SOFT TISSUE TUMOURS

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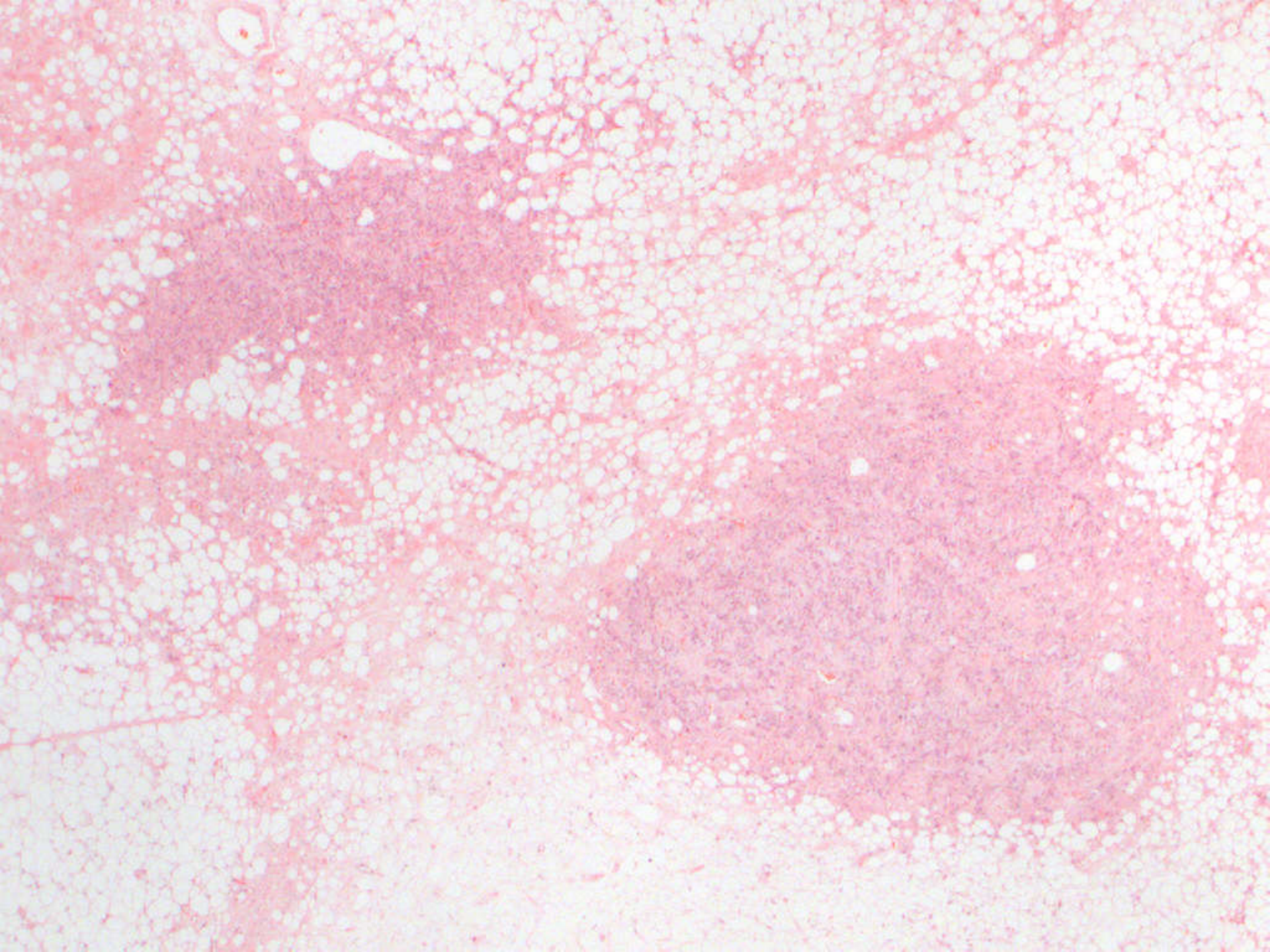
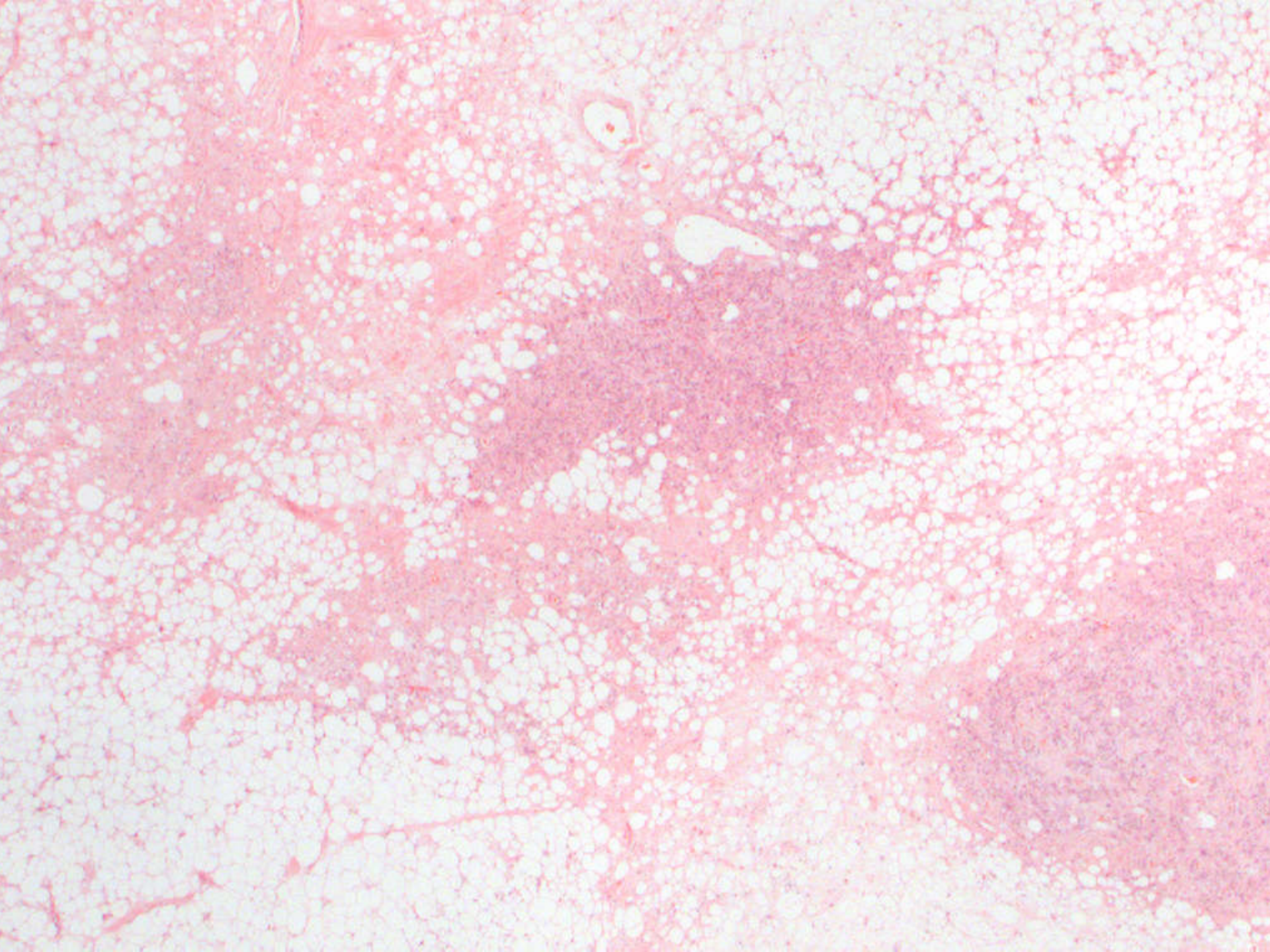
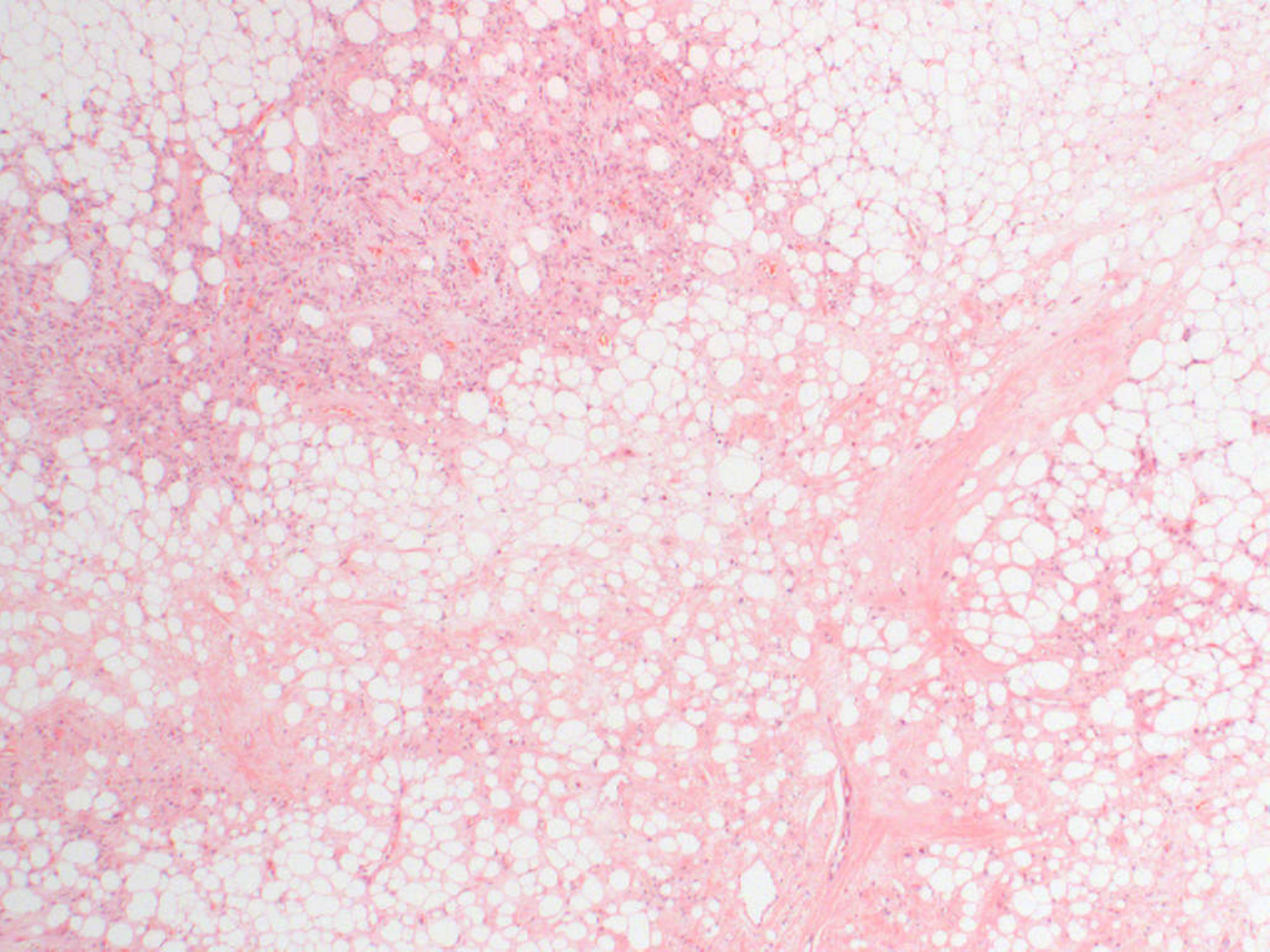
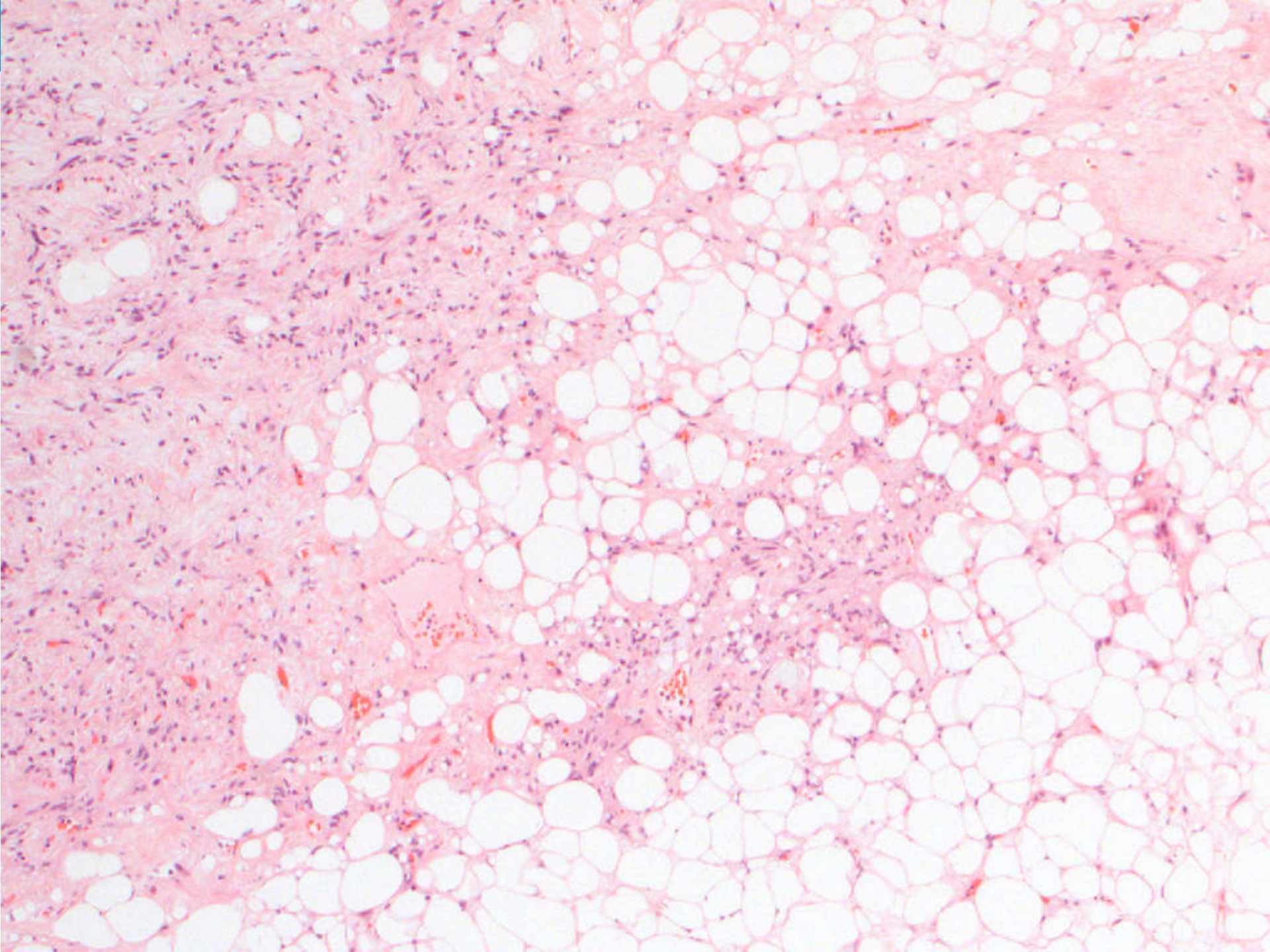
CLINICAL INFORMATION 1

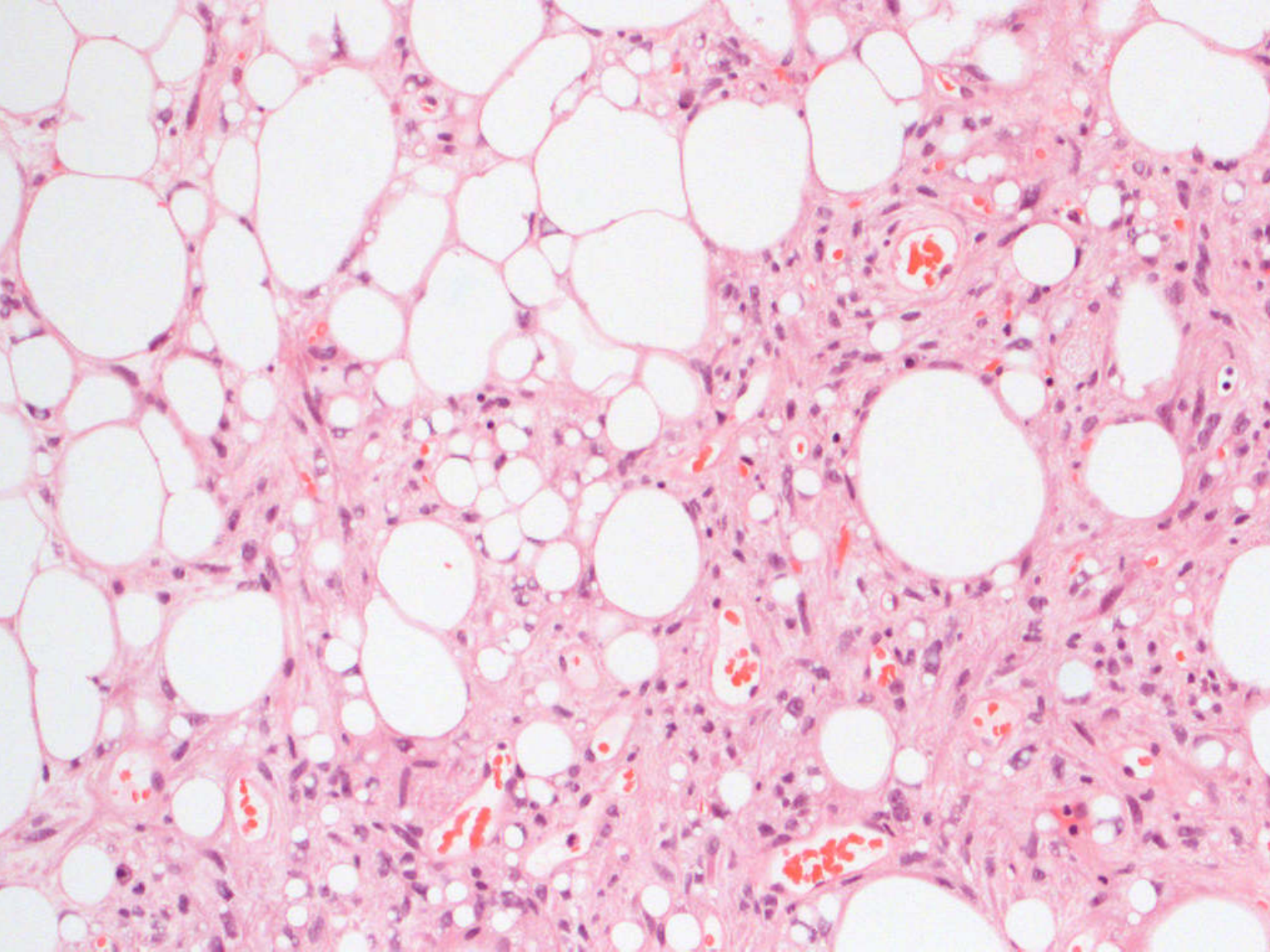
- Male, 73
- 5cm mass on shoulder.
- Deep to fascia/intramuscular.











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Spindle cell lipoma

- Cells are CD34+
- Mixture of adipocytes and bland spindle cells on a mixed myxoid, fibrous or collagenous background
- May have minimal to no fat
- DDx includes ALT/WDLS. Will have more cytological atypia with lipoblasts (but not necessary) – are MDM2 amplification positive

CLINICAL INFORMATION 1.1

- Male, 64
- 95cm mass R hamstring.
- Deep to fascia/intramuscular.

- Insert photos of case here ****

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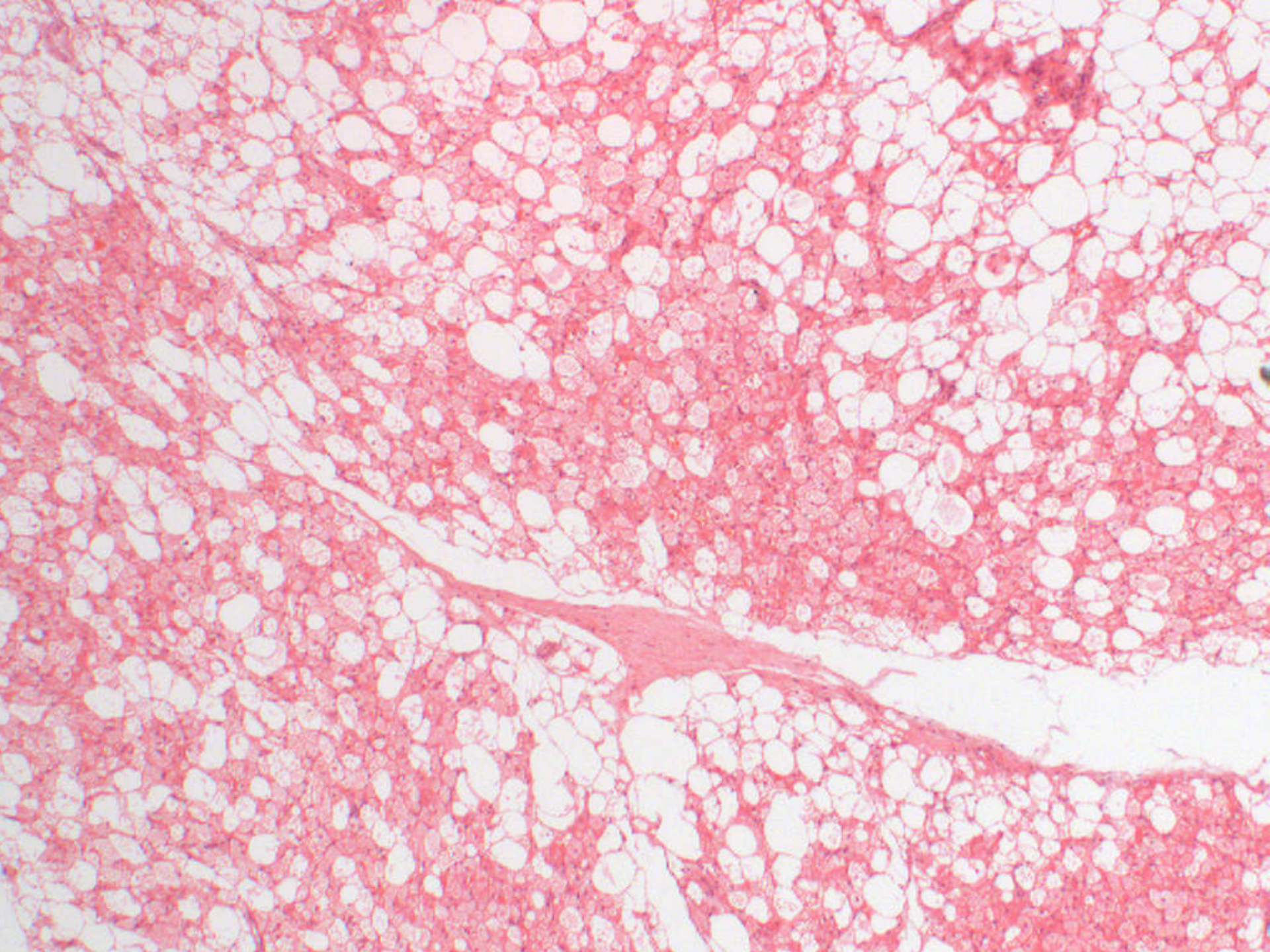
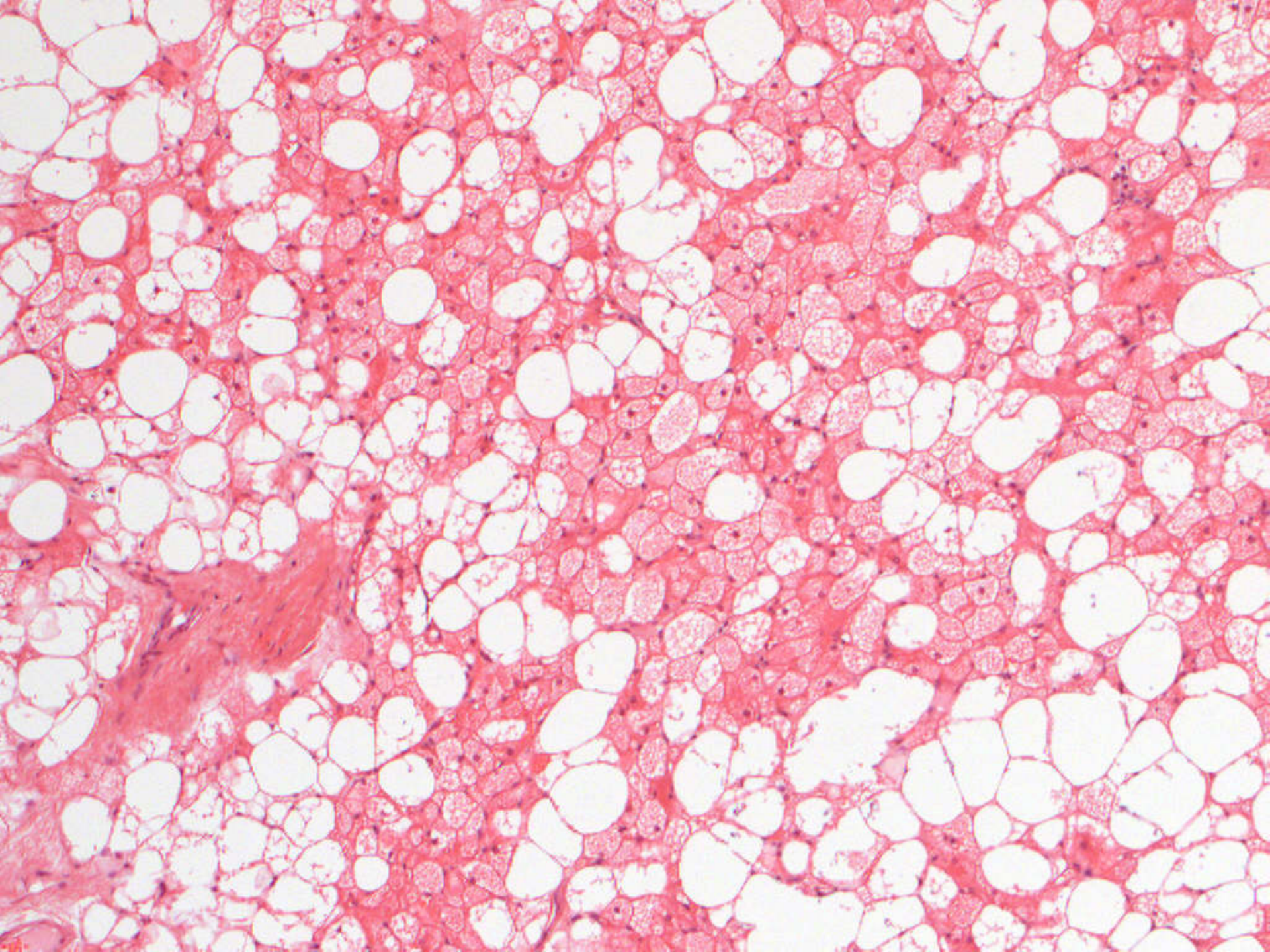
Pleomorphic lipoma

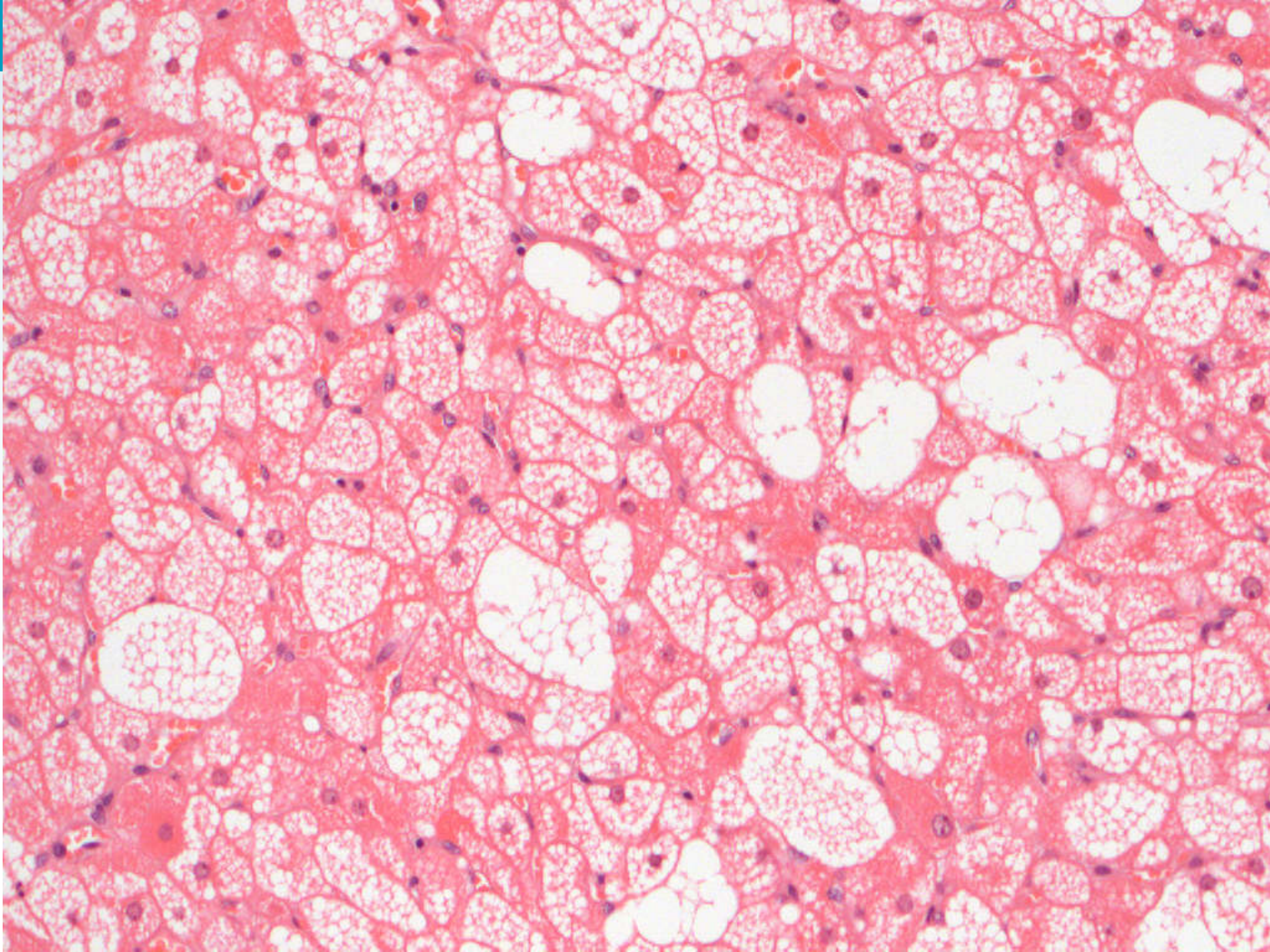
- Spindle cell/pleomorphic lipoma occur on a spectrum
- Fletcher recently proposed a separate entity to be called “atypical spindle cell/pleomorphic lipomatous tumour”
    - These are described as a low grade malignant counterpart to S/P lipoma
    - Said to show increased pleomorphism, increased and atypical lipoblasts, florets, infiltration and occurrence at unusual sites.
    - Additionally, recurrence rate higher when compared to S/P lipoma
- Both entities are CD34+, MDM2 negative and show deletion in RB1
    - We believe they are the same*
    - Pleomorphic liposarcoma will additionally show mitoses, necrosis, and will lack the low grade component.

CLINICAL INFORMATION 2

- Male, 35
- 15cm soft tissue tumour in thigh.
- Deep to fascia in muscle.







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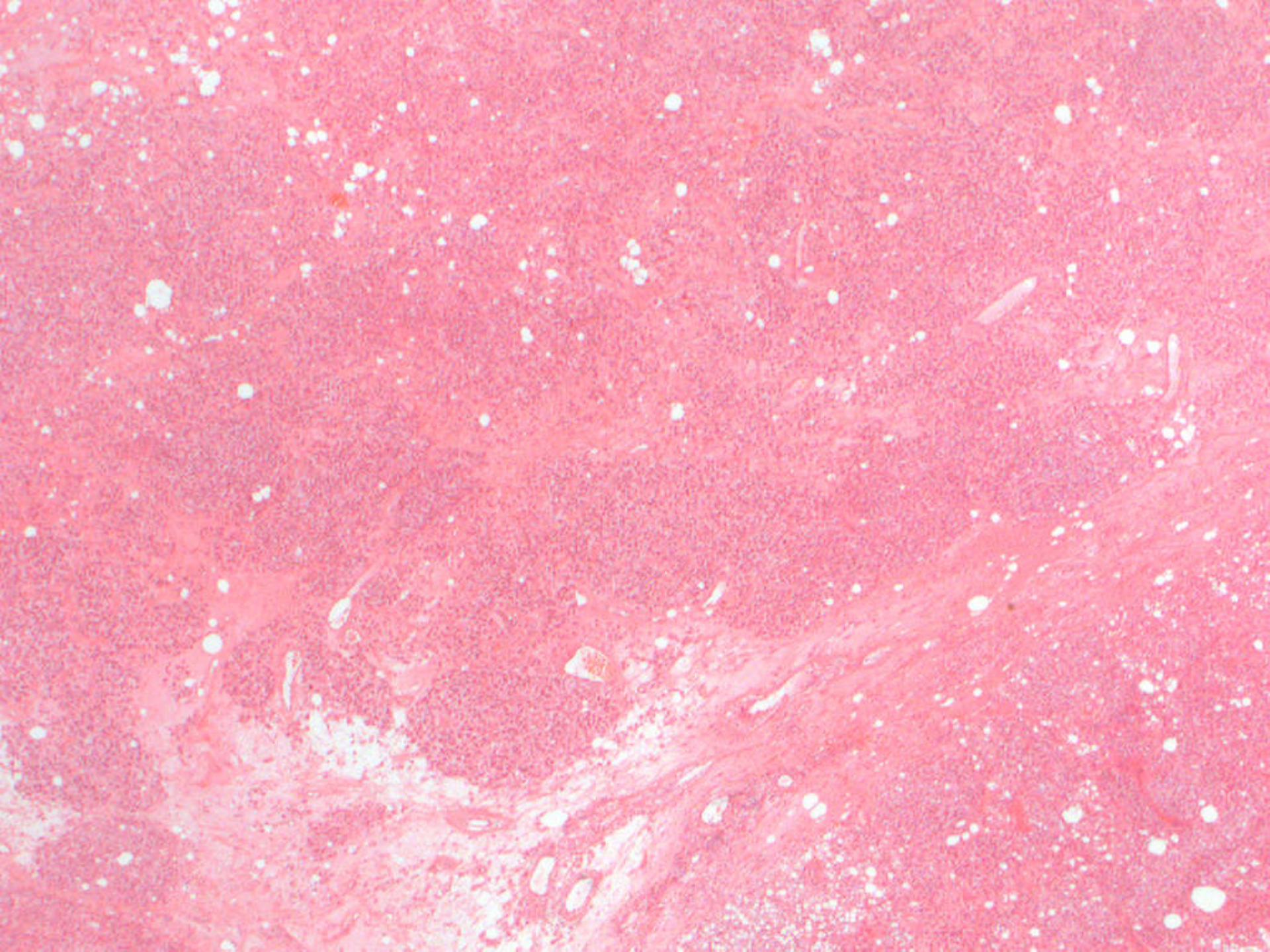
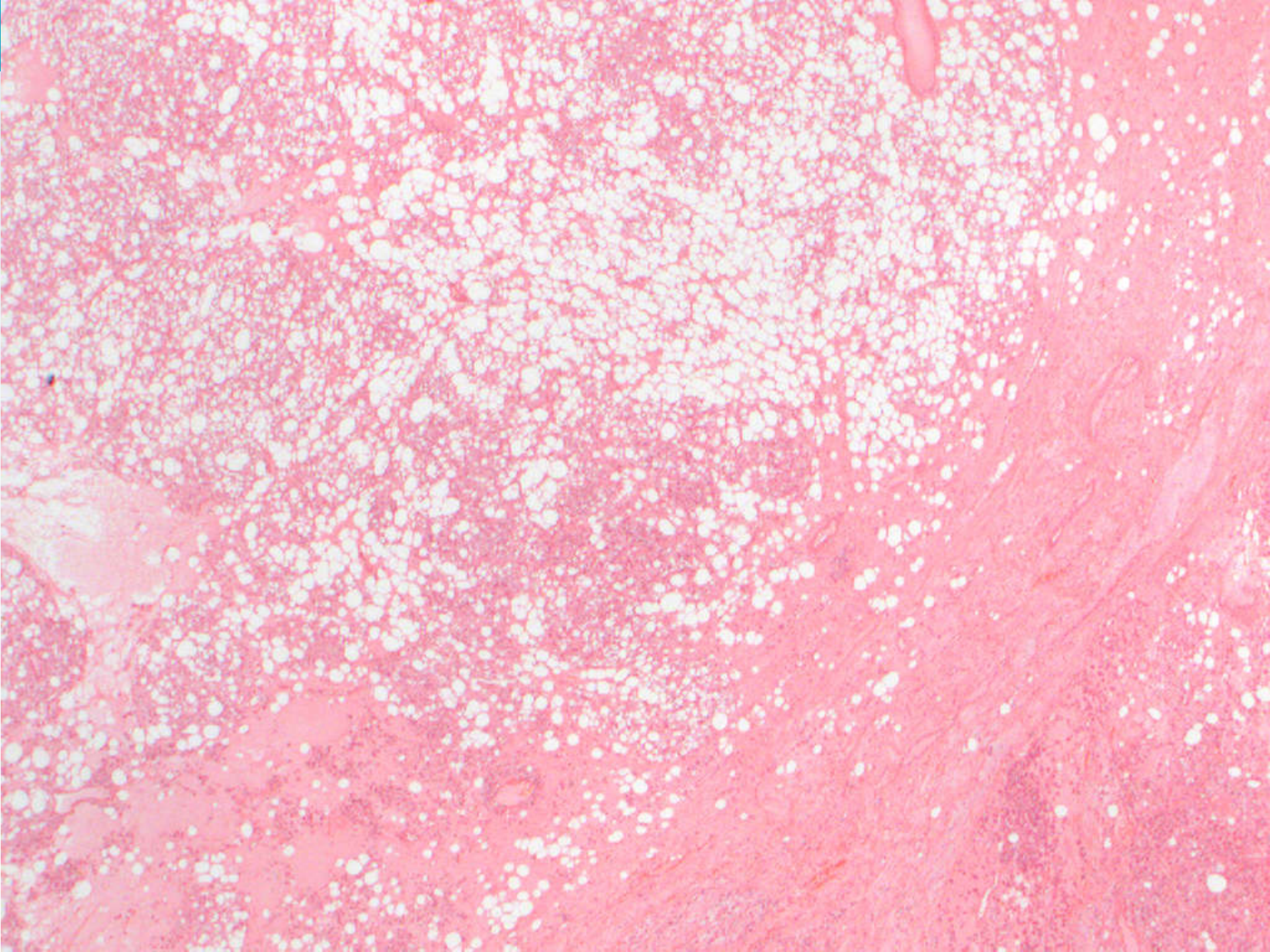
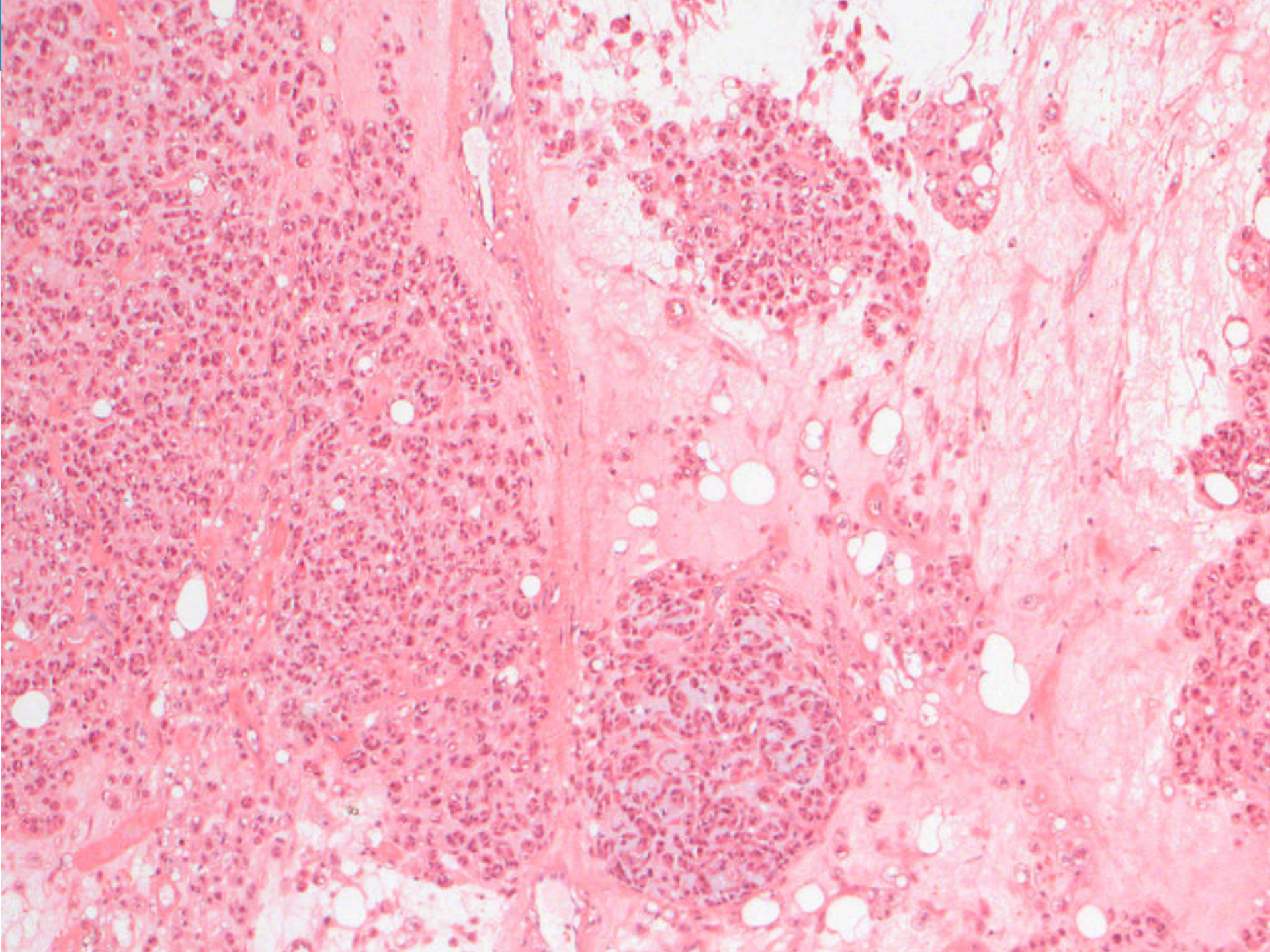
Hibernoma

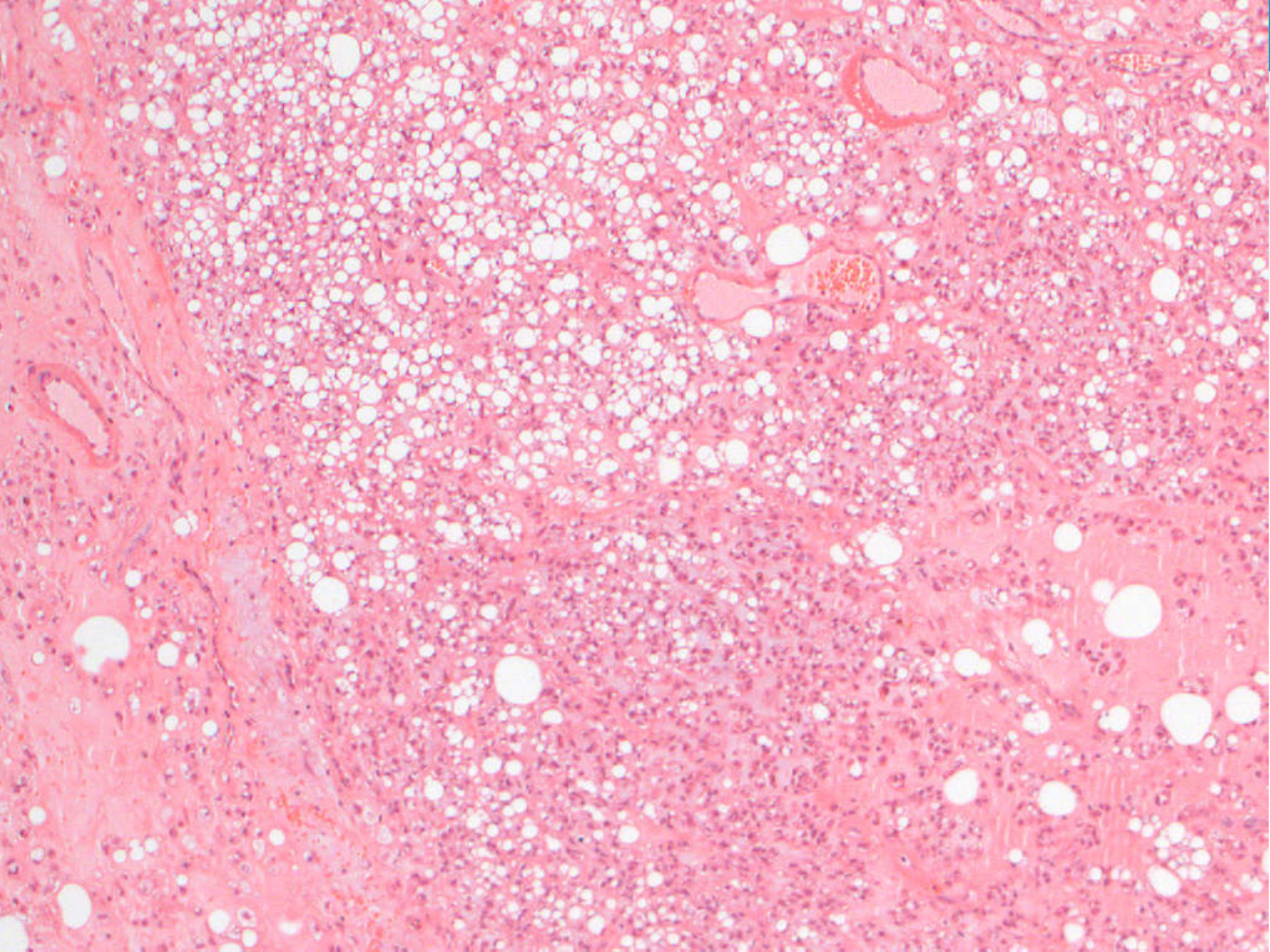
CLINICAL INFORMATION 3

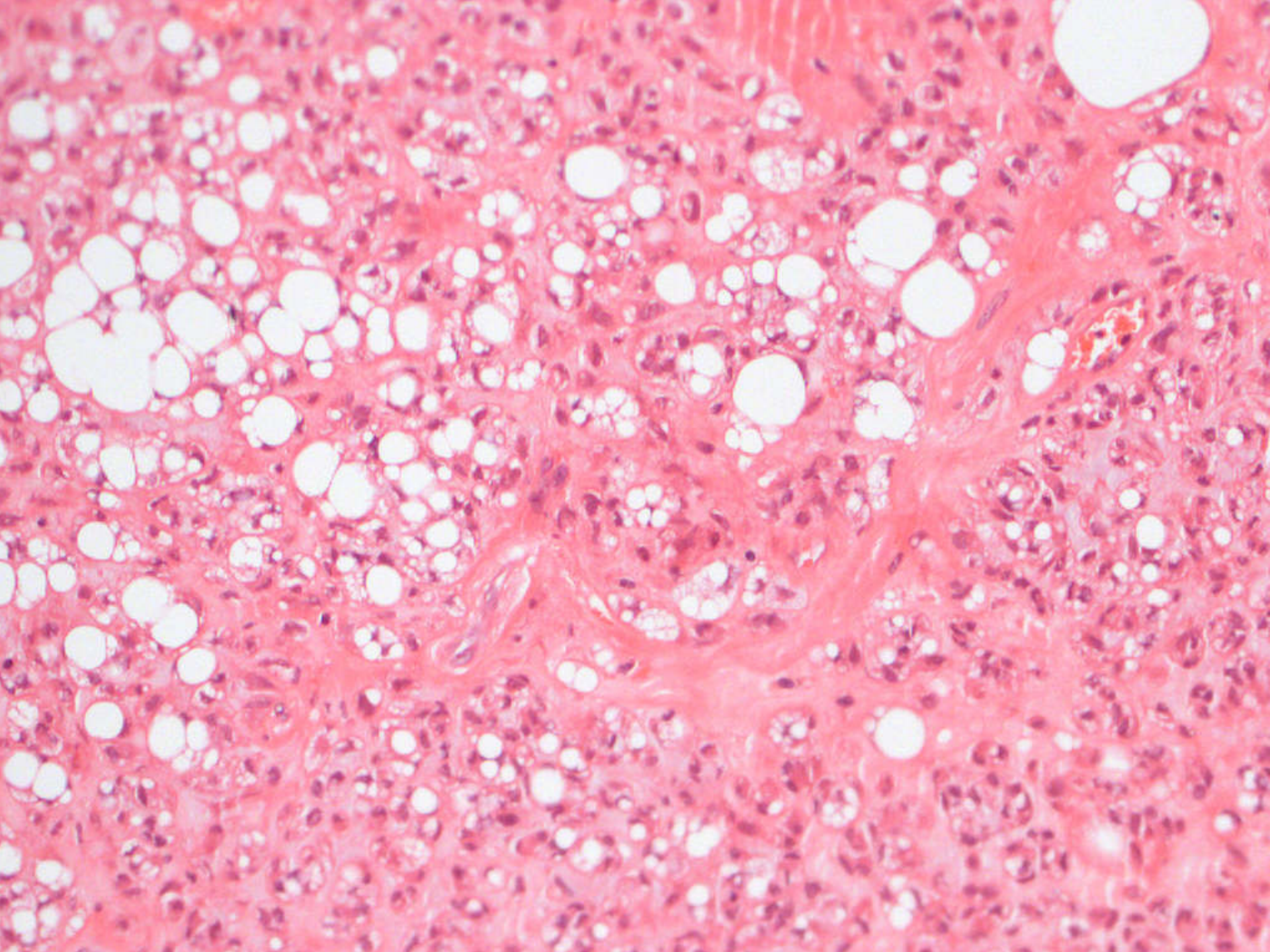
- Male, 48
- 8.5cm intramuscular mass in left thigh.











