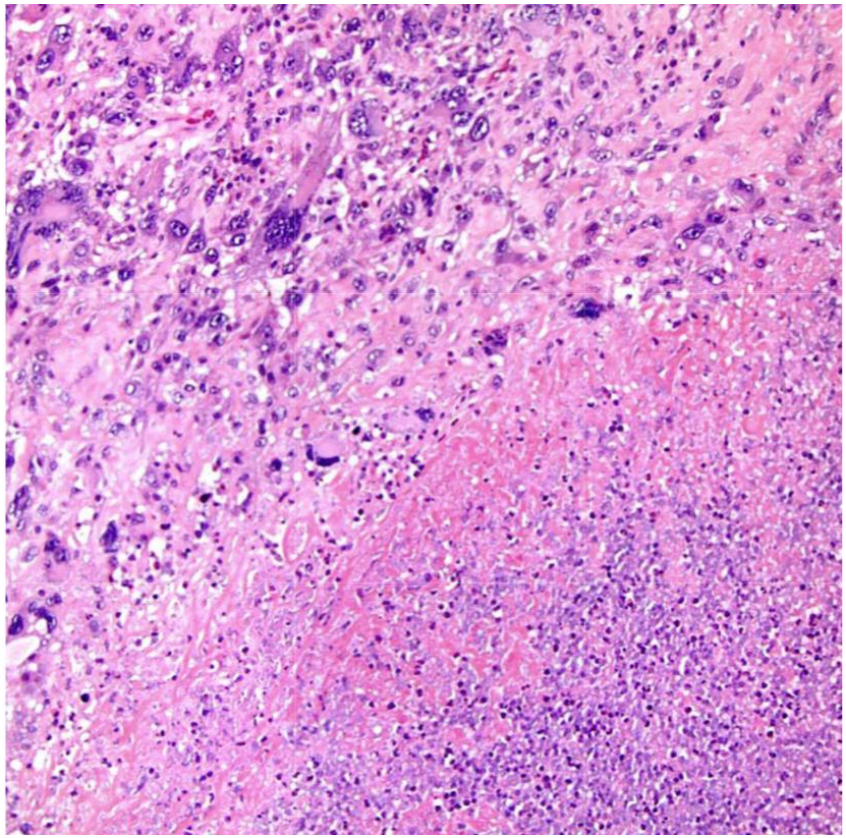
Storiform growth pattern



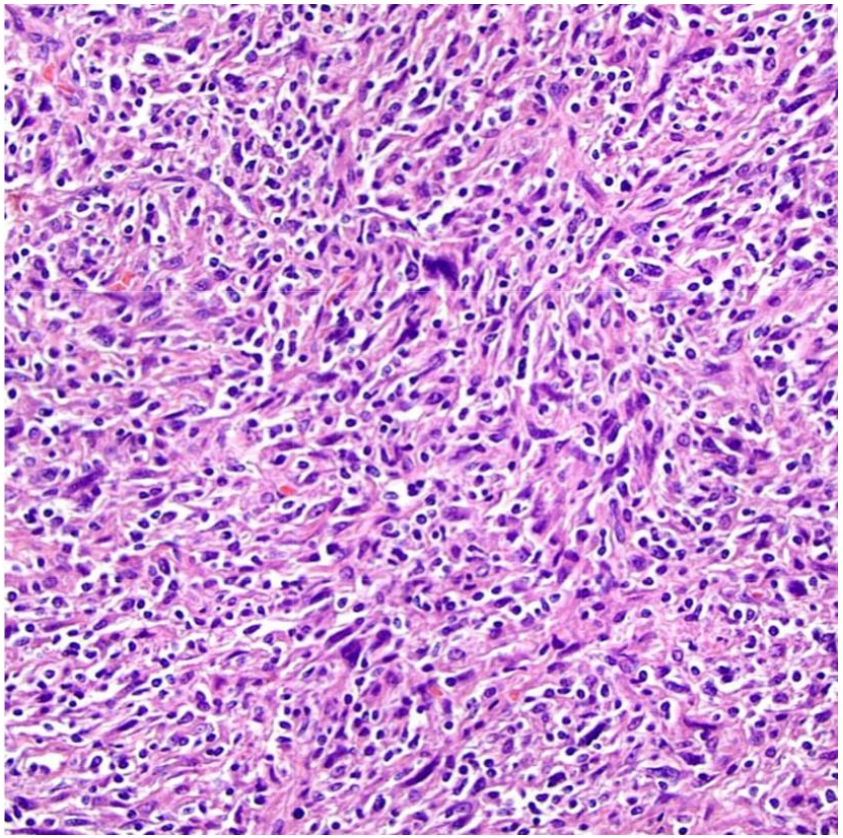
Fascicular growth



Coagulative necrosis



Chronic inflammation



Differential Diagnosis

- Dedifferentiated liposarcoma
- Other high-grade pleomorphic sarcomas
- Carcinoma, melanoma, lymphoma

By Diego Rivera
1886-1954