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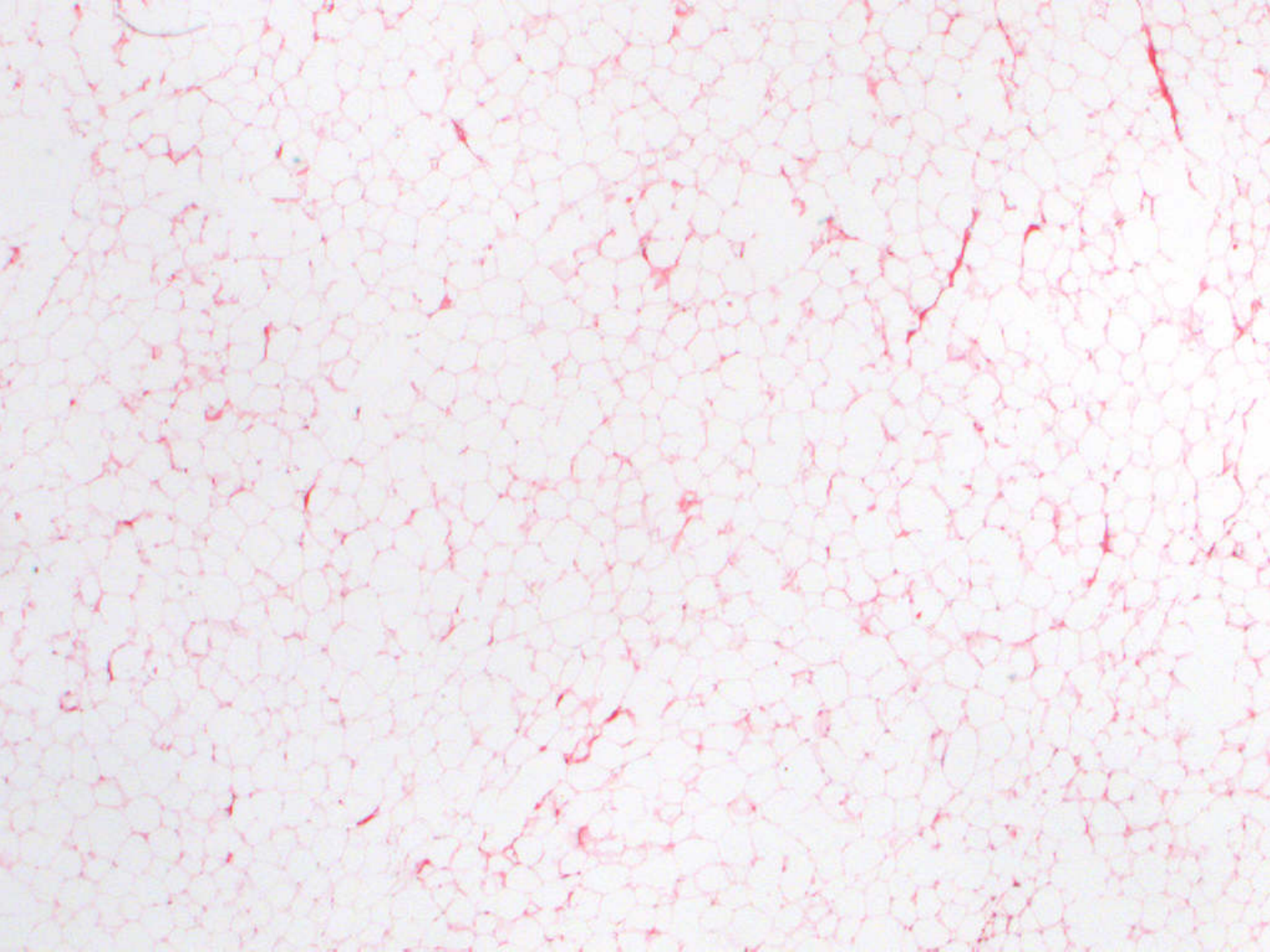
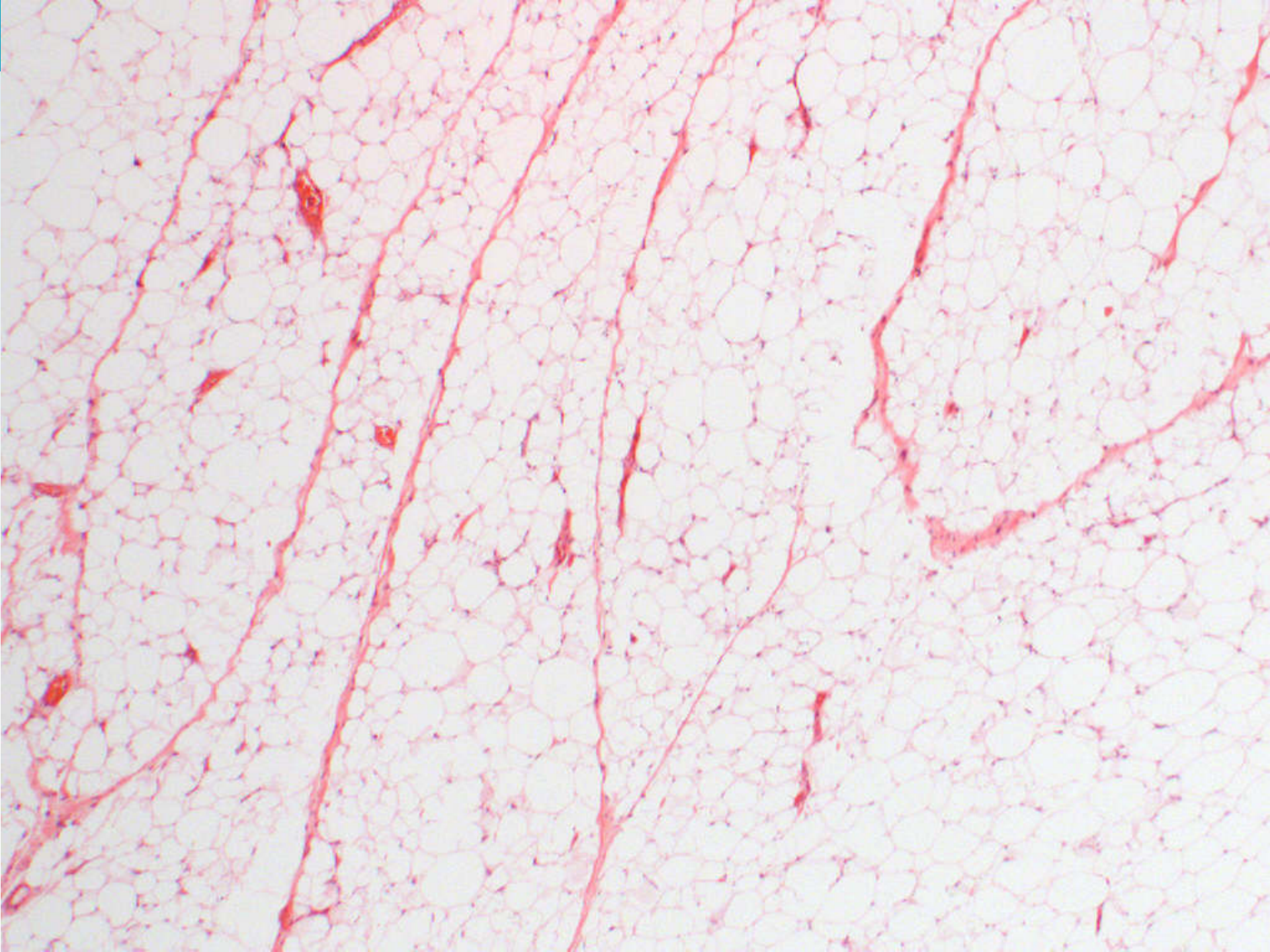
Chondroid Lipoma

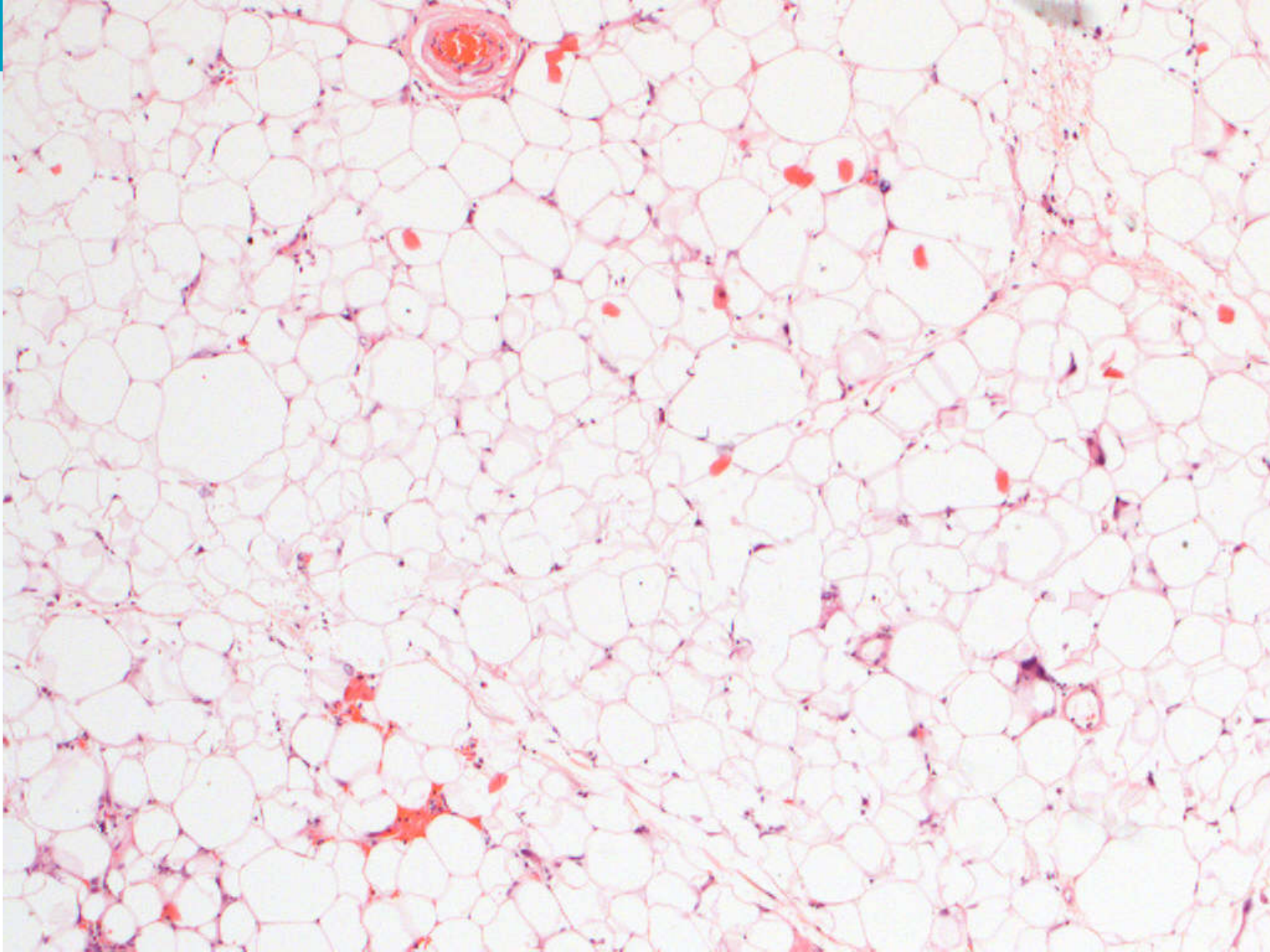
- Rare variant of adipocytic tumour
- Deep-seated, painless, circumscribed mass
- Composed of a mixture of adipocytes, chondroblast-like cells and lipoblasts set in a myxochondroid background

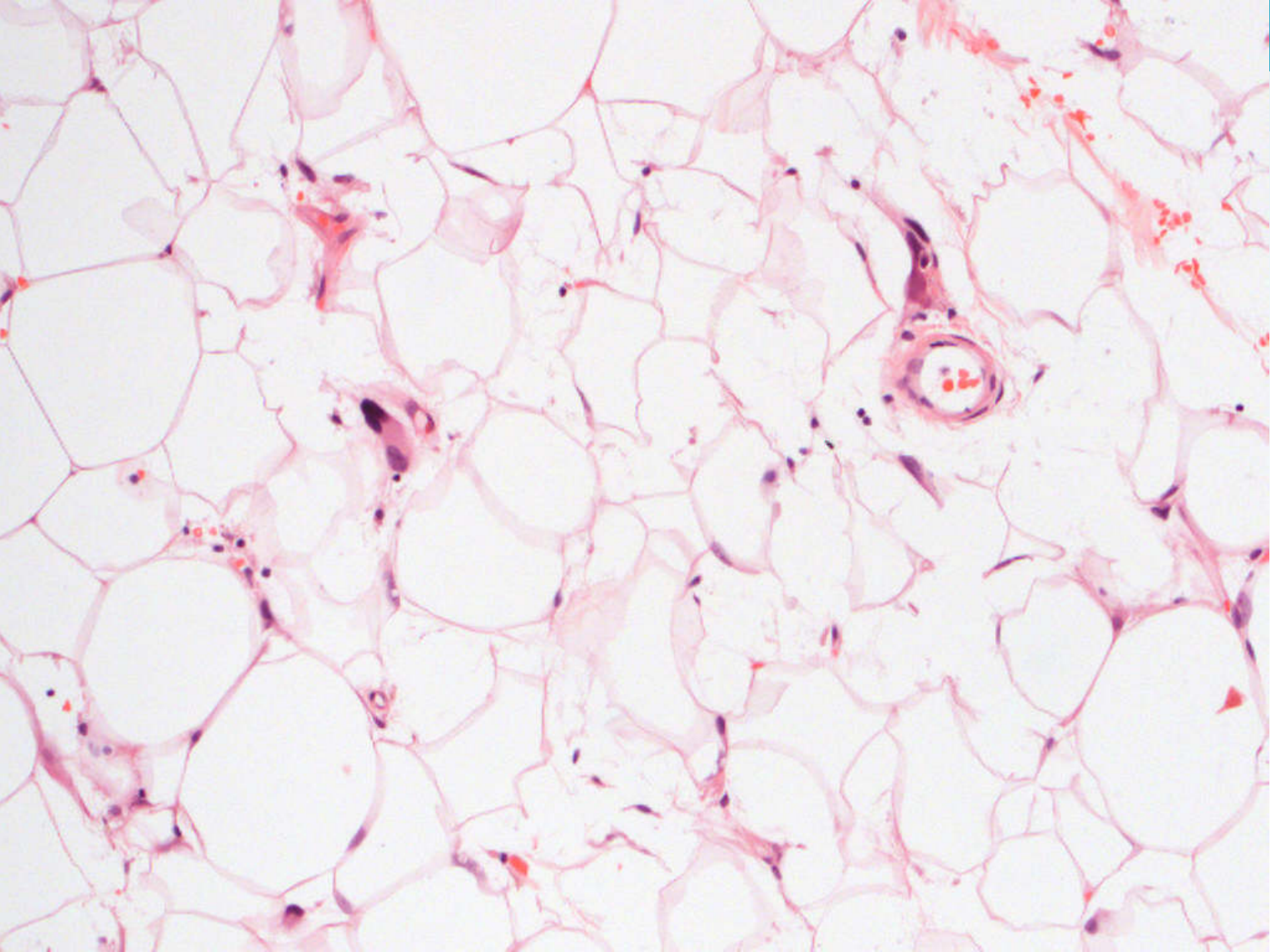
CLINICAL INFORMATION 4

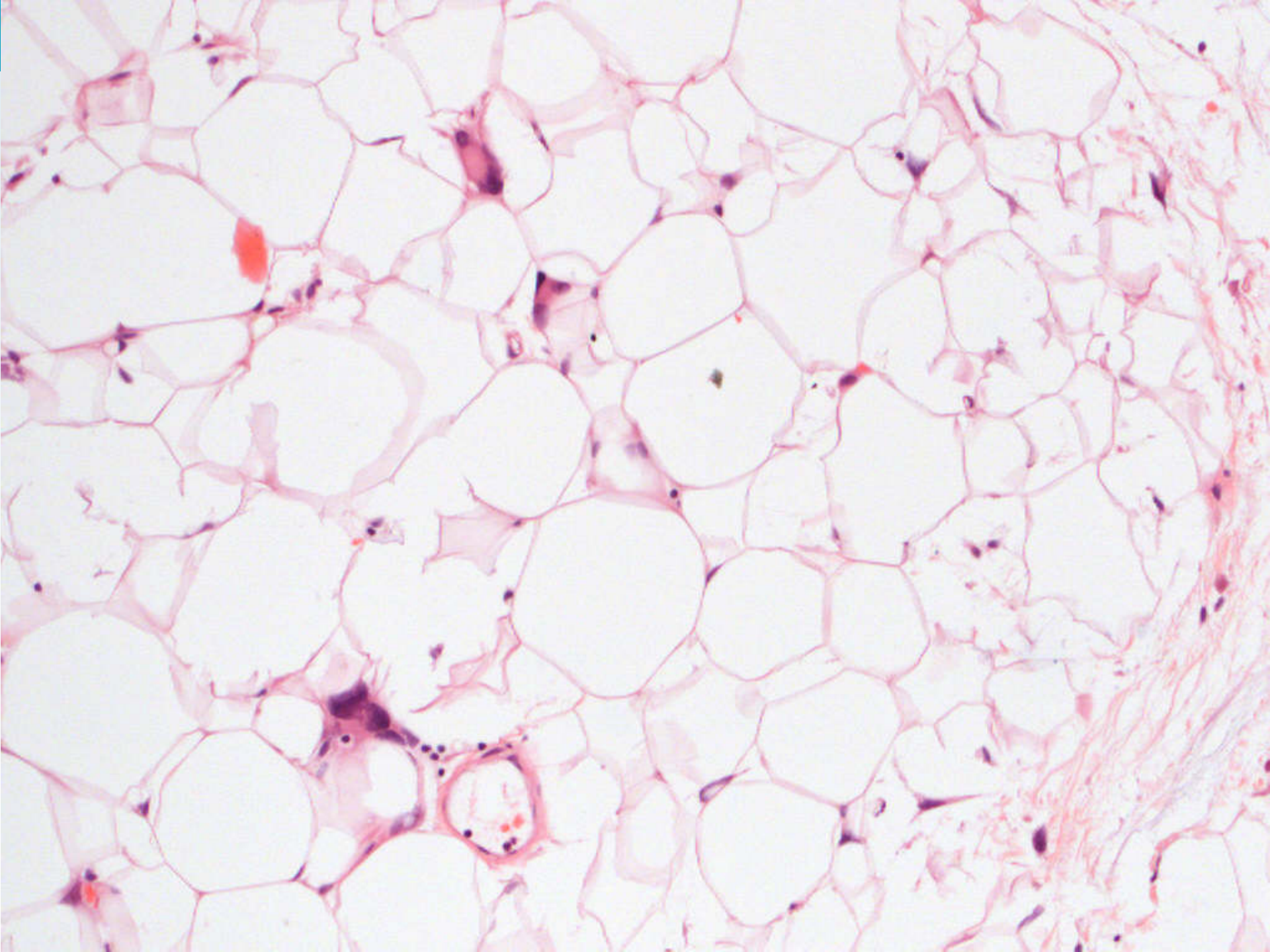
- Male, 78
- 20cm mass in thigh.
- Deep to fascia.











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Atypical lipomatous tumour/well differentiated liposarcoma

- Nomenclature depends on location and resectability
- Sample widely to look for dedifferentiation
- *MDM2* molecular highly sensitive
- Consider requesting *MDM2* on any trunk or limb girdle well differentiated lipomatous tumours that are deep seated and/or over 10cm.

Histologic Subtypes

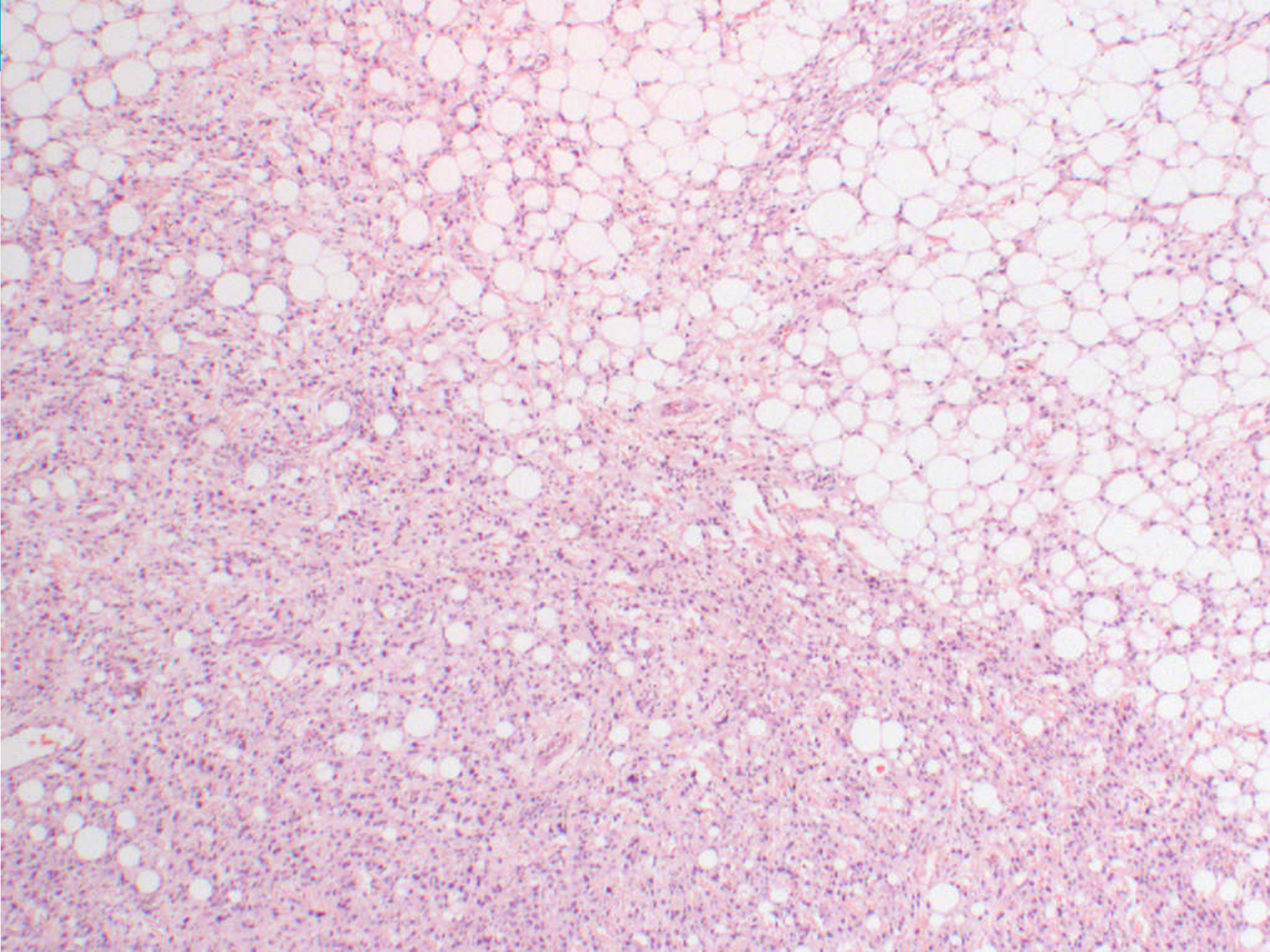
- 3 main variants with limited clinical significance
  - Lipoma-like
  - Sclerosing
  - Inflammatory
- Mixed subtype
- Rarest variants:
  - Lipoleiomyosarcoma. Both components low-grade.
  - Low-grade osteosarcomatous areas. Foci reminiscent of parosteal or low grade central OS.

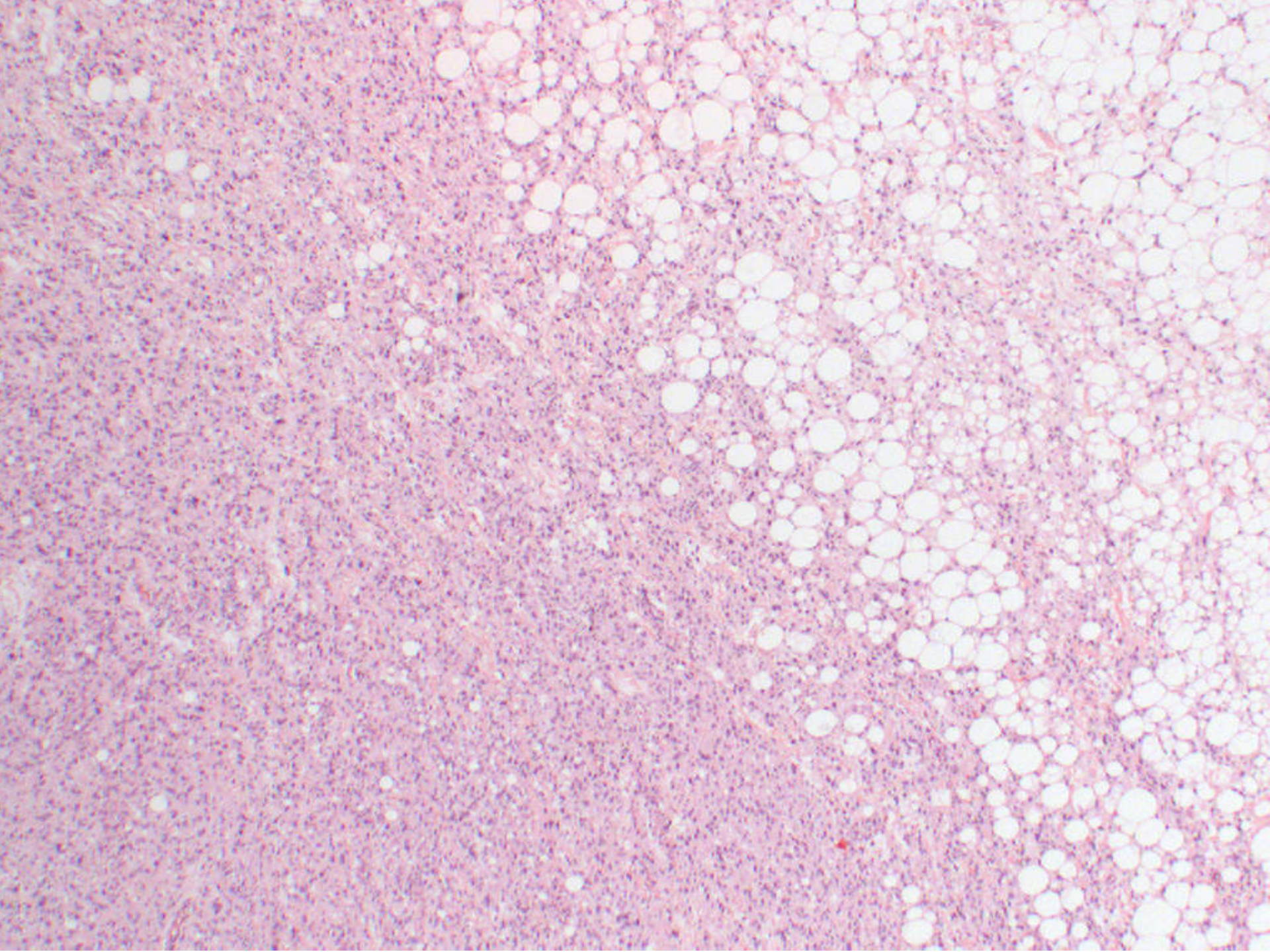
Additional comments:

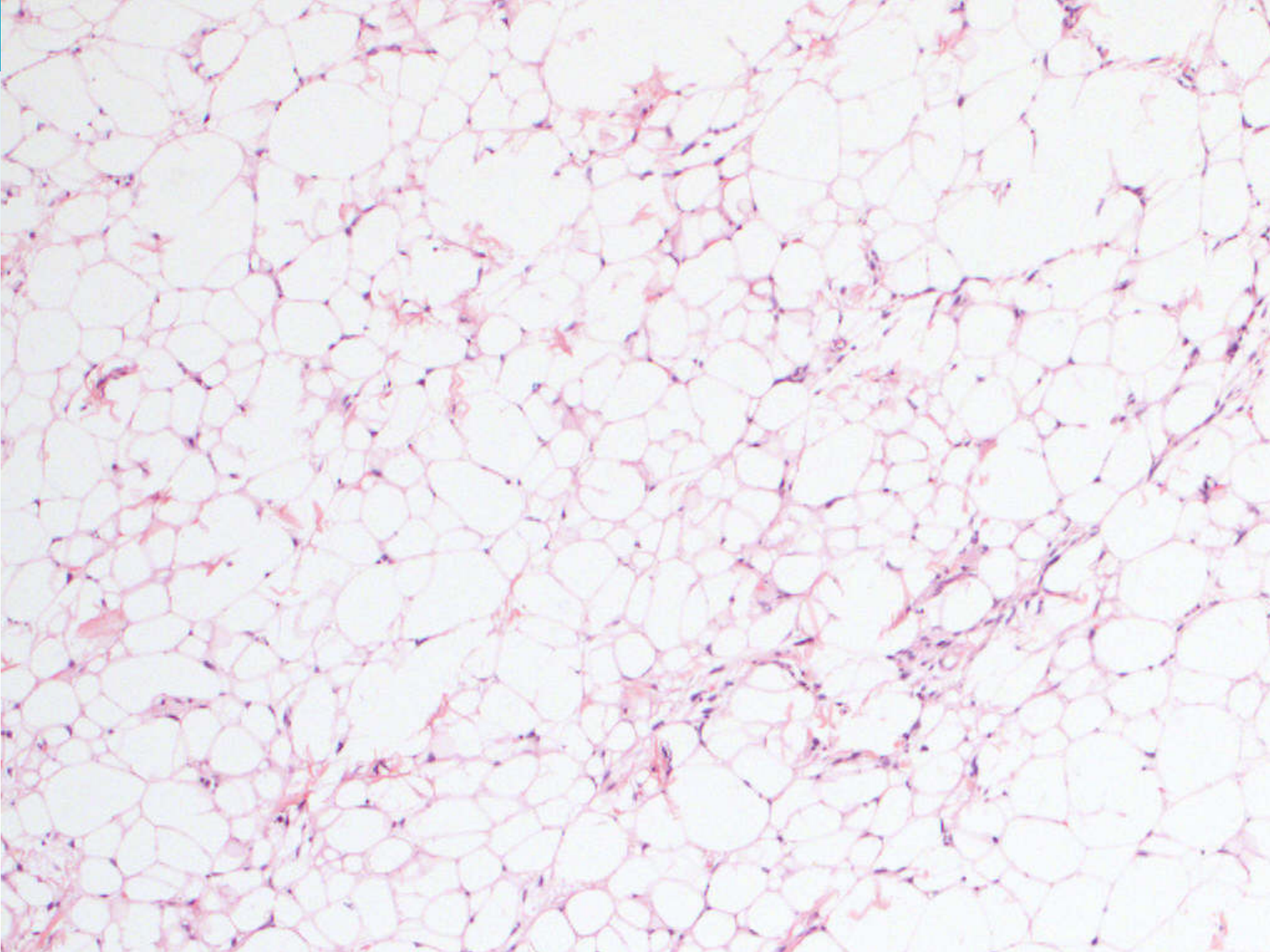
- The differential diagnosis now includes the recently classified “atypical pleomorphic/spindle cell lipomatous tumour.”
- Low grade adipocytic neoplasm with a pleomorphic lipoma-like appearance BUT additionally-
- Atypical morphologic features, including atypical spindle cells, bizarre pleomorphic multinucleated cells, pleomorphic lipoblasts and occasionally infiltrative growth.
- Negative for *MDM2* amplification
- P16 and CD34+
- A significant subset show deletions/losses of 13q14 including *RB1*

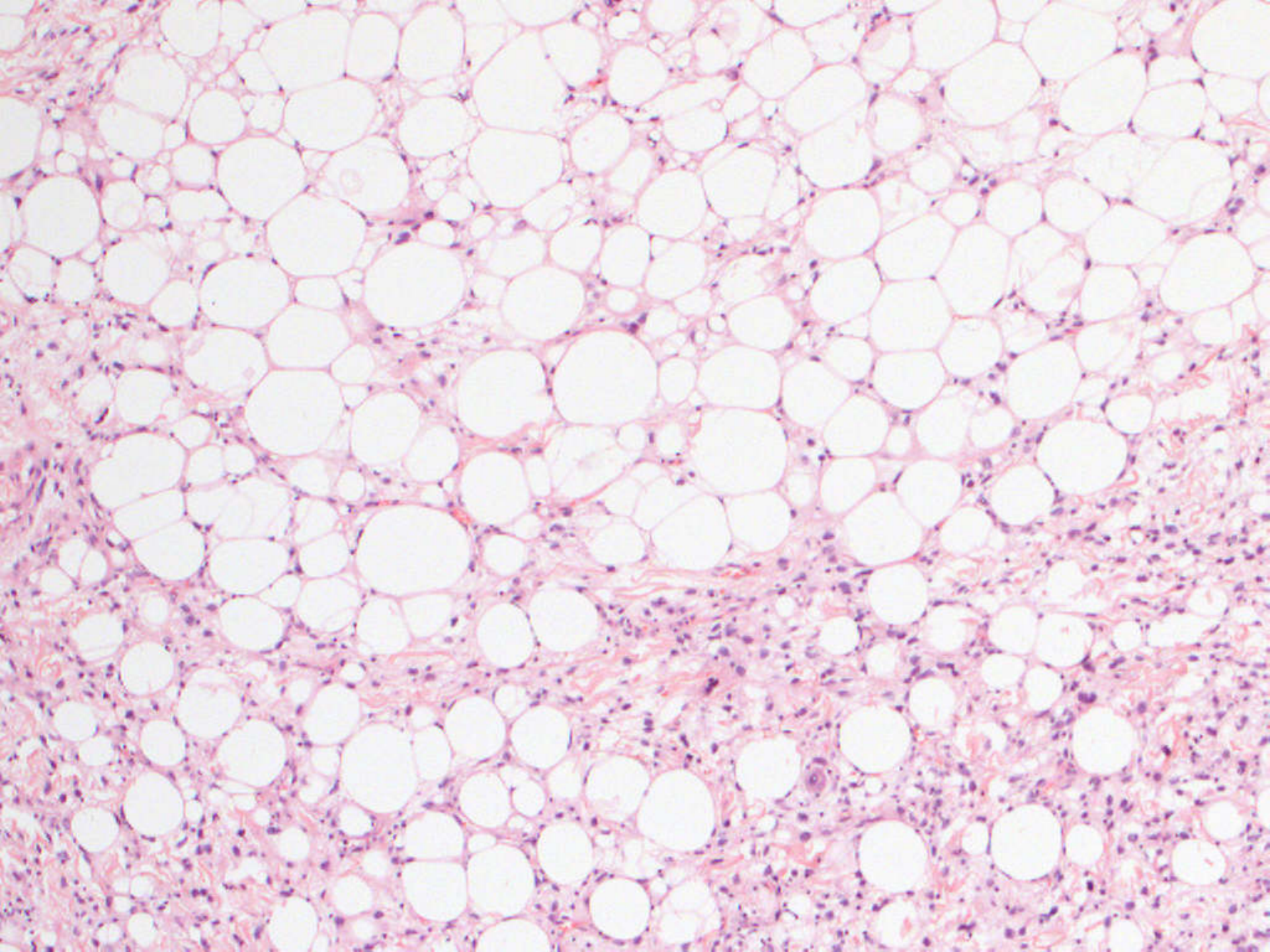
CLINICAL INFORMATION 5

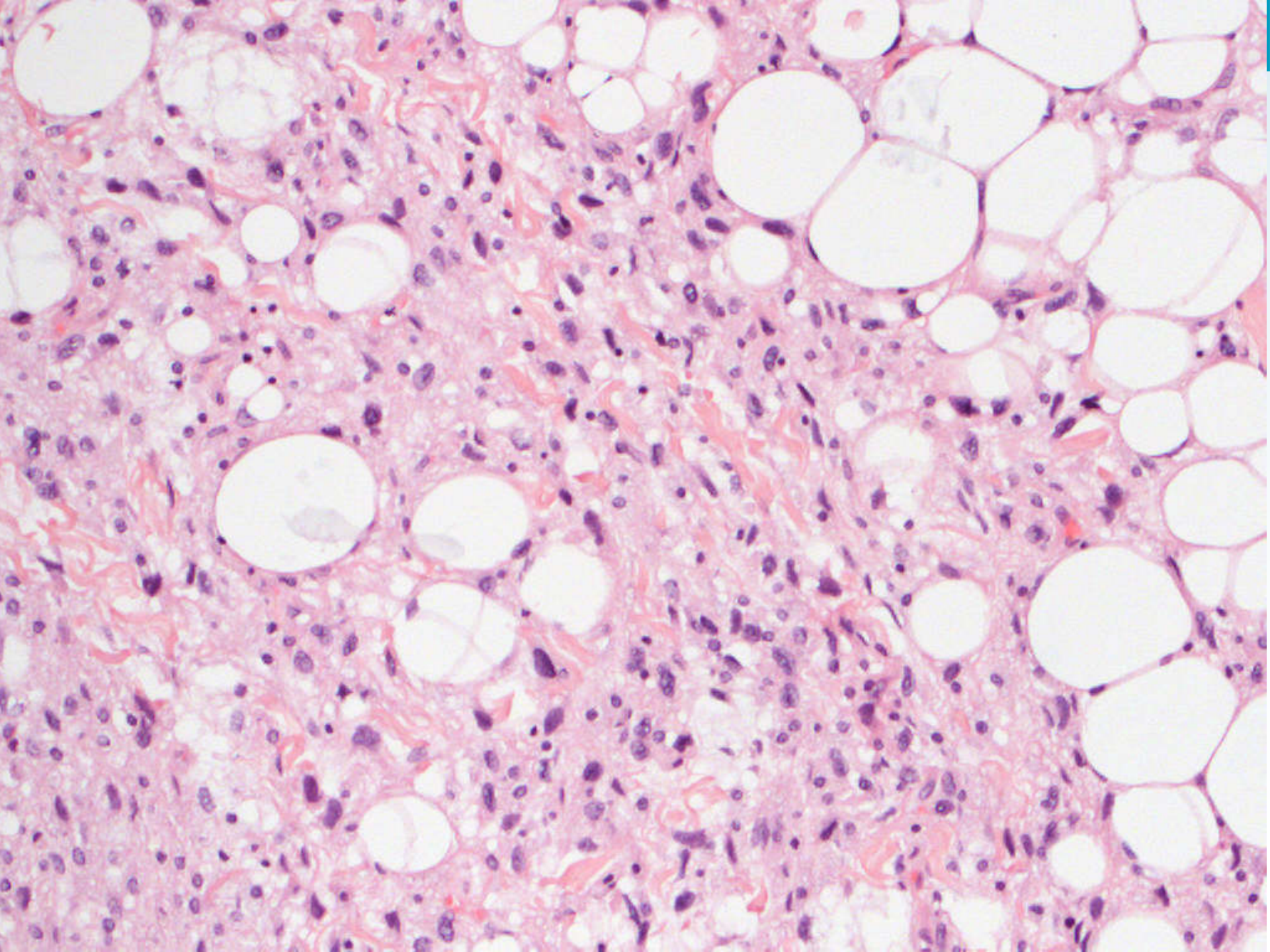
- Female, 65
- 21cm mass in femoral triangle.

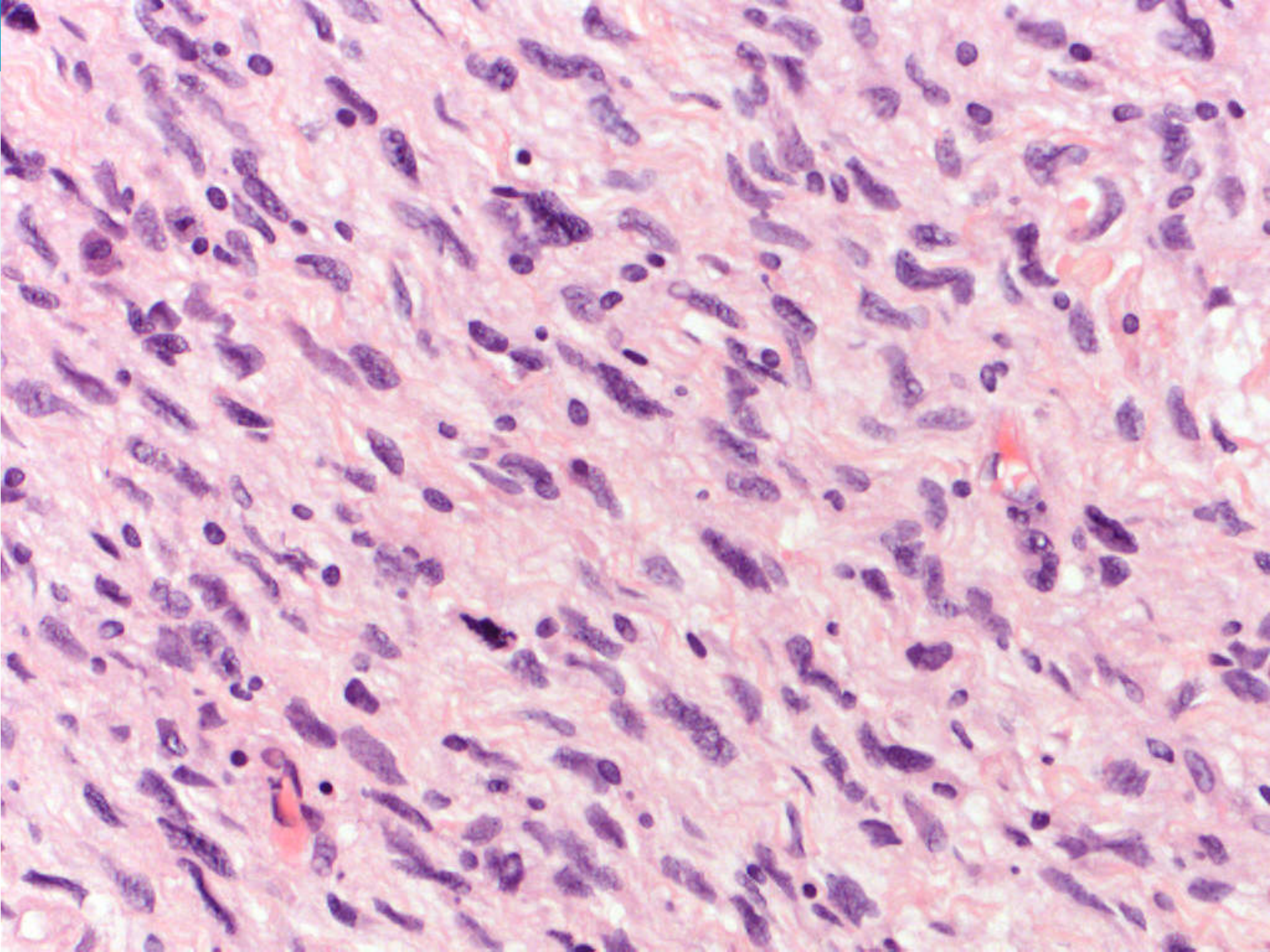












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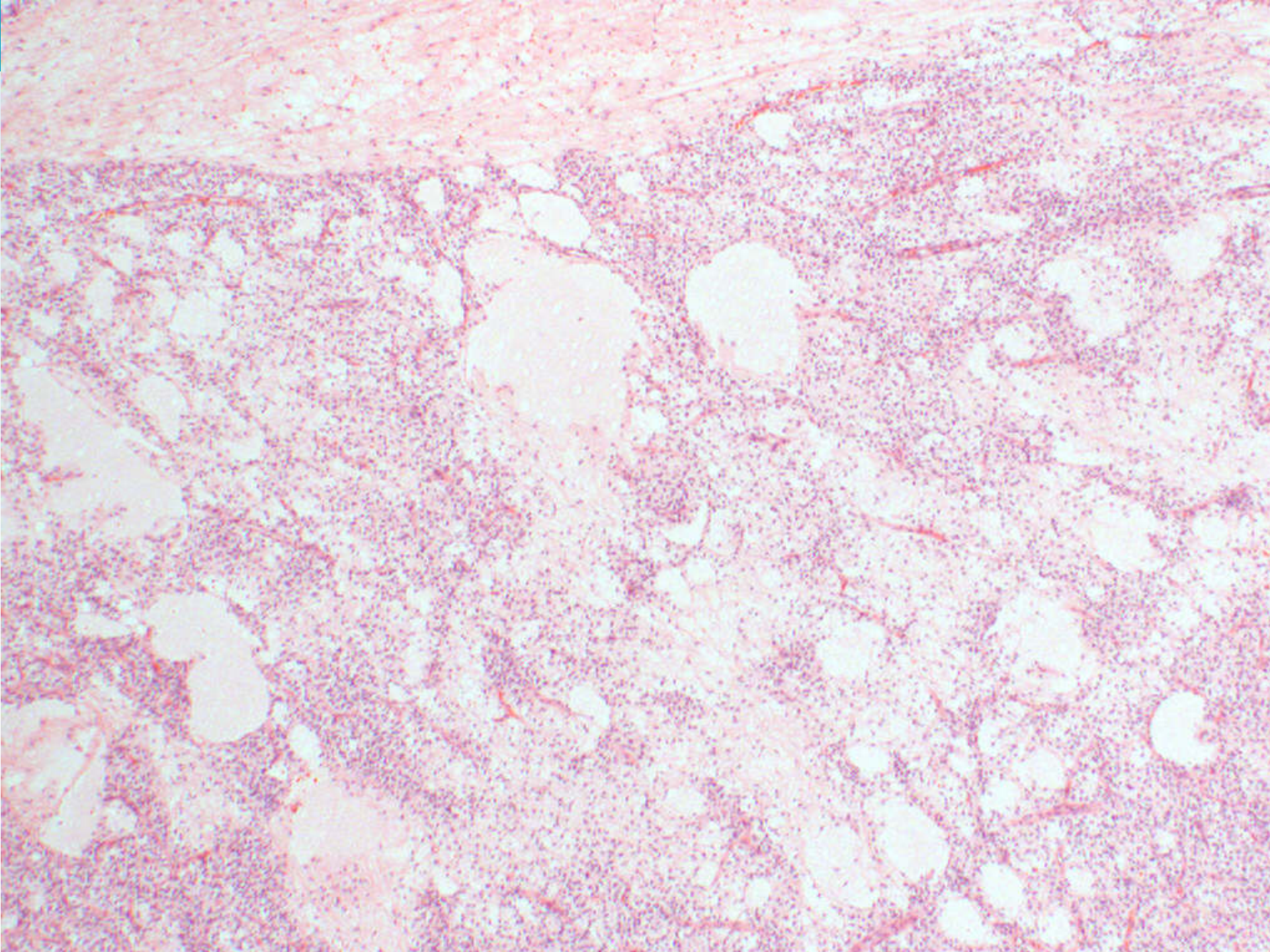
Dedifferentiated liposarcoma

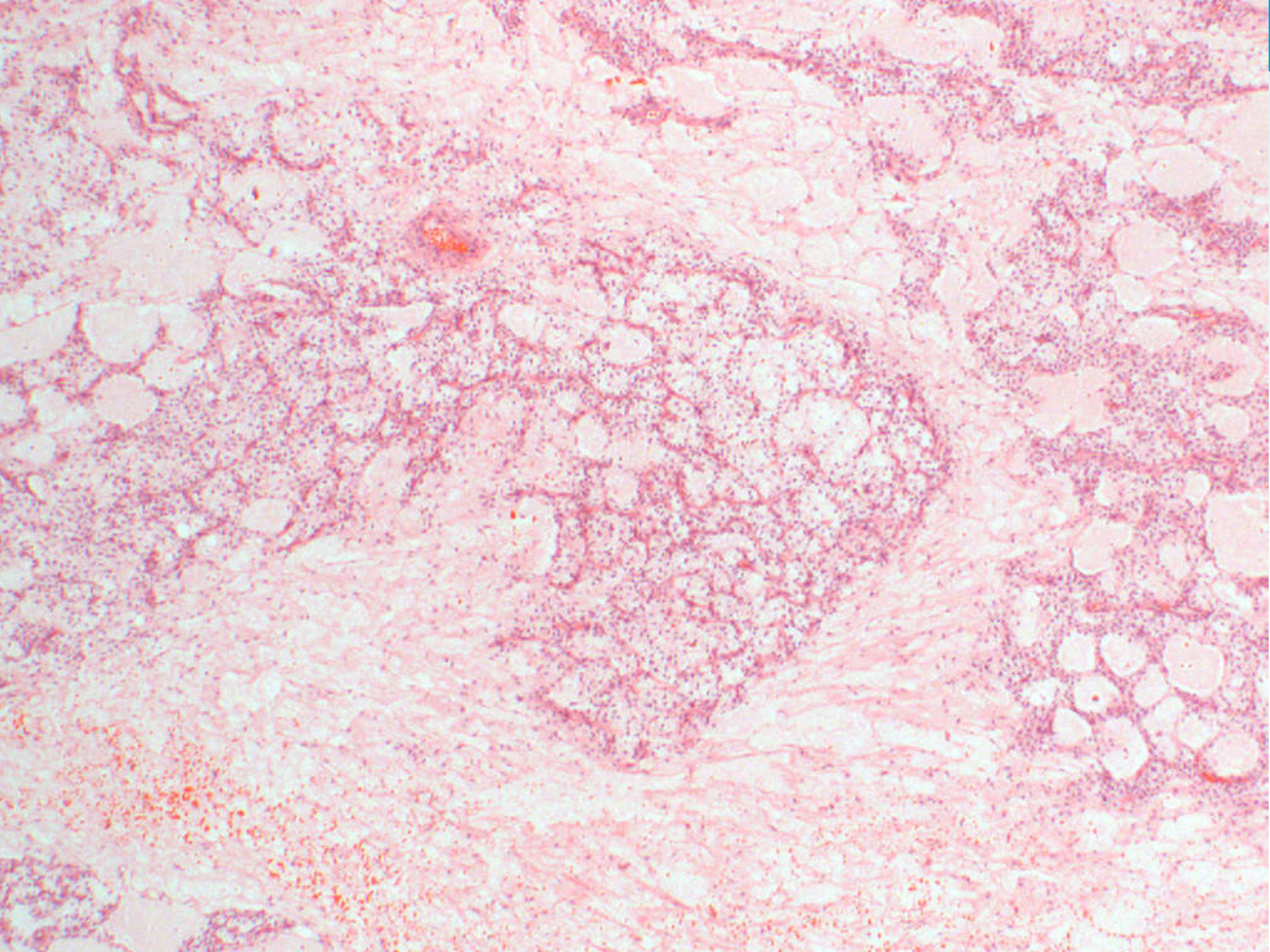
Additional comments:

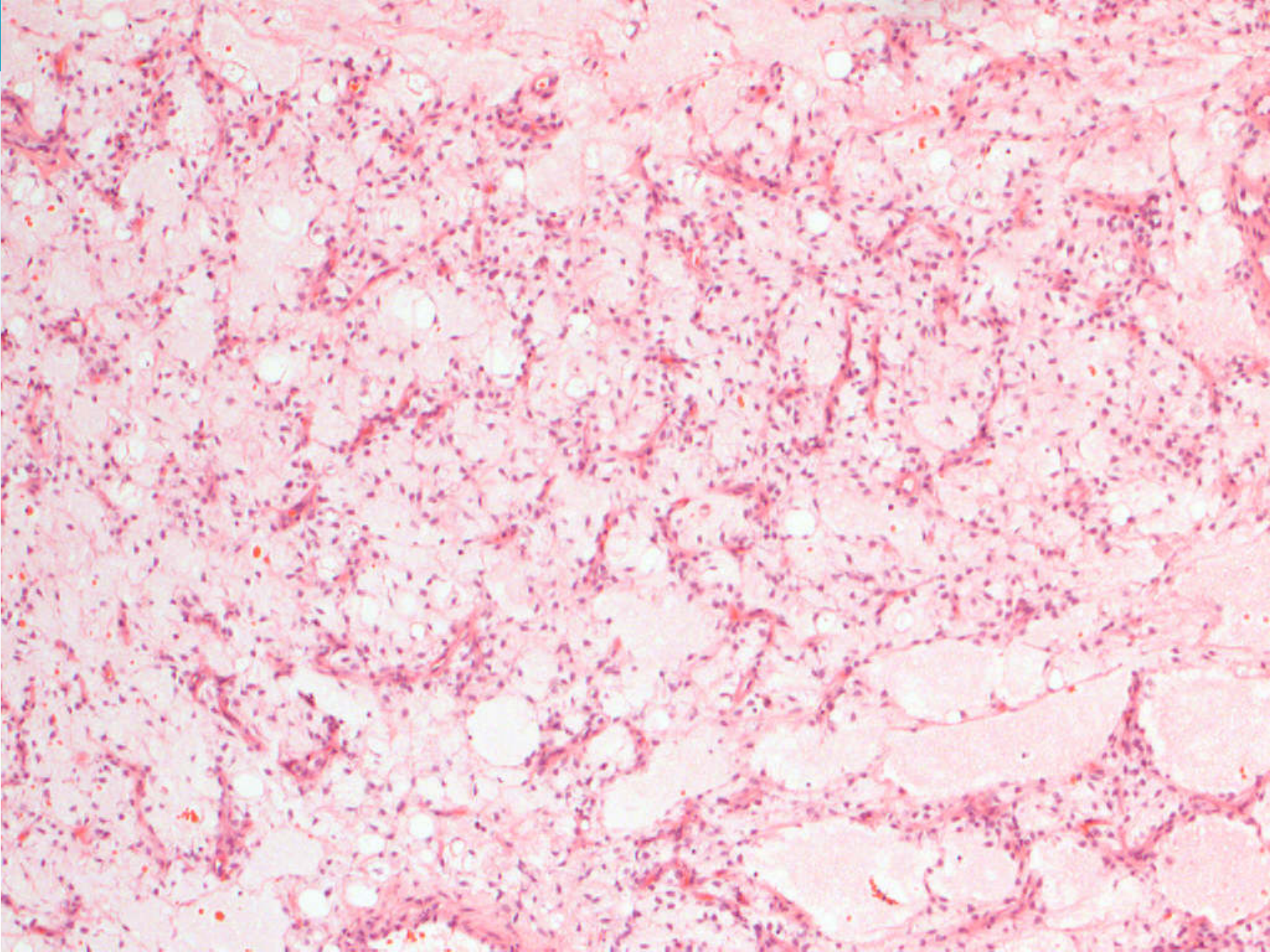
- De-differentiated liposarcoma should be the first diagnosis considered in any high grade retroperitoneal sarcoma in adults
- Look for the well-differentiated counterpart (which may be minimal) and correlate with imaging
- Both tumour components are MDM2 positive
- Dedifferentiated foci most often display features of undifferentiated pleomorphic sarcoma or myxofibrosarcoma, but may also display heterologous elements including
  - Neural and menigothelial differentiation
  - Leiomyosarcoma
  - Osteosarcoma/chondrosarcoma
  - Rhabdomyosarcoma
  - Pleomorphic liposarcoma (homologous lipoblastic differentiation)

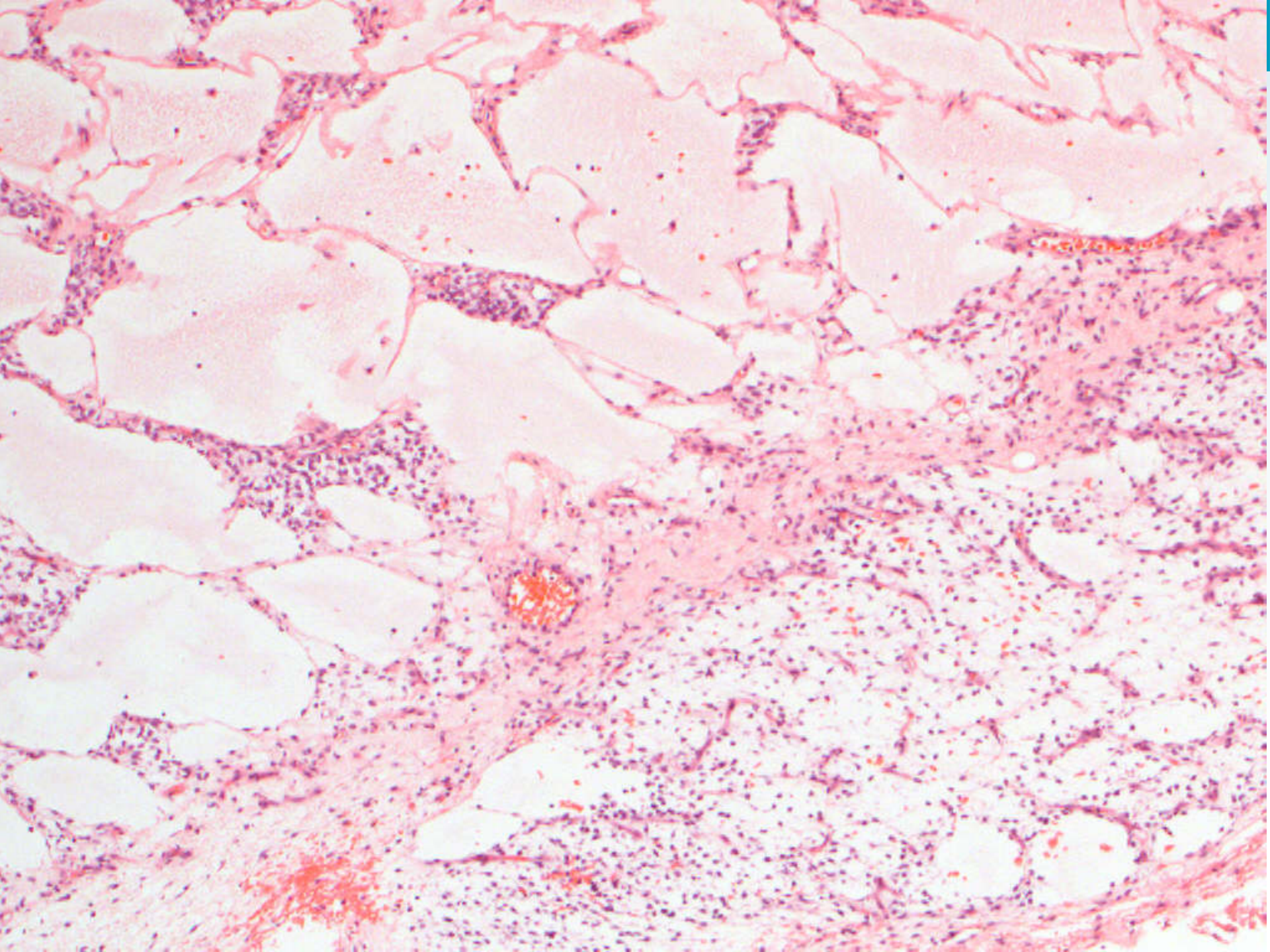
CLINICAL INFORMATION 6

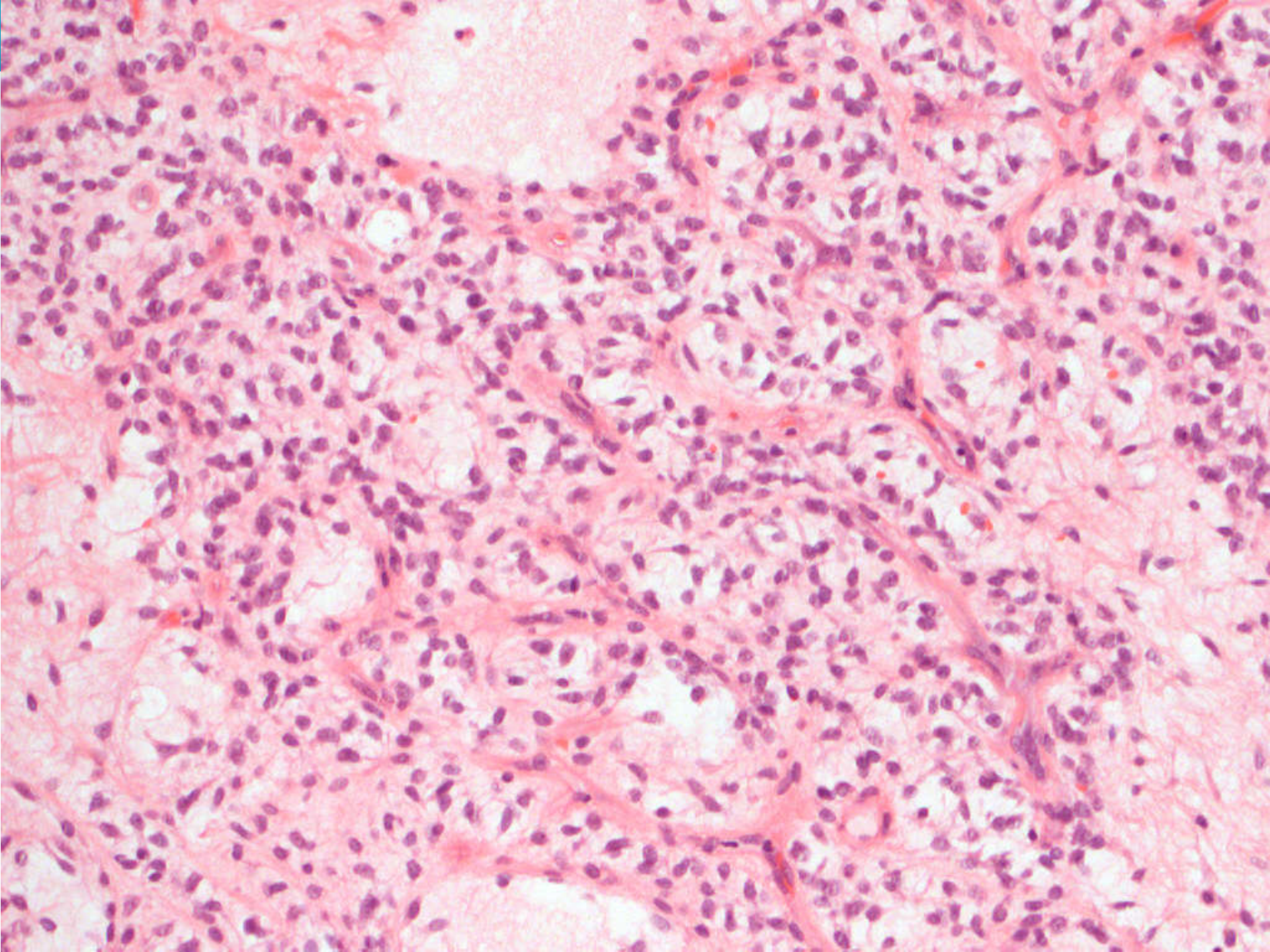
- Female, 46
- 11cm mass in thigh.
- Deep to fascia.











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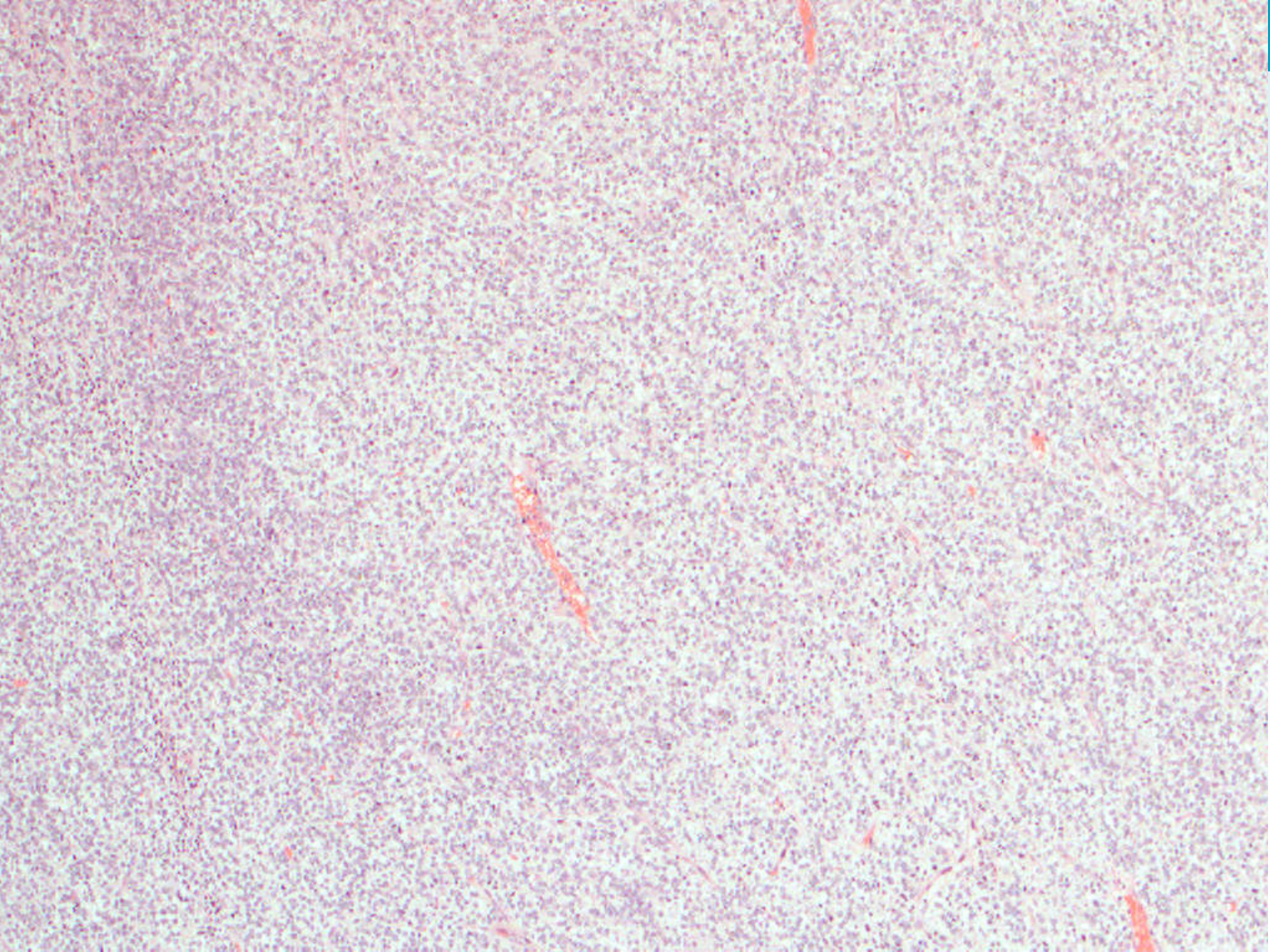
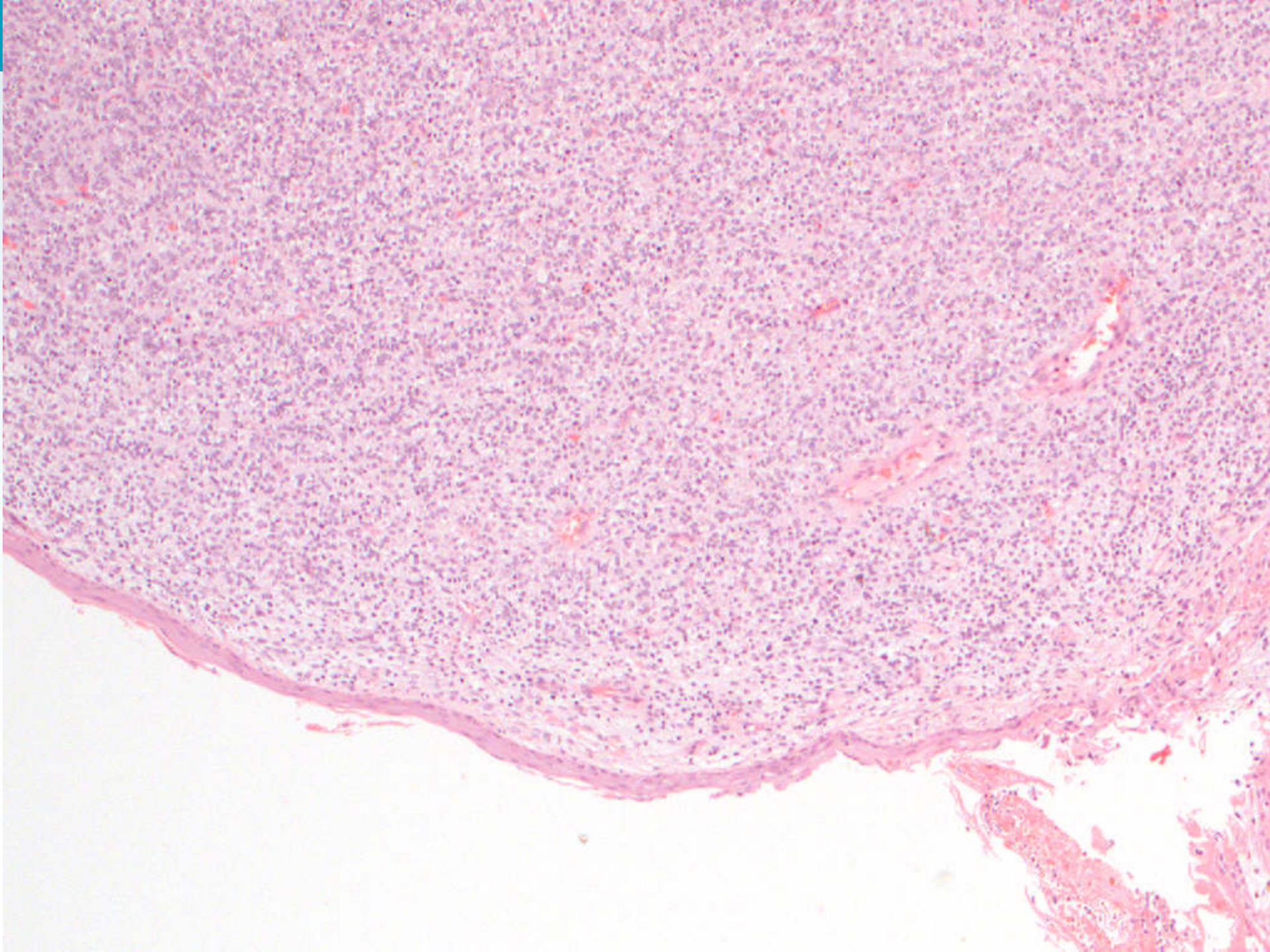
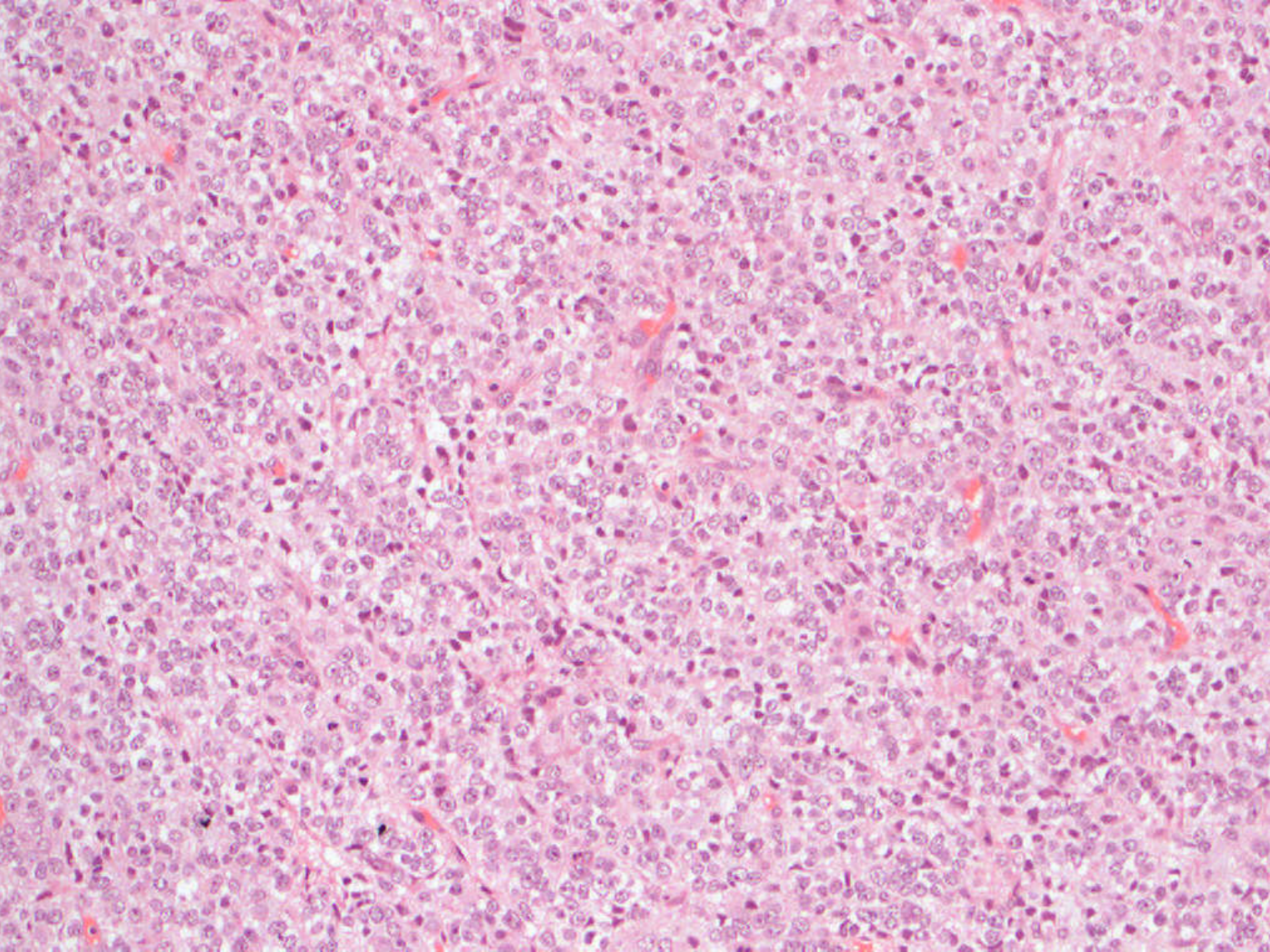
Myxoid liposarcoma

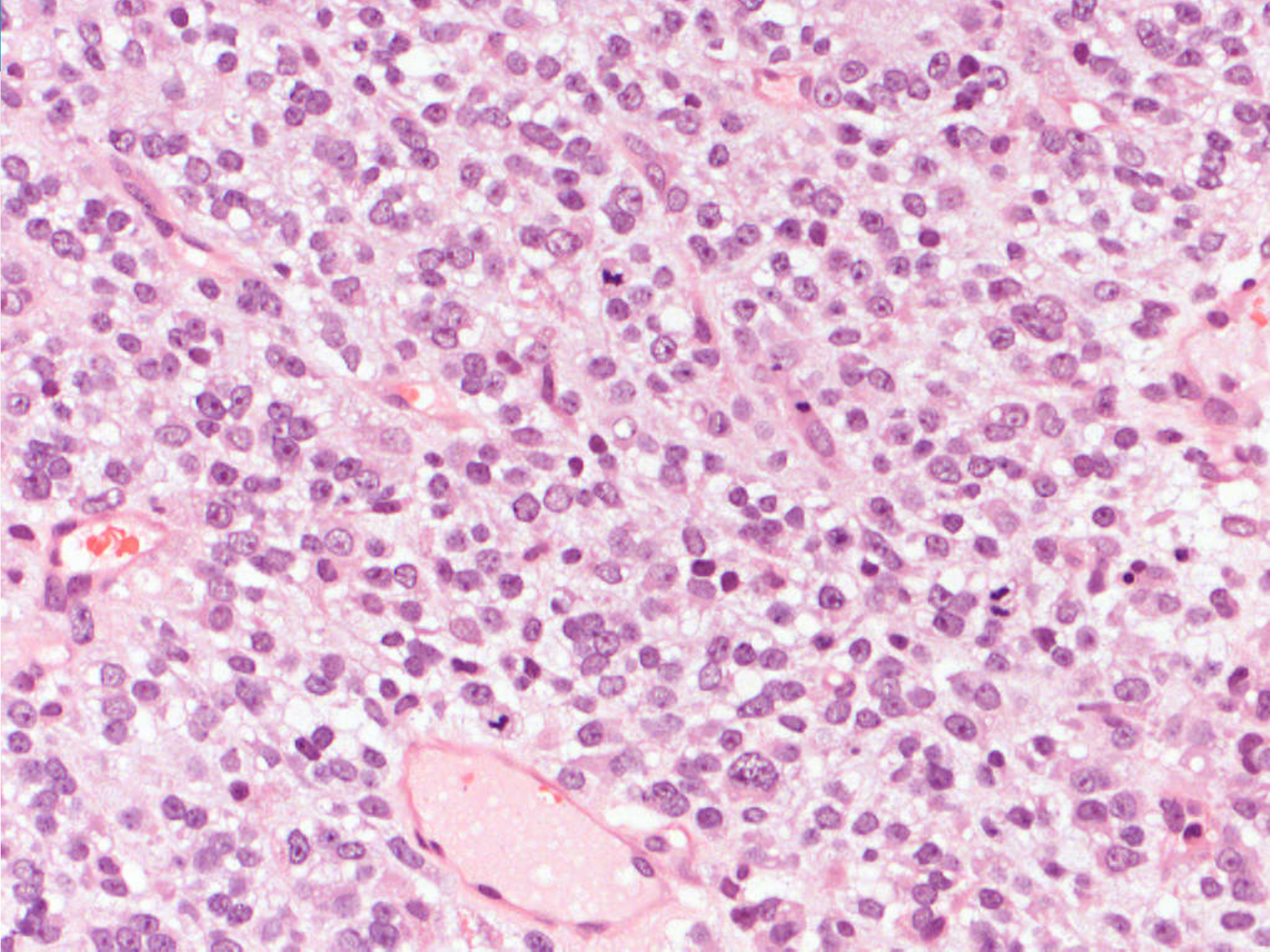
CLINICAL INFORMATION 7

- Female, 46
- Soft tissue tumour in foot.
- Deep to fascia [7cm max.dimension].









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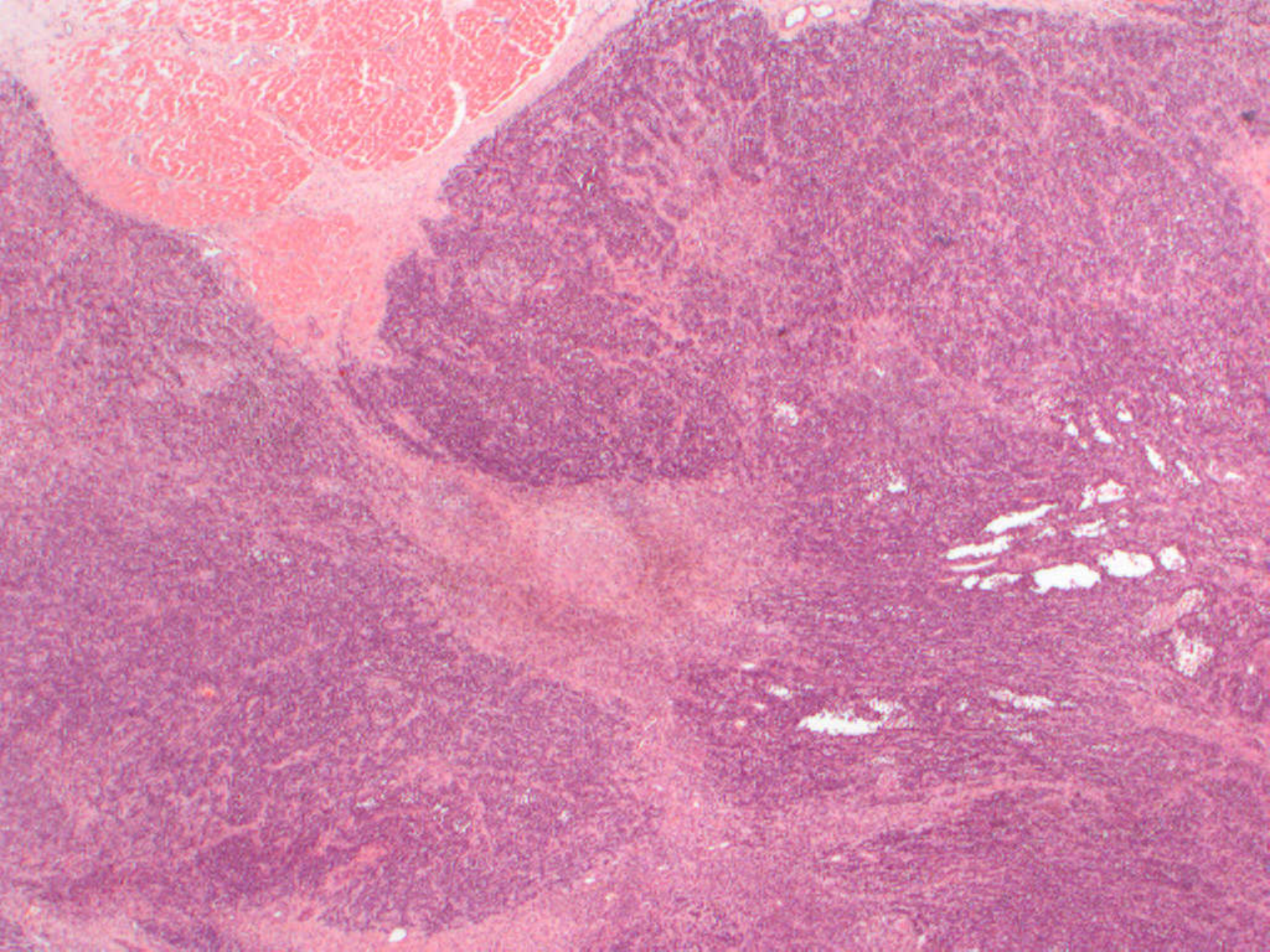
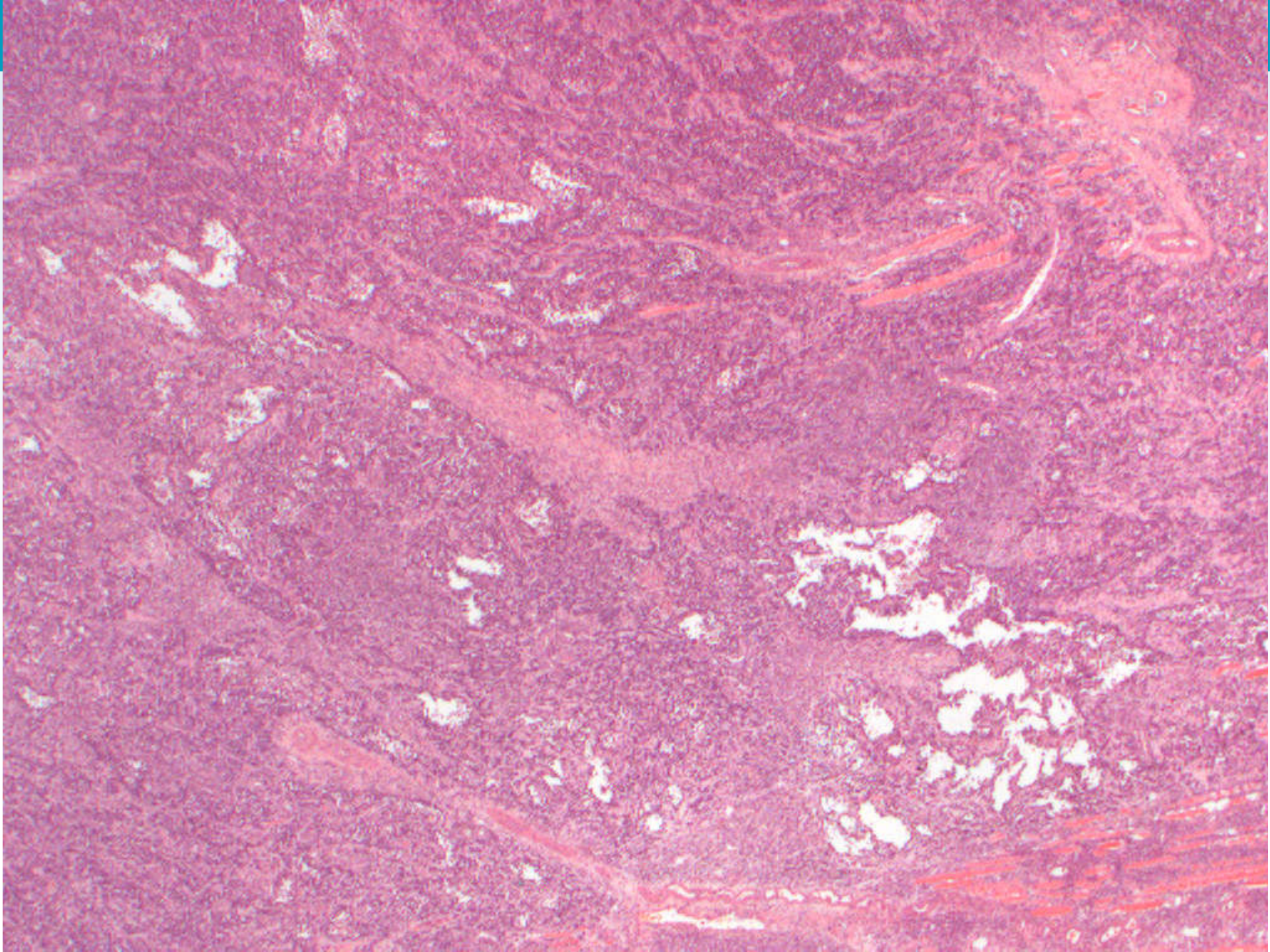
High Grade Myxoid Liposarcoma (previously round cell liposarcoma)

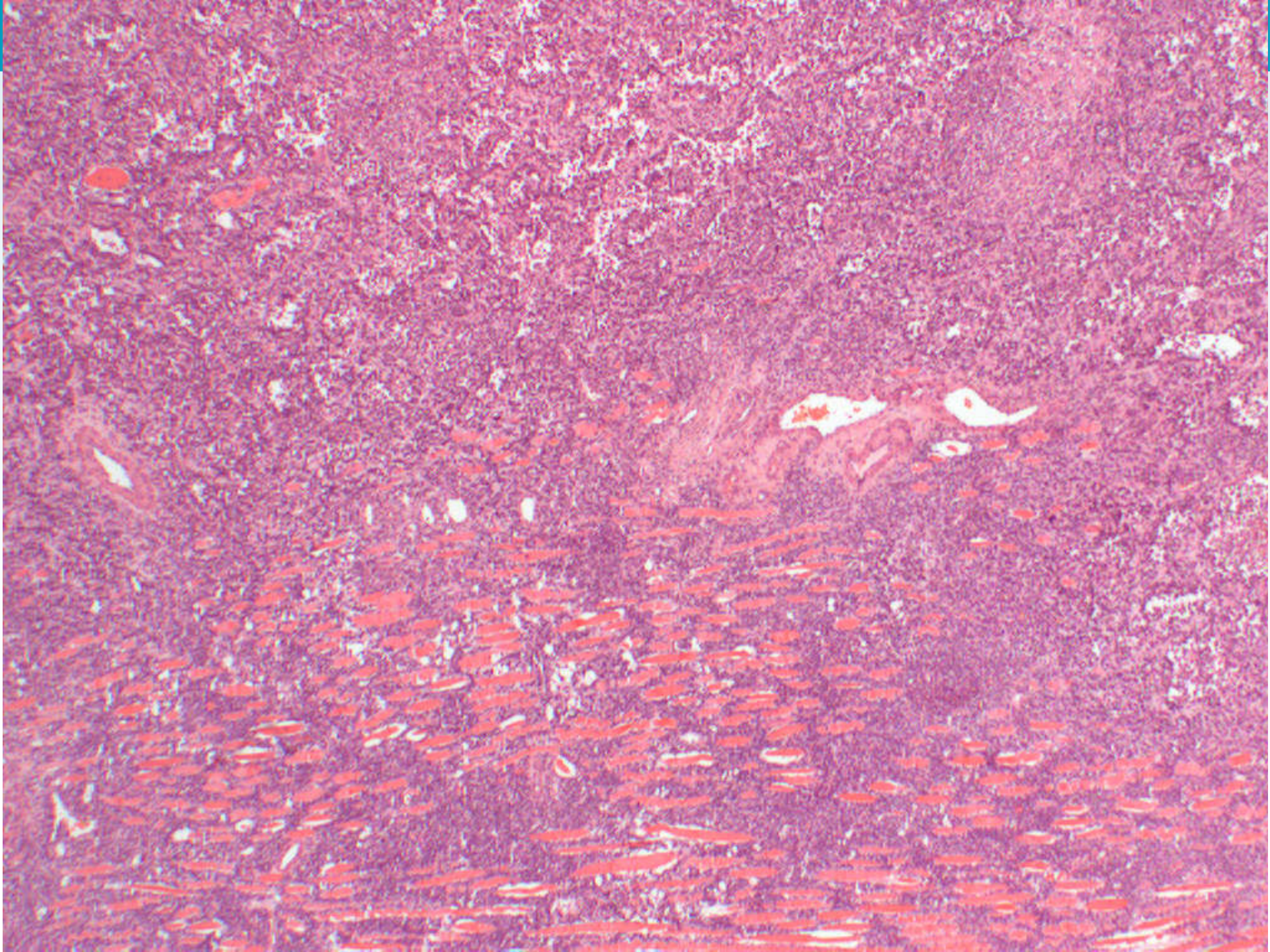
- Historically two separate entities
- Both characterised by the recurrent t(12;16)(q13;p11) translocation that results in *FUS-DDIT3* gene fusion
- Present in >95% of cases
- Remaining cases are *EWSR1-DDIT3* fused

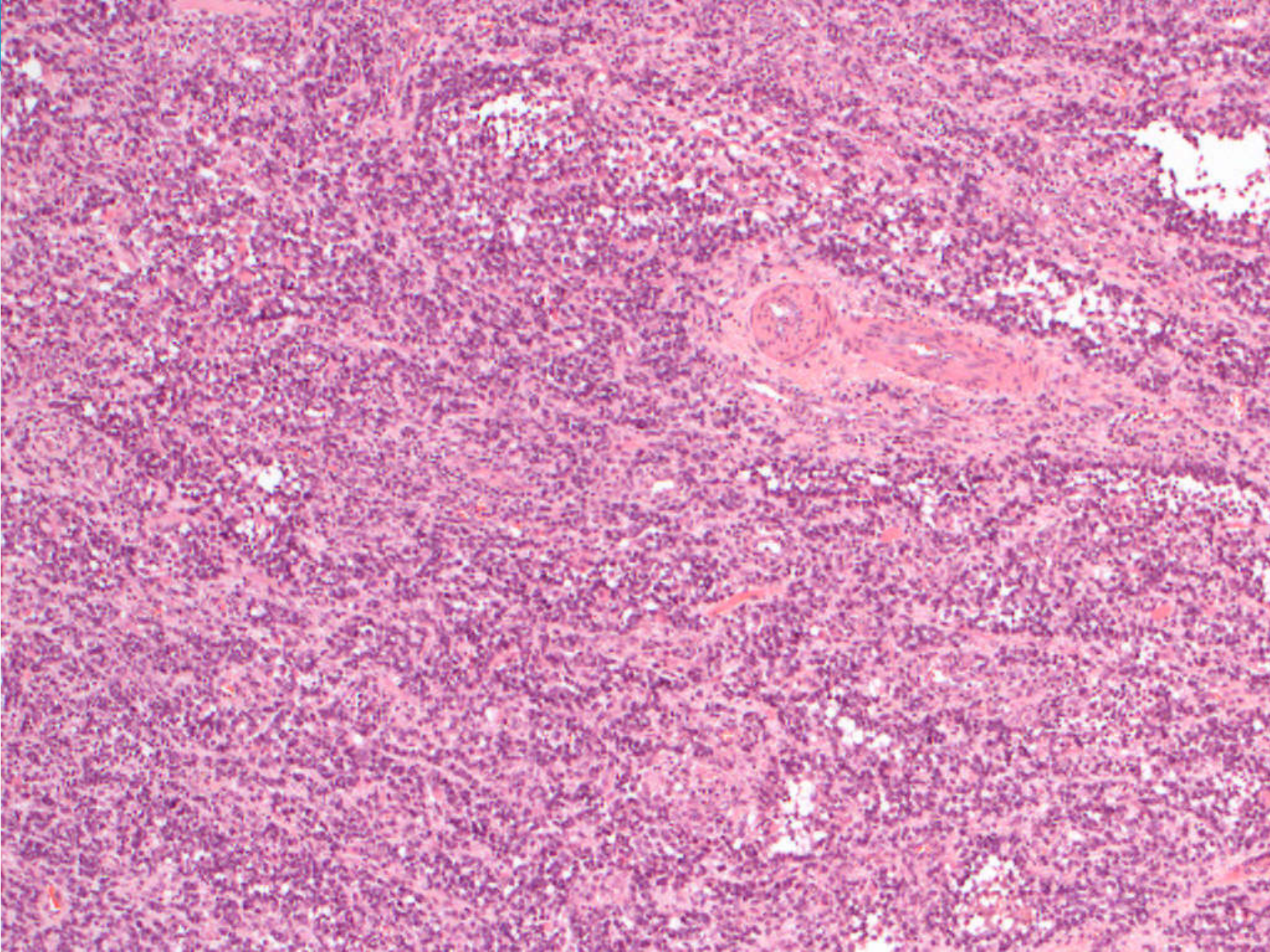
CLINICAL INFORMATION 8

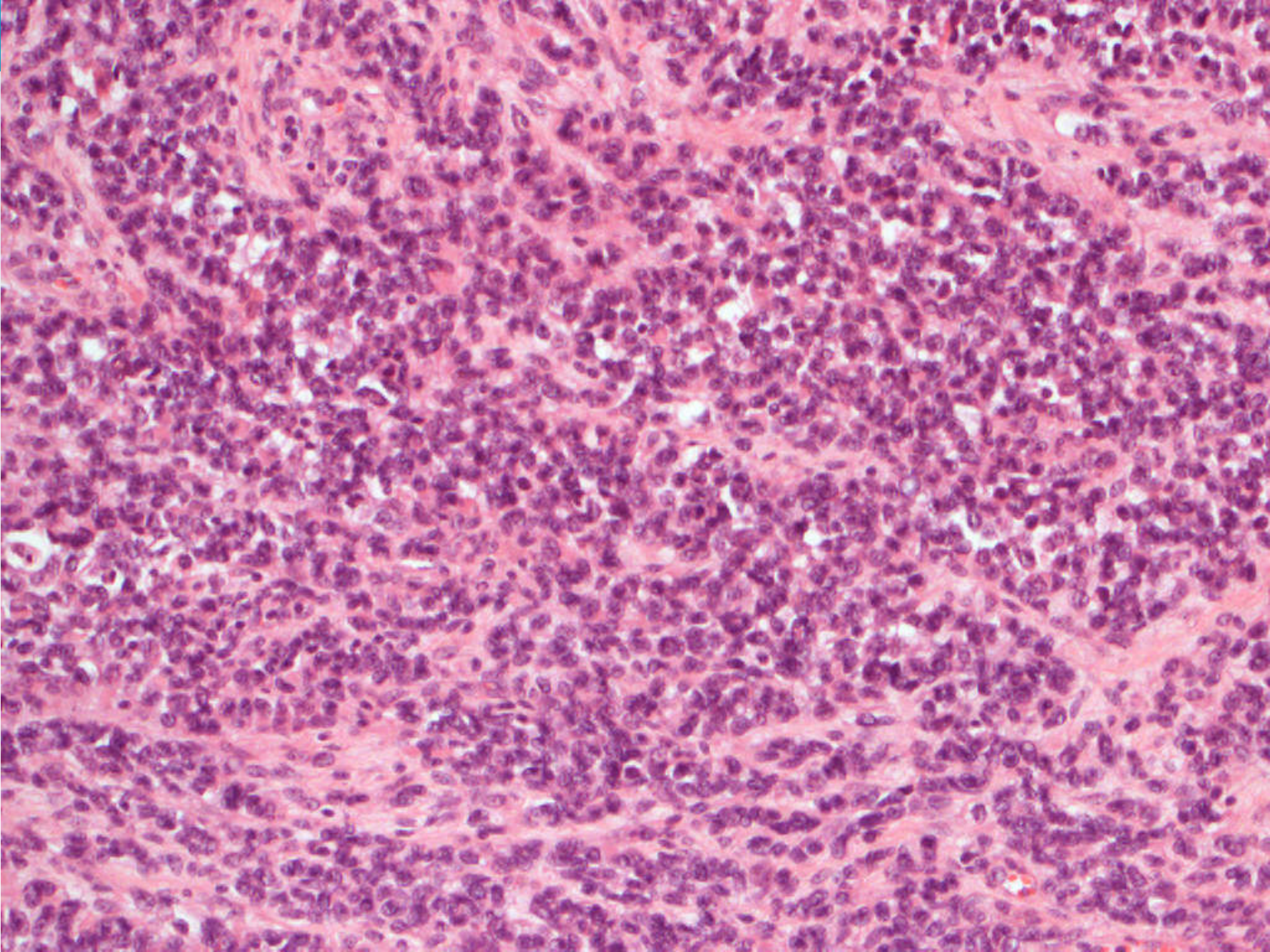
- Female, 8
- Soft tissue mass in volar aspect of forearm, lying deep to fascia but also in subcutaneous tissue.

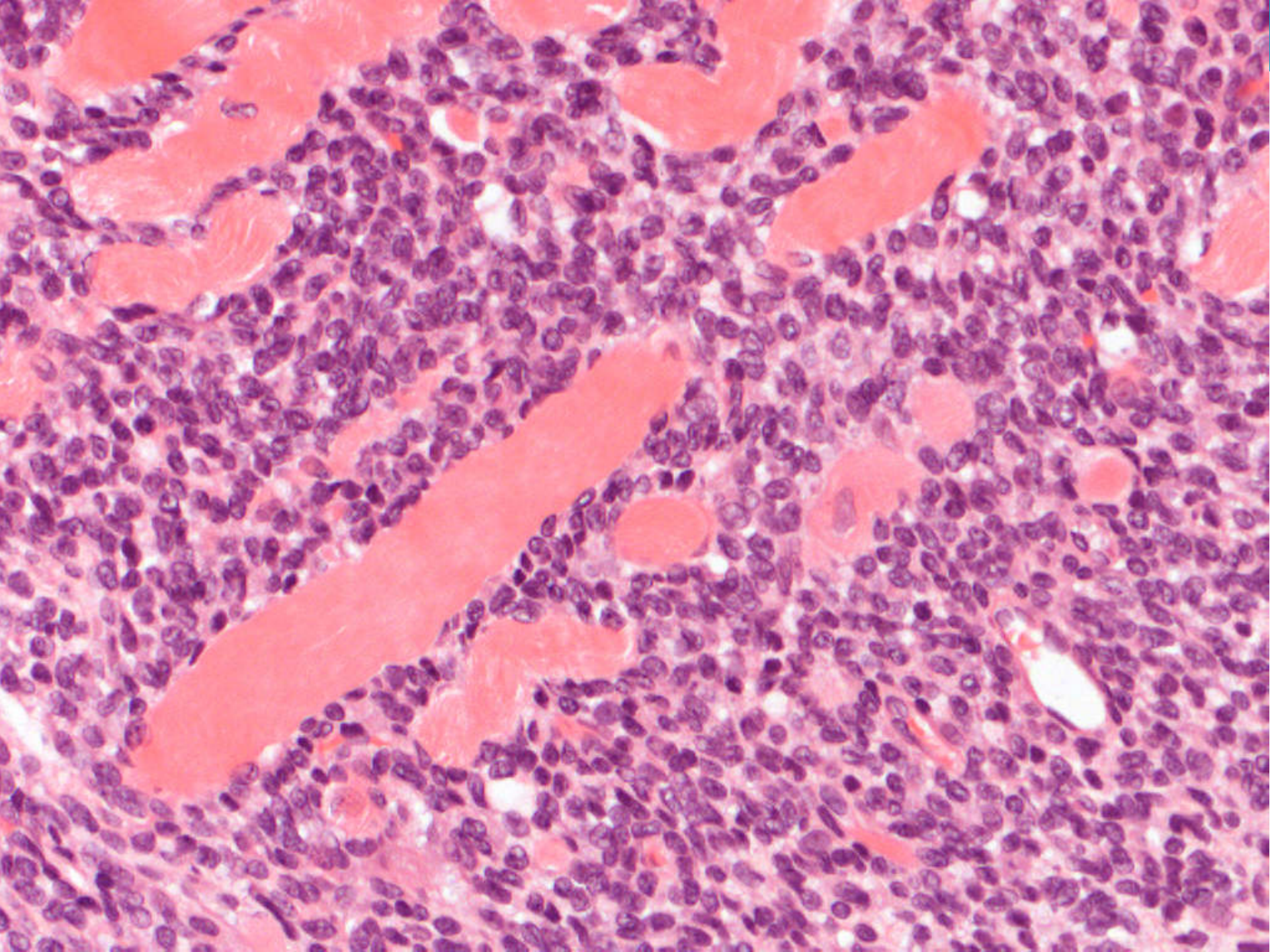


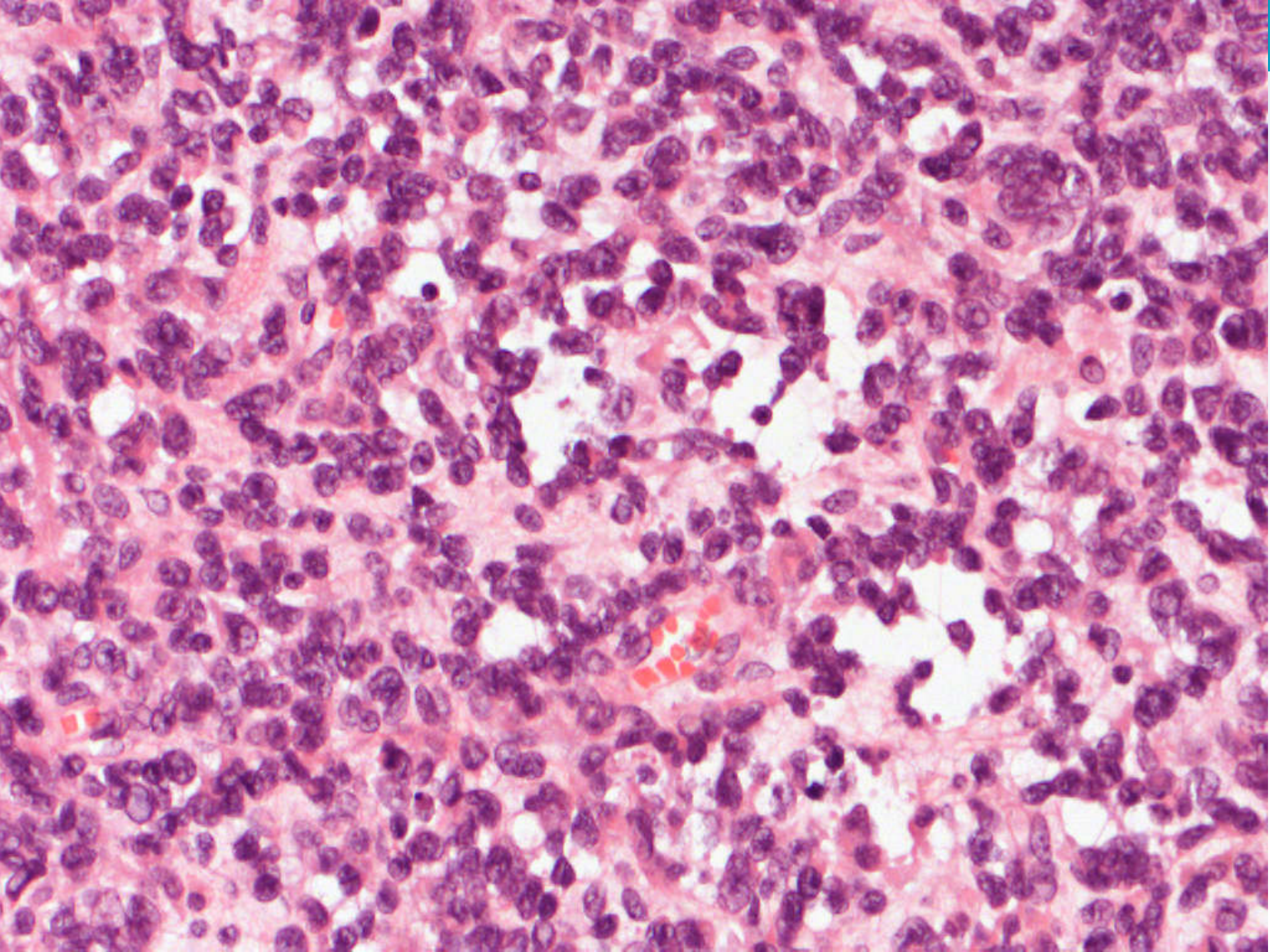












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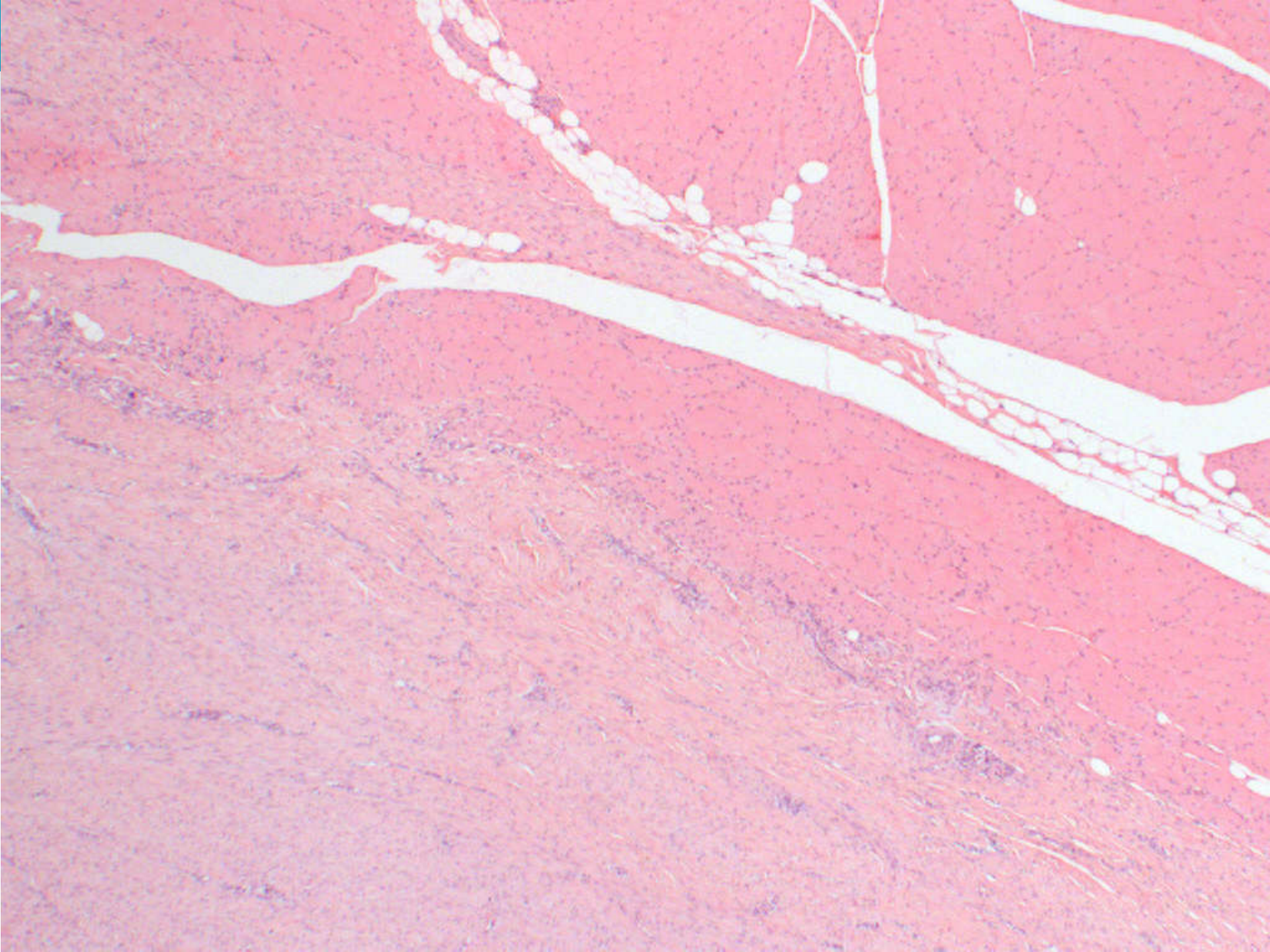
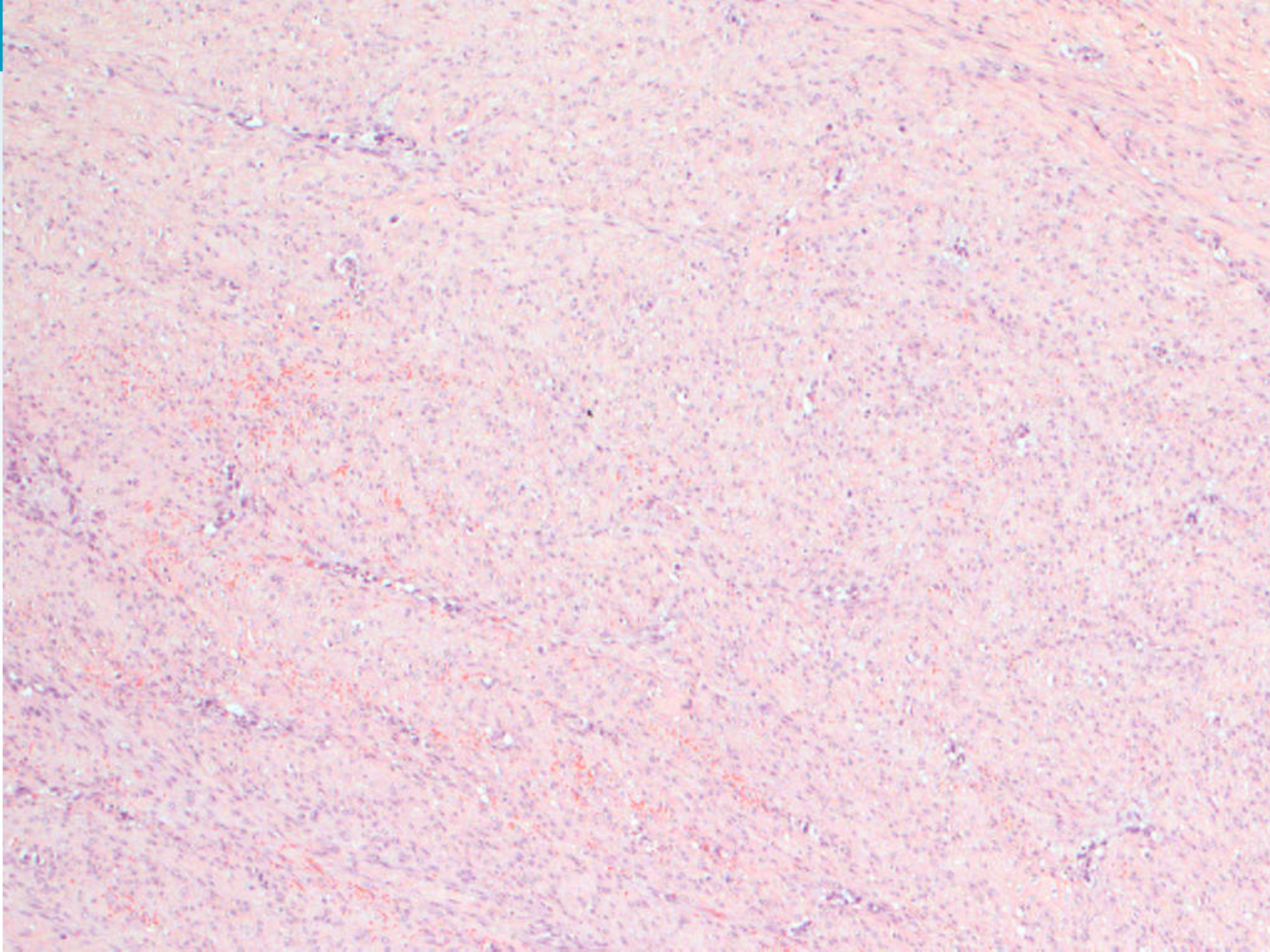
Alveolar rhabdomyosarcoma

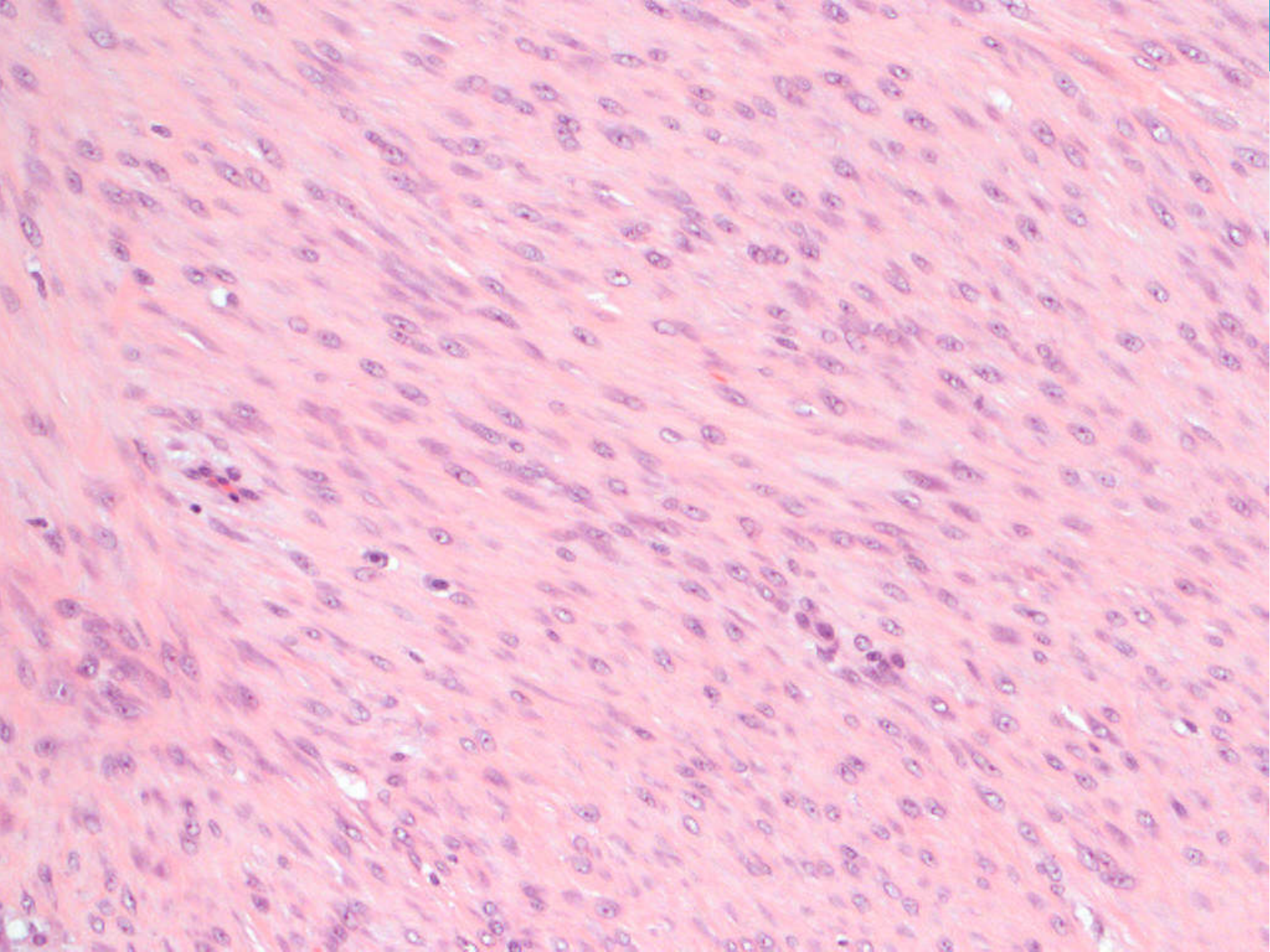
- Recurrent, consistent translocations with either *PAX3-FOX01* or *PAX7-FOX01* fusion.
- "Alveolar" pattern may be subtle or absent
- Diffuse and strong nuclear labelling for myogenin correlates with decreased survival
- Positive labelling for keratins and neuroendocrine markers can occur and cause confusion

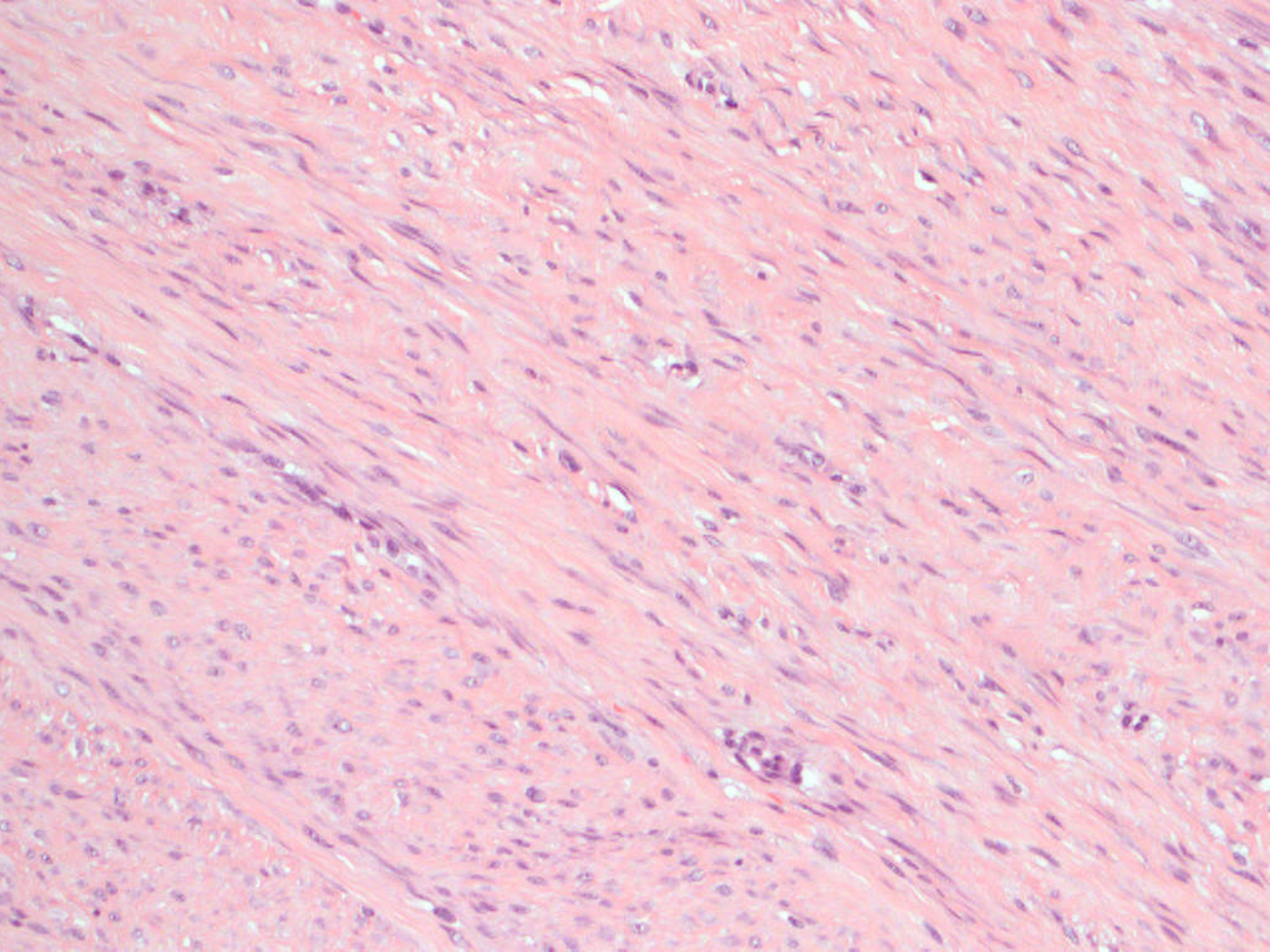
CLINICAL INFORMATION 9

- Female, 21
- Open biopsy from right buttock.
- 17cm mass.









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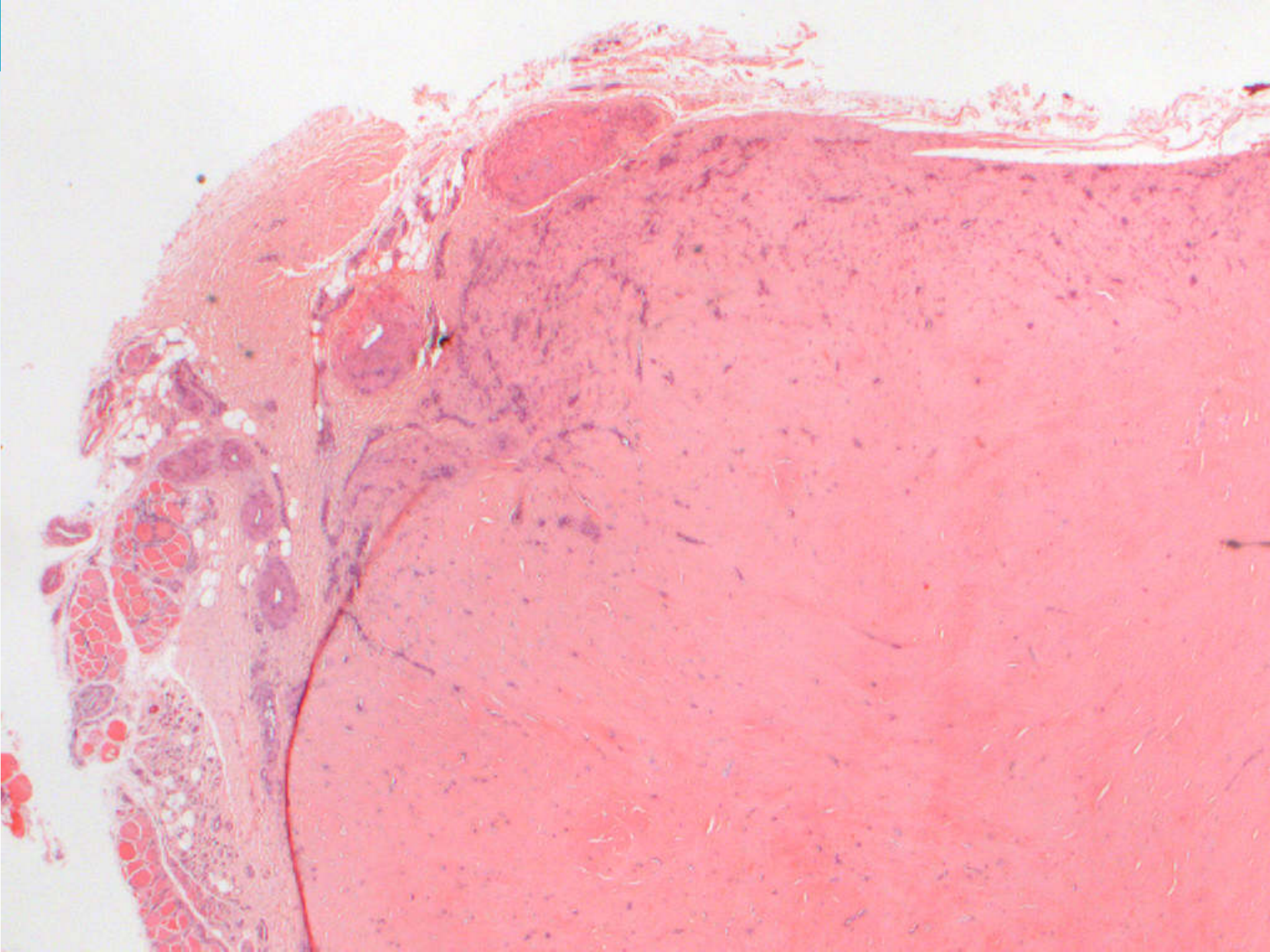
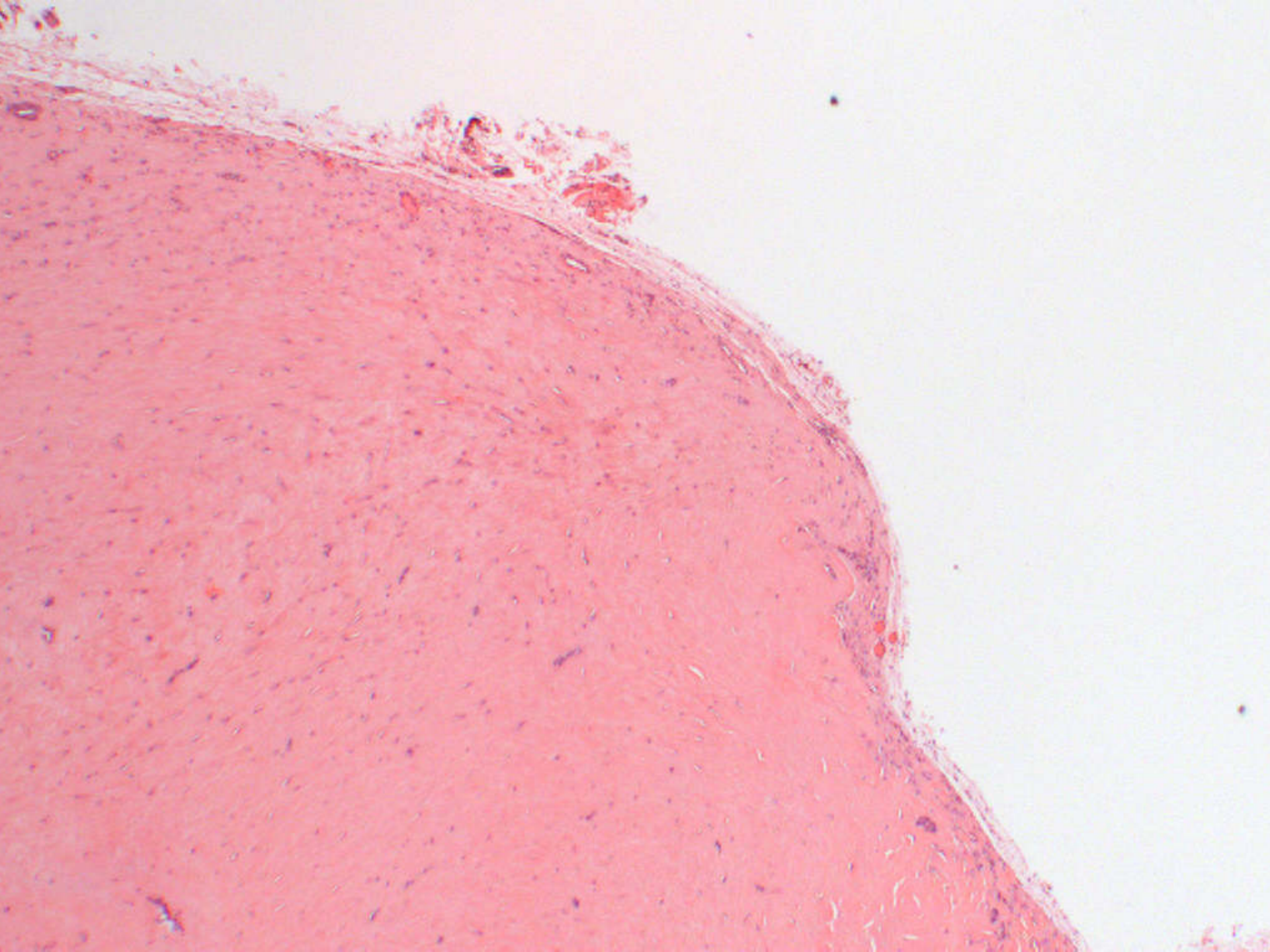
Desmoid-type fibromatosis

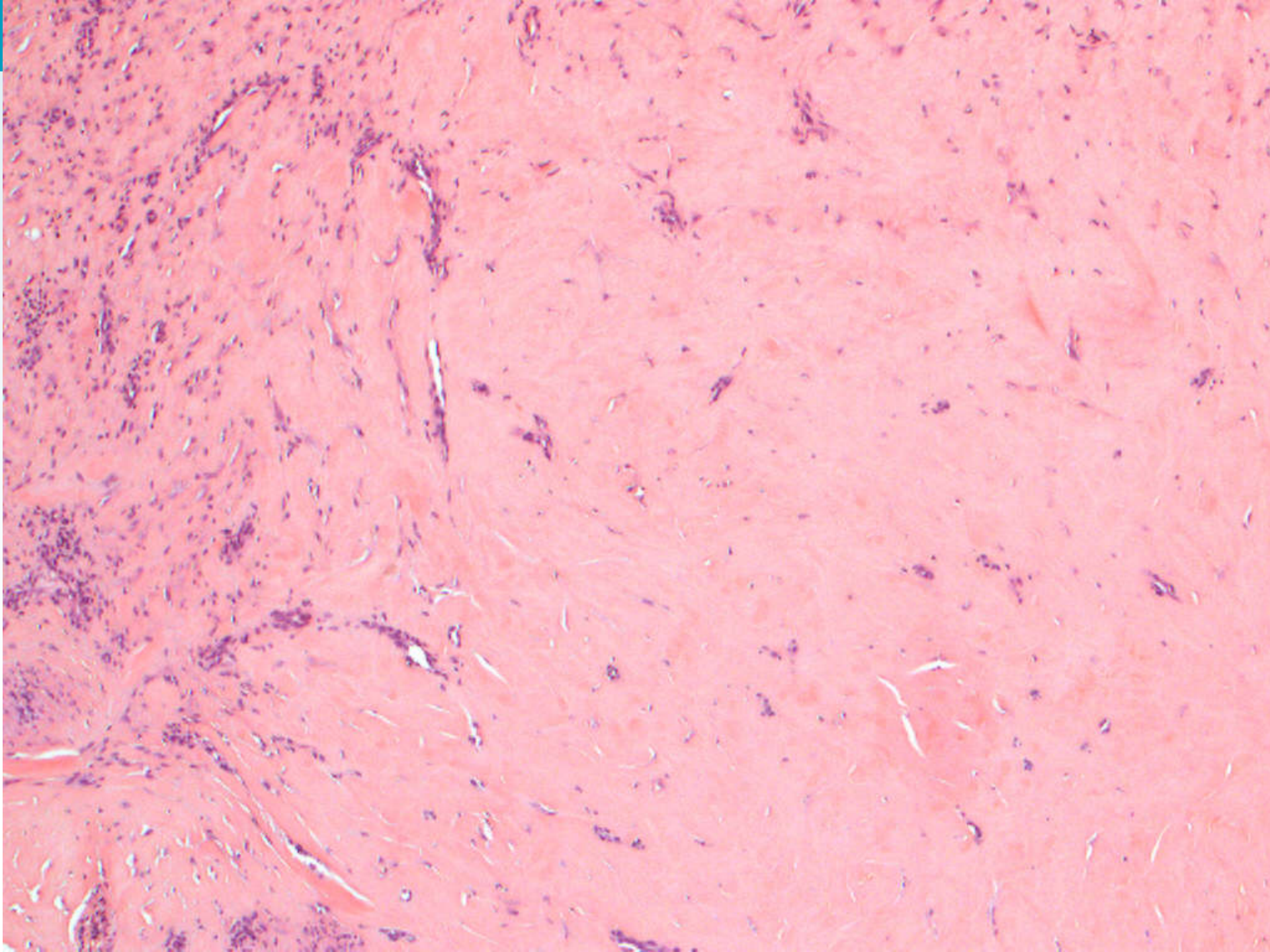
- Poorly circumscribed lesions of bland, spindled to stellate cells with infiltrative margins
- 70-75% show nuclear positivity for beta-catenin
- Tumours arising in the setting of Gardner-type FAP harbour inactivating mutations in *APC* gene
- Up to 85% of sporadic lesions harbour mutations of the *CTNNB1* gene

CLINICAL INFORMATION 10

- Male, 65
- Excision of lump on dorsum of right foot [30x25x12mm].







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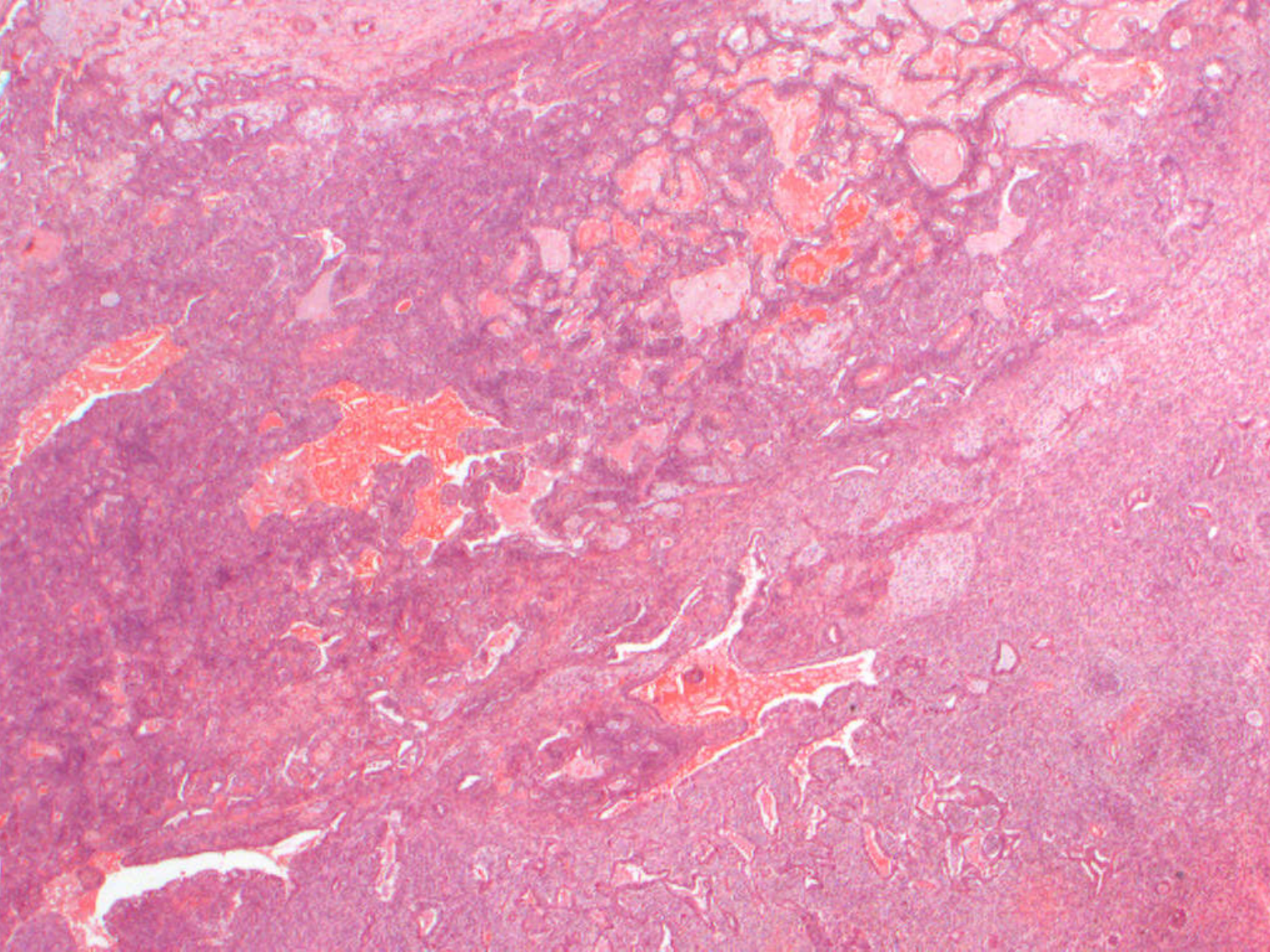
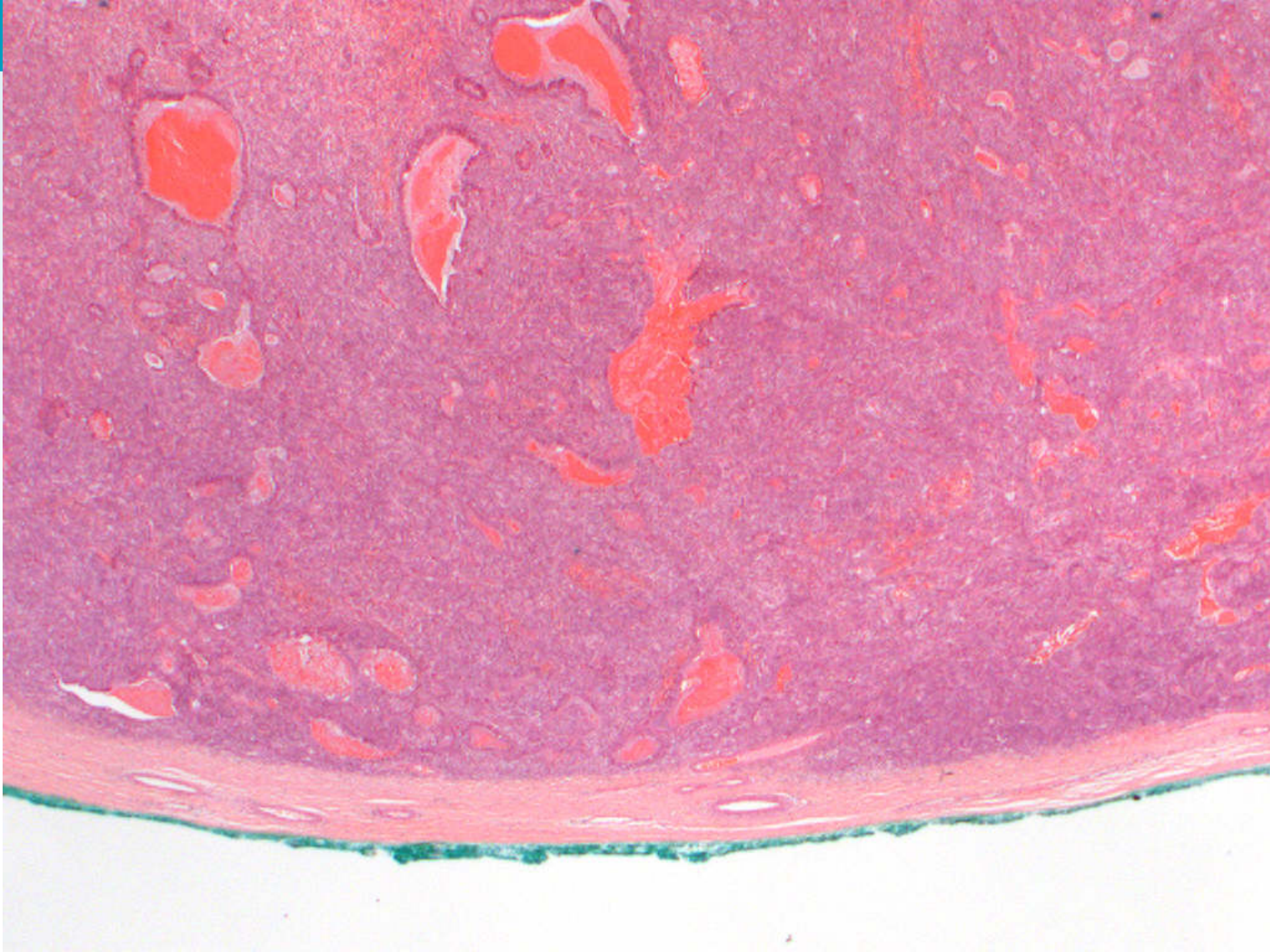
Fibroma of tendon sheath

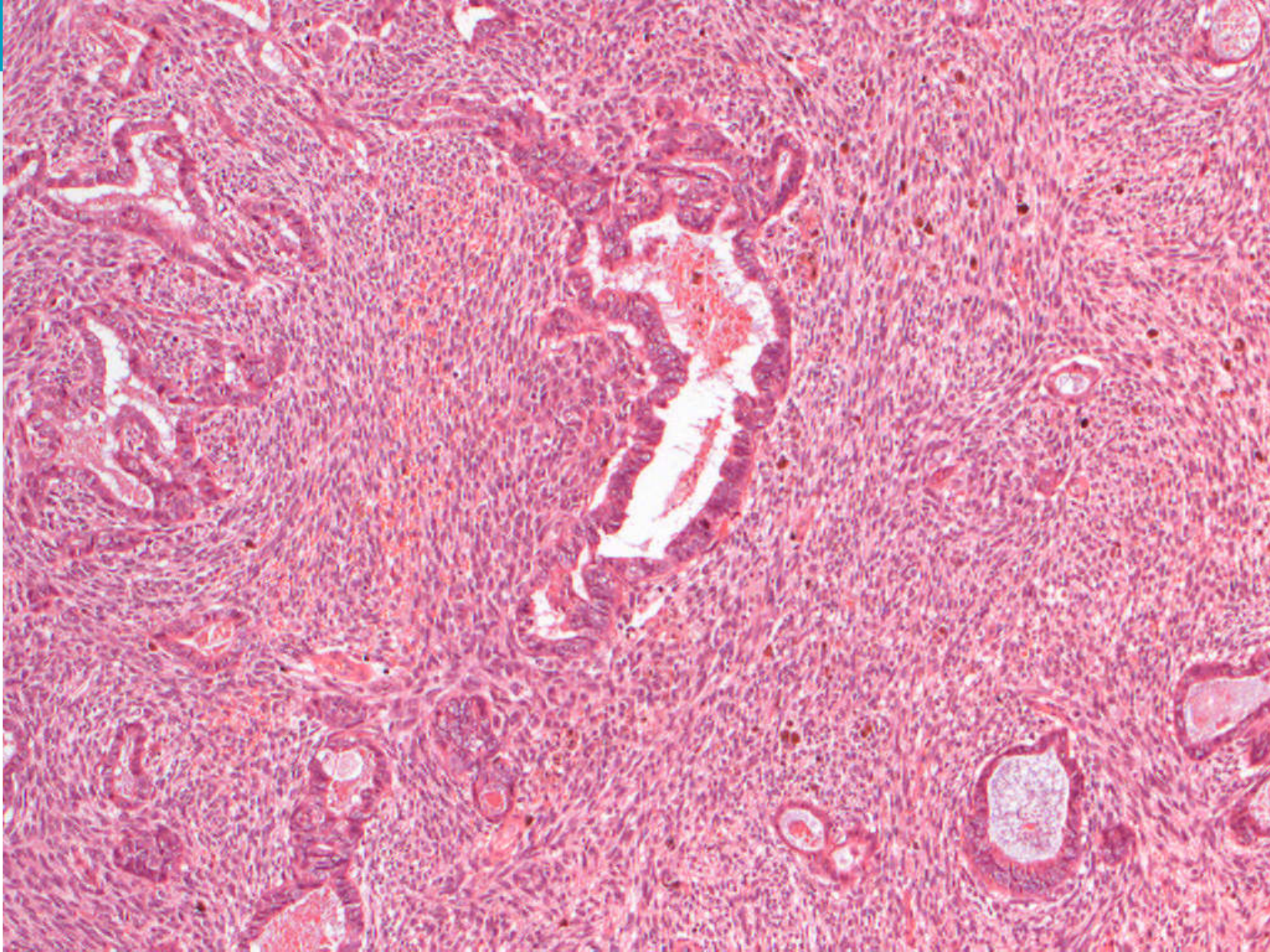
- Benign fibroblastic nodular neoplasm, usually attached to a tendon
- Usually paucicellular, small (<3cm) and contains bland fibroblastic/myofibroblastic cells in a dense collagenous stroma
- Elongated, thin-walled “slit-like” vessels
- Degenerative myxoid change, chondroid or osseous metaplasia occur rarely

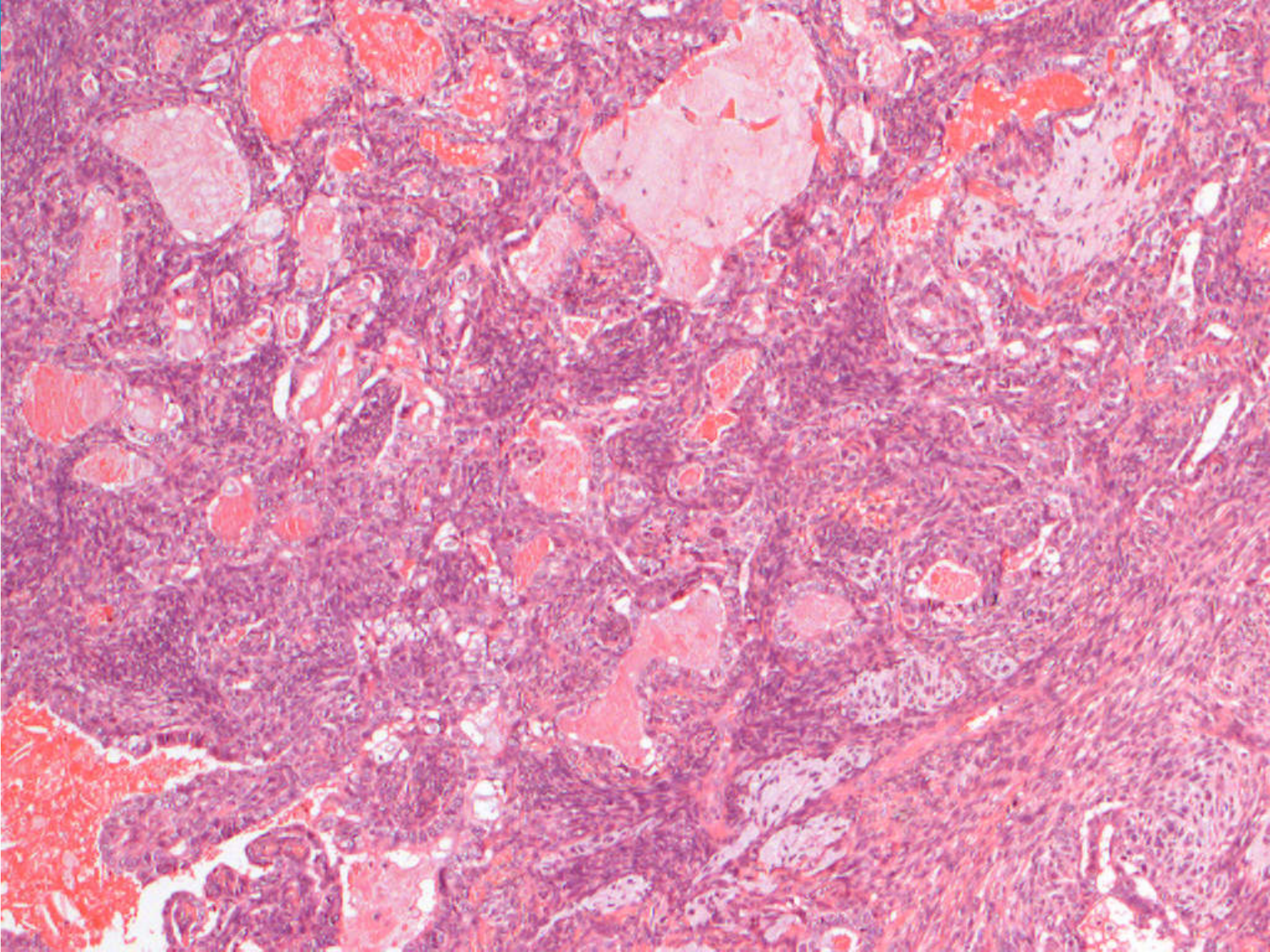
CLINICAL INFORMATION 11

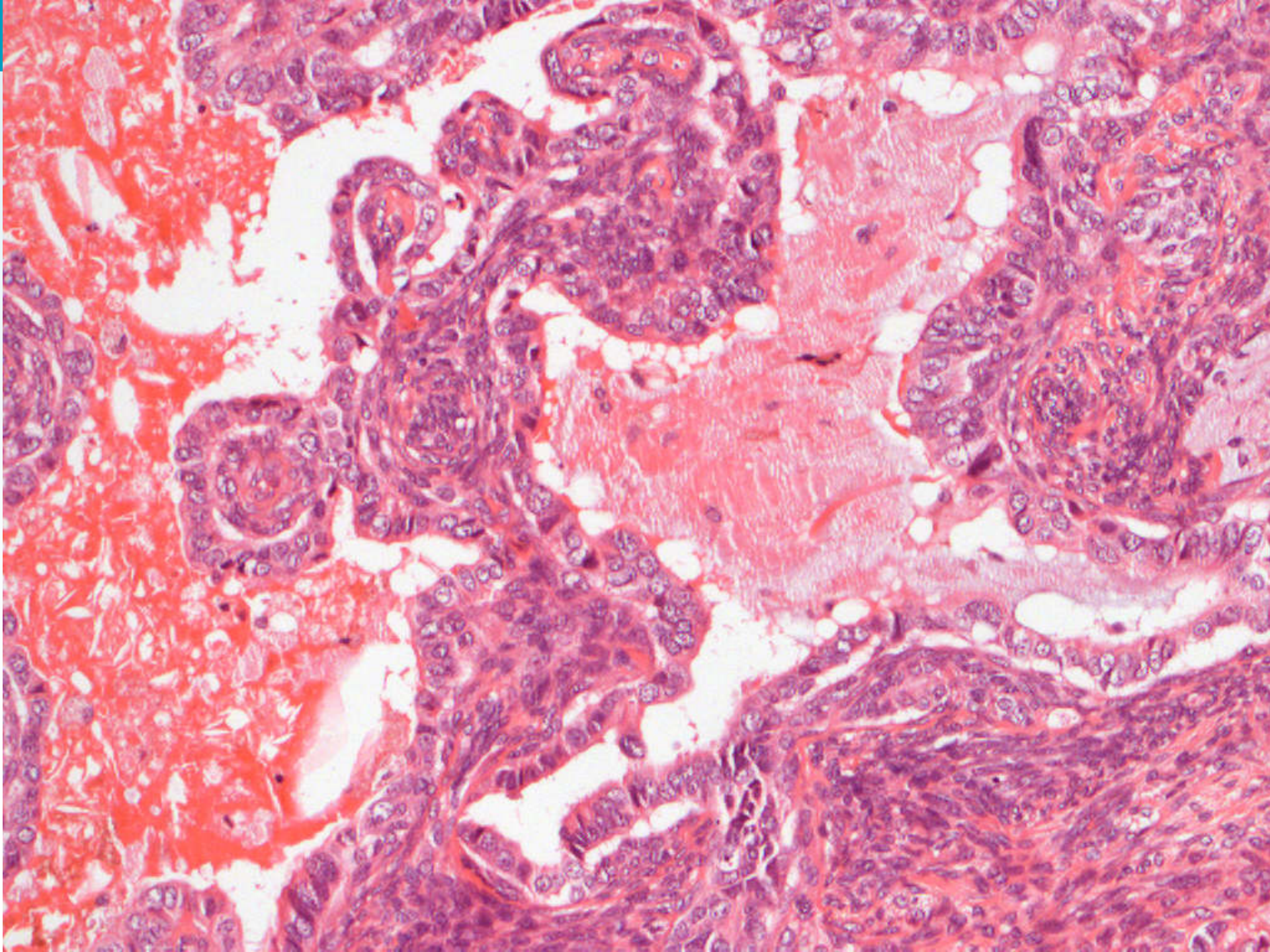
- Male, 41
- 4cm nodule present on dorsum of foot for five years.

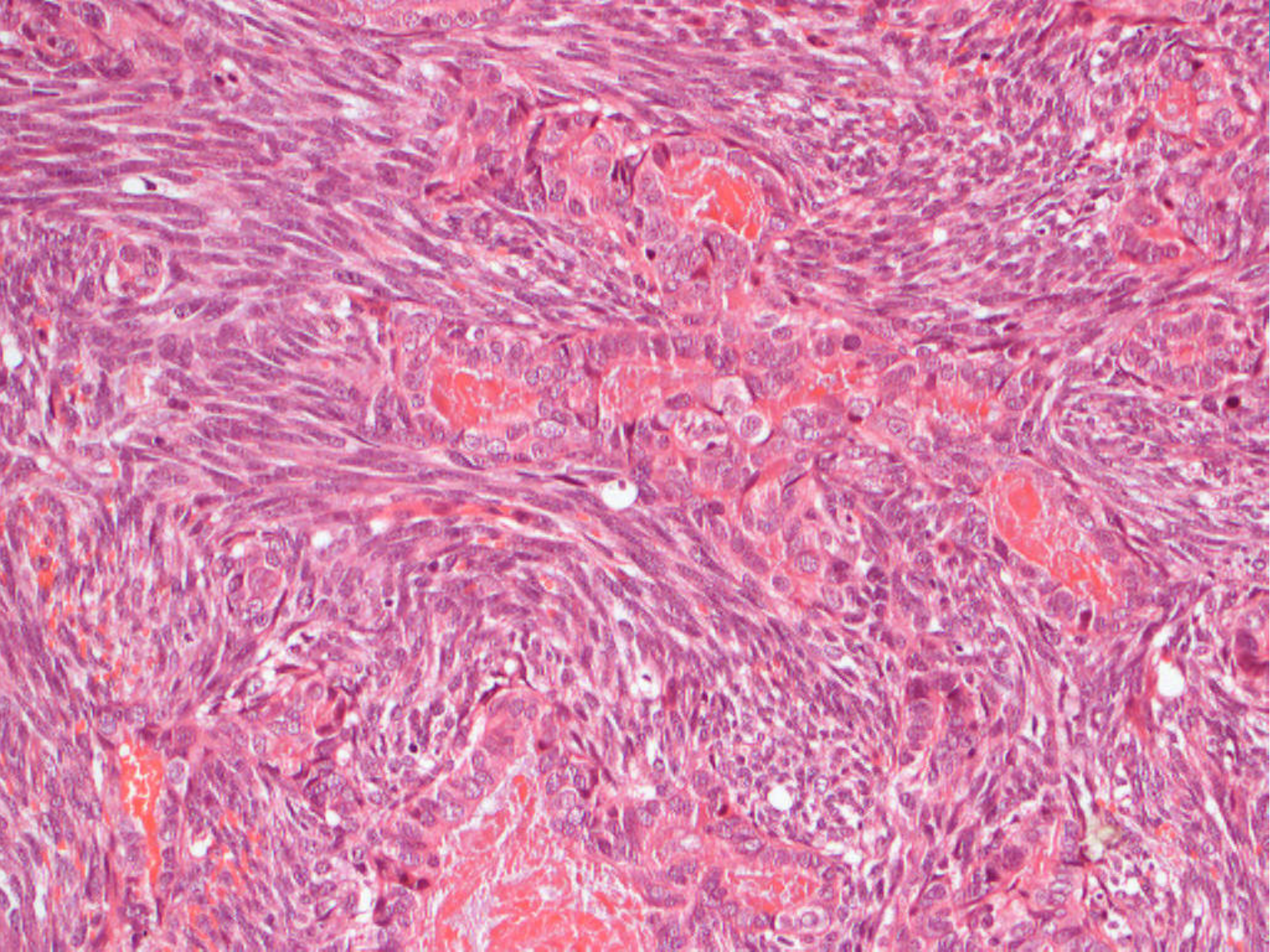


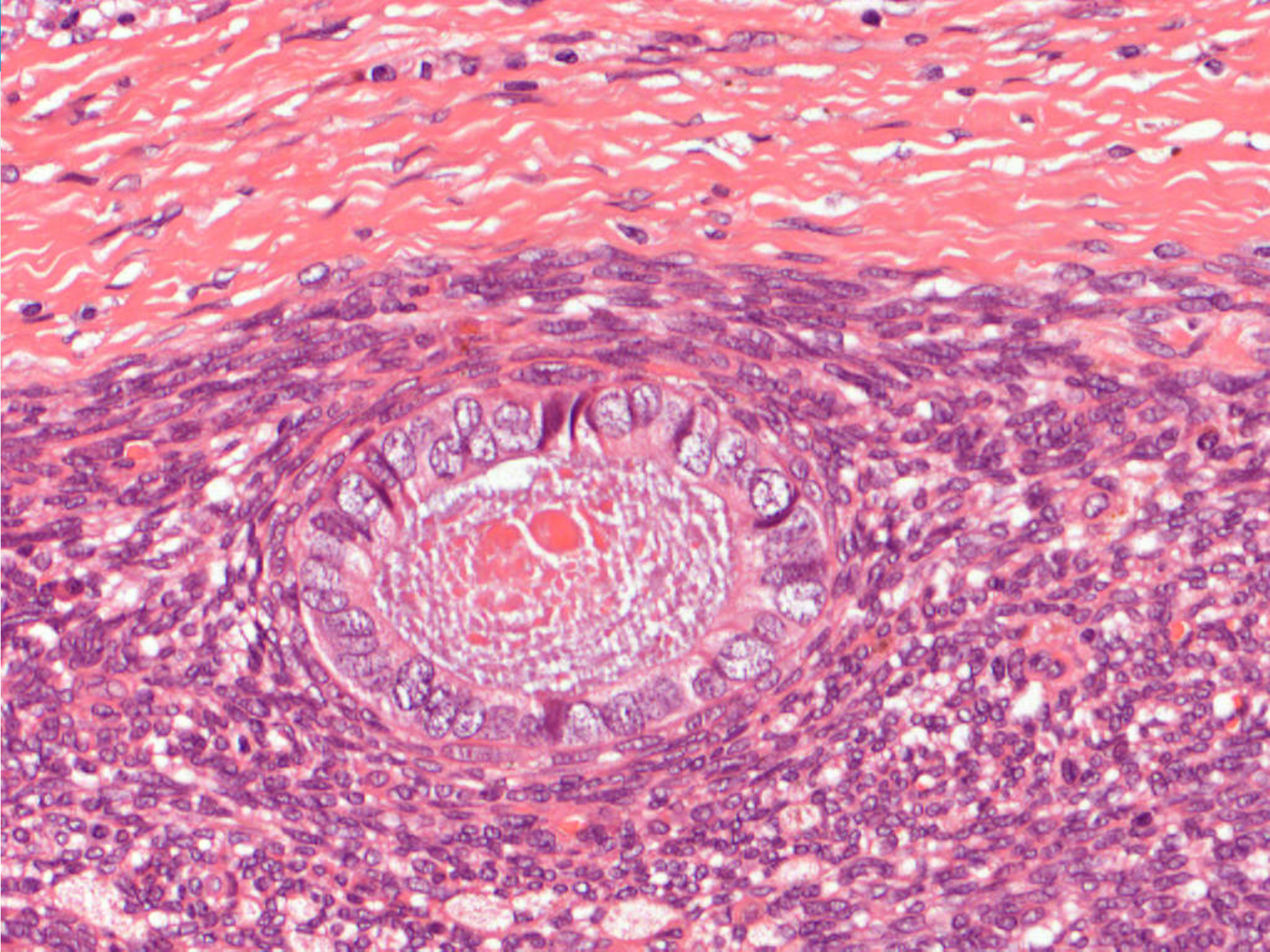












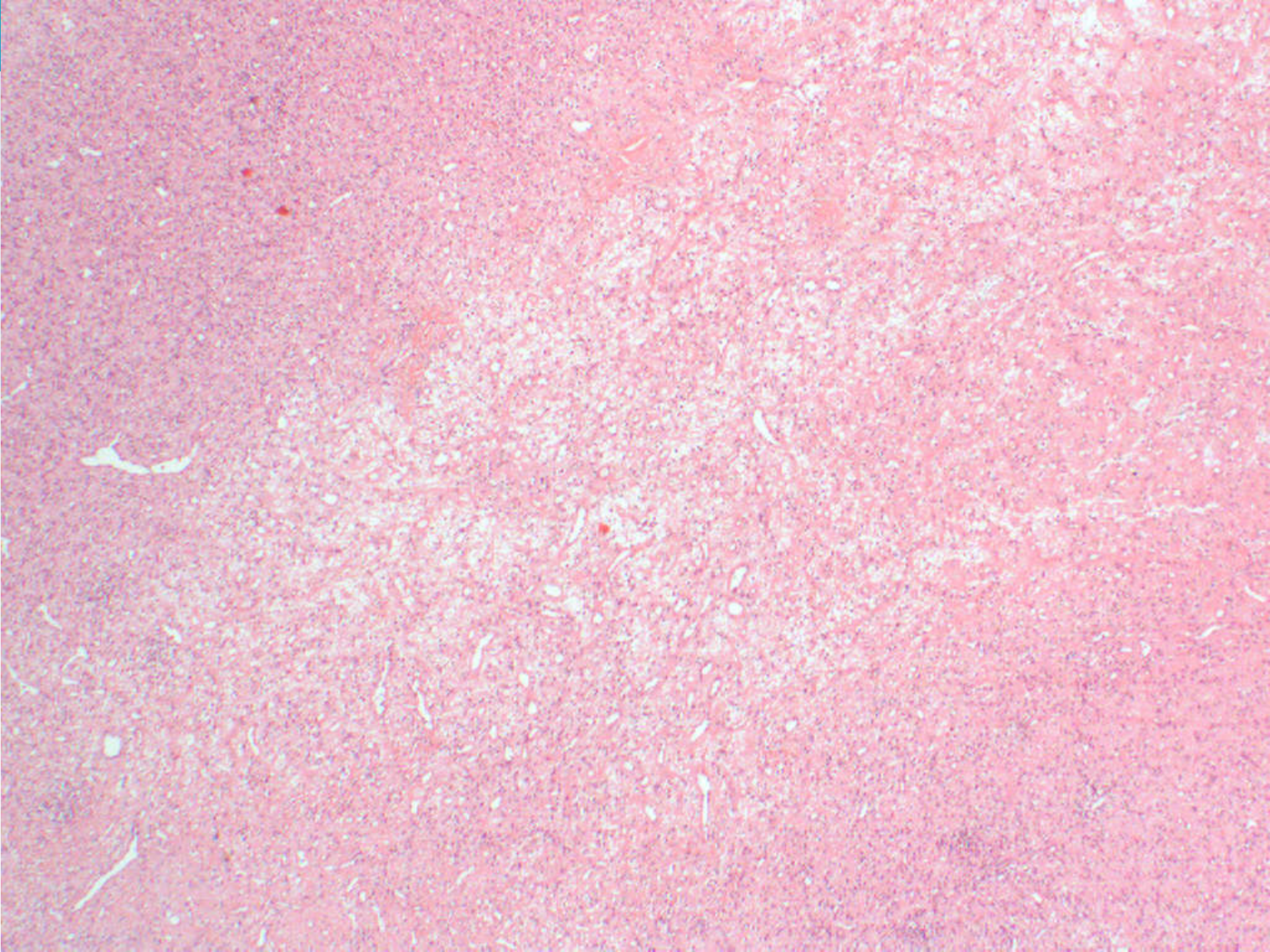
DX: Soft Tissue 11 Adv Path Course

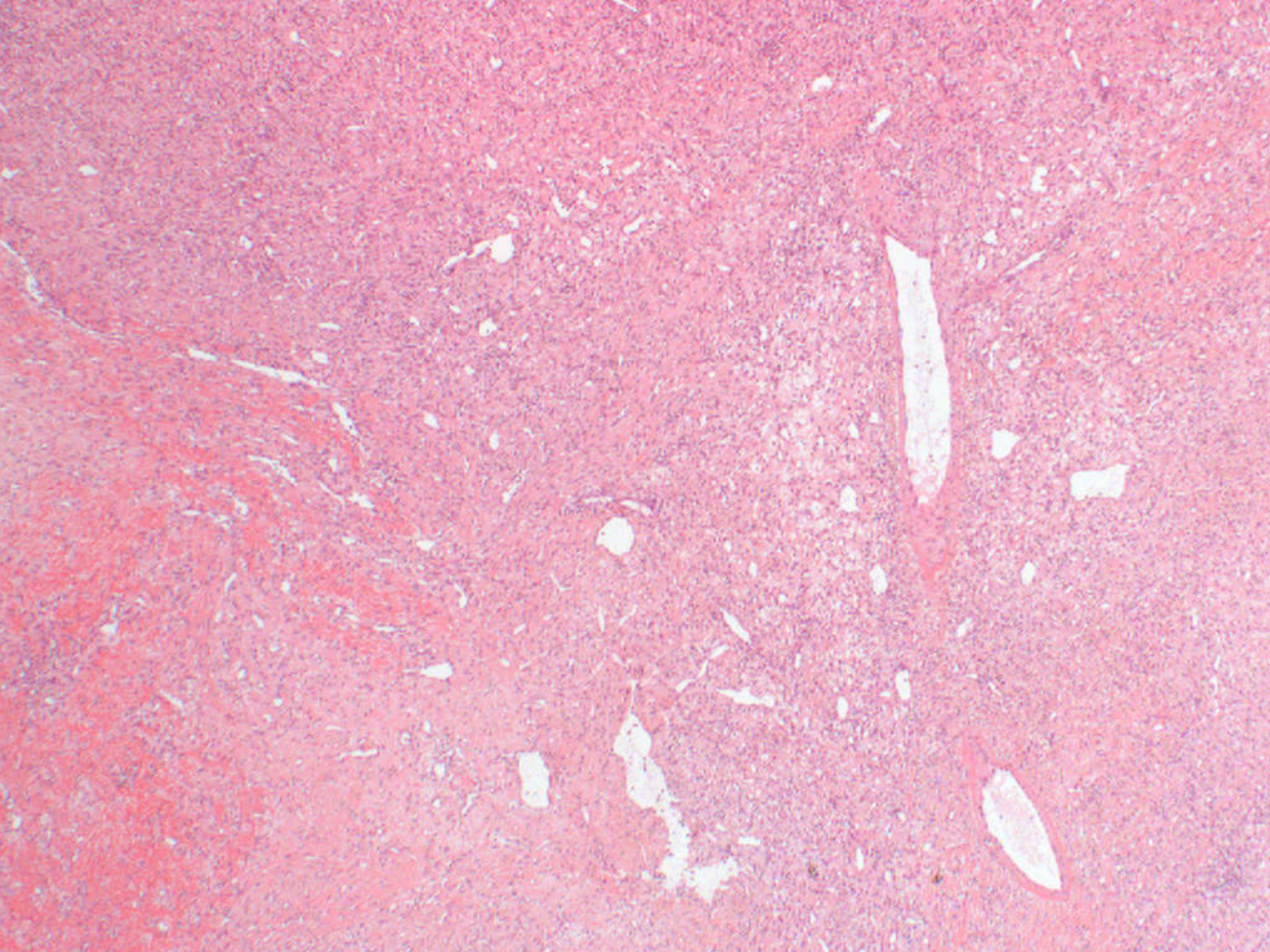
Biphasic Synovial Sarcoma

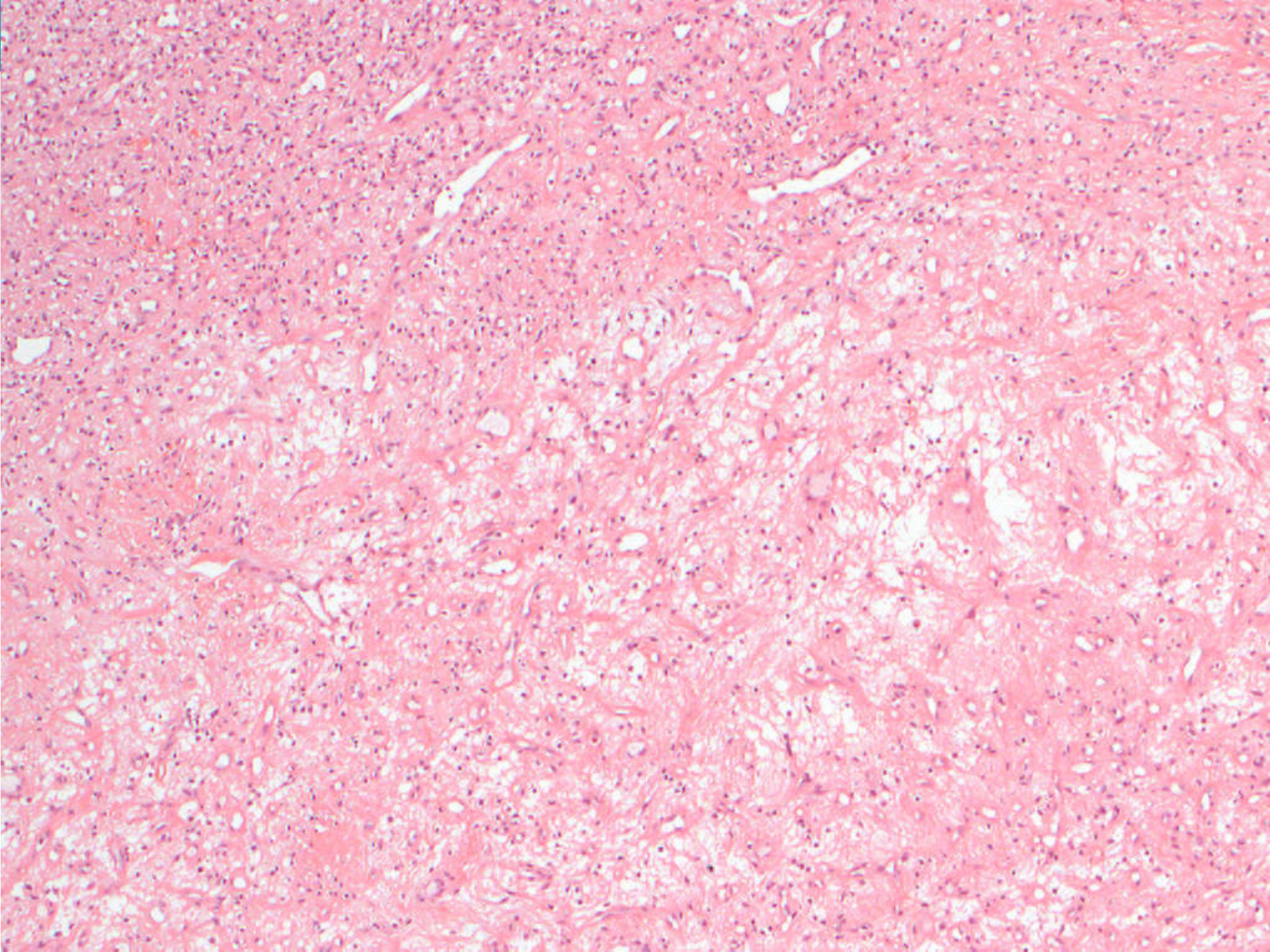
- Variable epithelial differentiation in numerous patterns
- Specific translocation resulting in *SS18-SSX* fusion in >95%
- May show myxoid change, hyaline collagen bundles and calcifications
- IHC: Usually EMA+, CD99+ (beware Ewings) nuclear TLE1+ in 80% (beware can also be + in MPNST and SFT)

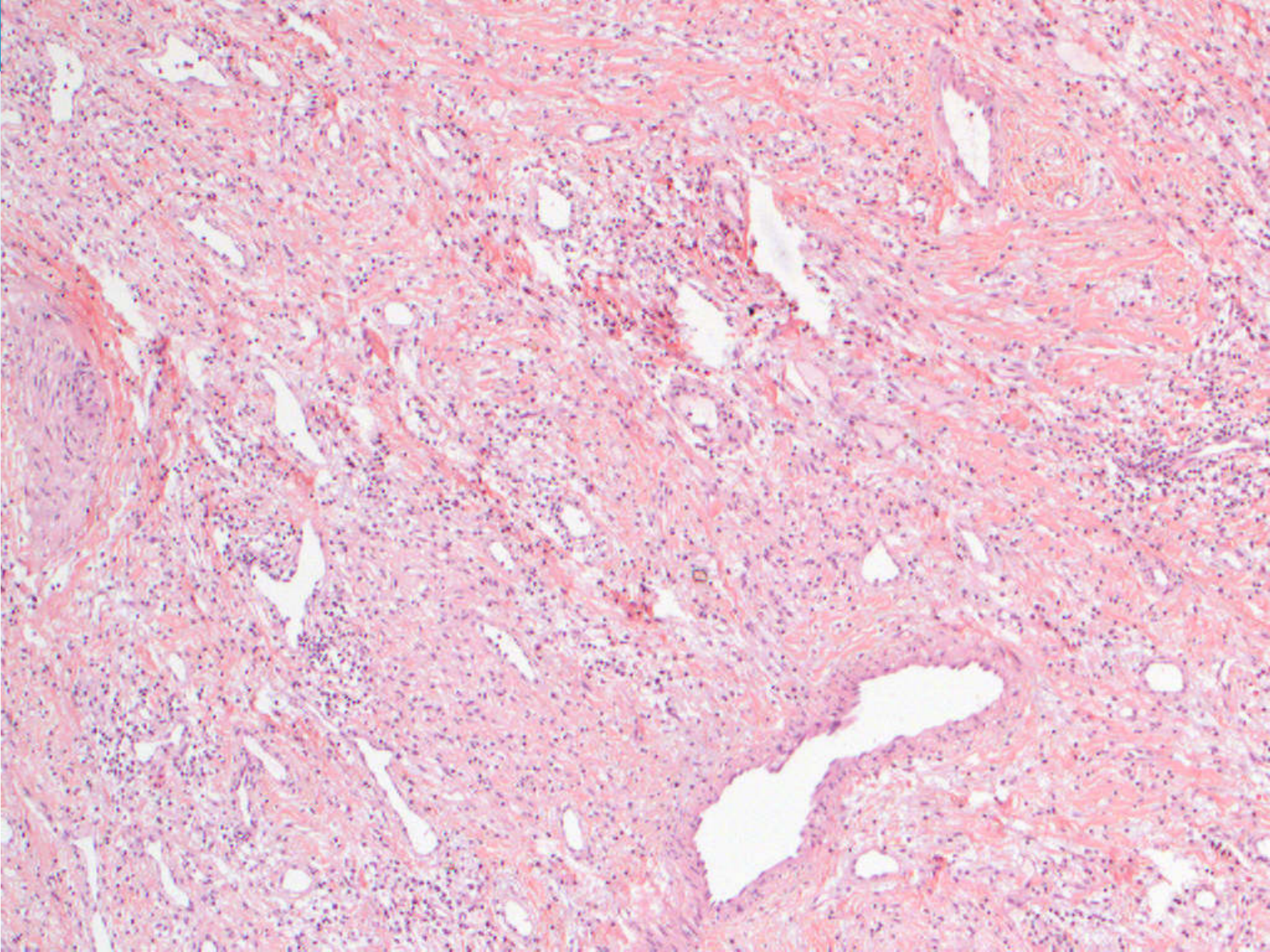
CLINICAL INFORMATION 12

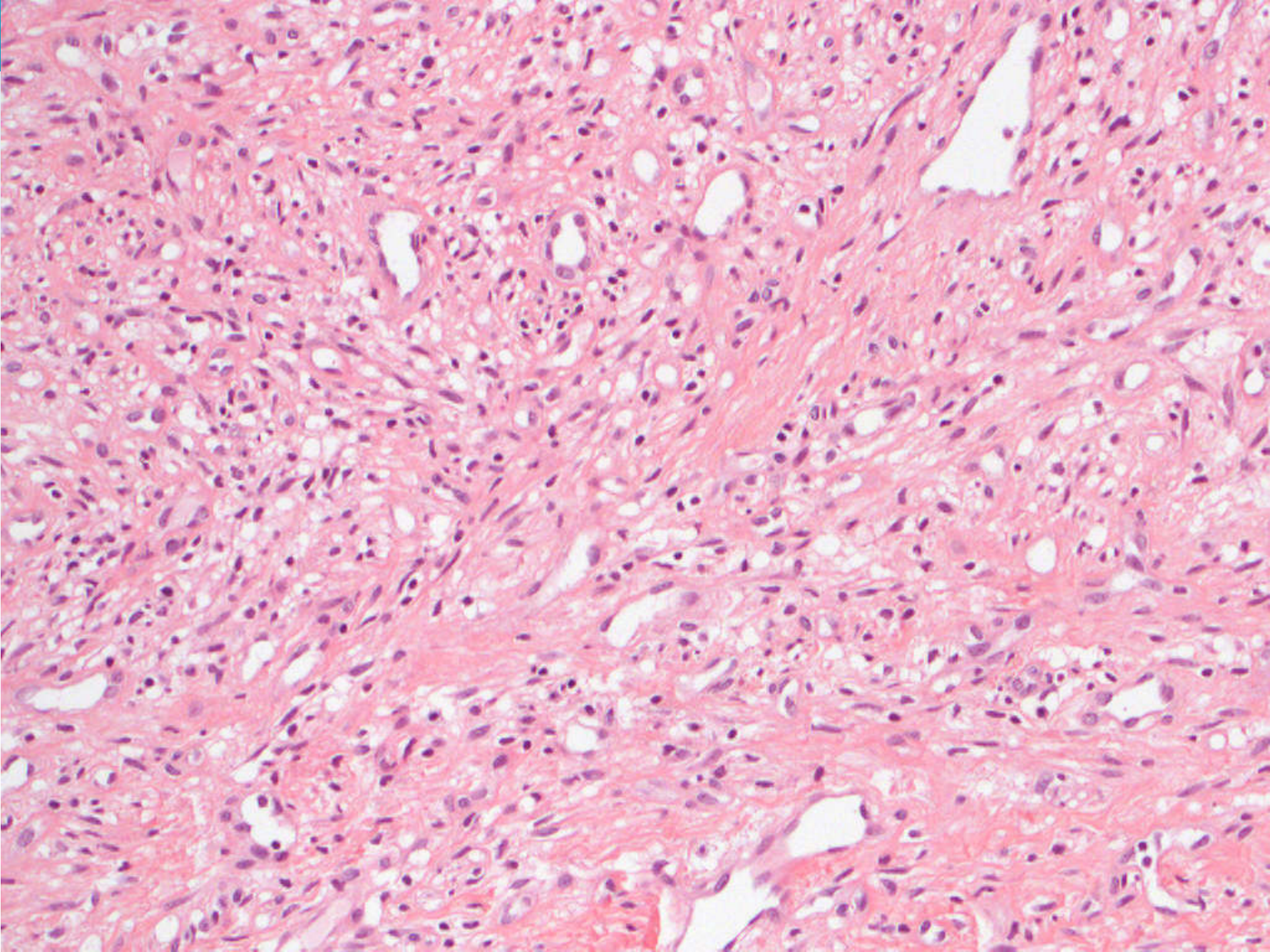
- Female, 46
- Soft tissue mass [40x30x30mm] in femoral triangle and stuck to vessels.











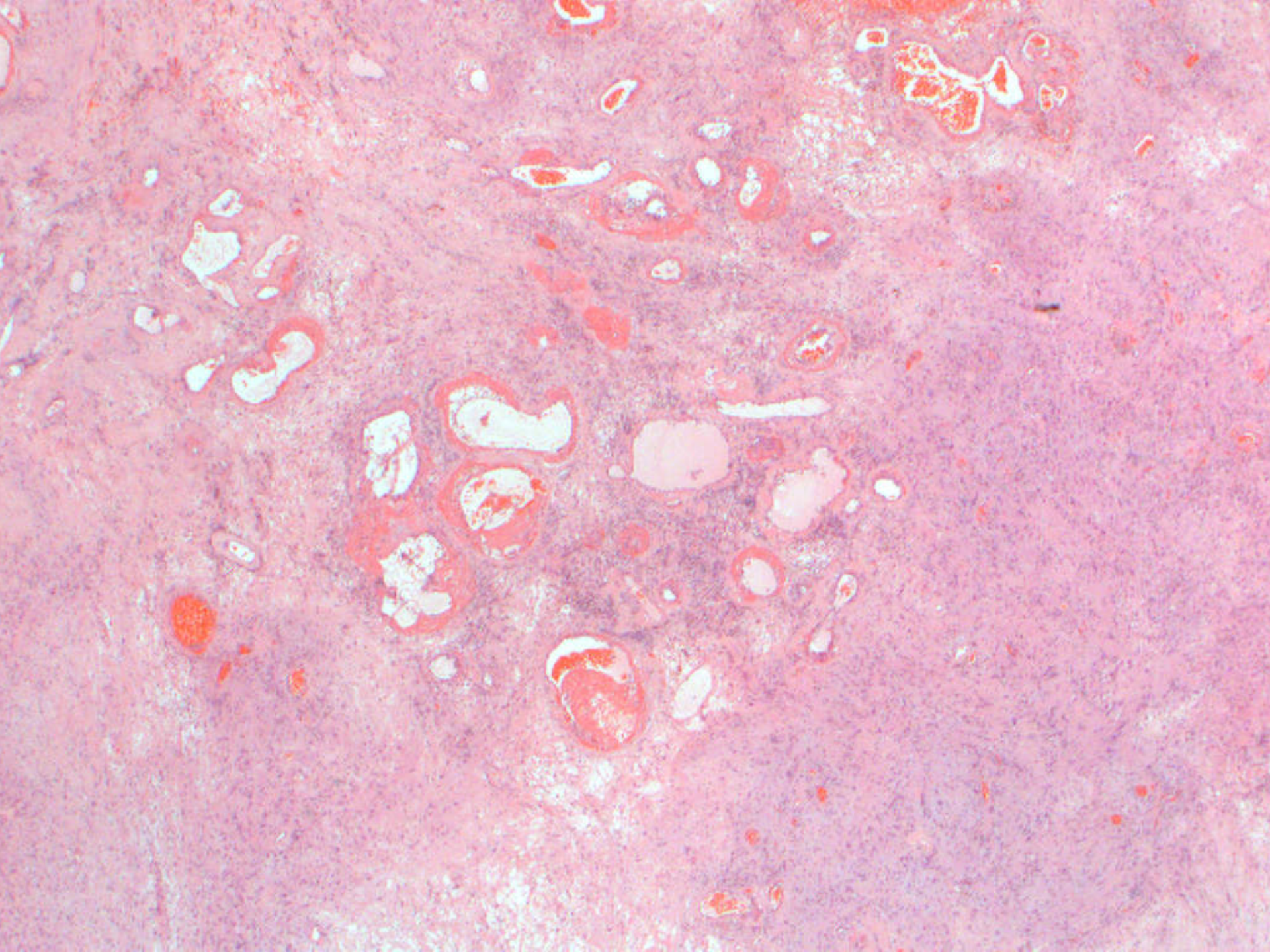
DX: Soft Tissue 12 Adv Path Course

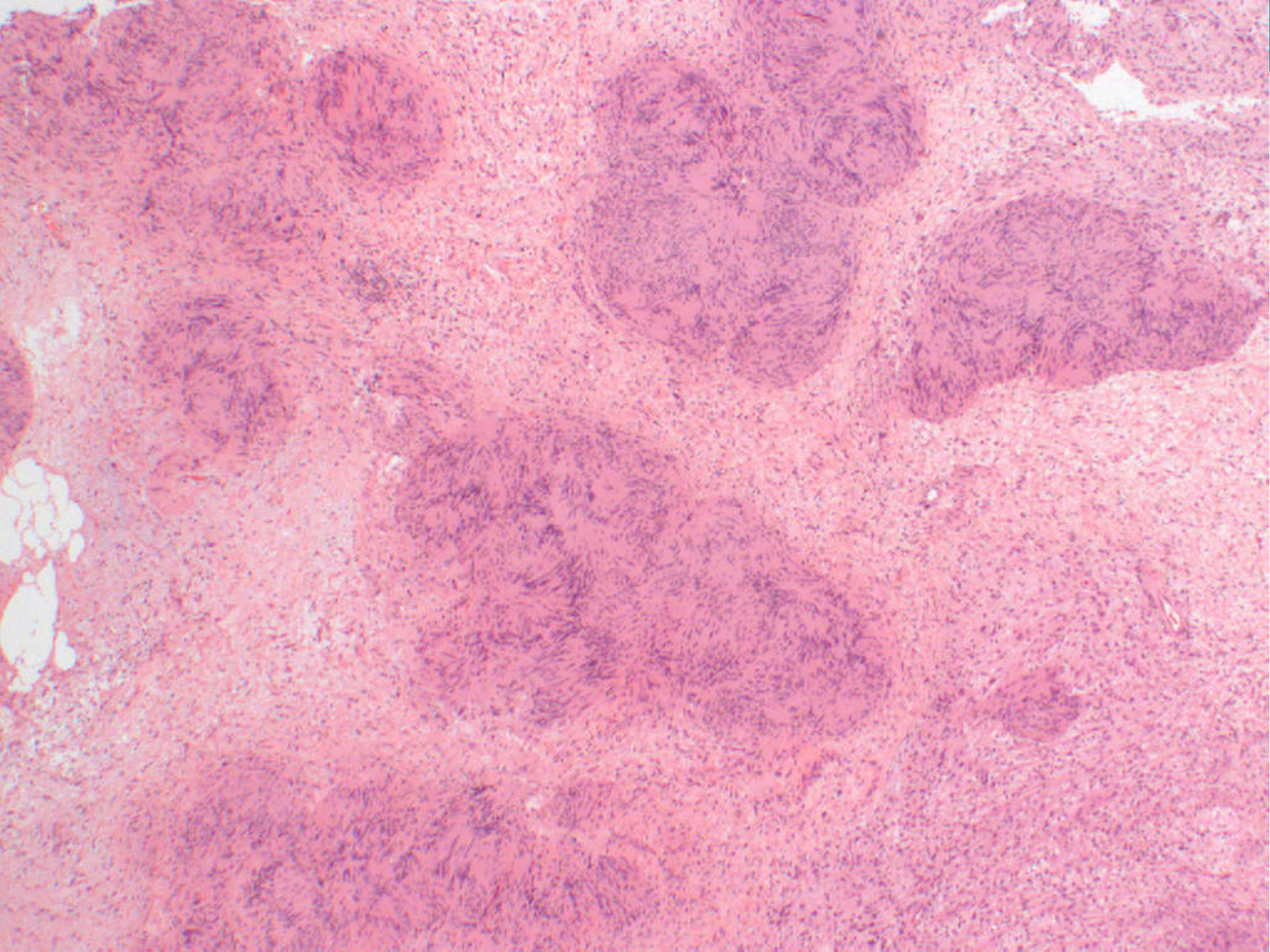
Solitary fibrous tumour

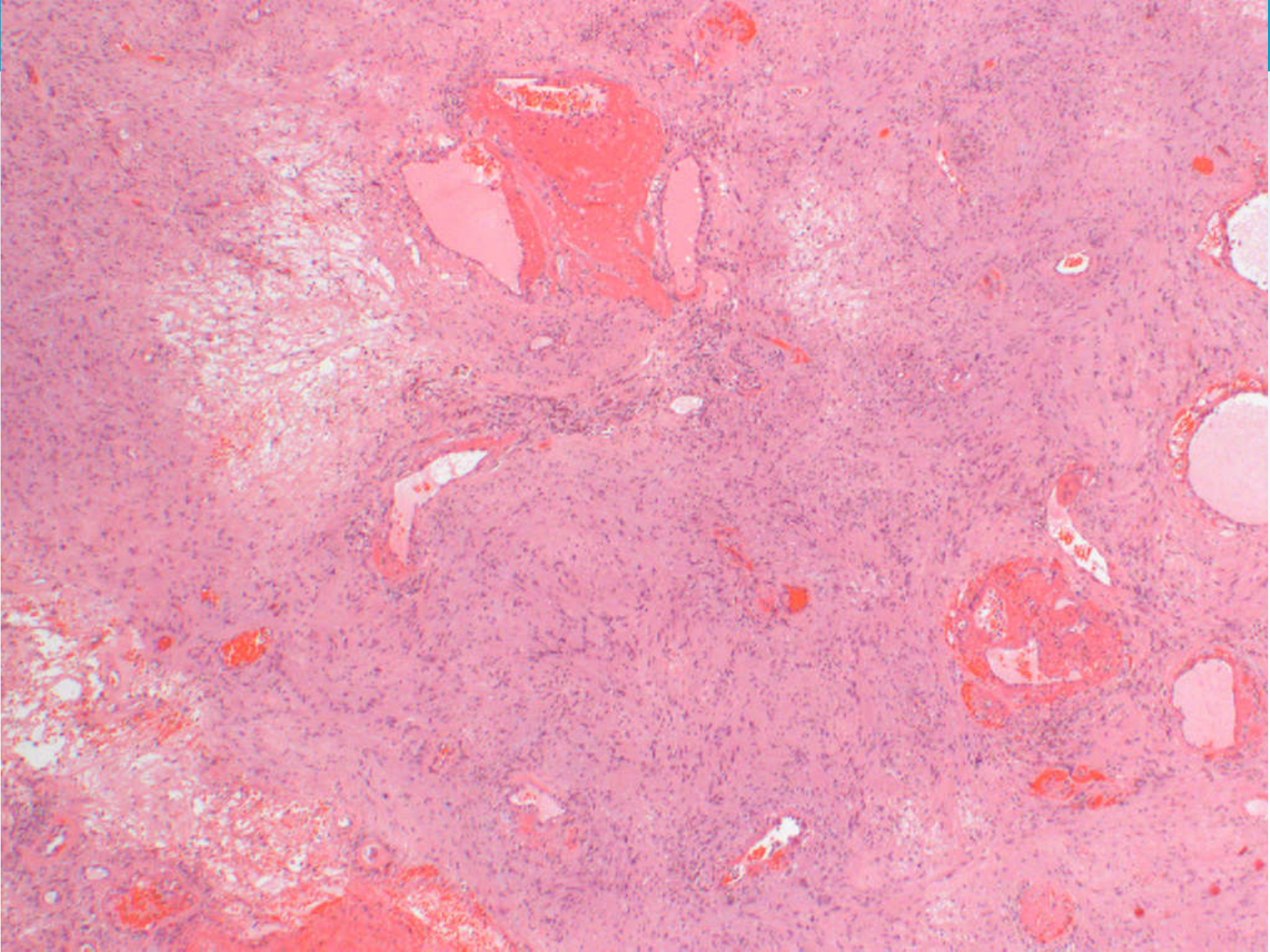
- Fibroblastic mesenchymal tumour with haemangiopericytoma-like branching vessels
- "Patternless" architecture, variable cellularity and variably fibrous
- Cellular and lipomatous variants exist
- Malignant features include
    - Mitoses >4/10 HPF
    - Variable cytologic atypia
    - Infiltrative margins and/or necrosis
- STAT6, CD34 and CD99+. Variable EMA, SMA and keratin.

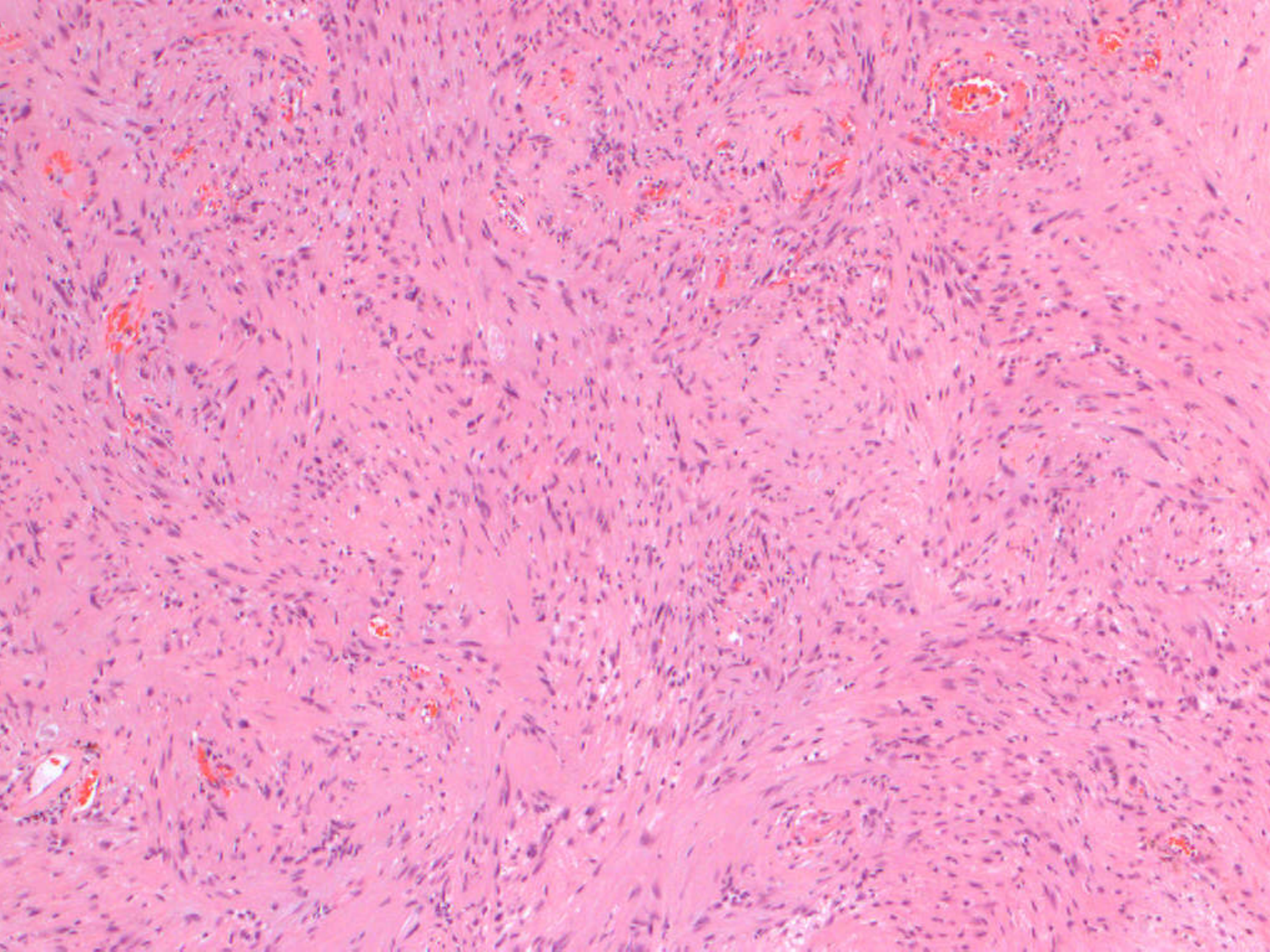
CLINICAL INFORMATION 13

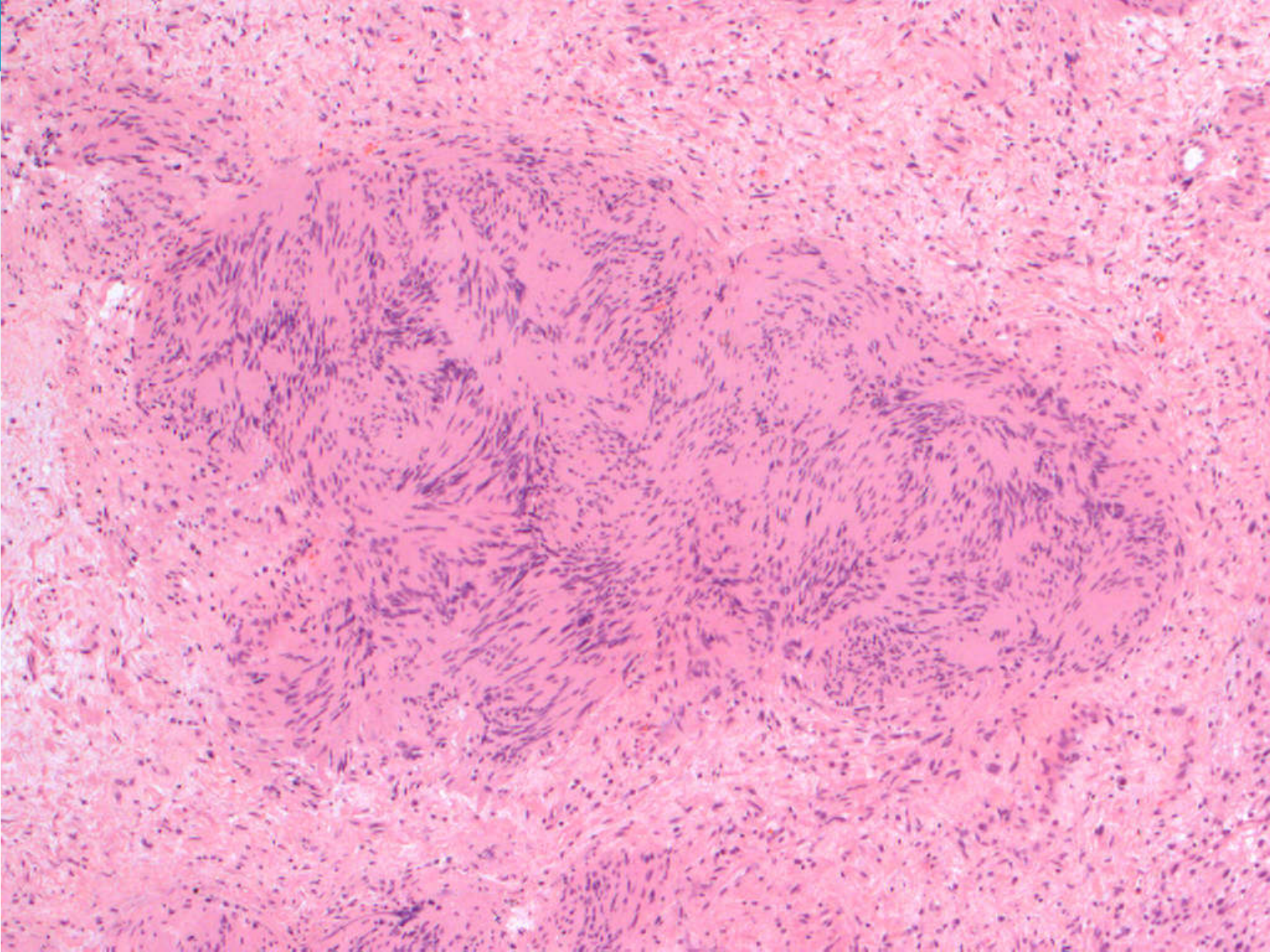
- Male, 59
- Soft tissue lesion [30x18x10mm] on lower leg.

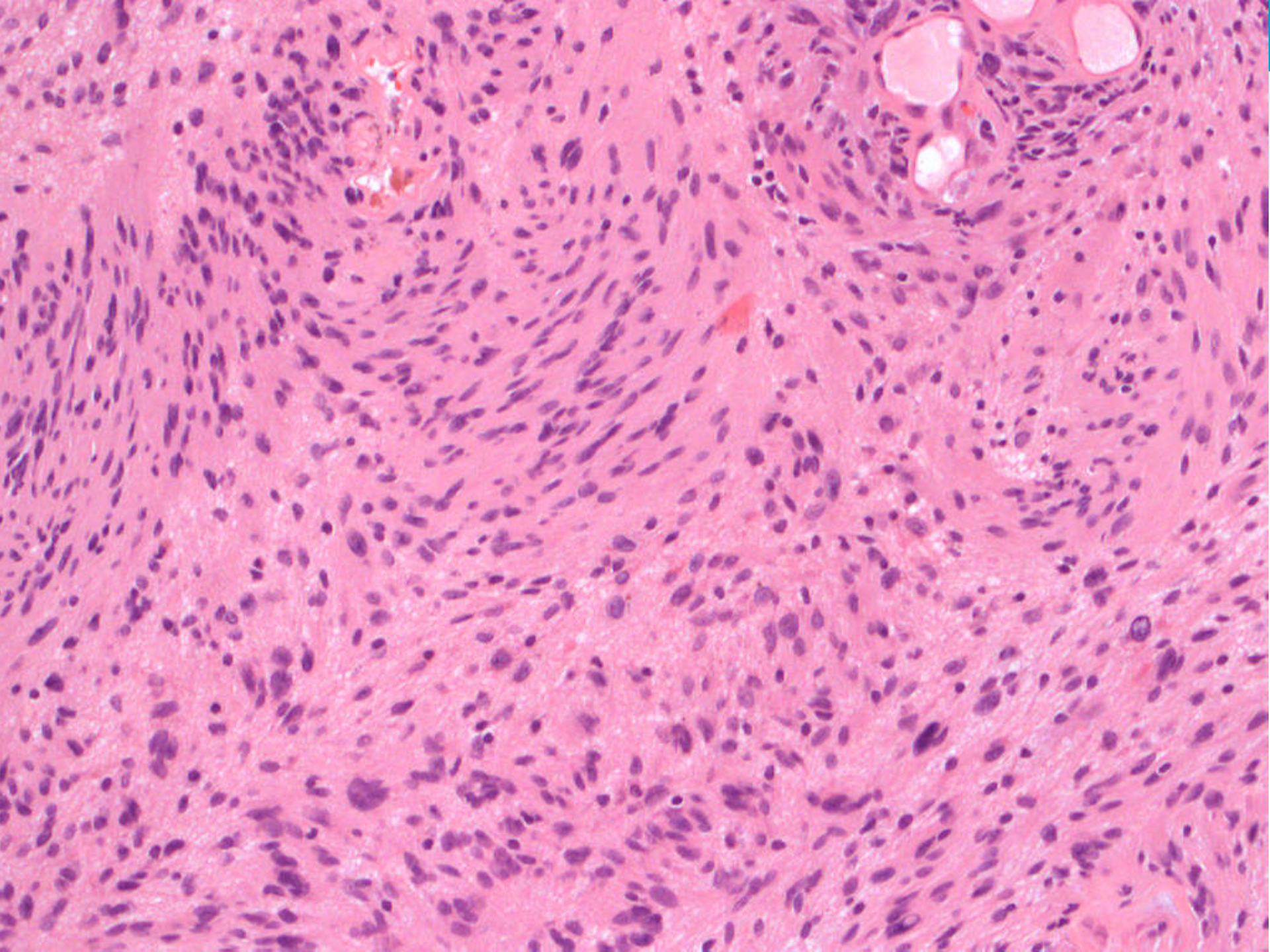


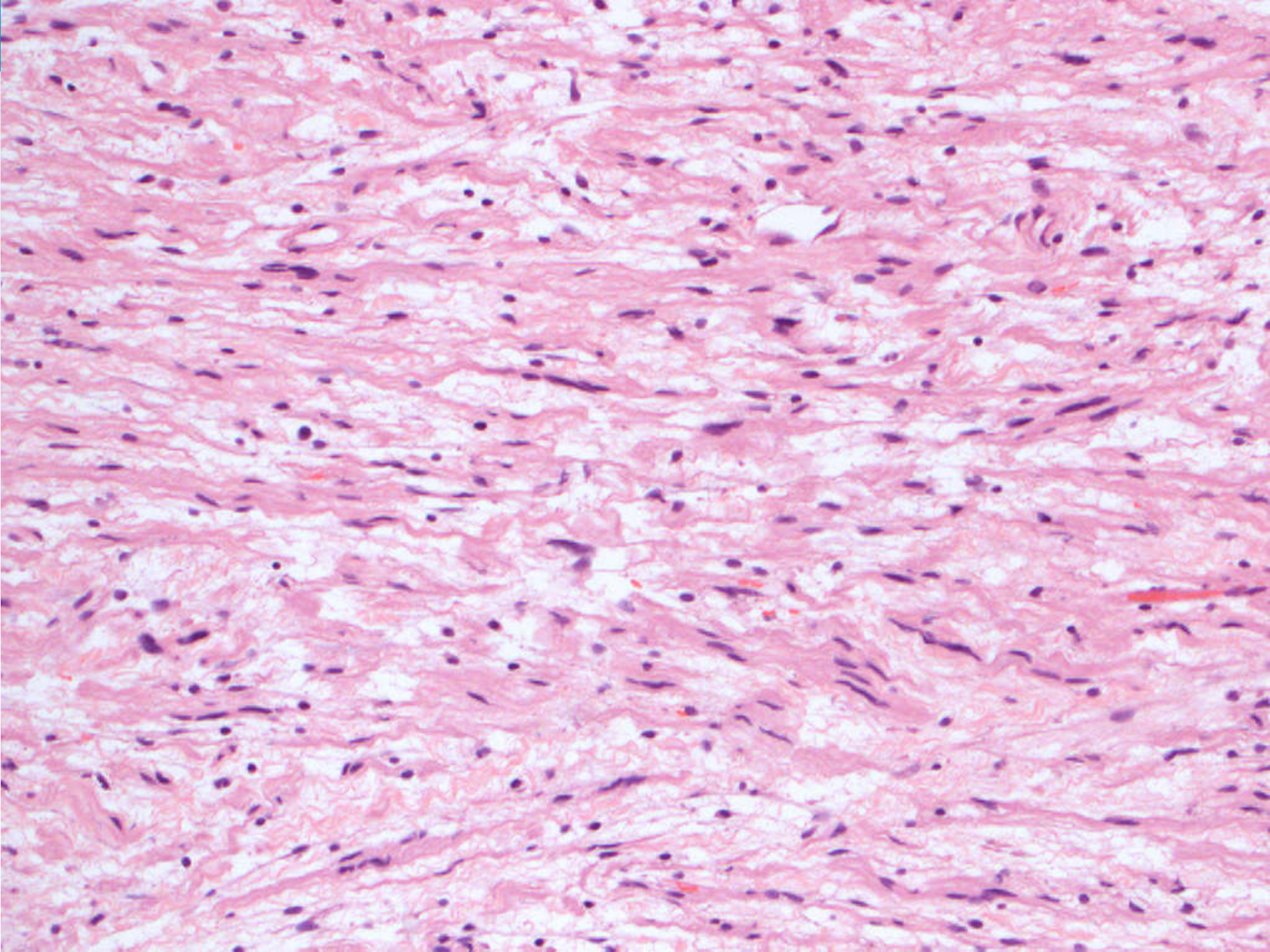












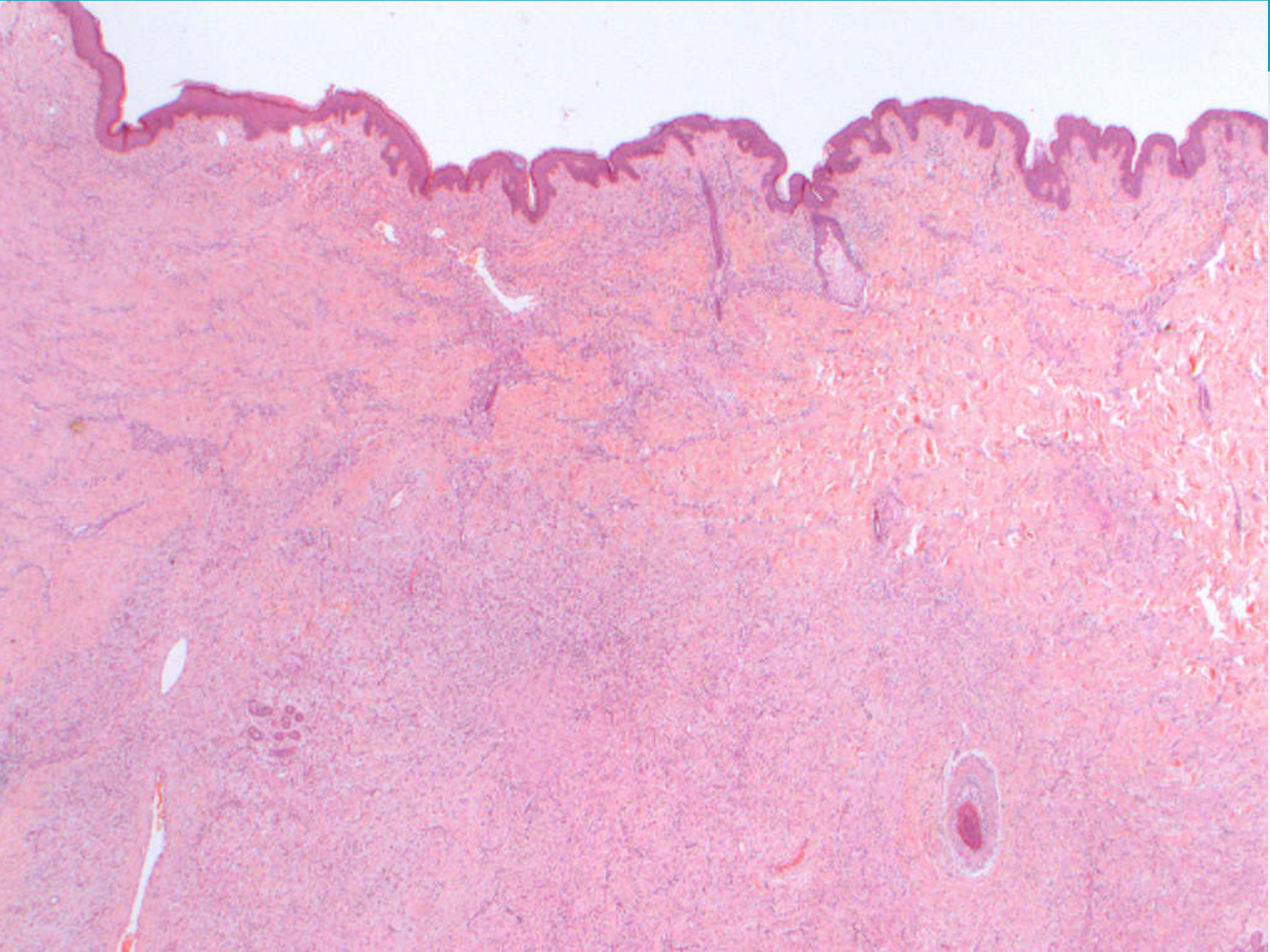
DX: Soft Tissue 13 Adv Path Course

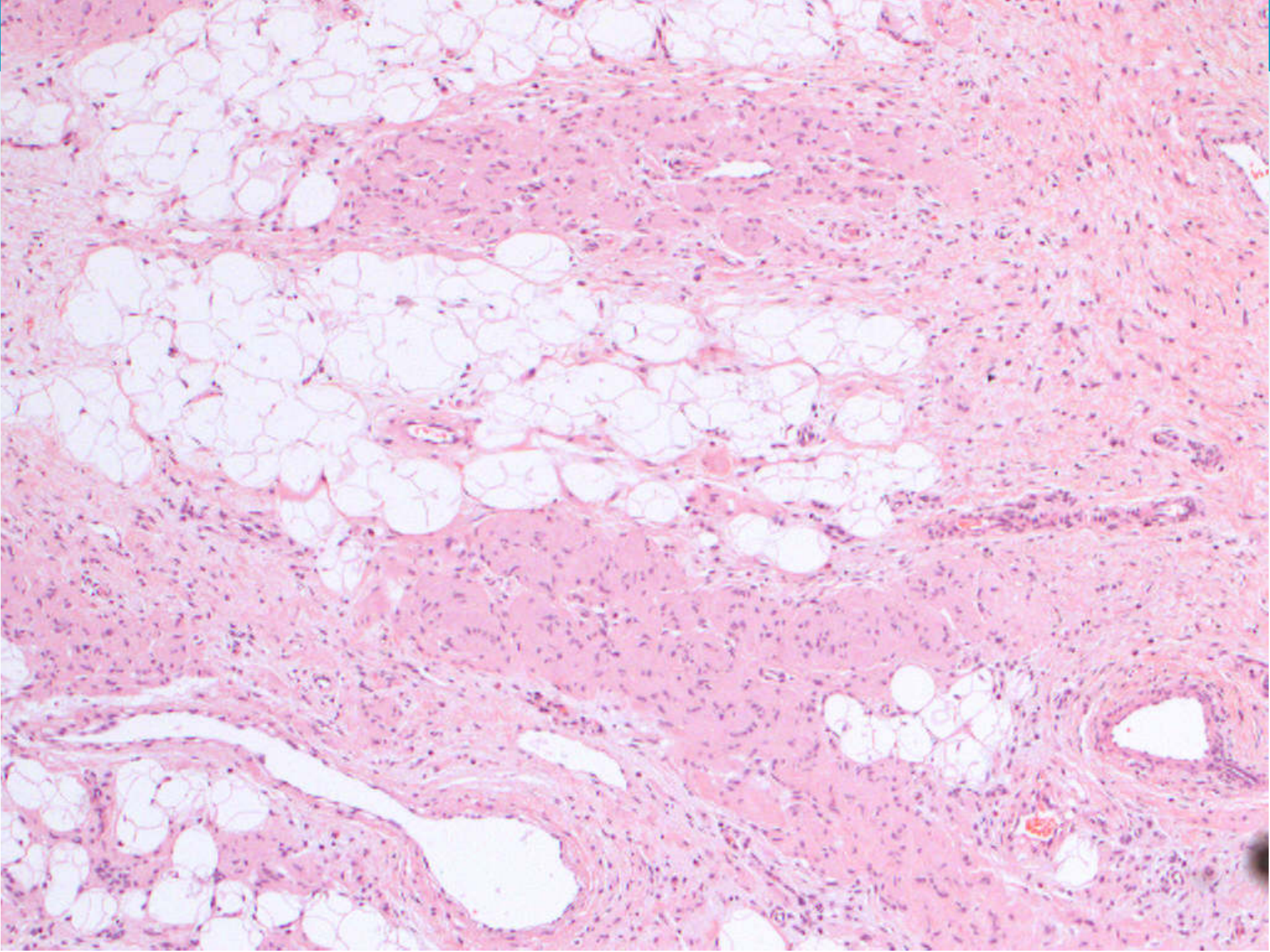
Schwannoma

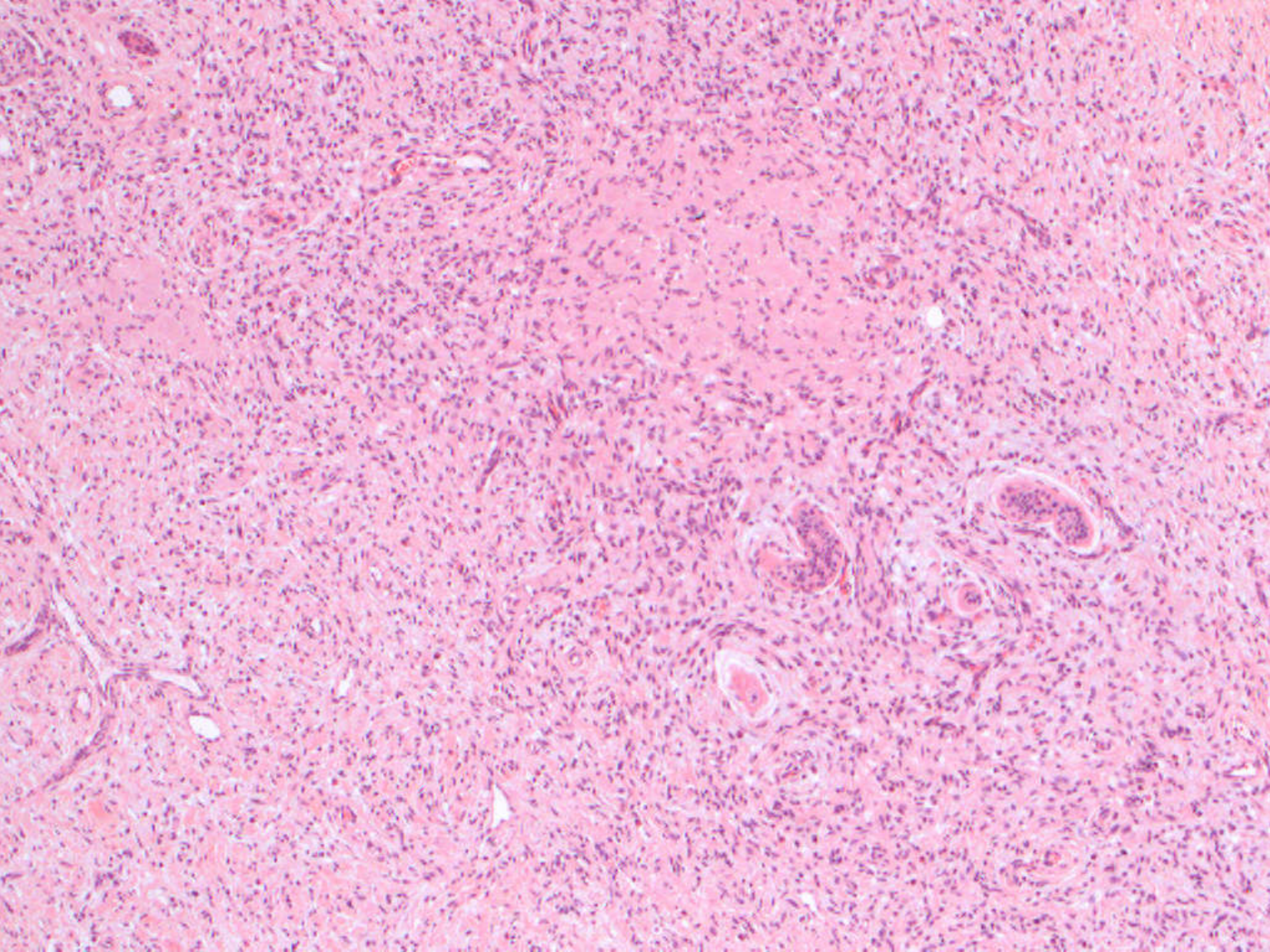
- Over 90% are solitary and sporadic
- Multiple schwannomas are a feature of NF2, schwannomatosis and Gorlin-Koutlas syndrome
- Bilateral vestibular schwannomas are the hallmark of NF2
- May be conventional, cellular, plexiform or microcystic/reticular
- May erode bone, show ancient change and increased mitoses, BUT
- Schwannoma does not represent a precursor of MPNST; malignant change is EXCEPTIONALLY rare. (This is in contrast to melanotic schwannoma which is rarely metastasizing, and occurs in spinal roots and GI tract).

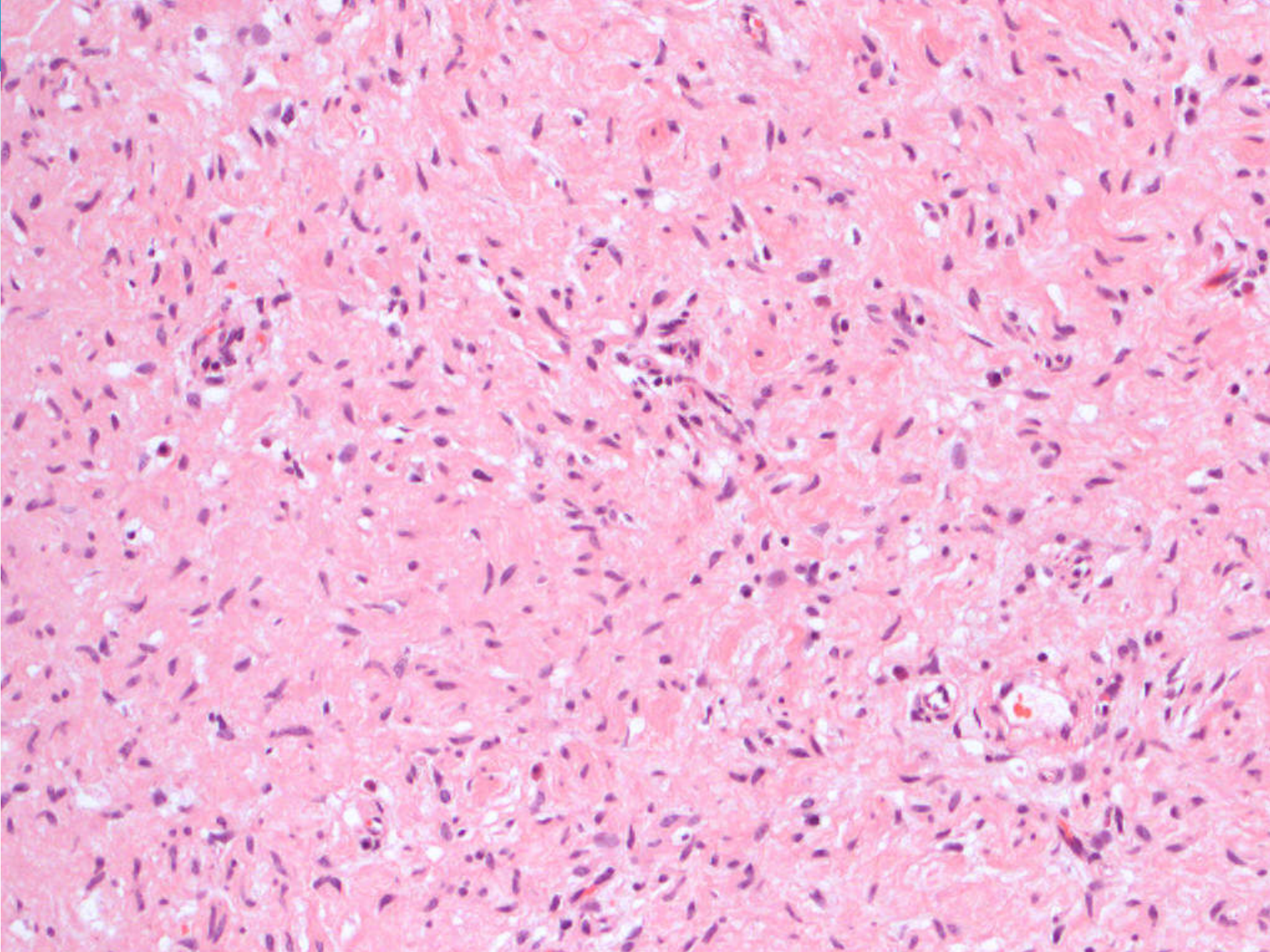
CLINICAL INFORMATION 14

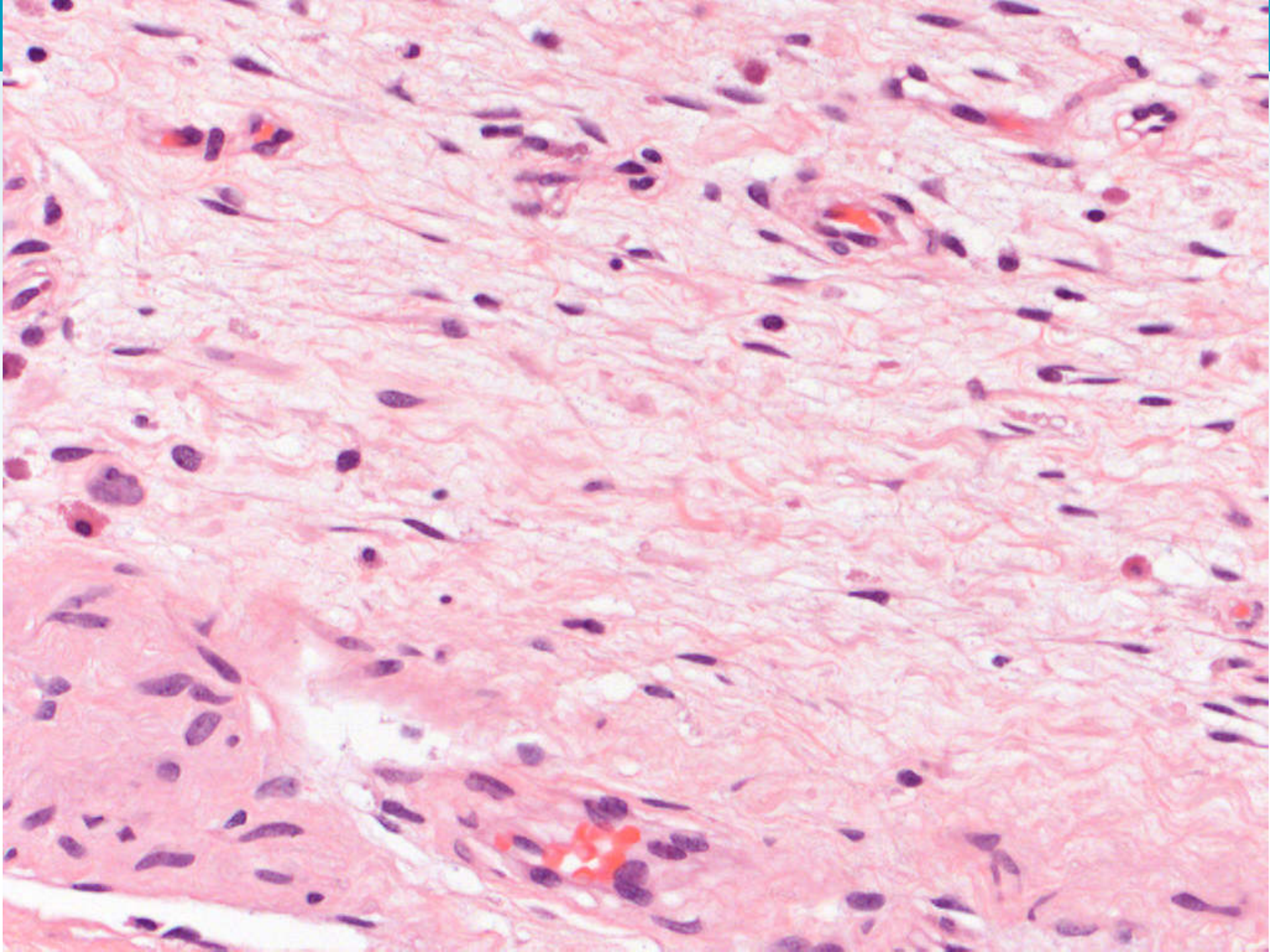
- Female, 23
- Large [15cm] subcutaneous chest wall lesion.











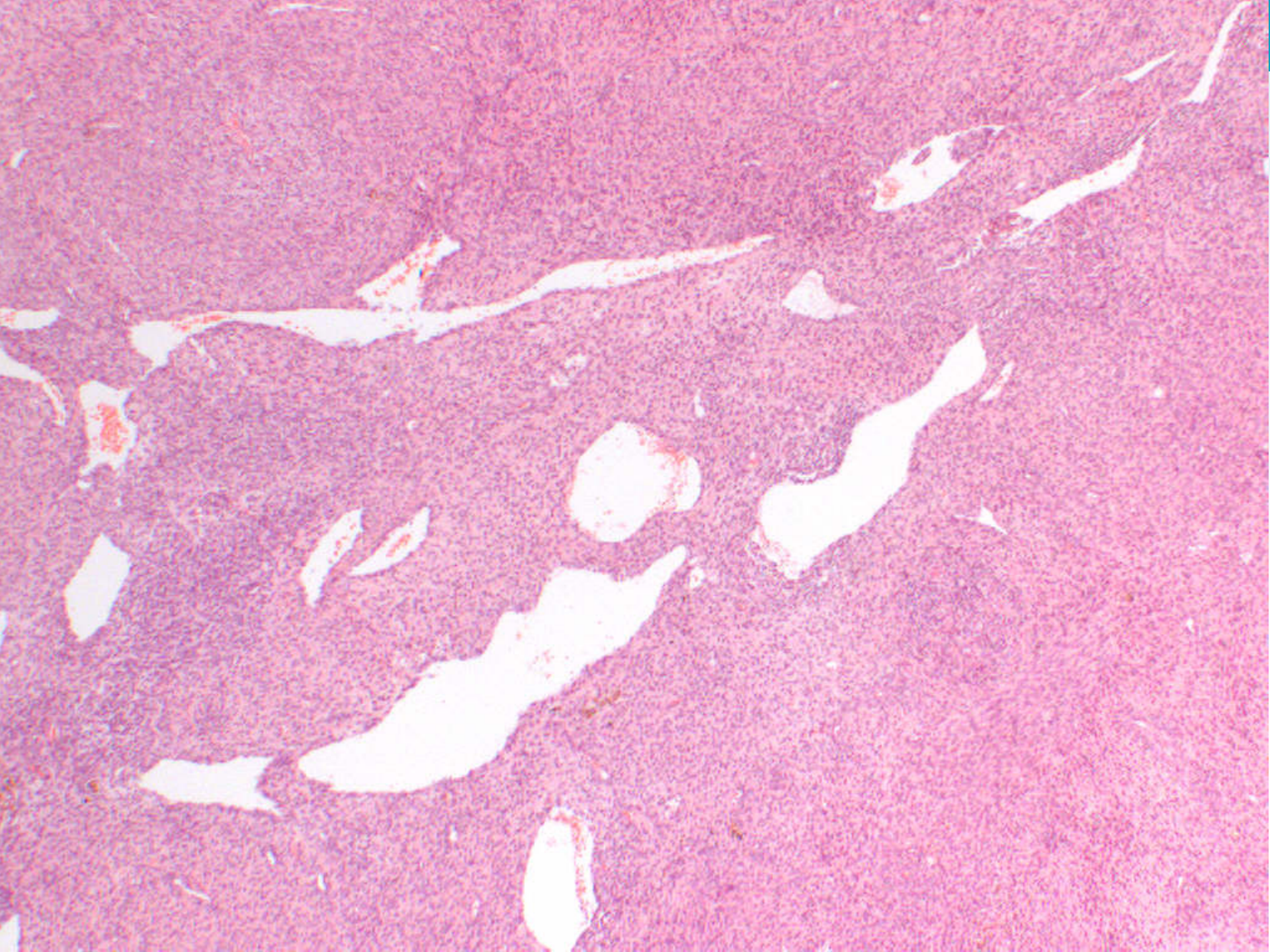
DX: Soft Tissue 14 Adv Path Course

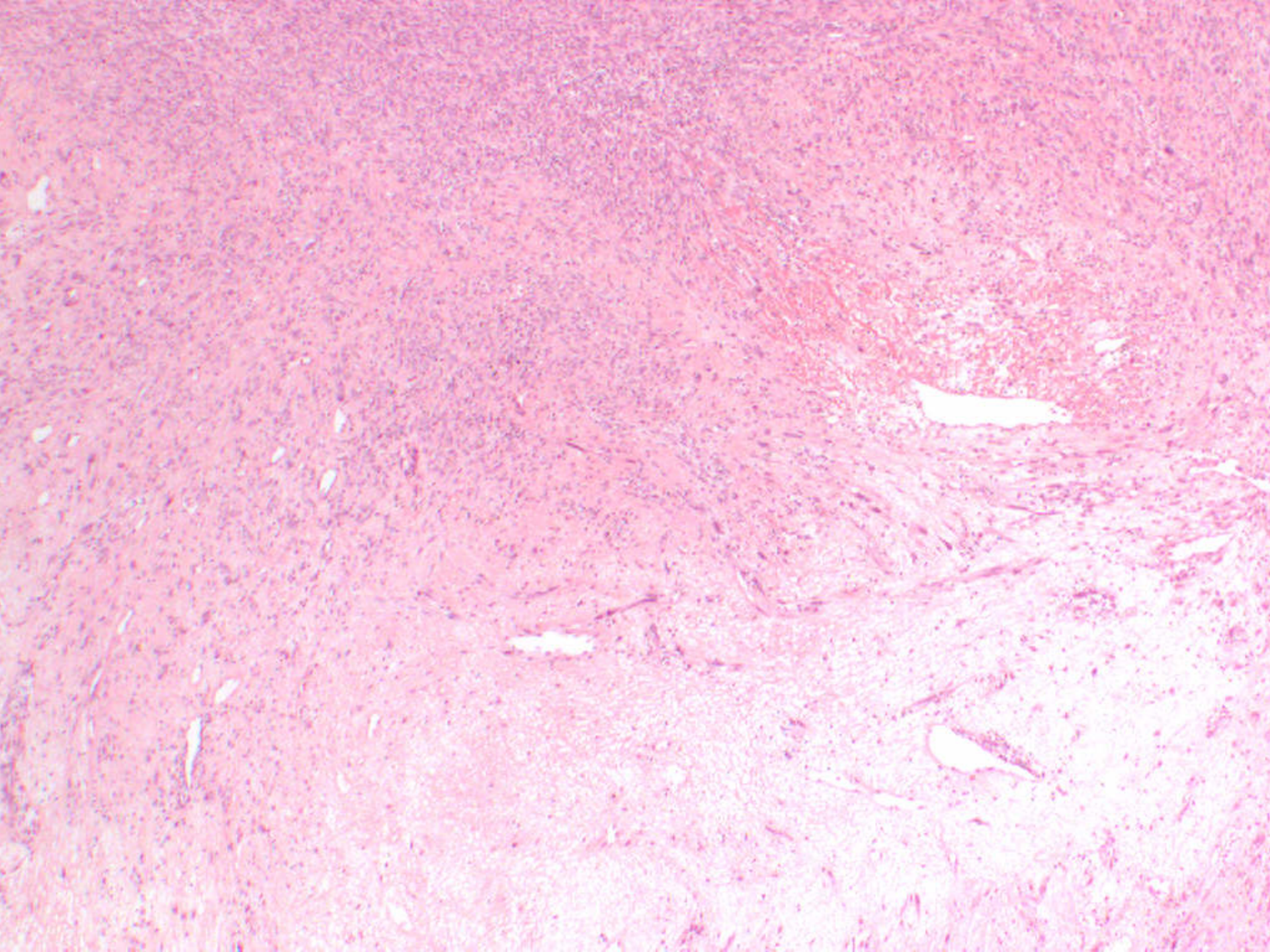
Neurofibroma

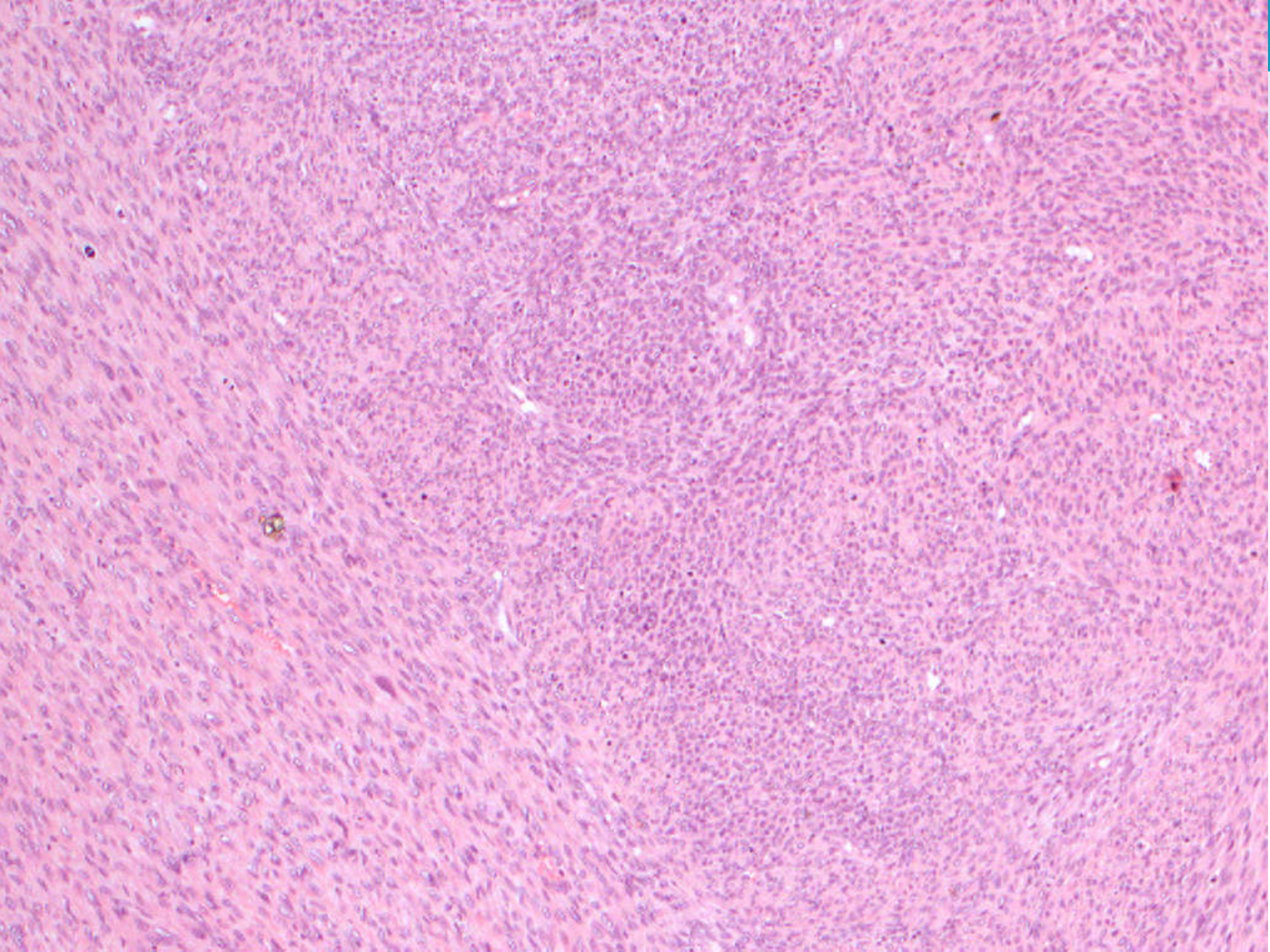
- May be sporadic or occur in NF1, usually multiple
- May be polypoid, plexiform or diffusely infiltrative
- Rarely contain melanin-pigmented cells
- Plexiform neurofibromas and solitary intraneural neurofibromas in sizeable nerves are precursor lesions of some MPNSTs
- Beware of overdiagnosing an “atypical neurofibroma” as malignant
- These may show hypercellularity, hyperchromasia or mitotic activity

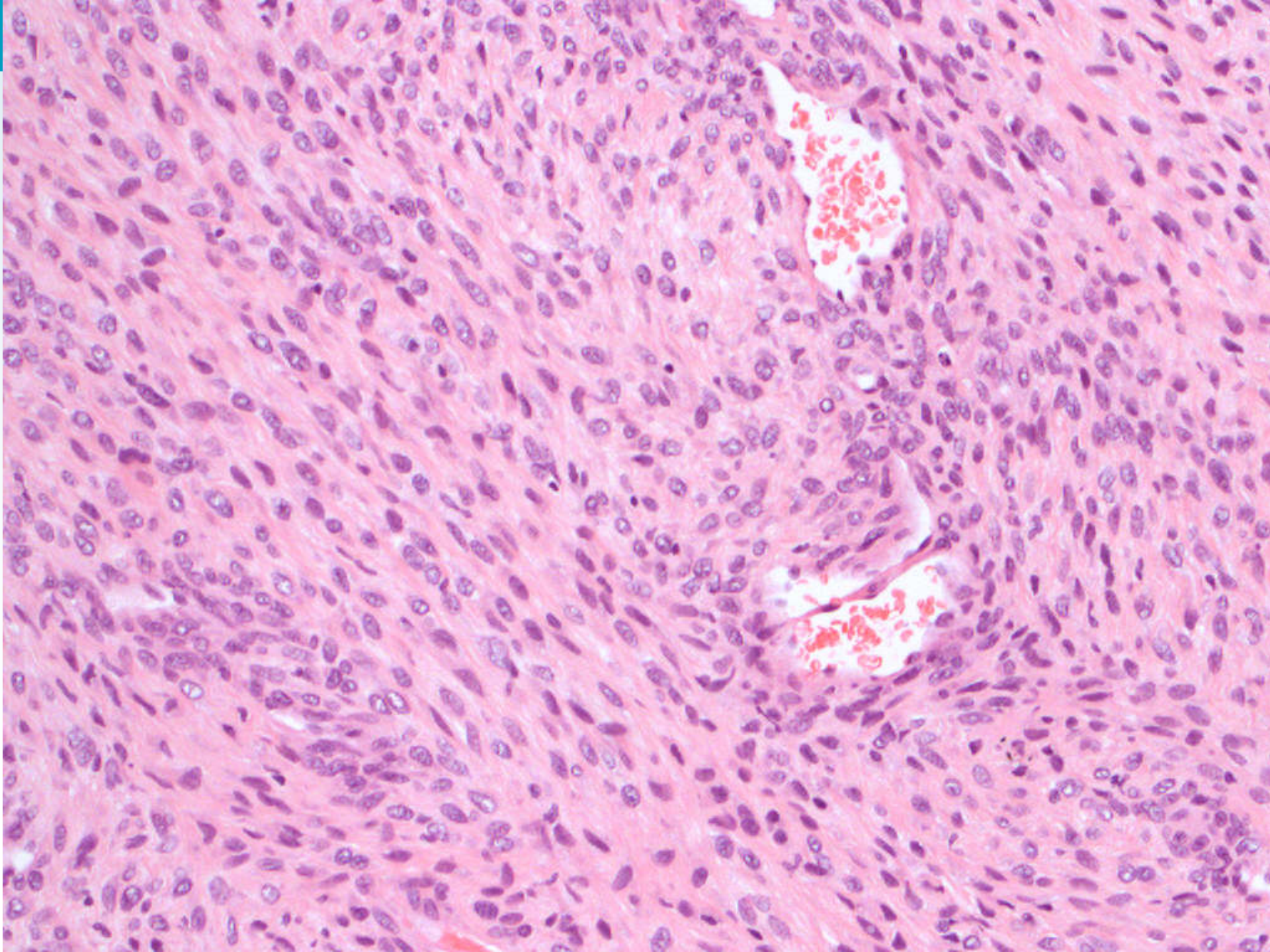
CLINICAL INFORMATION 15

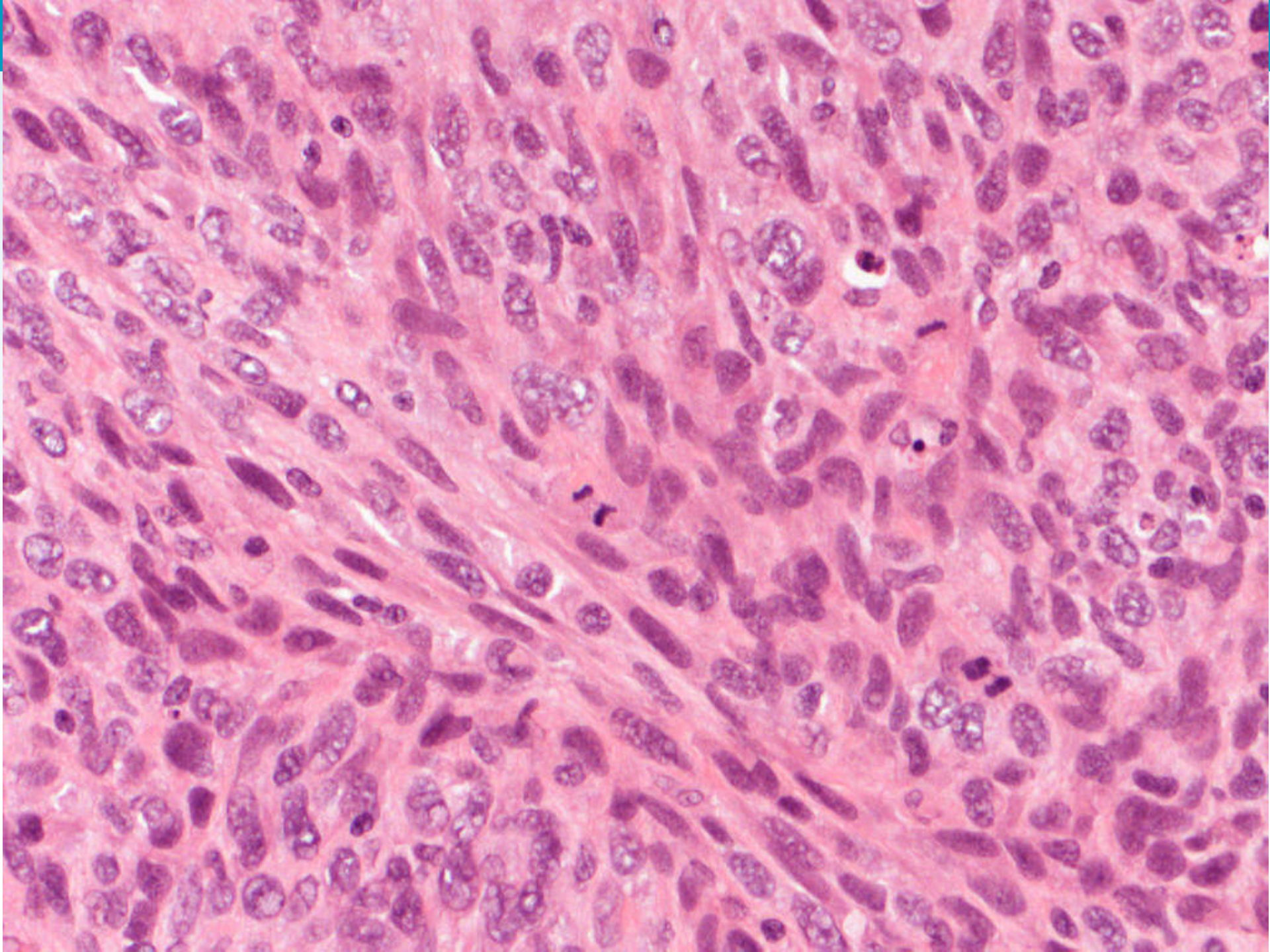
- Female, 48
- Soft tissue oval-shaped mass [90x80x45mm] in thigh.











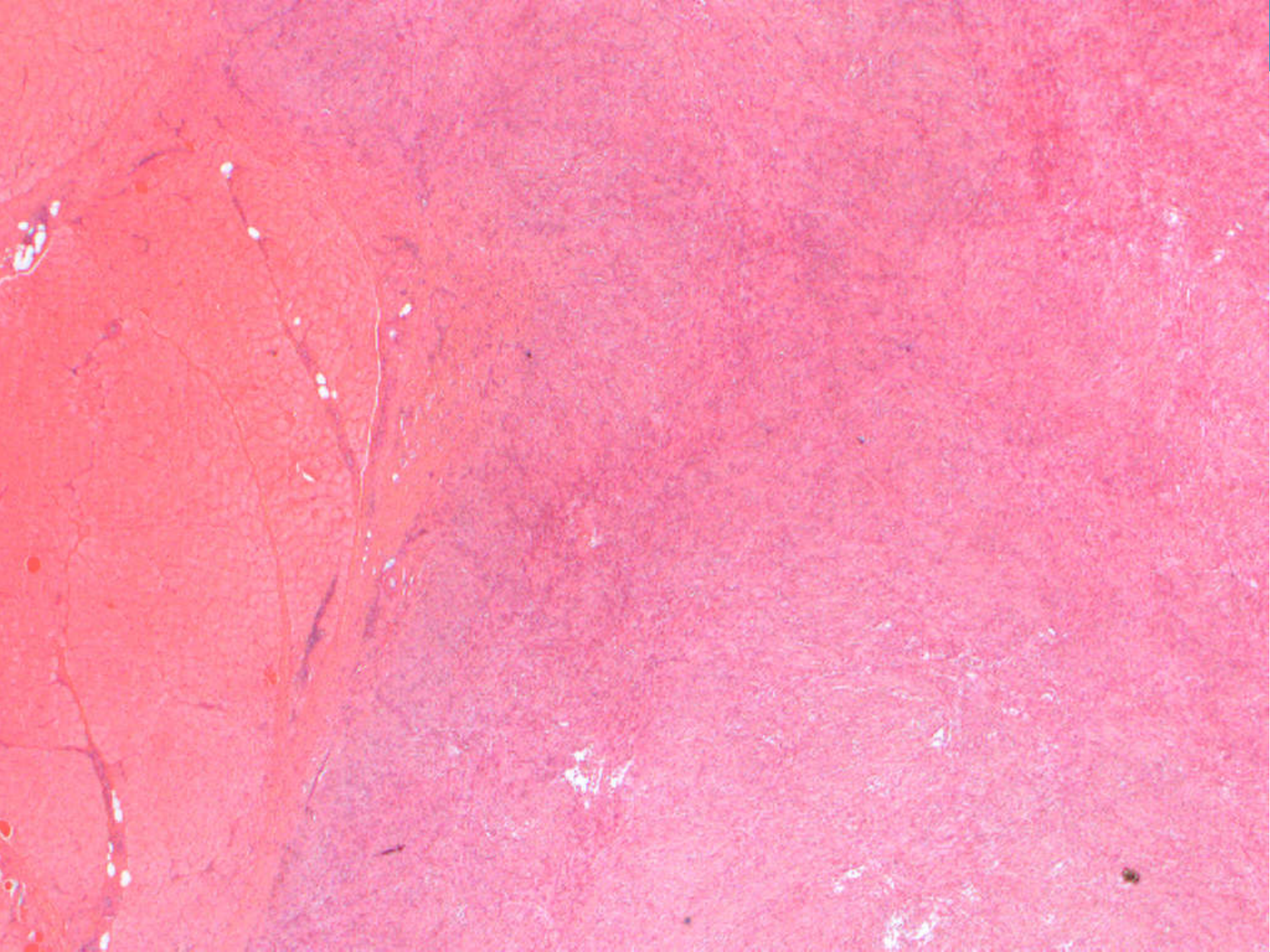
DX: Soft Tissue 15 Adv Path Course

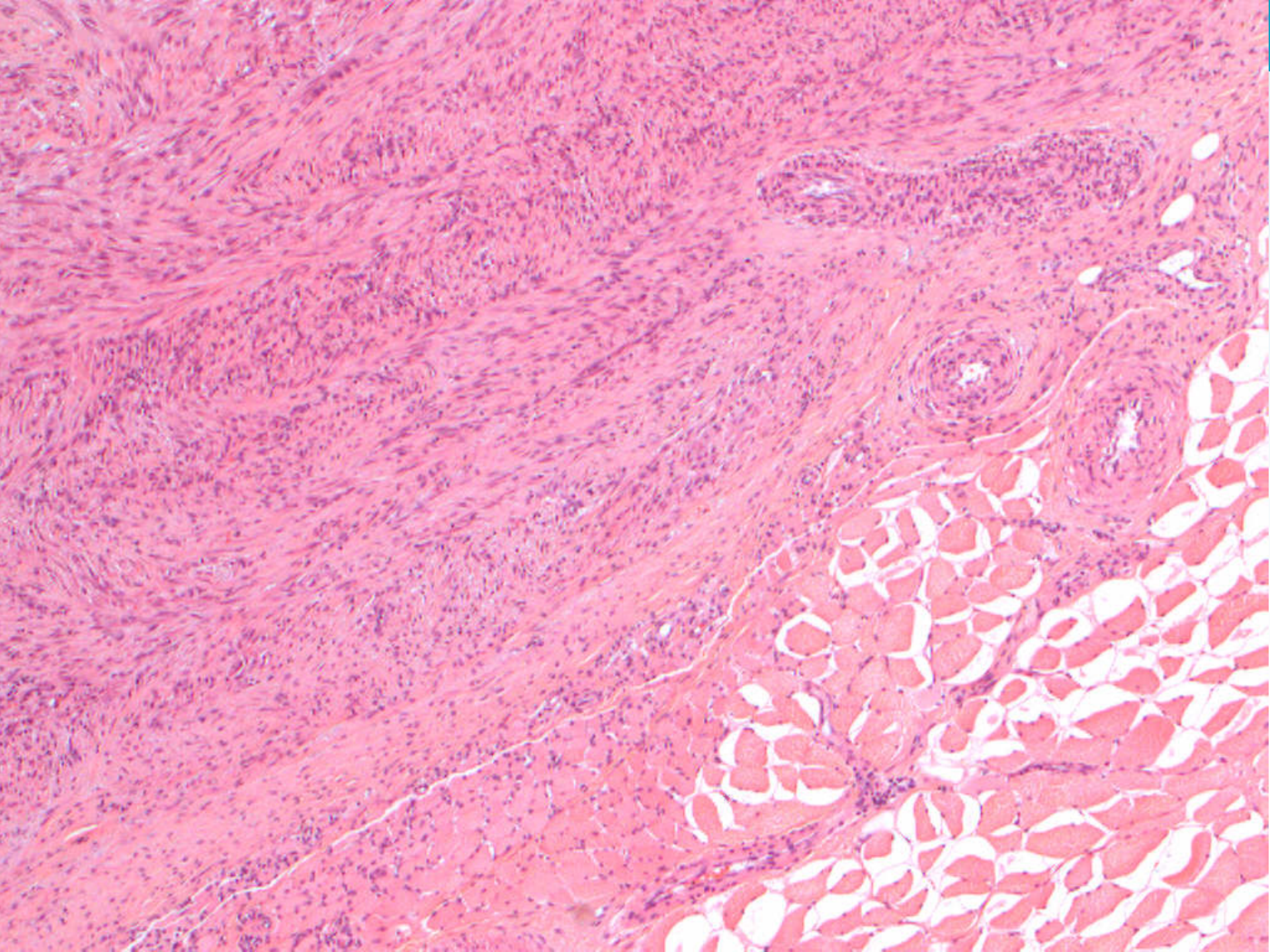
Malignant peripheral nerve sheath tumour

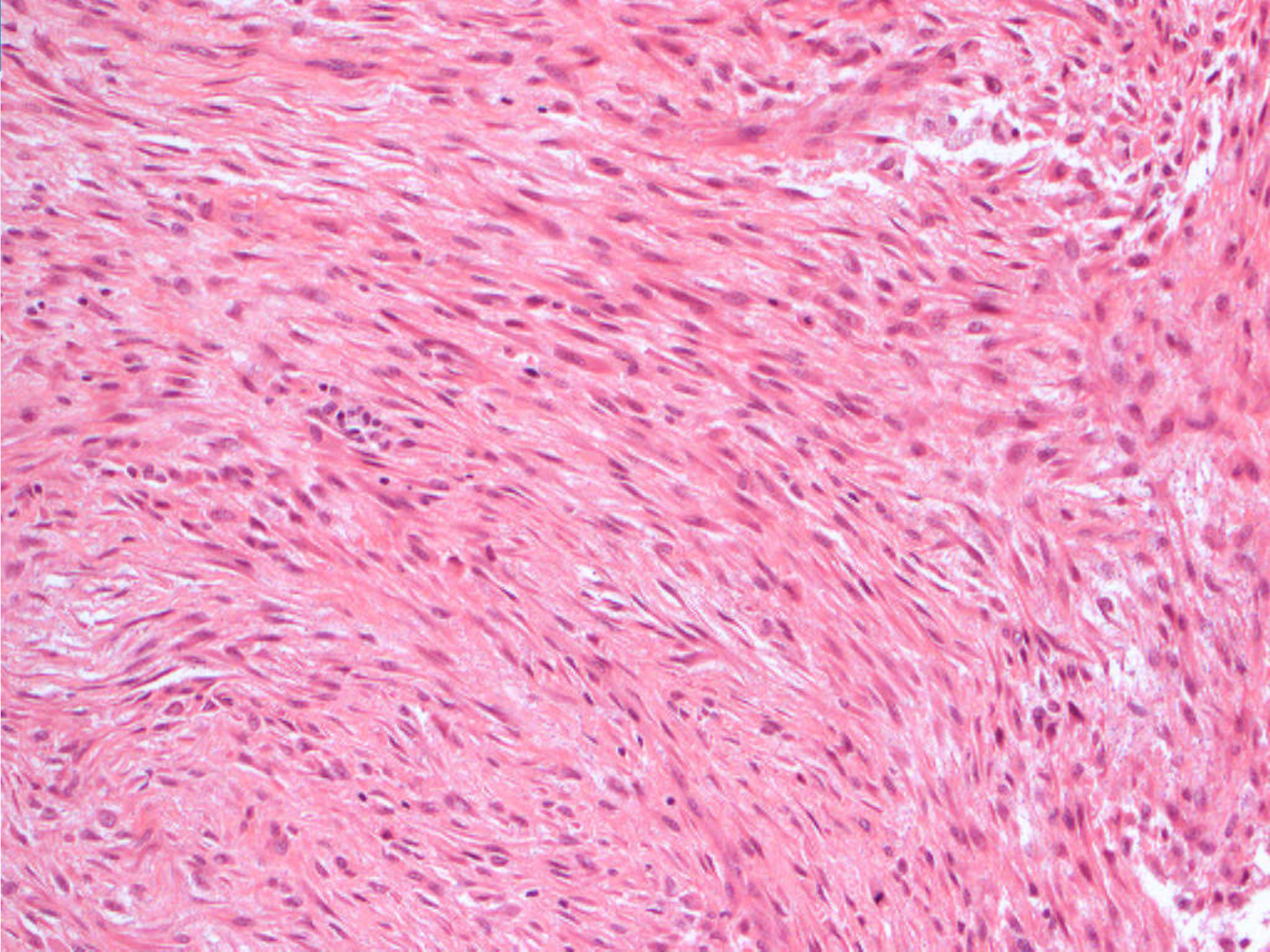
- Show increased cellularity AND hyperchromasia AND atypia AND frequent mitoses
- Usually have a heterogenous appearance. Geographic necrosis common.
- Heterologous elements (skeletal muscle, bone, cartilage and vessels) are rarely observed
- Variants include epithelioid type (not NF1-associated) and malignant Triton tumour
- May contain melanin pigment or areas with a pleomorphic undifferentiated appearance
- IHC variable. S100 + in <50%, usually focal. Many show loss of H3k27me3 (in contrast to epithelioid MPNST which retain H3k27me3, have more diffuse S100 labelling and show loss of INI1/SMARCB1 +/- keratin positivity)

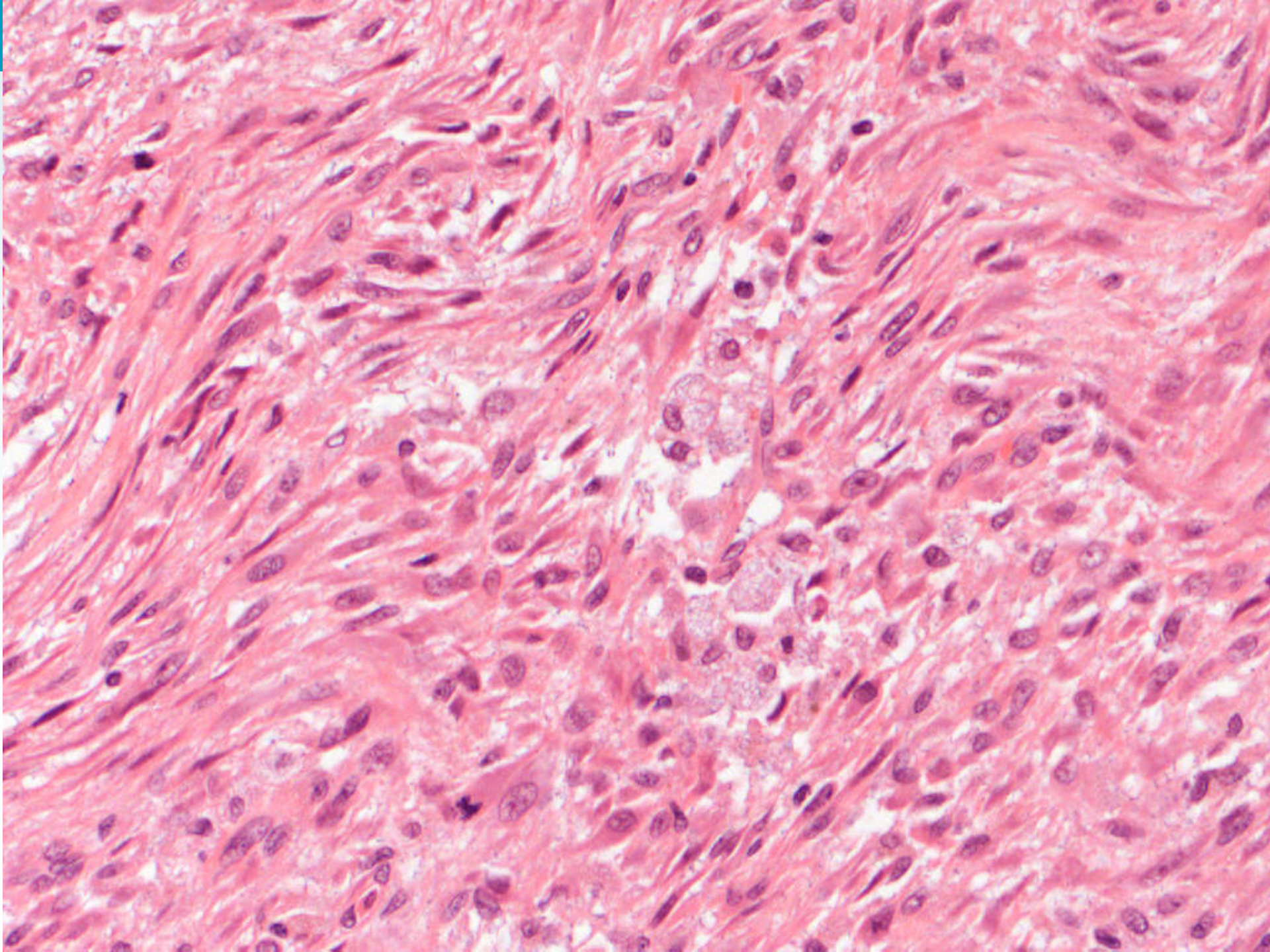
CLINICAL INFORMATION 16

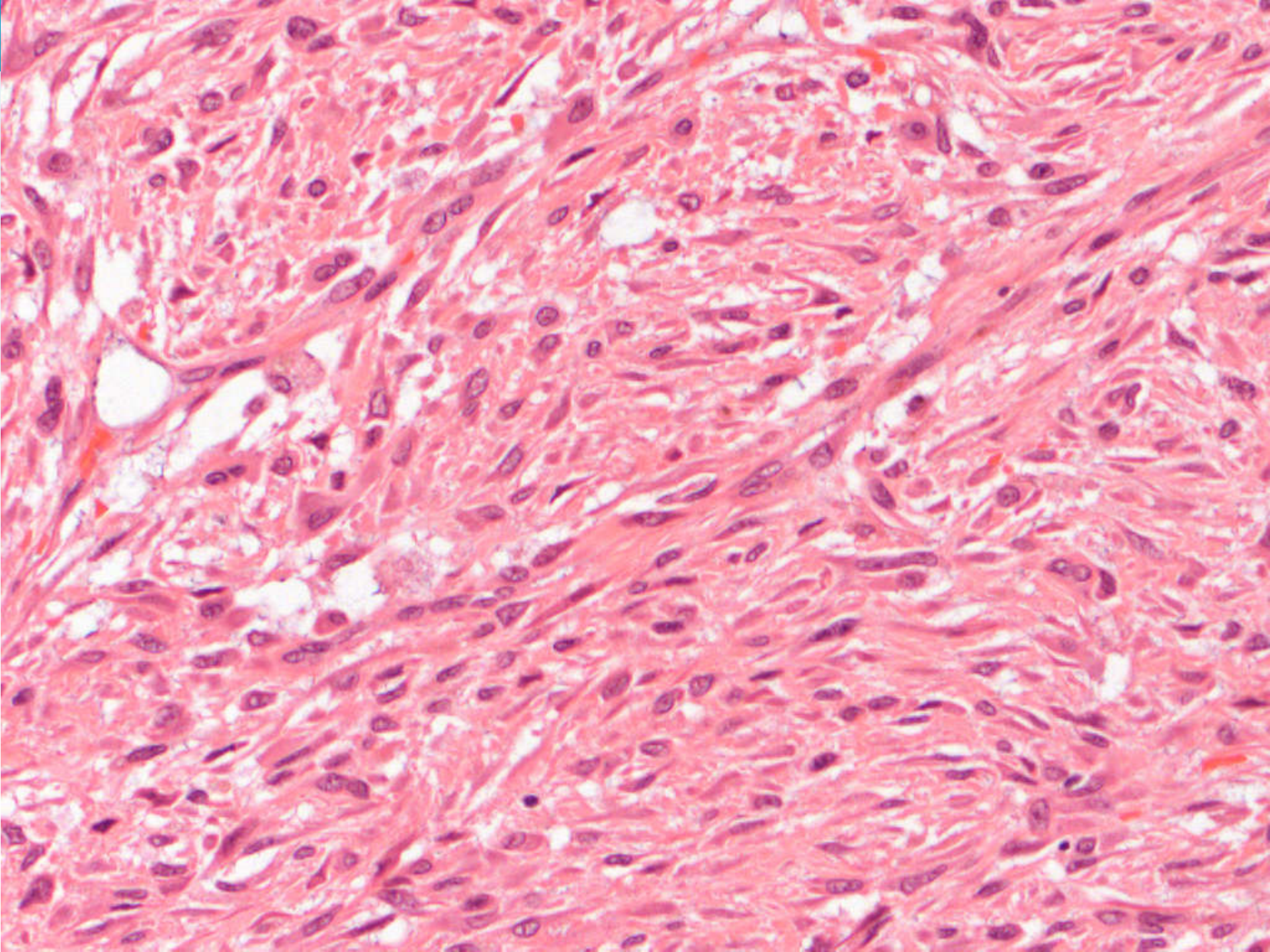
- Female, 20
- Soft tissue lesion [70mm maximum dimension] surrounded by muscle and sited in the vastus medialis.
- Patient also had pigmented nevus excised.











DX: Soft Tissue 16 Adv Path Course

Nodular fasciitis

- Prototypical pseudosarcomatous neoplasm, often misdiagnosed
- Generally self-limiting, subcutaneous, rapidly growing, infiltrative lesion of plump, uniform myofibroblastic cells
- Rarely >5cm, cranial or intravascular
- Mitoses may be plentiful but not atypical
- Usually SMA+
- Recently, USP6 fusion confirms neoplastic nature

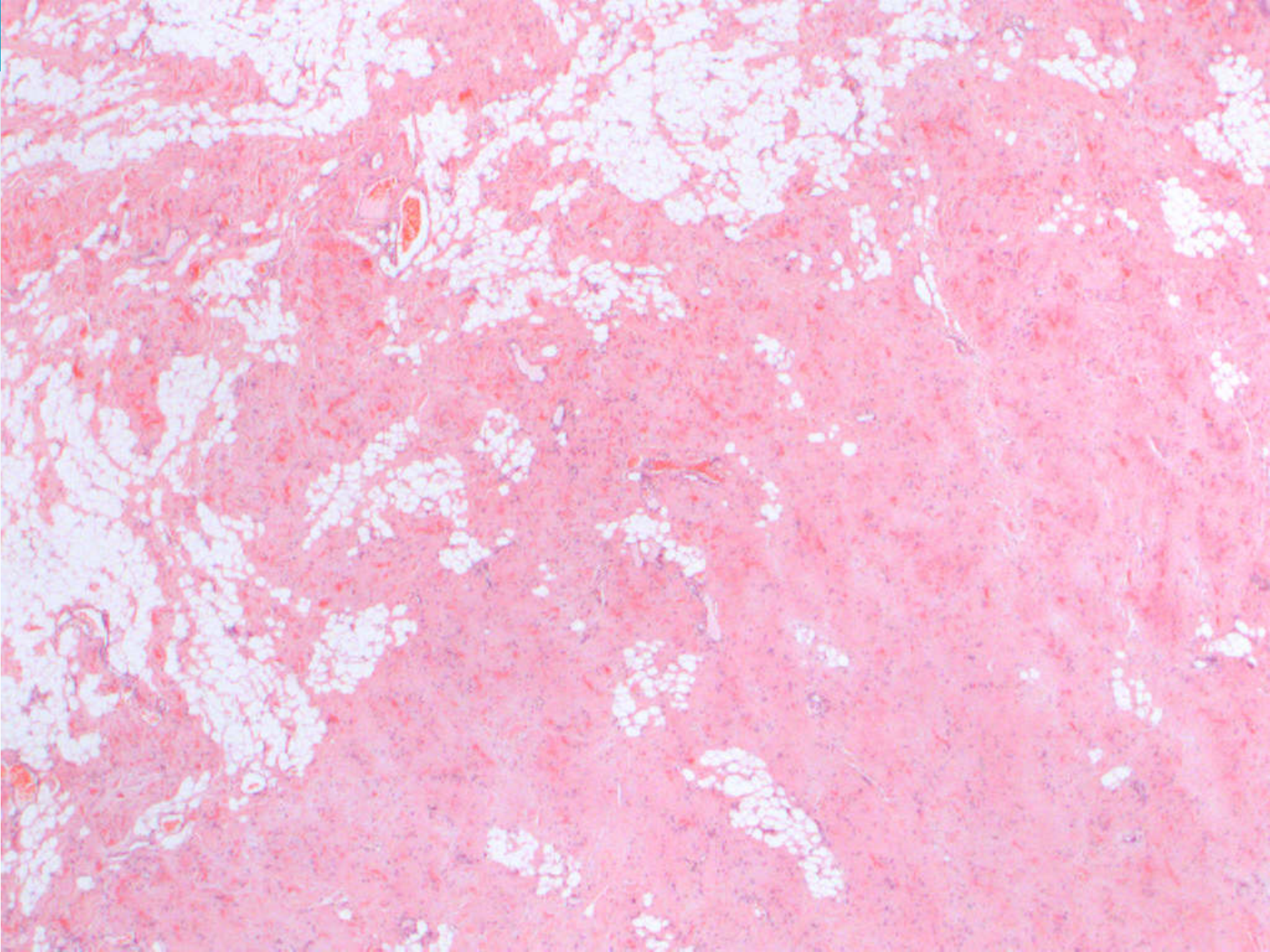
Osseous metaplasia = fasciitis ossificans

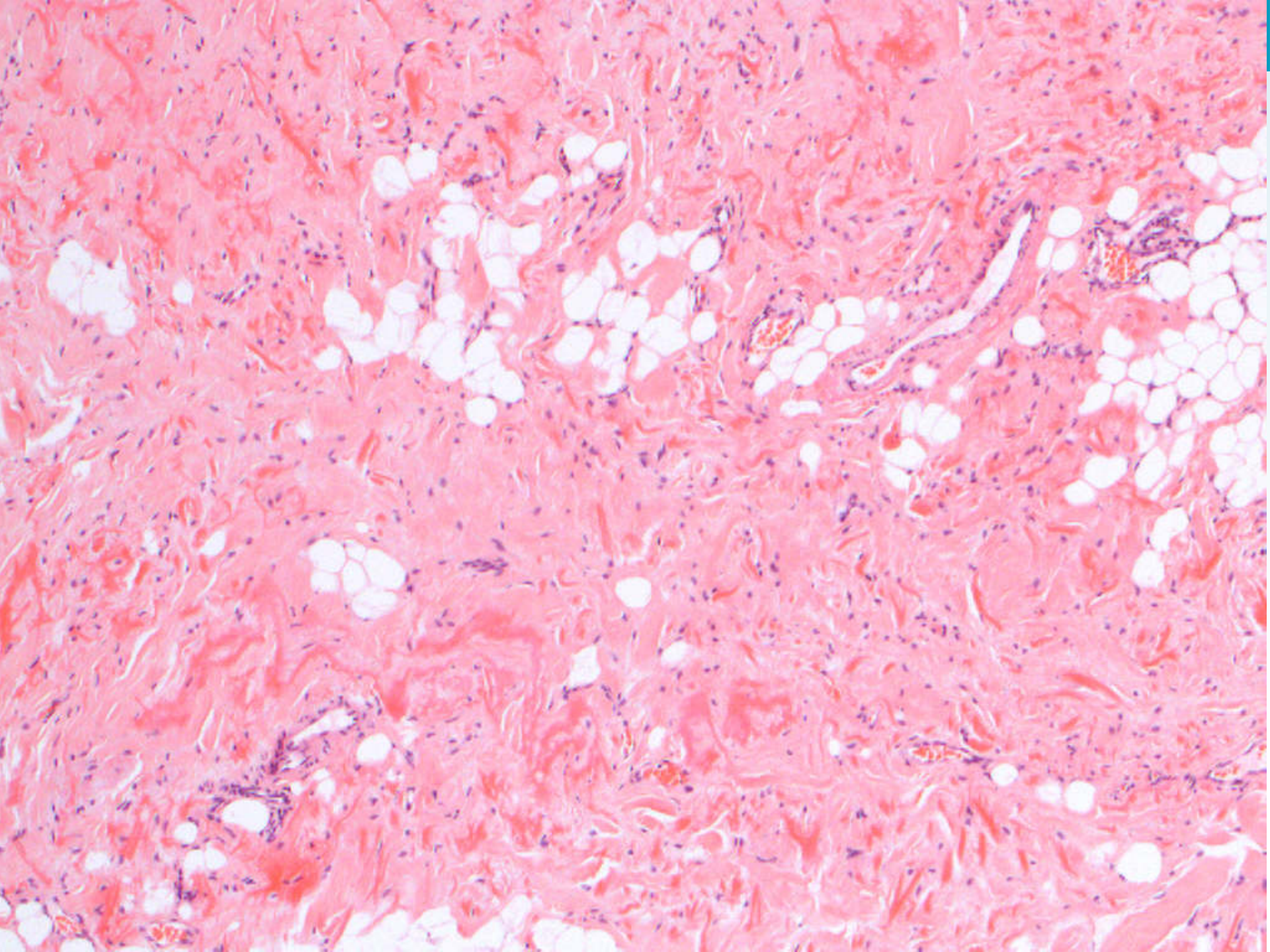
Ganglion cells = proliferative fasciitis/myositis

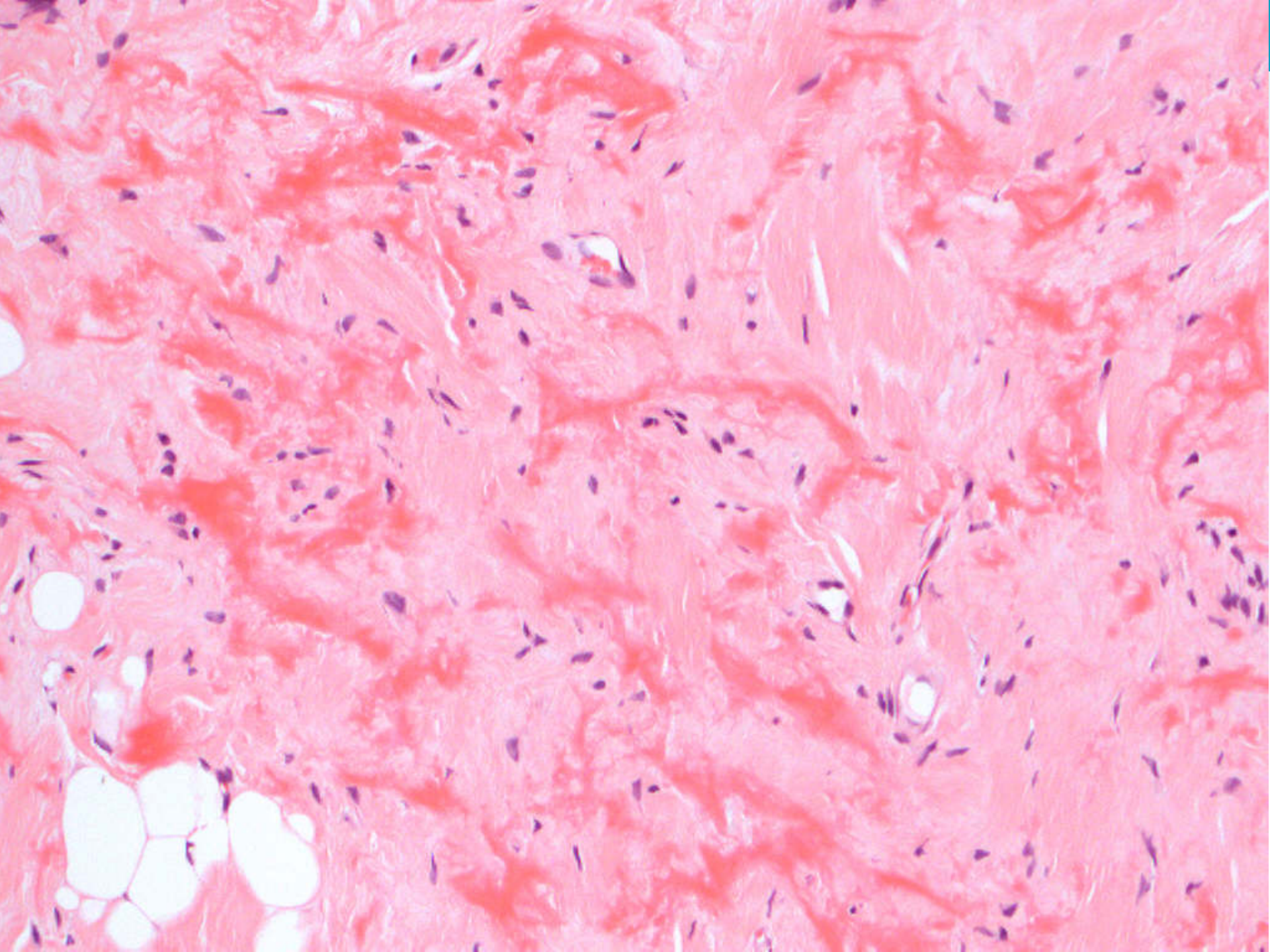
Zonal appearance with necrosis = ischaemic fasciitis

CLINICAL INFORMATION 17

- Female, 74
- Lump at base of each scapula.







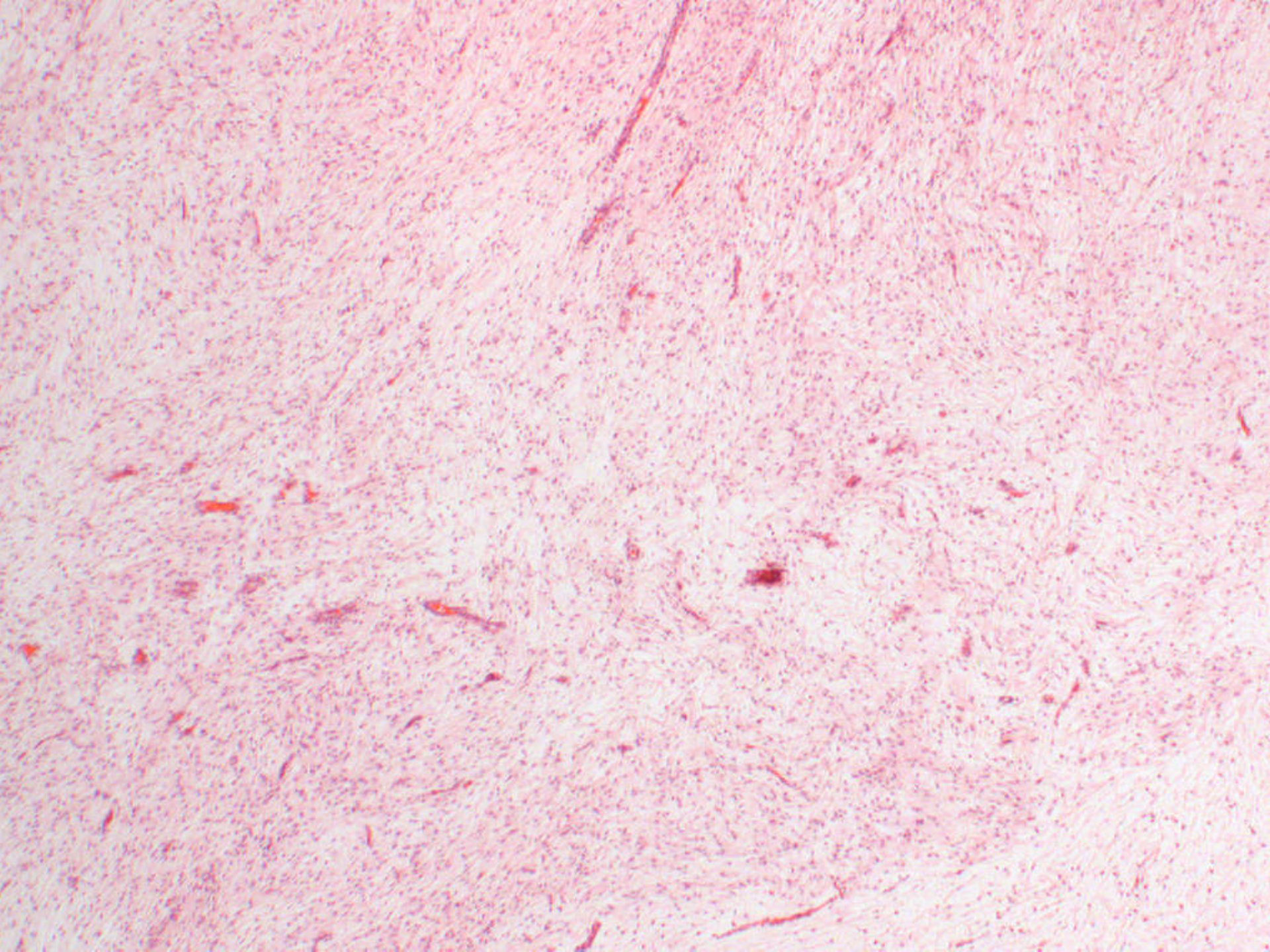
DX: Soft Tissue 17 Adv Path Course

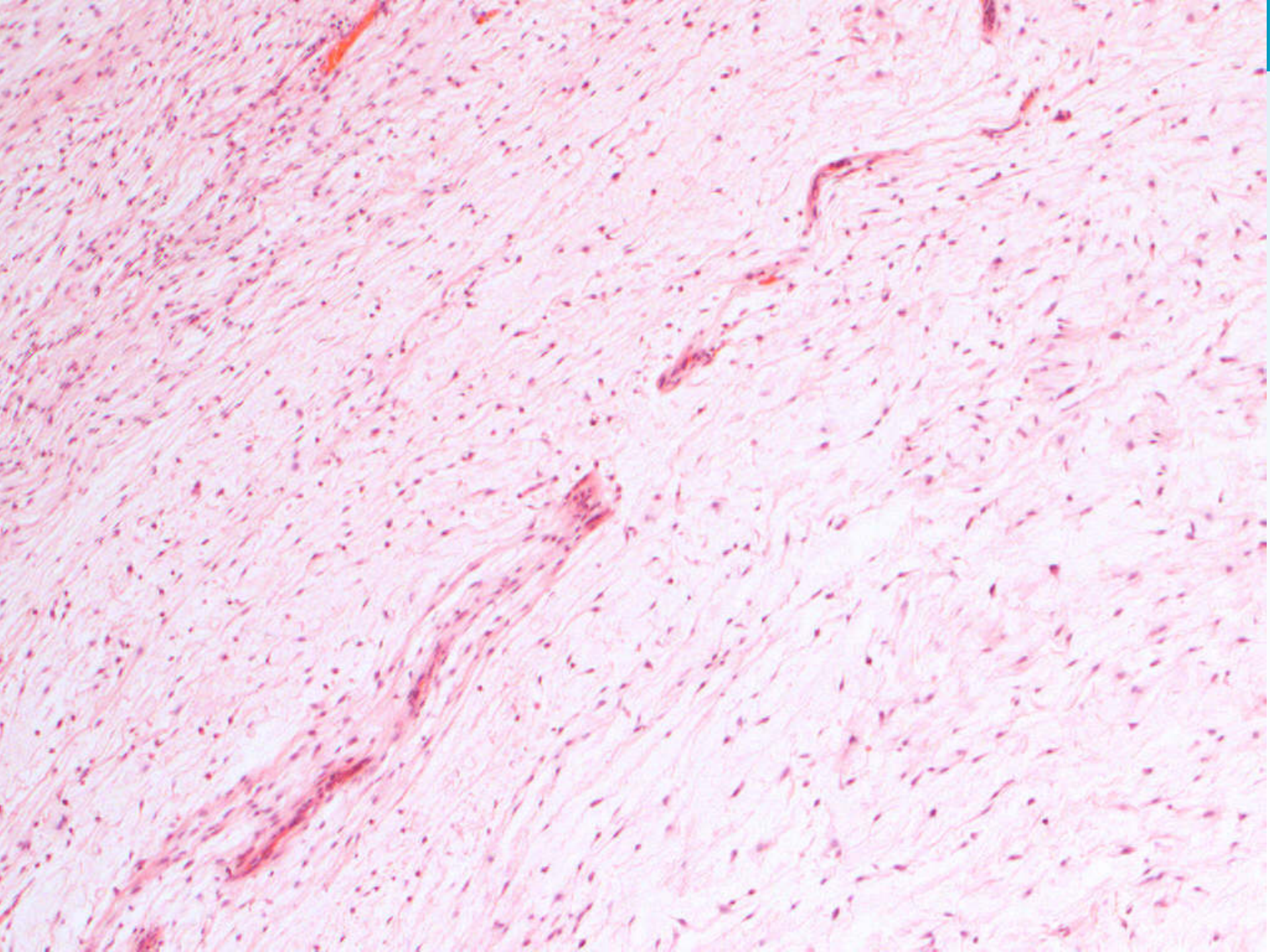
Elastofibroma

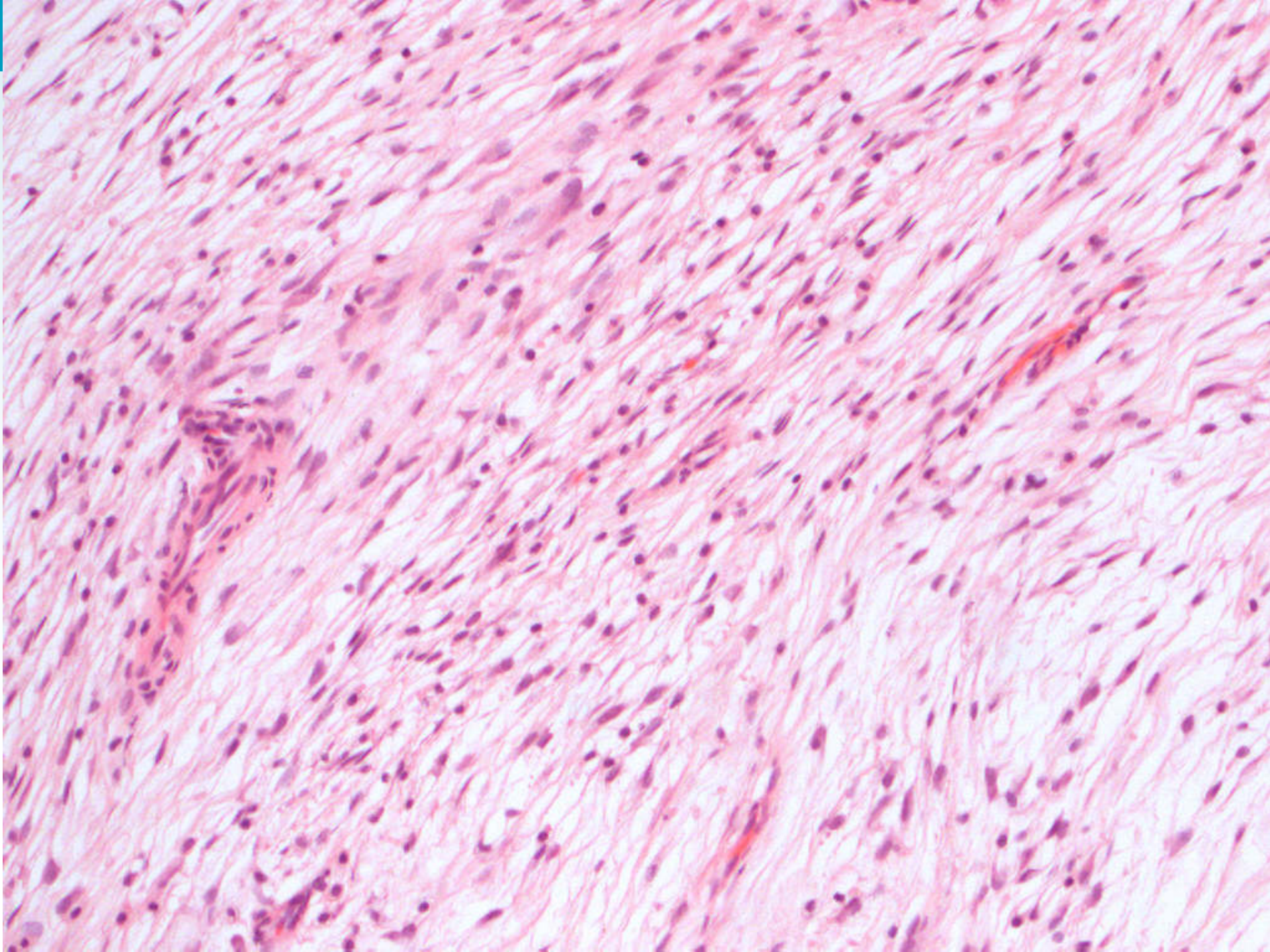
- Ill-defined proliferation of elasto-fibrous tissue
- Myxoid change common
- May be unilateral, bilateral or multiple
- Rarely occurs in extracapsular locations

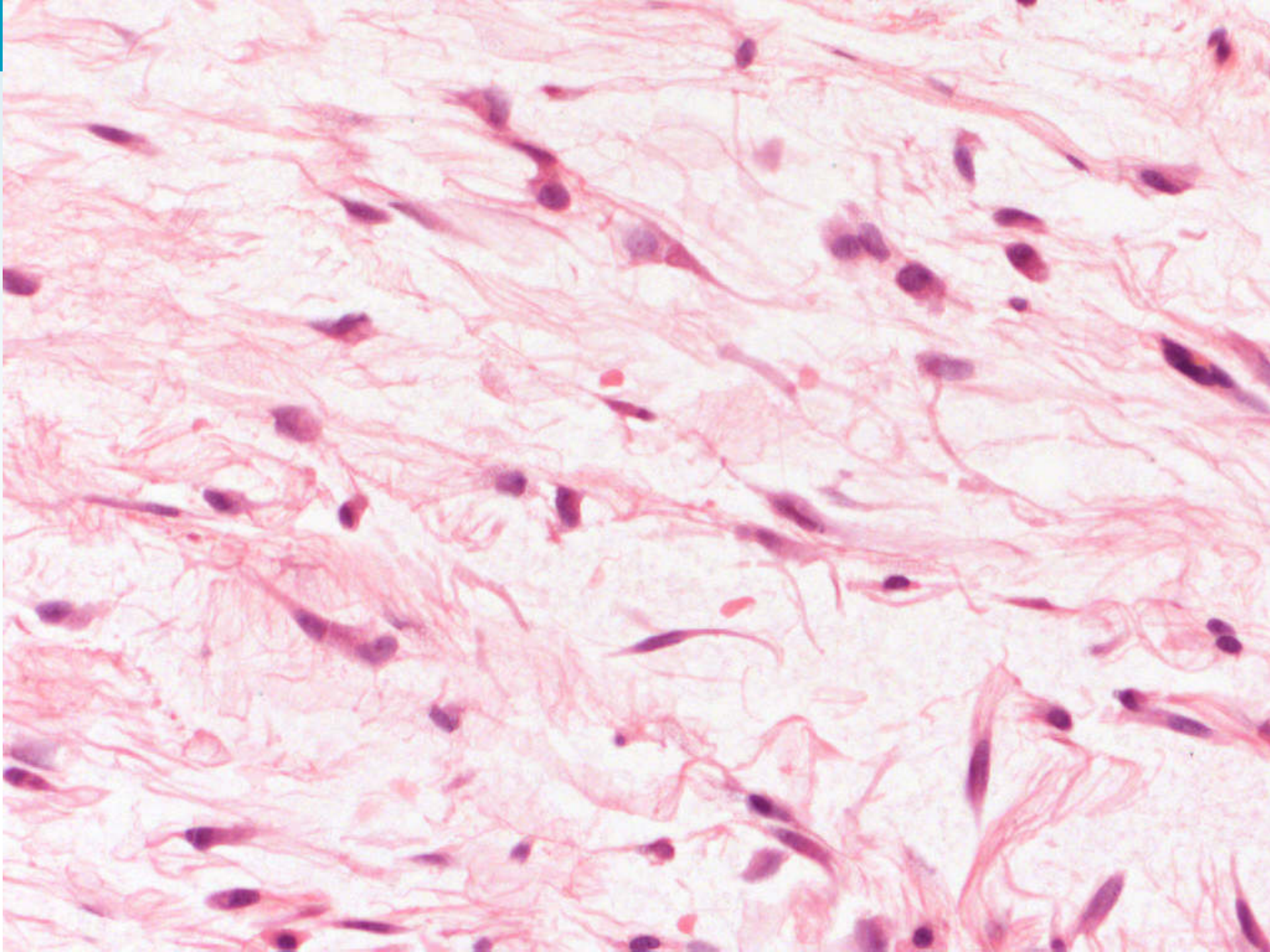
CLINICAL INFORMATION 18

- Female, 59
- Intramuscular soft tissue lesion, left biceps [60x30x35mm].









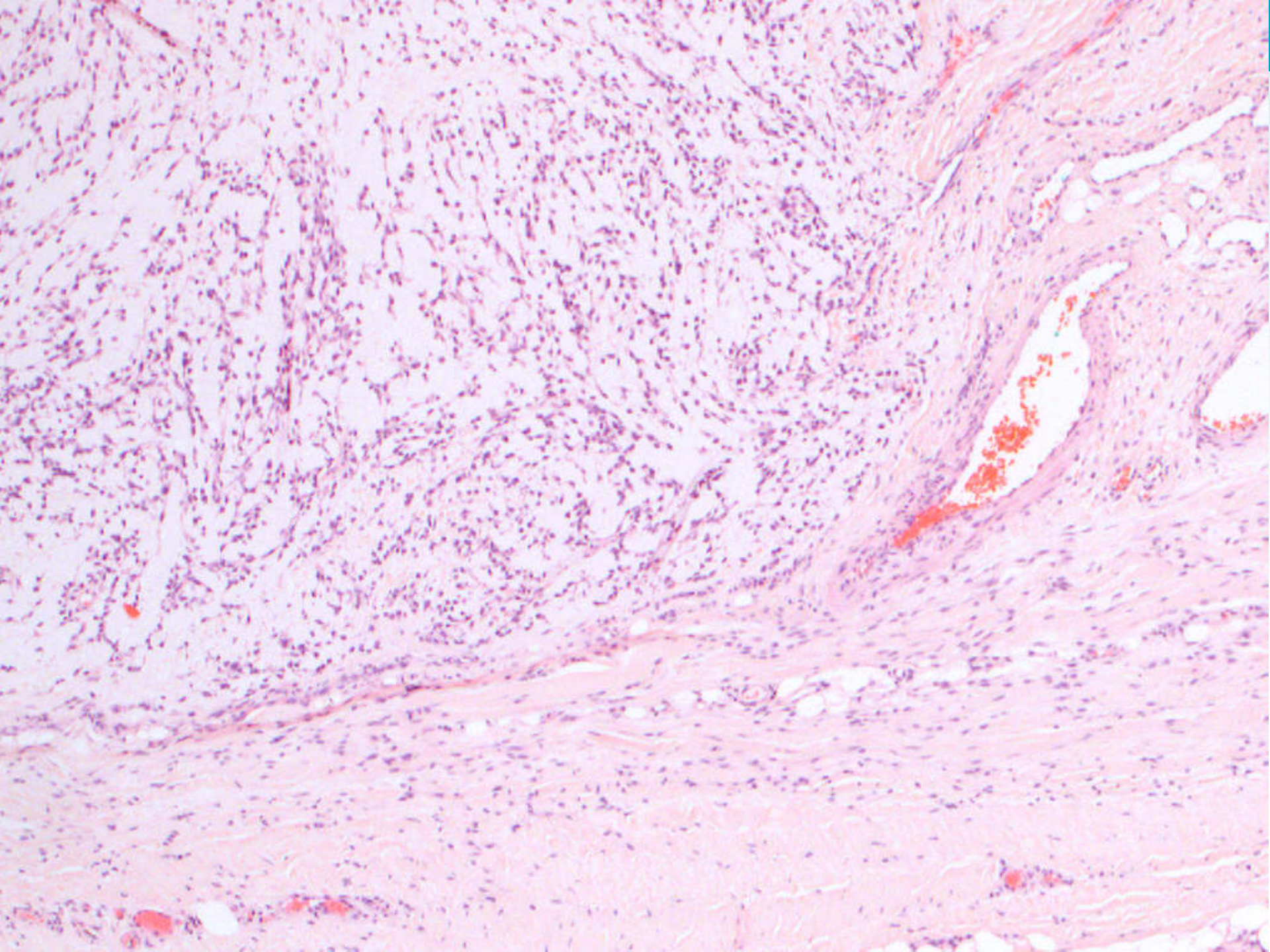
DX: Soft Tissue 18 Adv Path Course

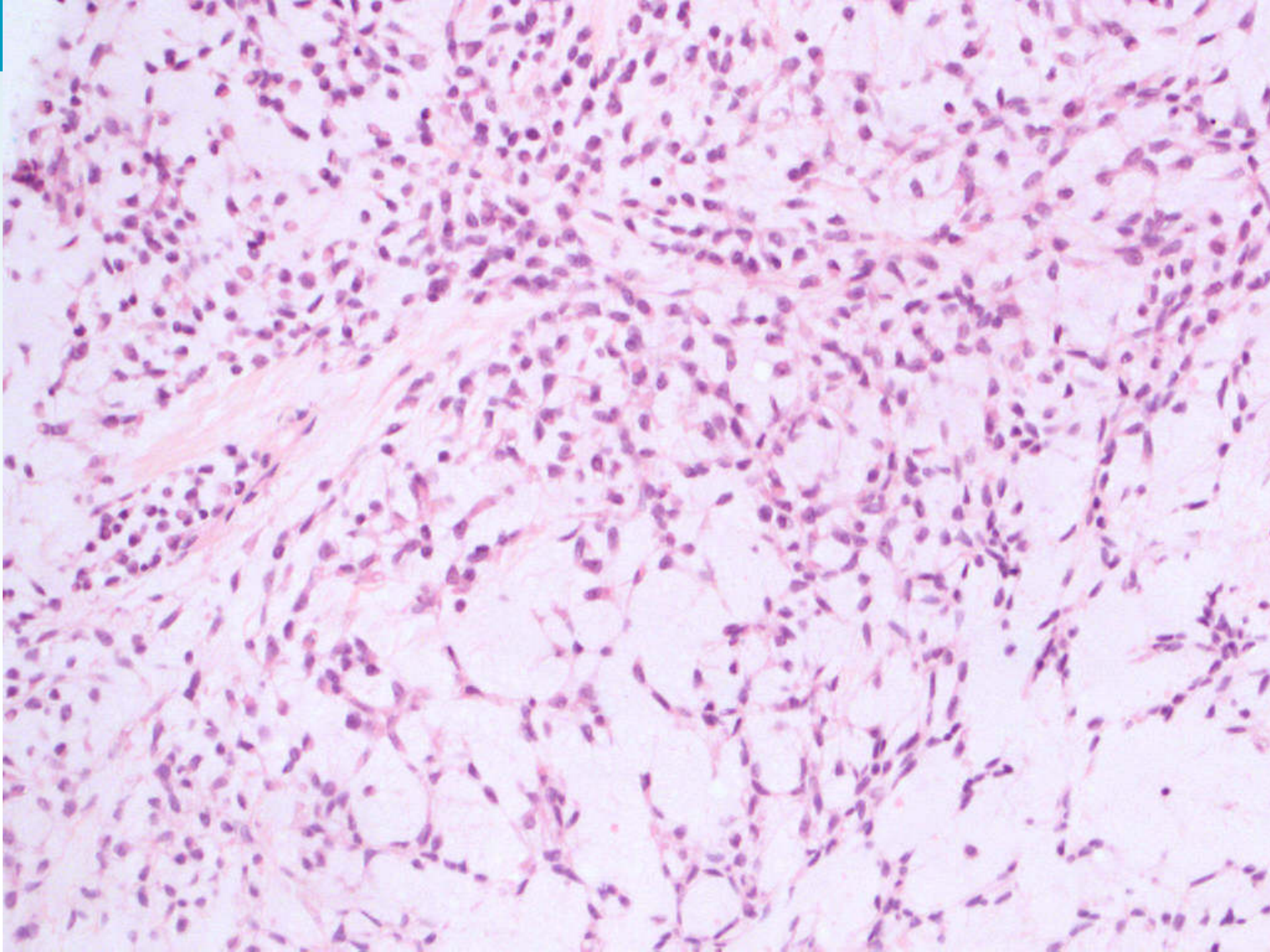
Intramuscular myxoma

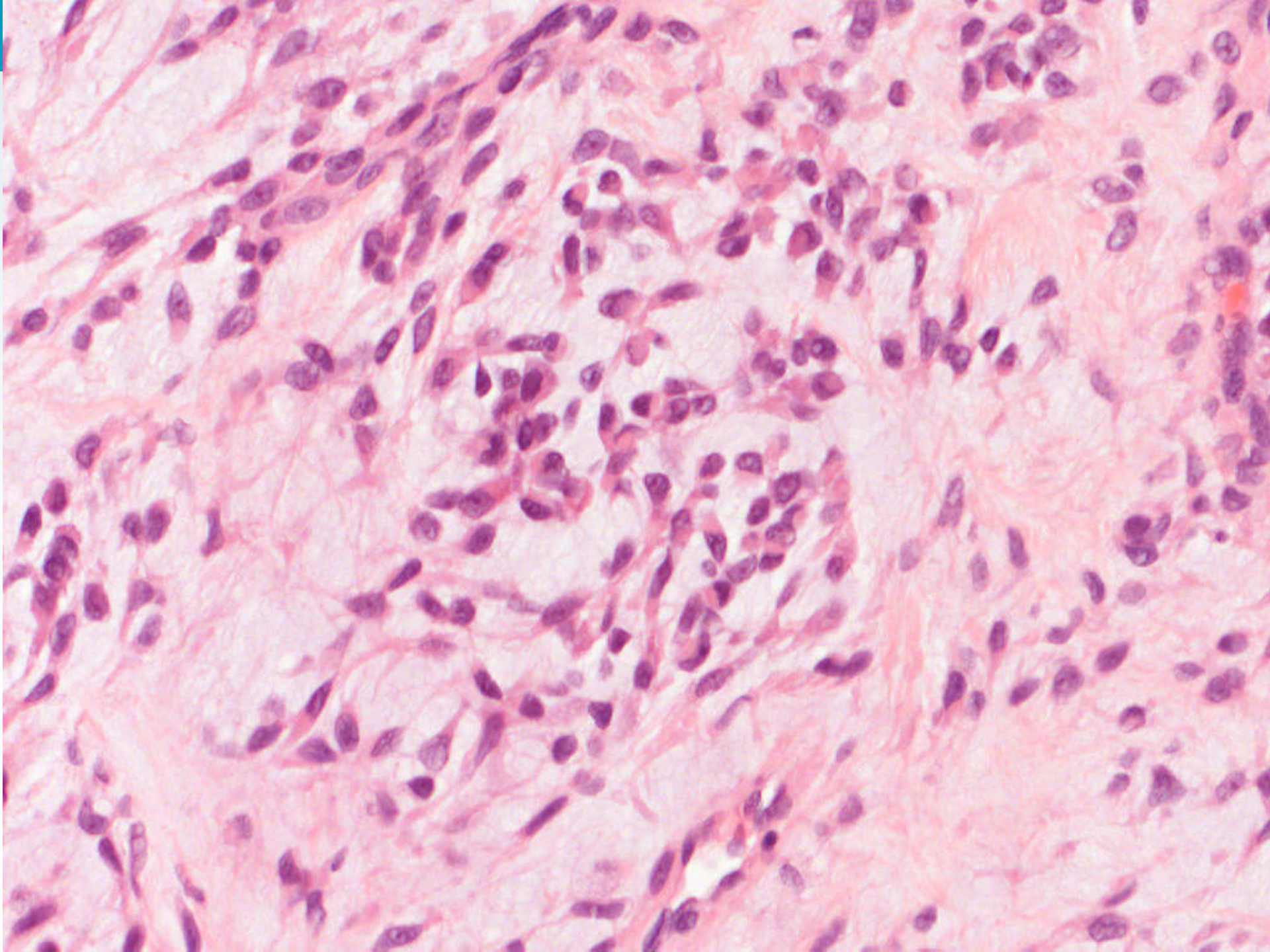
- Gelatinous, paucicellular tumour of bland spindle cells in myxoid stroma
- Fibrous dysplasia + intramuscular myxoma(ta) = Mazabraud
- May show cystic change and cellular foci, but atypia, necrosis and mitoses are lacking
- Don’t miss low-grade myxofibrosarcoma, particularly in a limited sample. Always correlate with imaging studies.

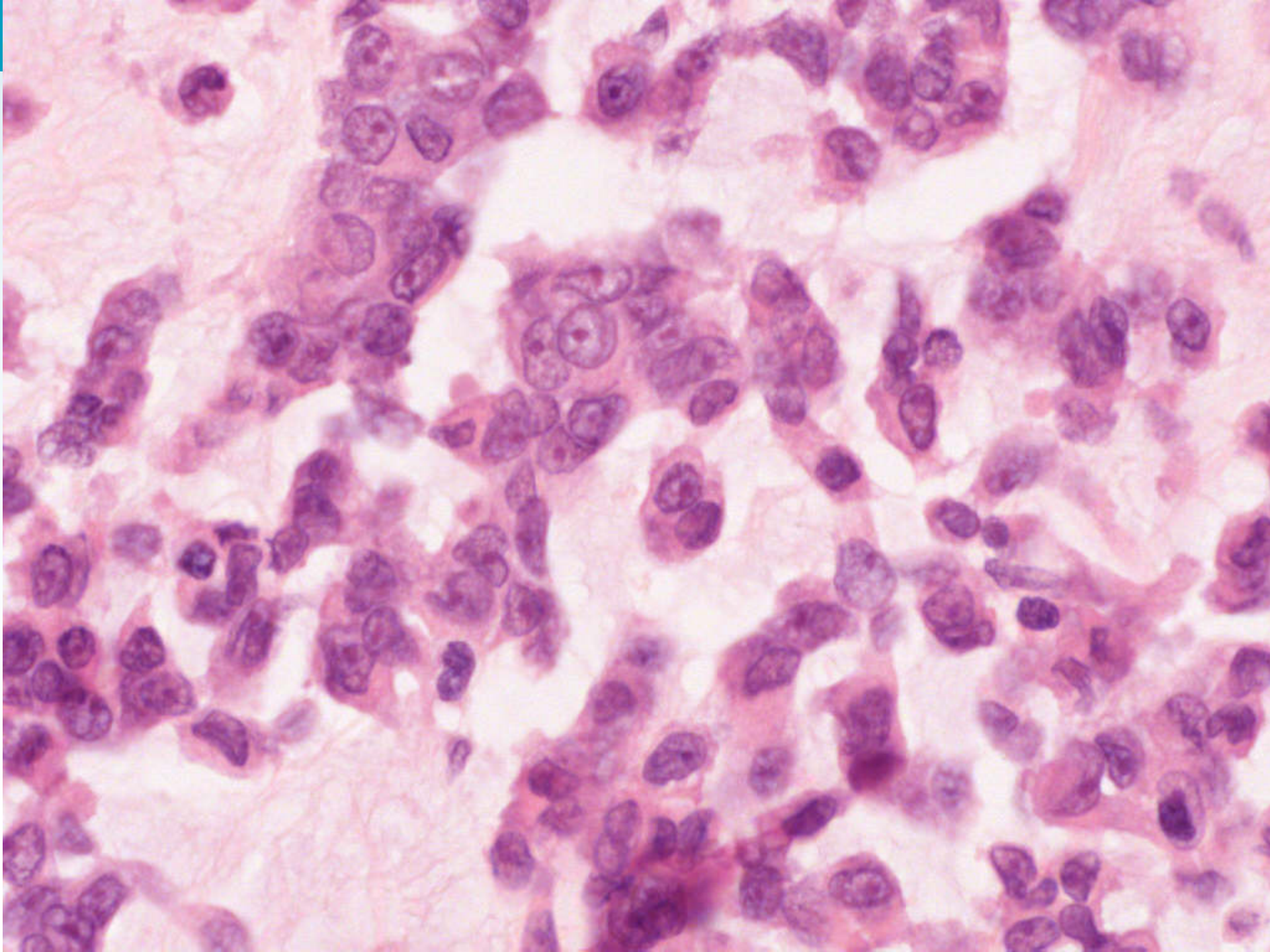
CLINICAL INFORMATION 19

- Female, 43
- Resection of soft tissue mass from right thigh [70x60x40mm].









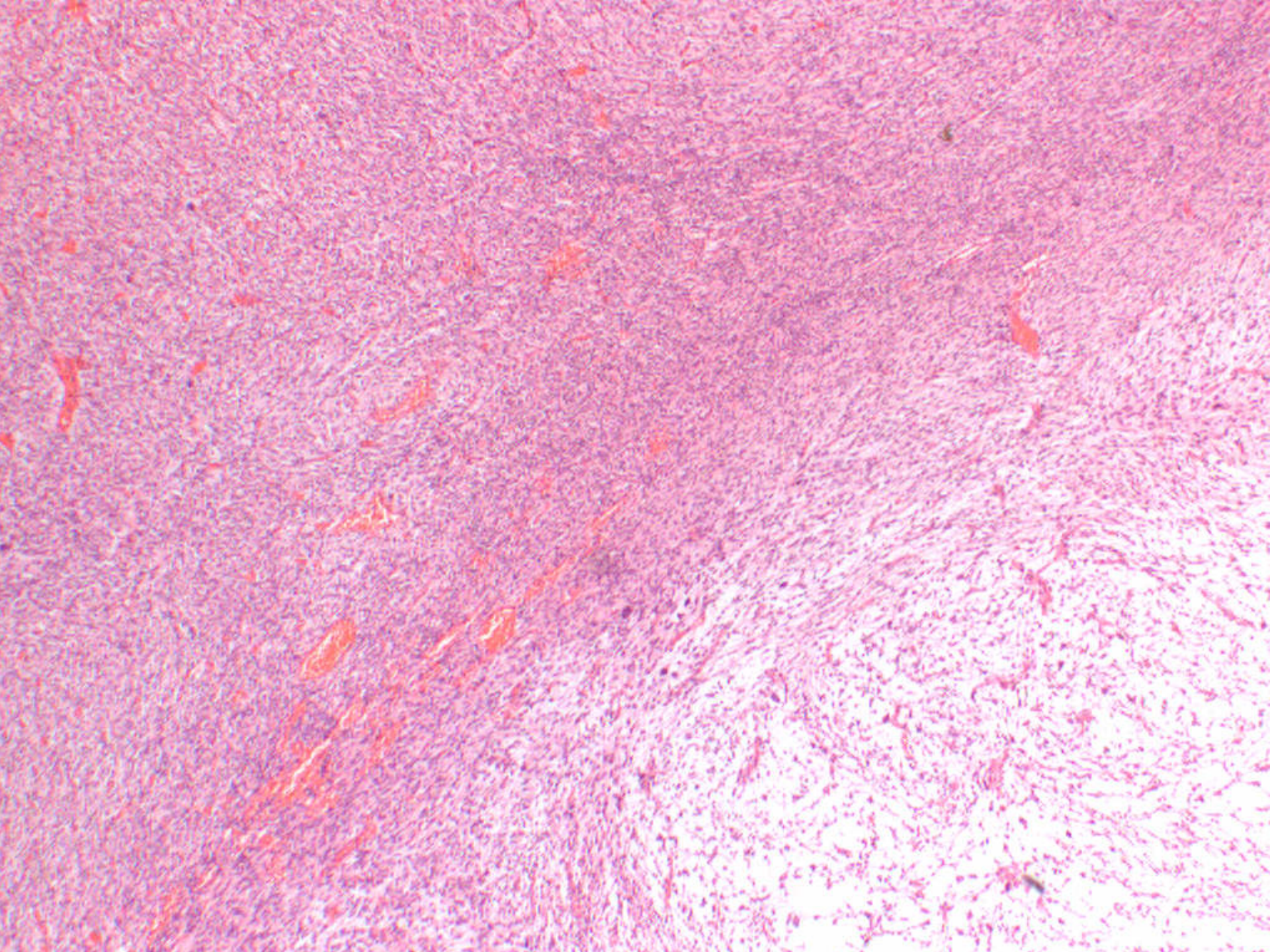
DX: Soft Tissue 19 Adv Path Course

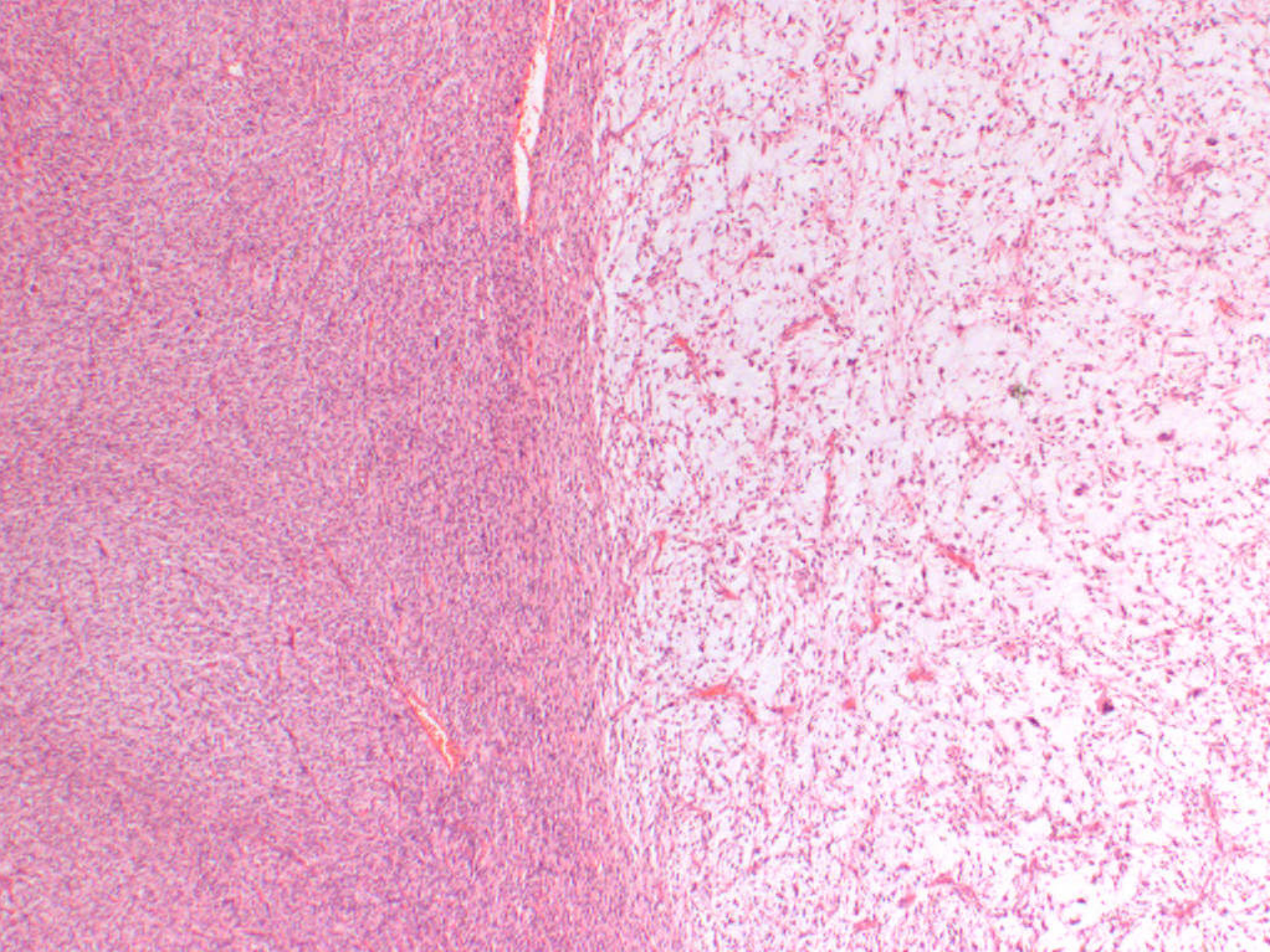
Extraskeletal myxoid chondrosarcoma

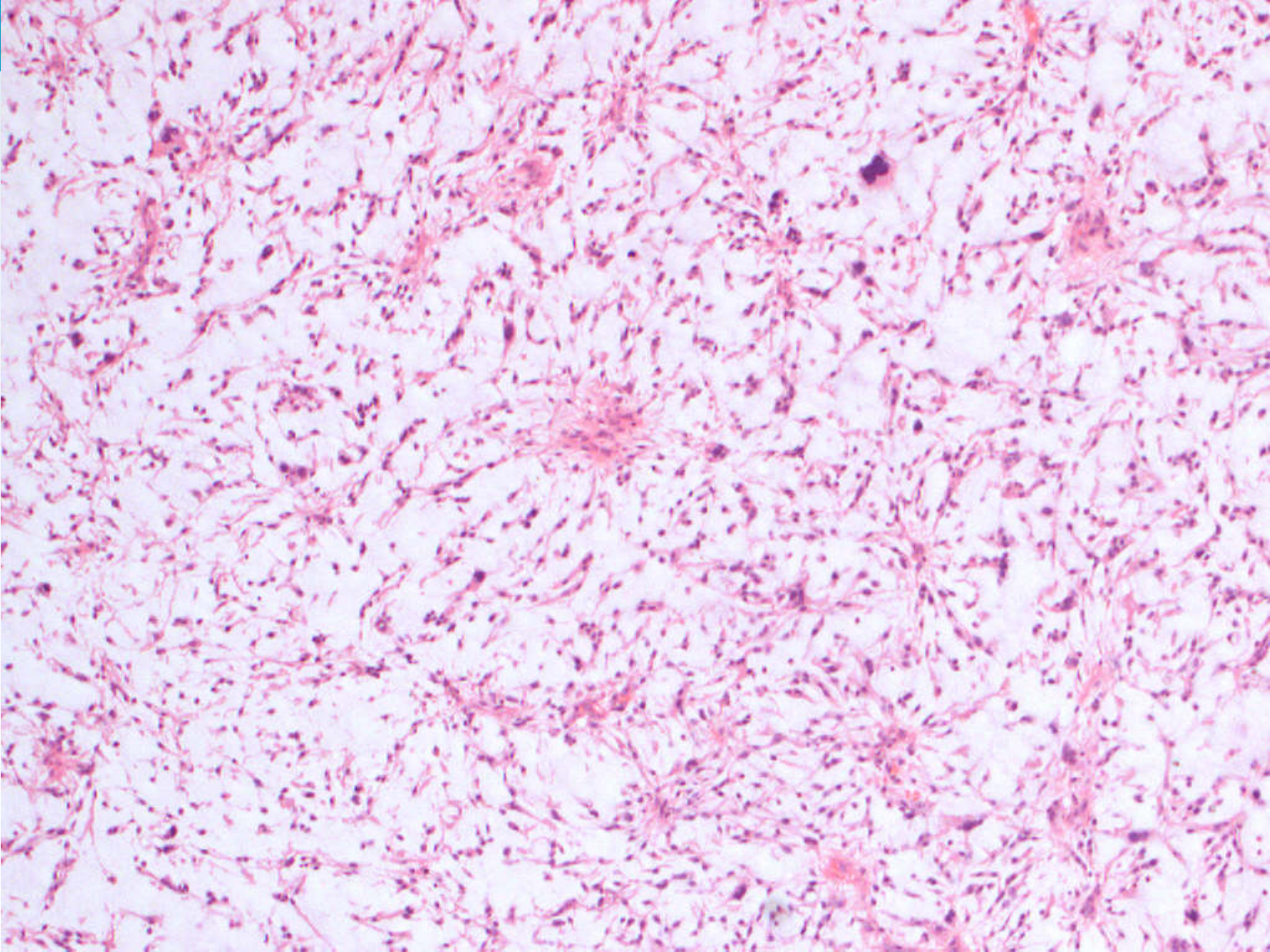
- Malignant mesenchymal tumour of uncertain differentiation
- Despite name, no convincing evidence of cartilagenous differentiation
- Only rarely seen in children or adolescents
- Differential diagnosis is myoepithelioma/myoepithelial carcinoma
- The tumour is characterised by a recurrent *NR4A3* rearrangement

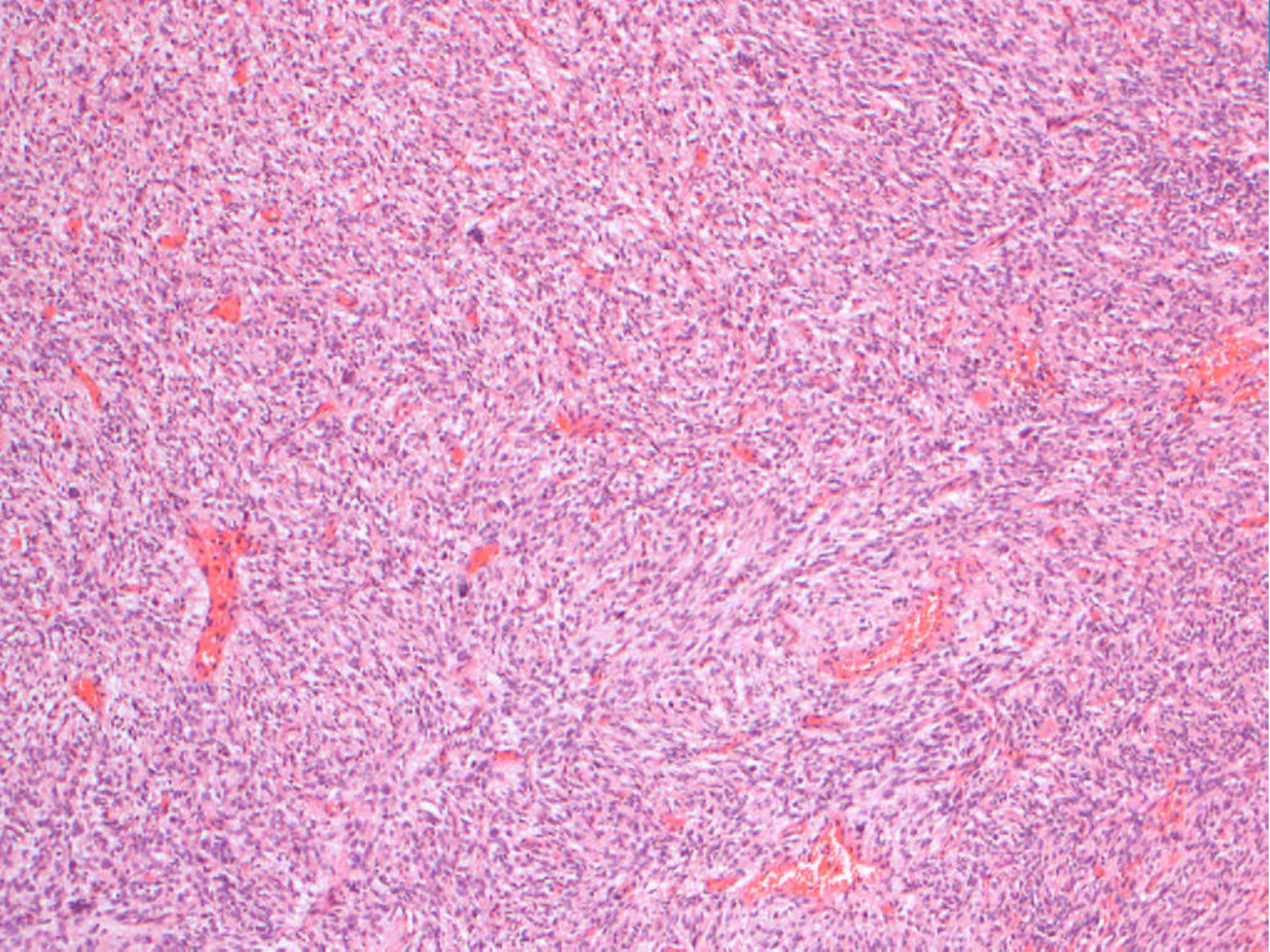
CLINICAL INFORMATION 20

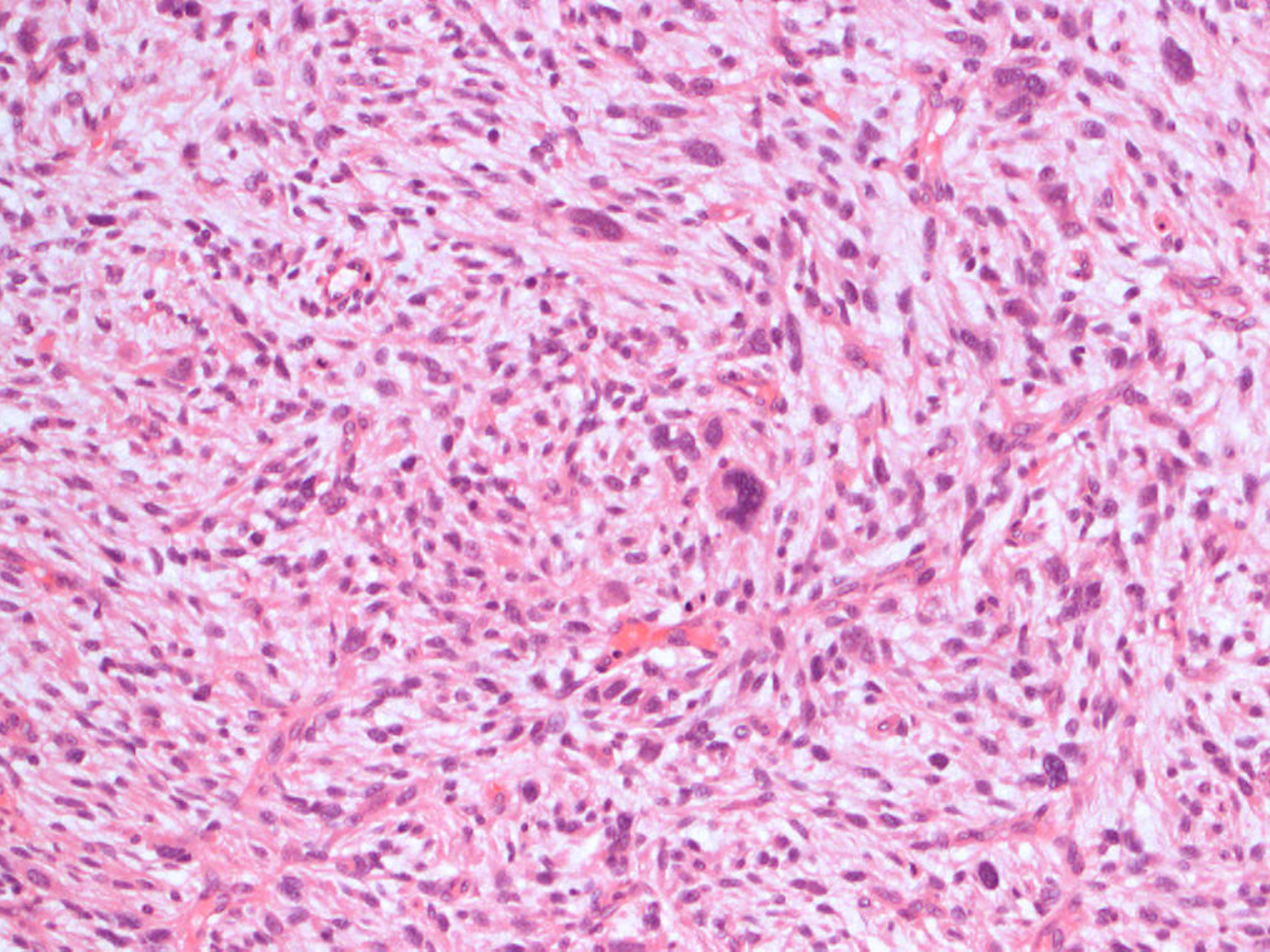
- Male, 76
- Subcutaneous recurrent mxyoid lesion in paraspinal region.

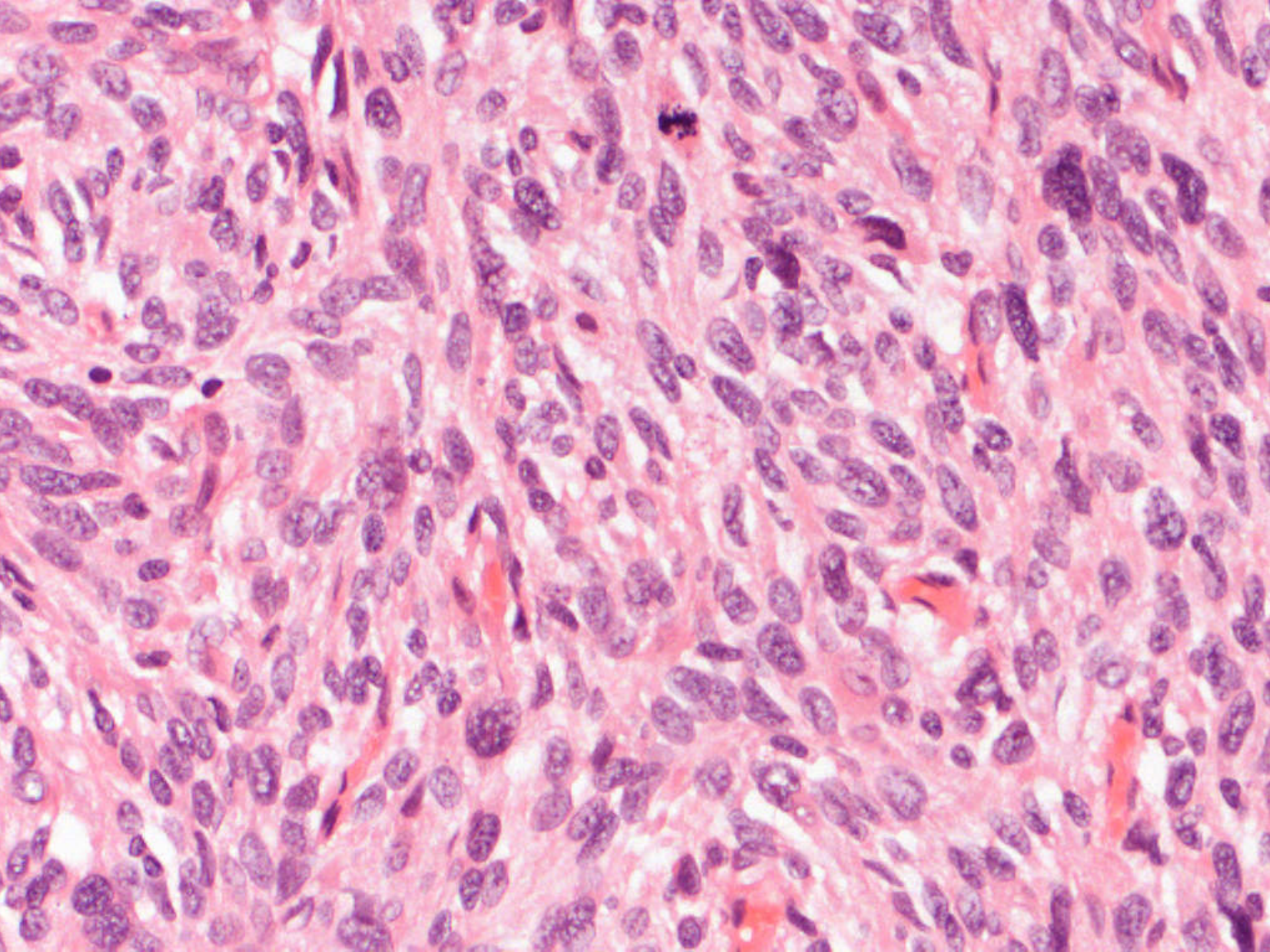












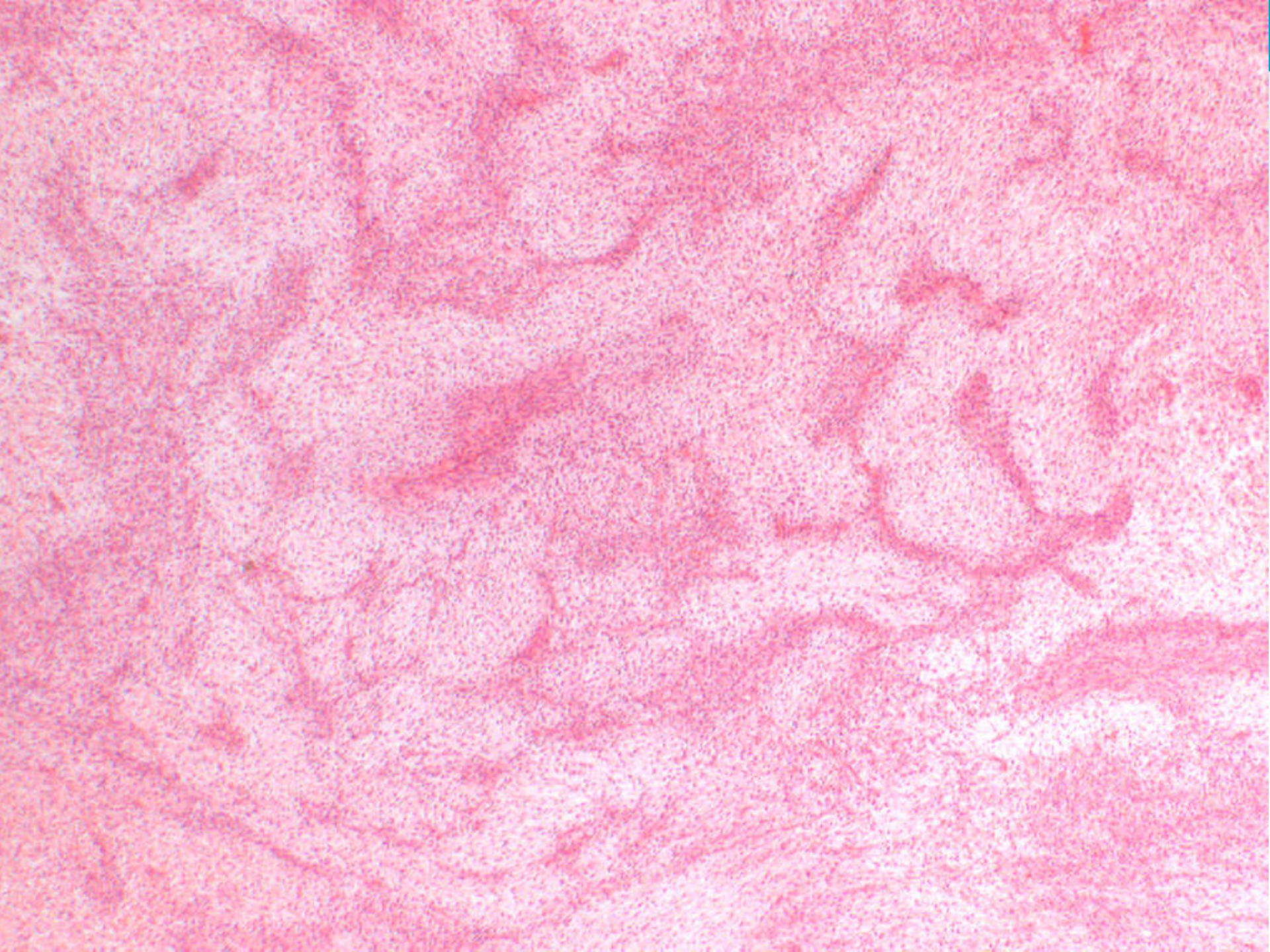
DX: Soft Tissue 20 Adv Path Course

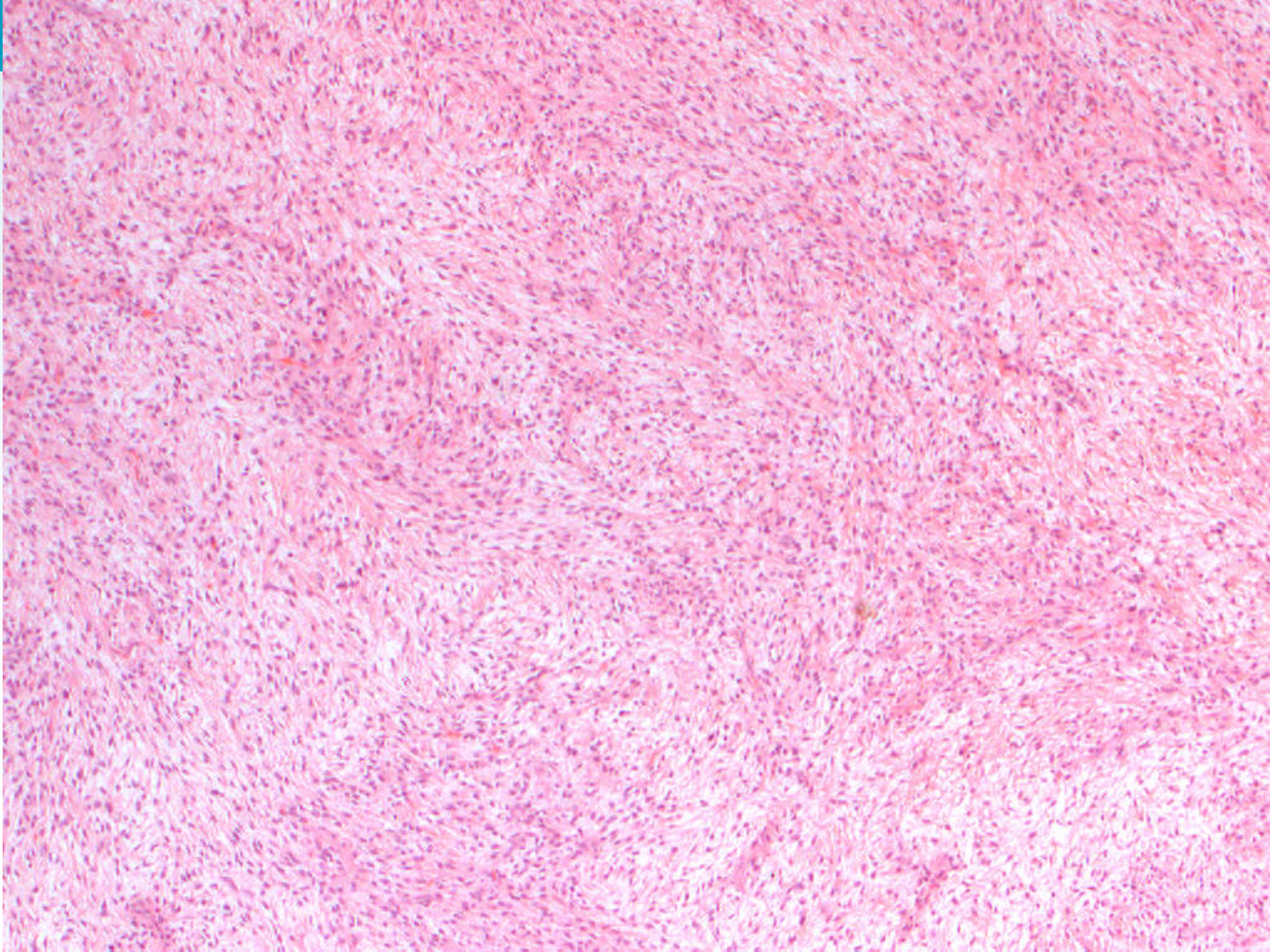
Myxofibrosarcoma

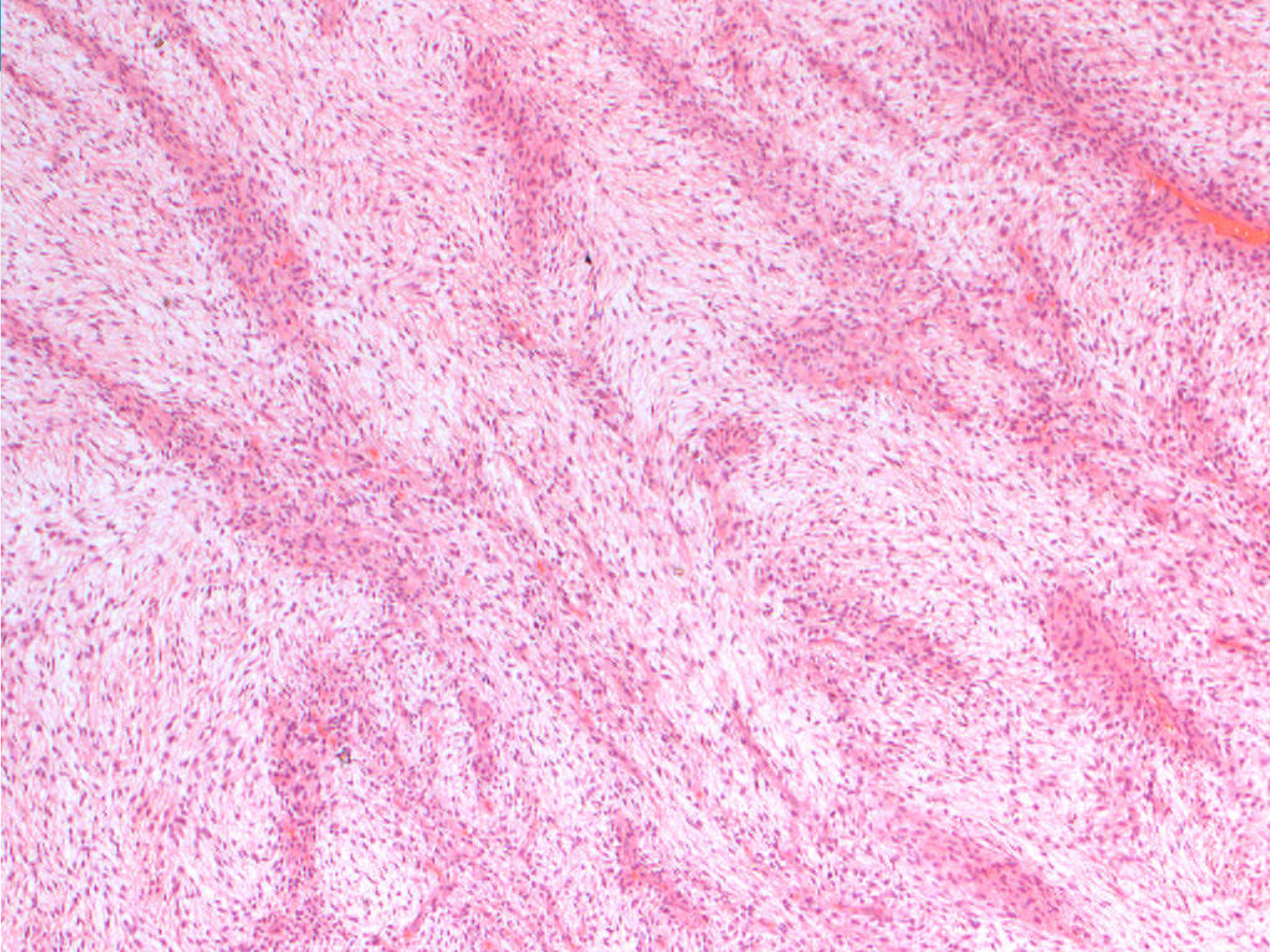
- One of the most common sarcomas of the elderly
- Comprises a spectrum of malignant fibroblastic neoplasms (low to high grade) with variably prominent myxoid stroma, cellular pleomorphism and curvilinear vessels
- May show patchy staining for SMA, others generally negative
- Beware of the rare epithelioid variant which may cause diagnostic confusion

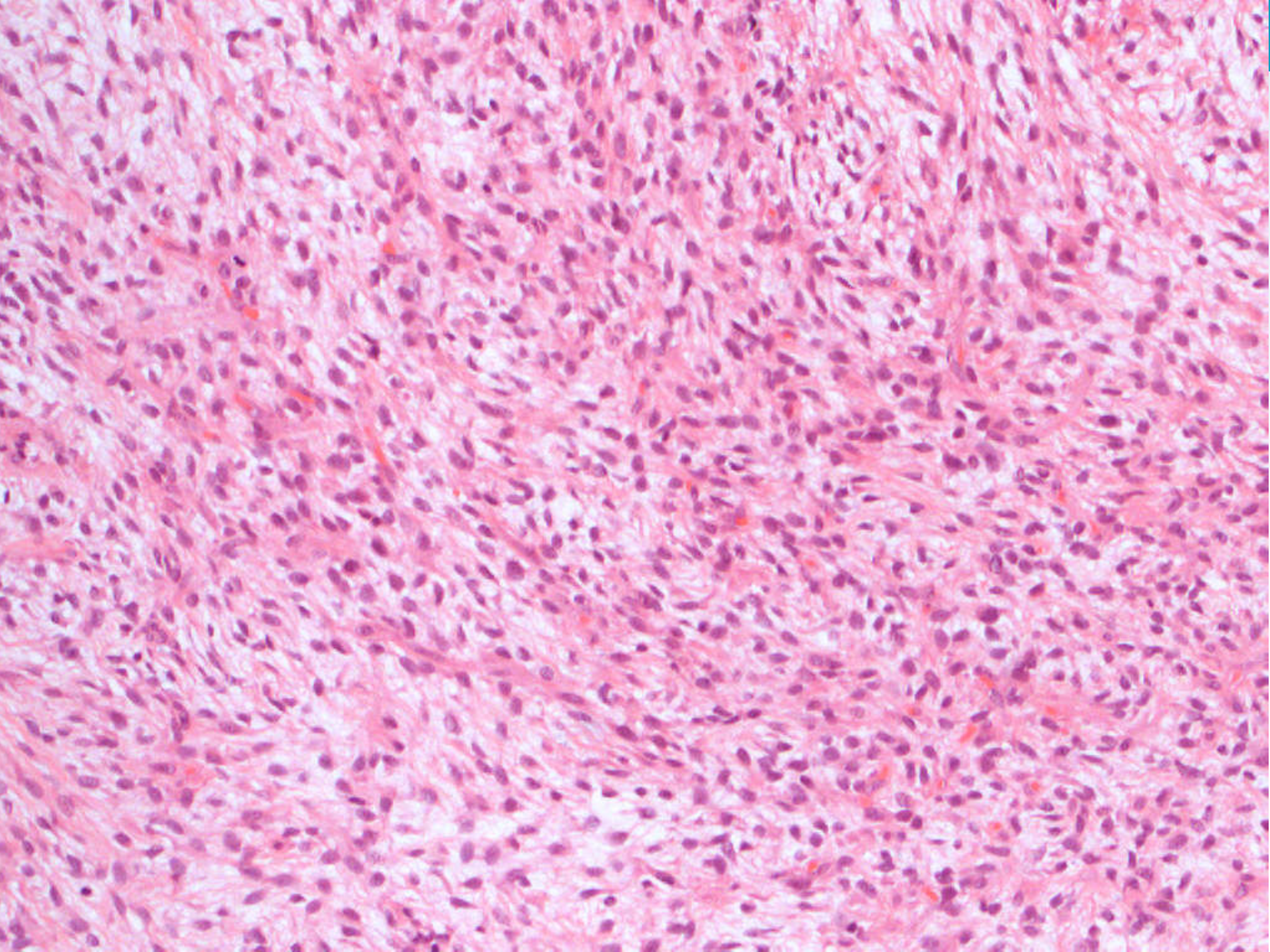
CLINICAL INFORMATION 21

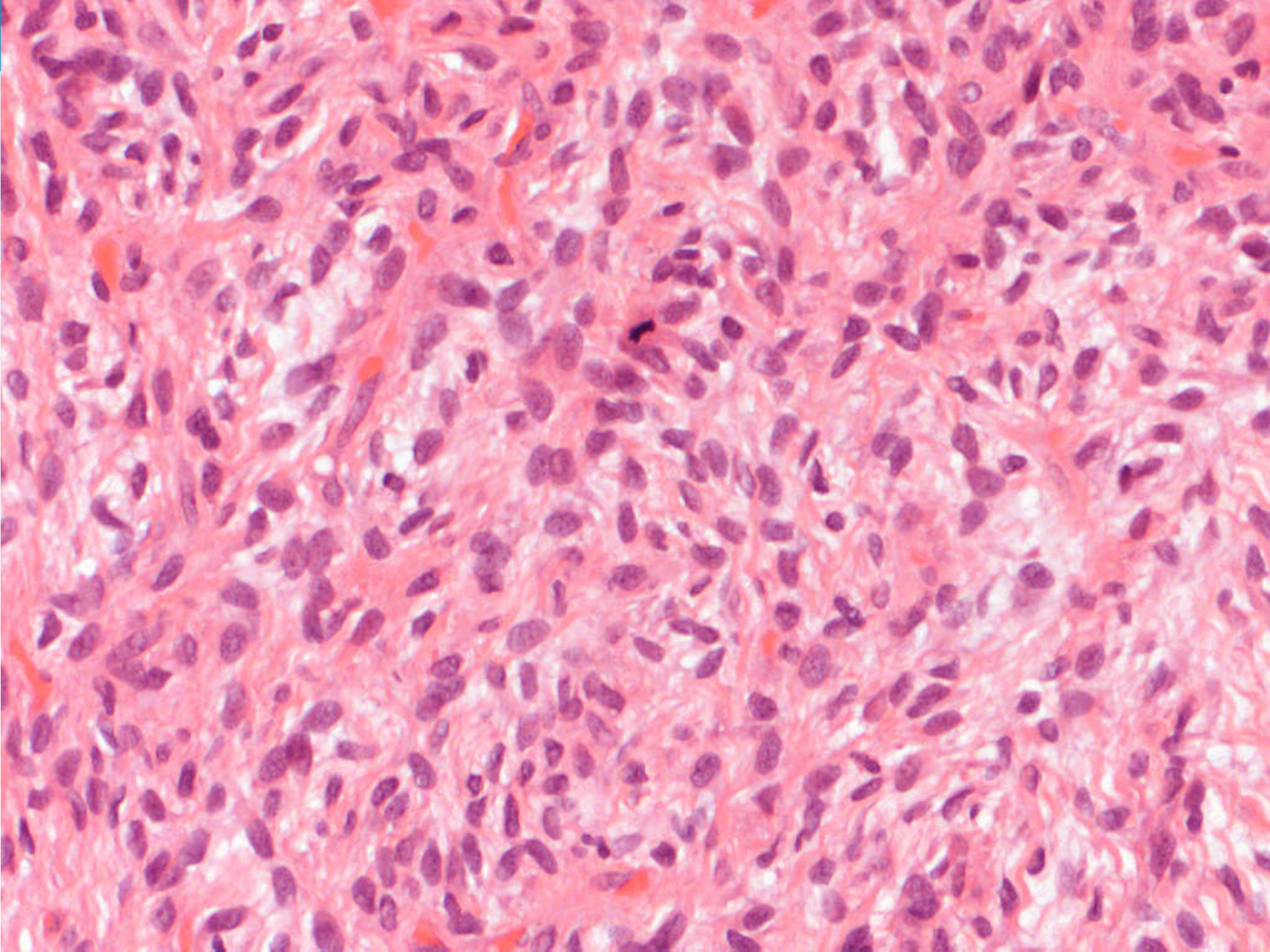
- Male, 9
- Soft tissue subcutaneous mass [5cm maximum dimension].

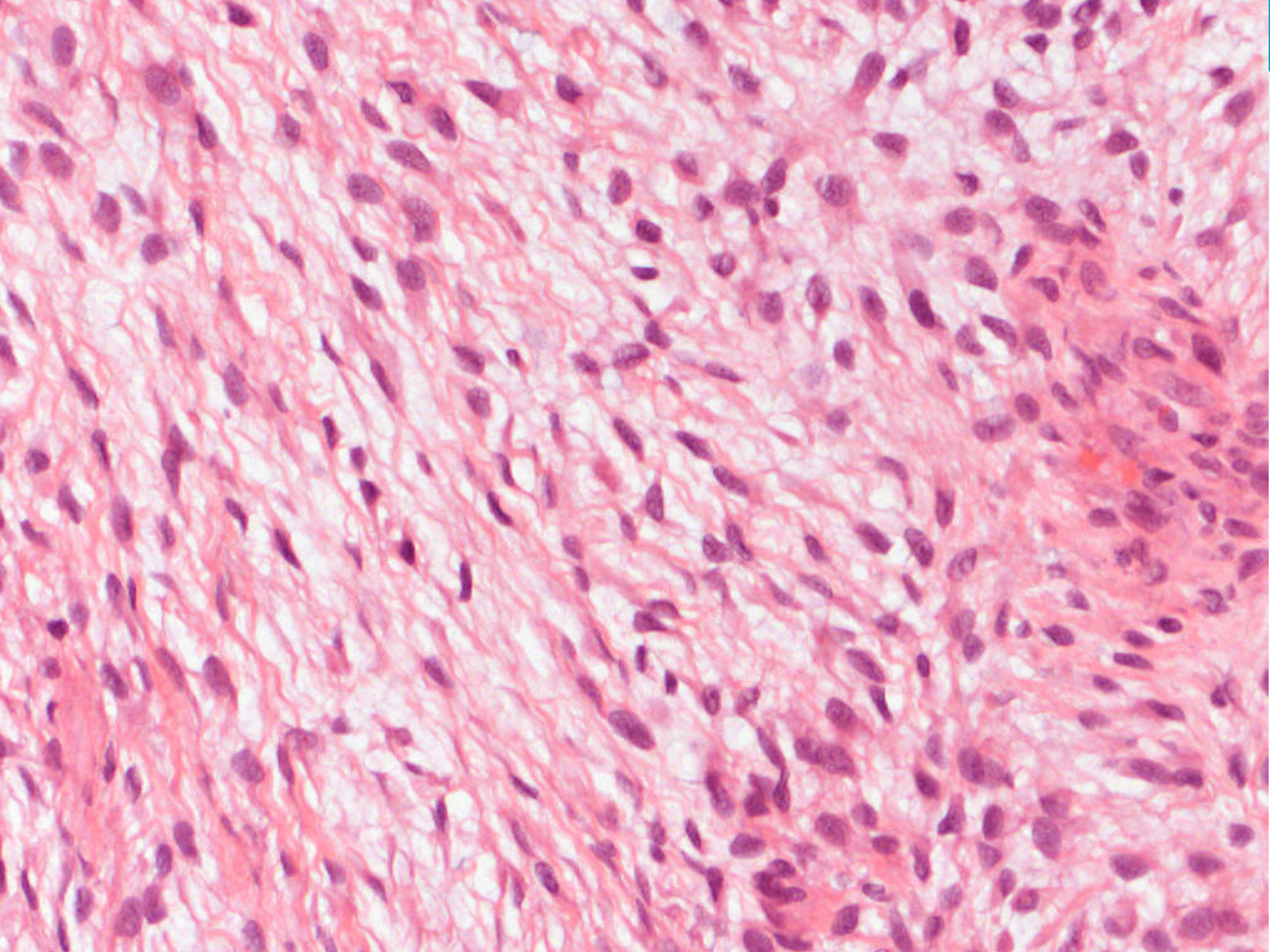












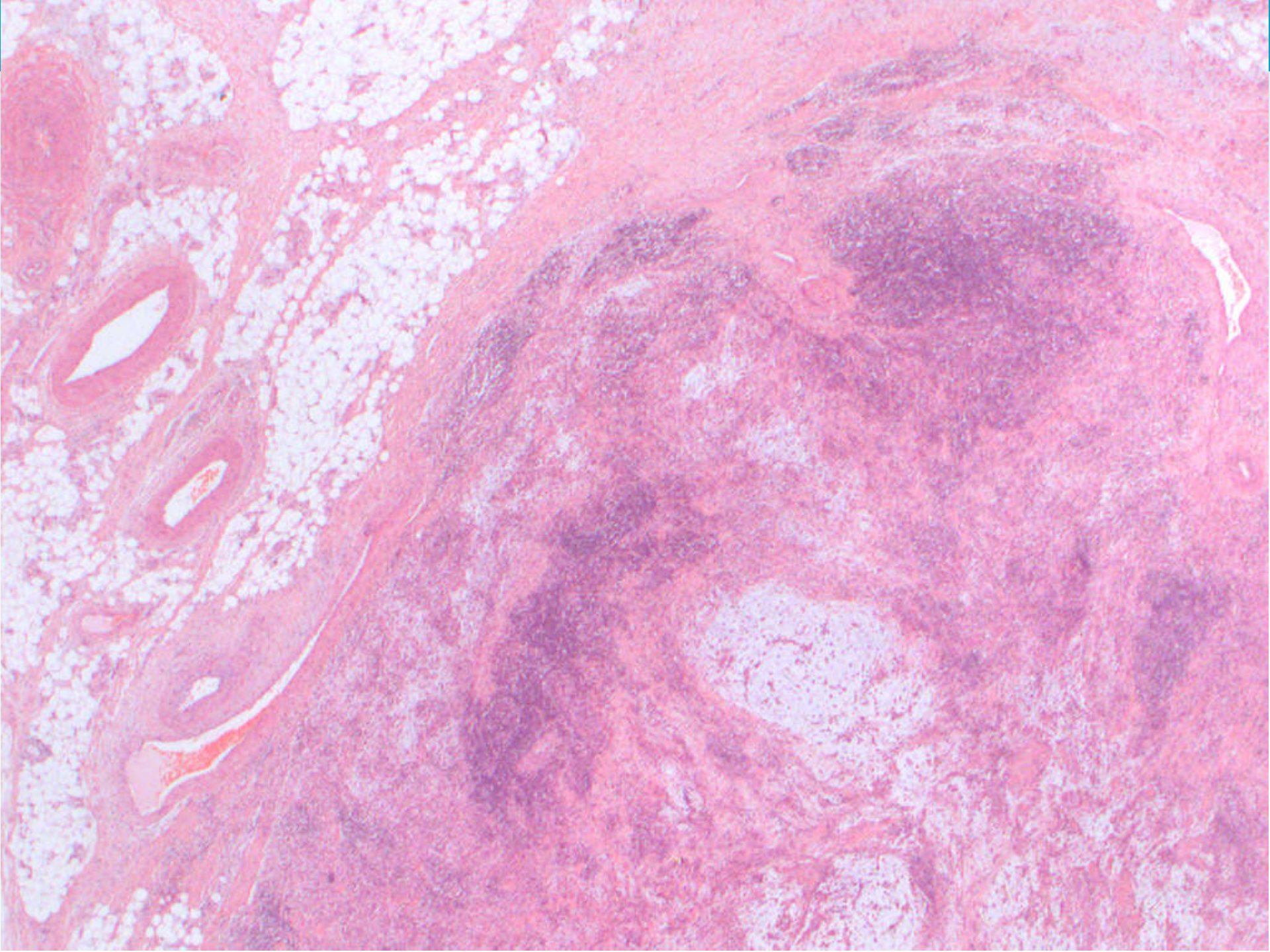
DX: Soft Tissue 21 Adv Path Course

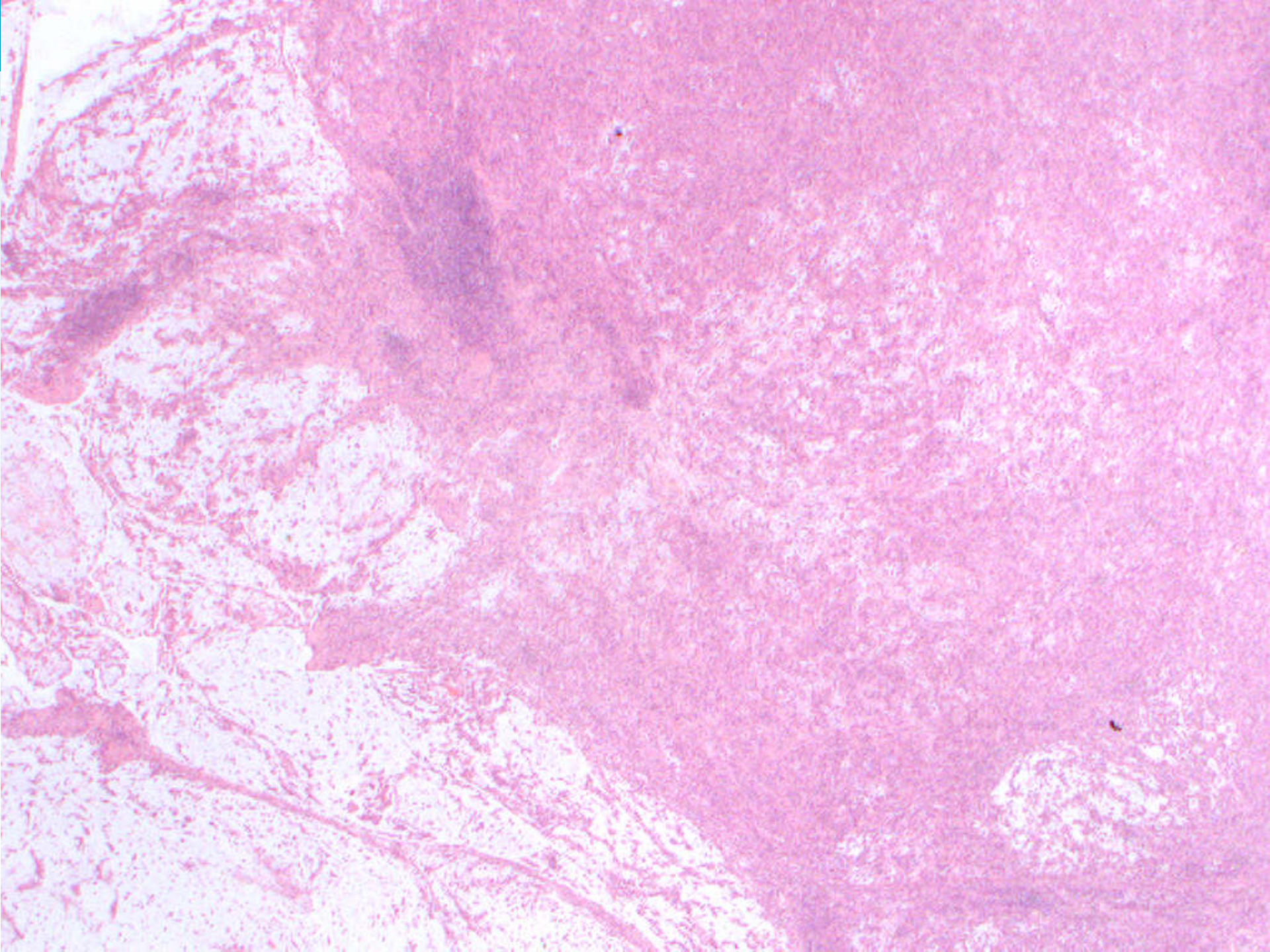
Low grade fibromyxoid sarcoma

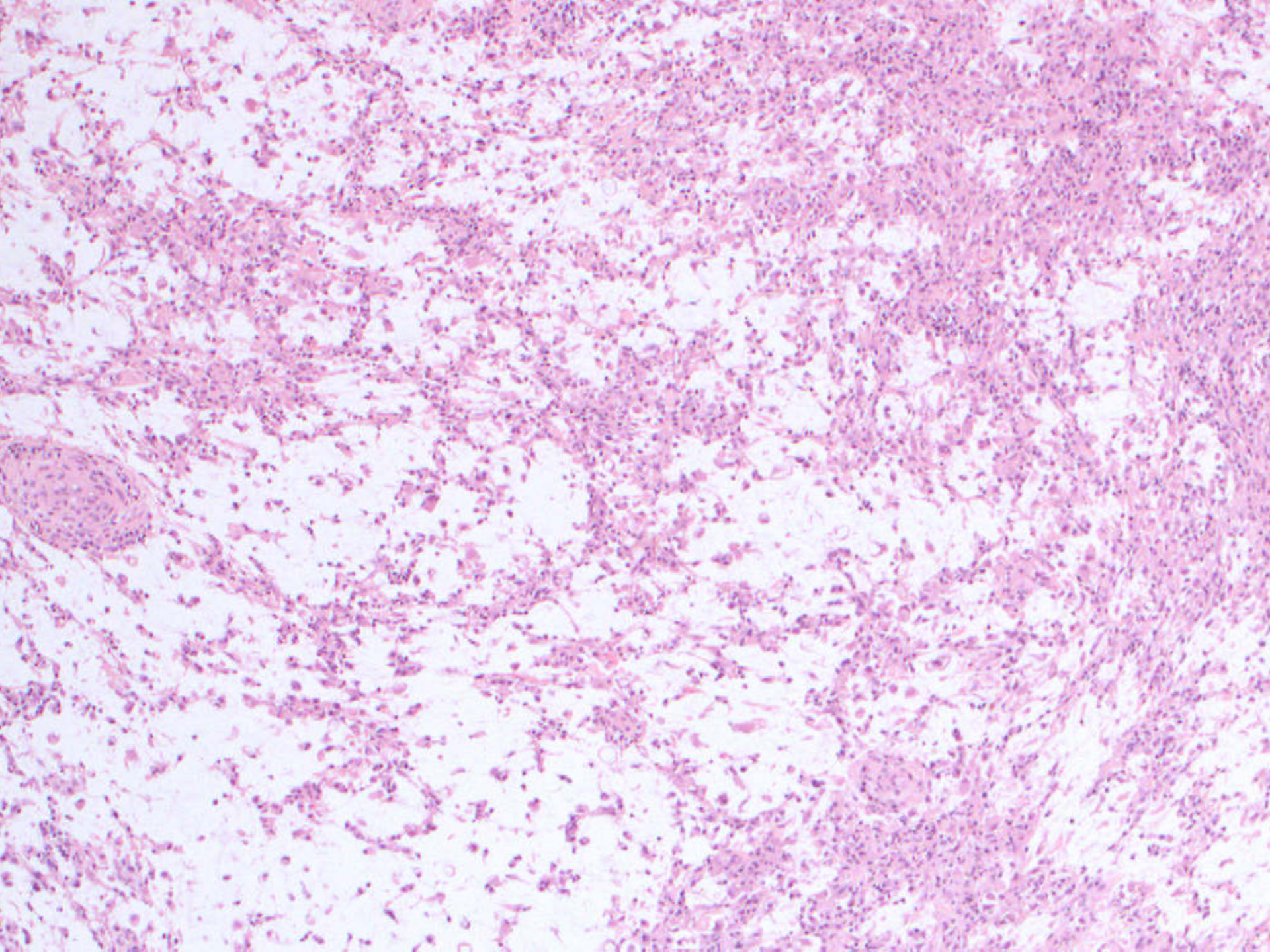
- Malignant fibroblastic neoplasm with both heavily collagenised and myxoid zones (and occasionally collagen rosettes)
- Deceptively bland spindle cells and arcades of curvilinear vessels
- Can occur at any age, typically proximal extremity or trunk
- EMA and SMA usually positive. MUC4 is highly sensitive and specific
- Consistently demonstrate either a *FUS-CREB3L2* or *FUS-CREB3L1* fusion

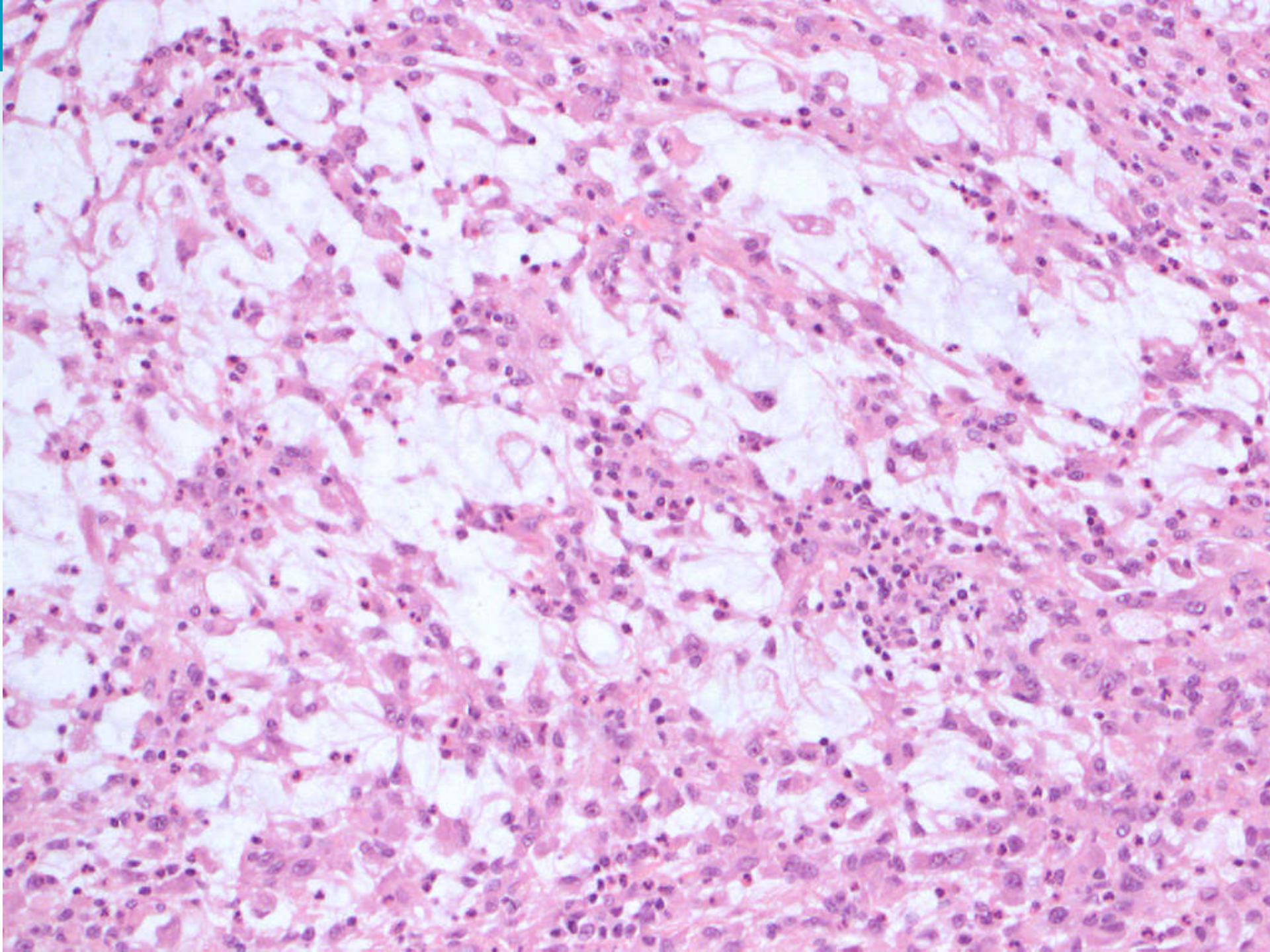
CLINICAL INFORMATION 22

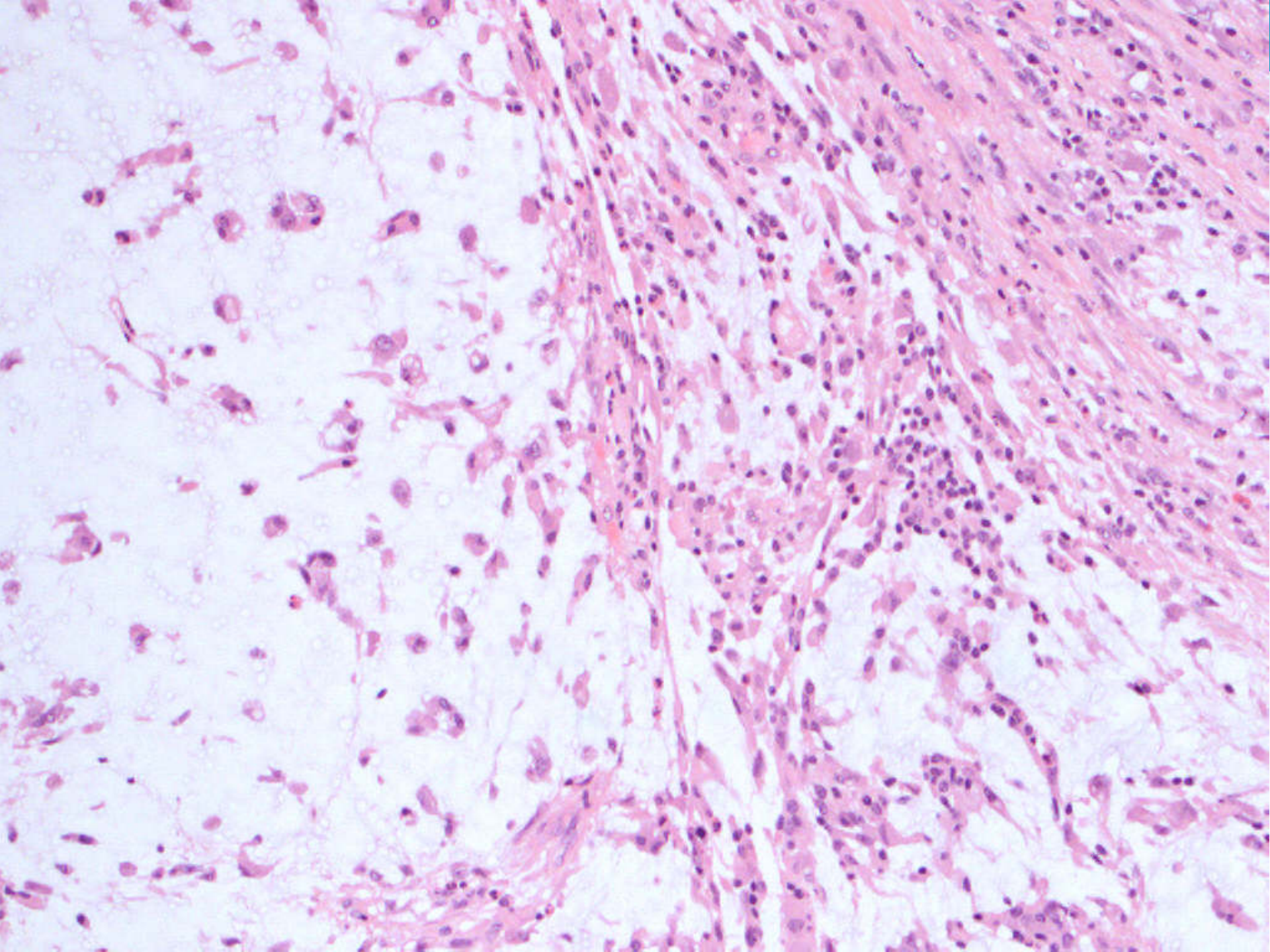
- Female 57
- Soft tissue swelling medial aspect of the tibia.
- Lesion [90mm maximum dimension].











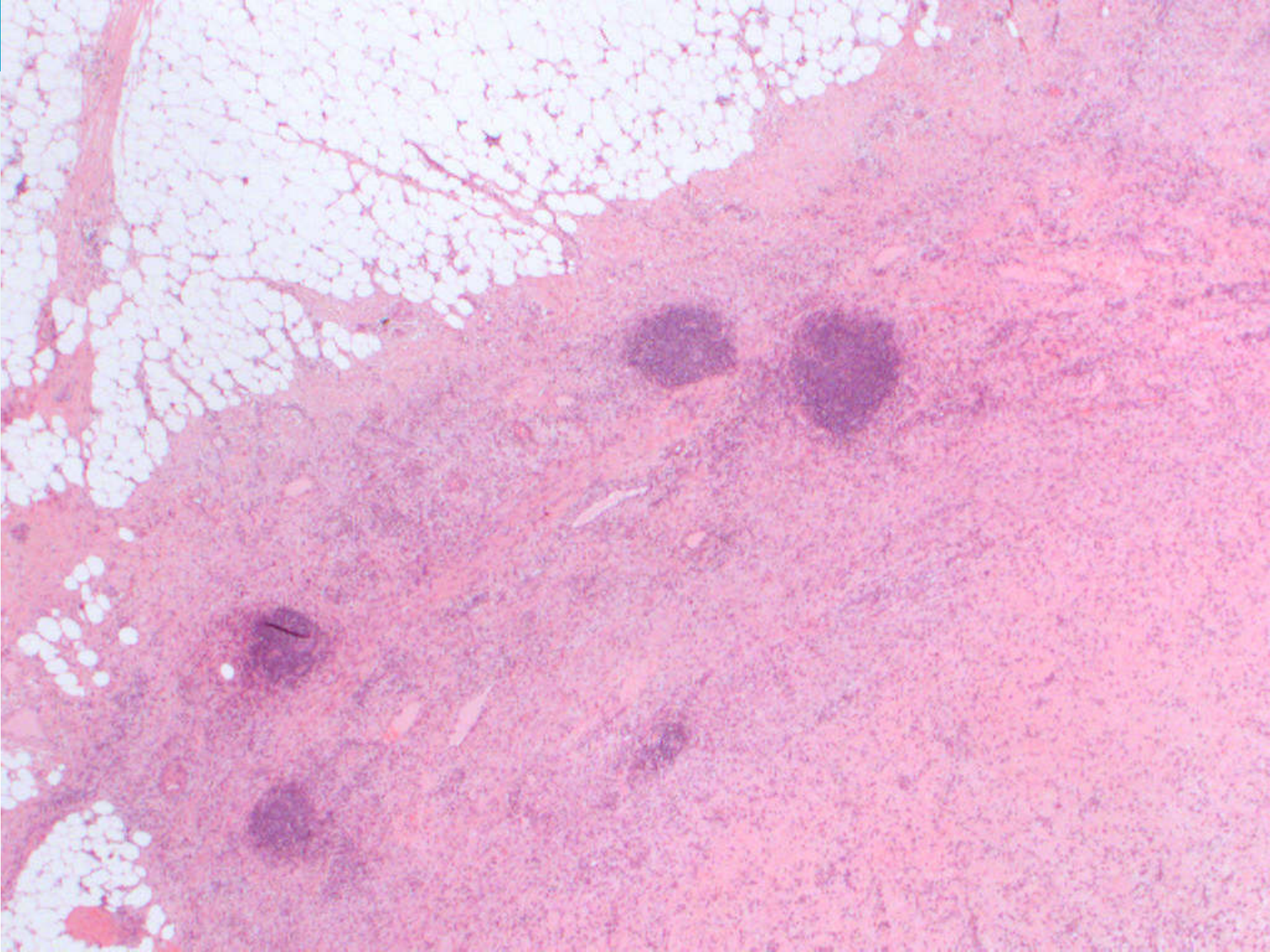
DX: Soft Tissue 22 Adv Path Course

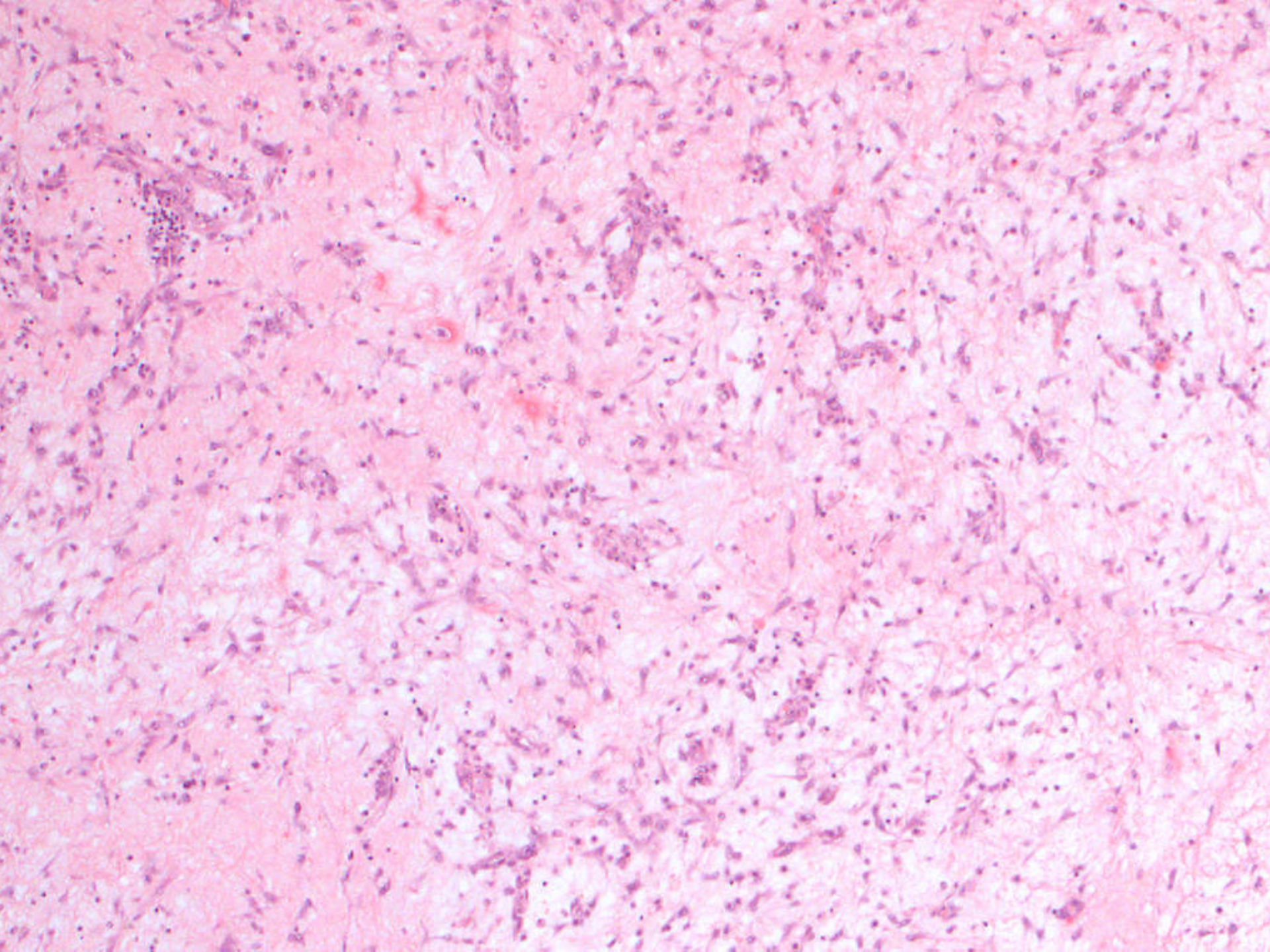
Myxoinflammatory fibroblastic sarcoma

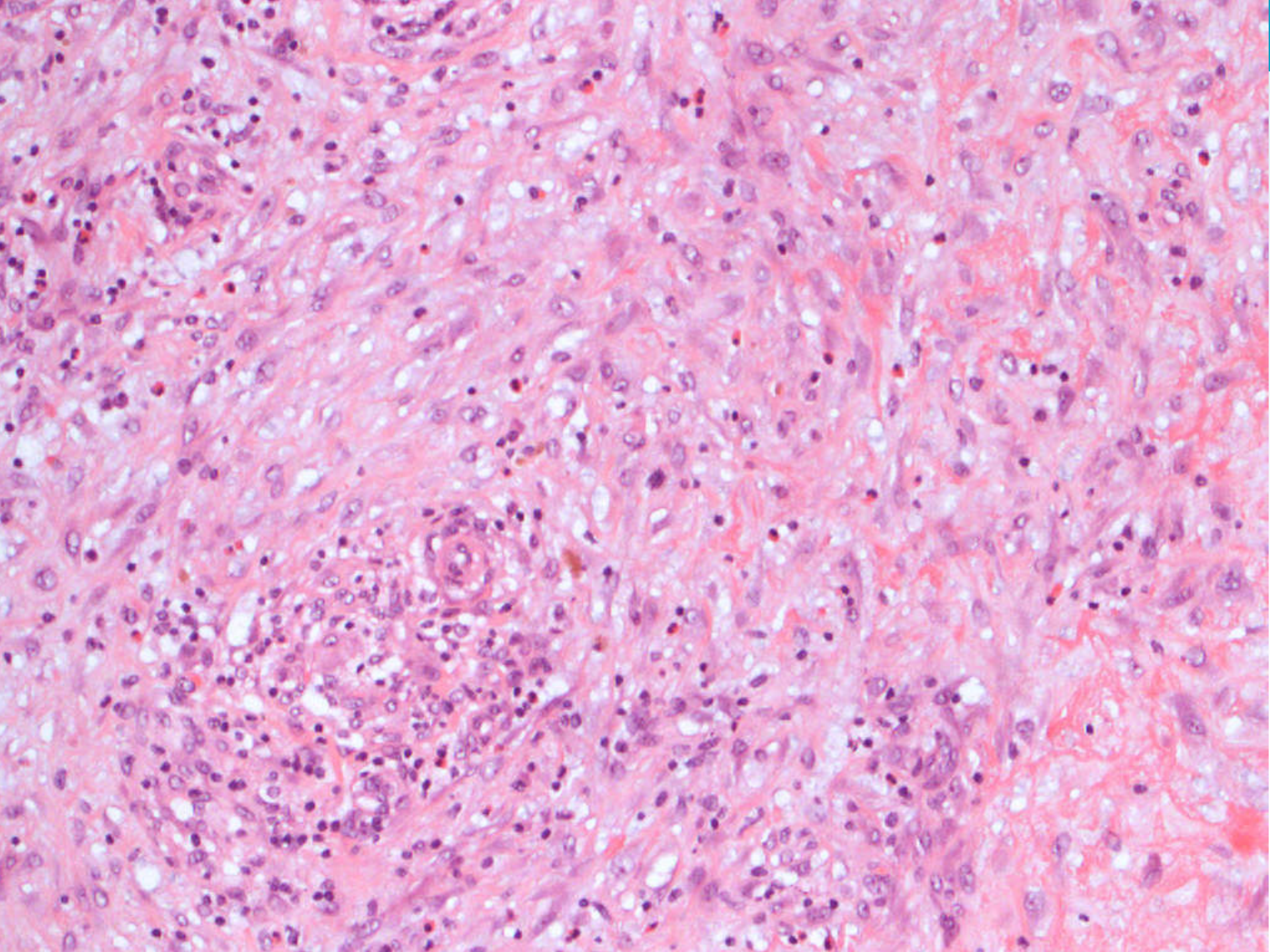
- Primarily observed in distal extremities of middle aged patients
- Involvement of tenosynovial structures typical
- Epithelioid fibroblasts with macronucleoli interspersed with prominent mixed inflammatory infiltrate and myxoid matrix
- Look for haemosiderin pigment and vacuolated, virocyte-like cells
- Variable positivity foe CD68, CD34, SMA and keratin. Lymphoid markers like CD30 negative

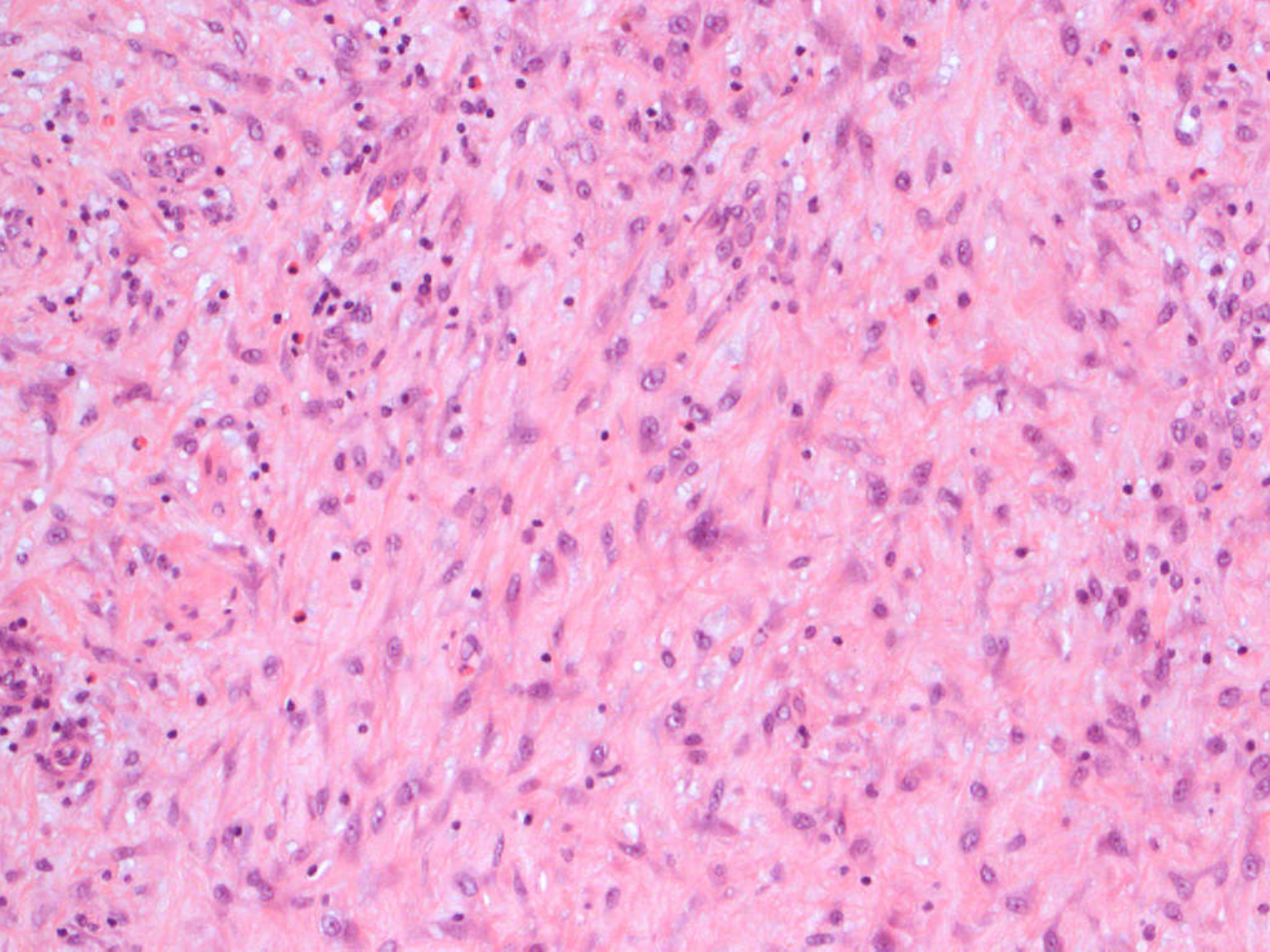
CLINICAL INFORMATION 23

- Male, 88
- Lump in right groin.
- Lesion [3cm maximum dimension].









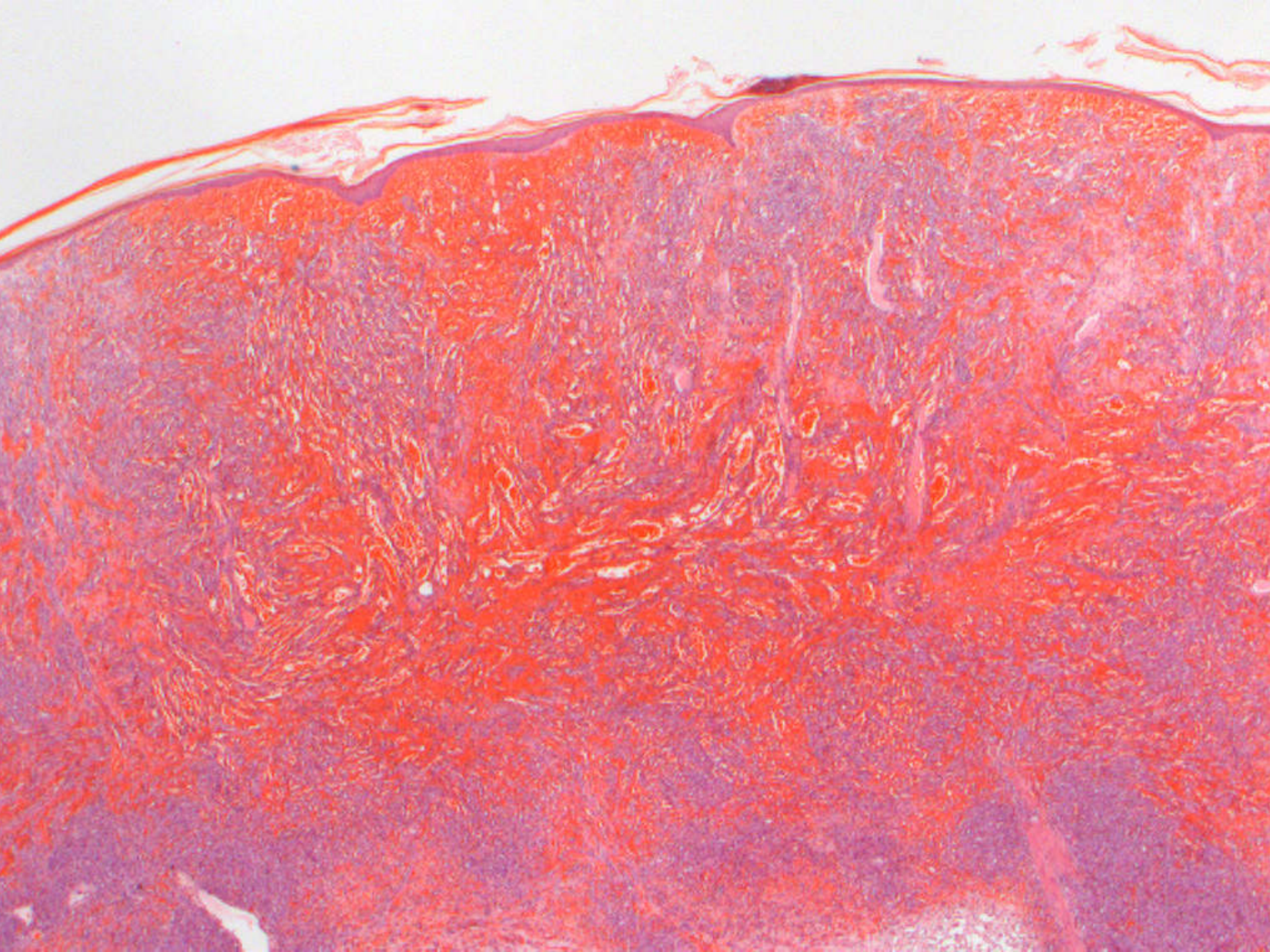
DX: Soft Tissue 23 Adv Path Course

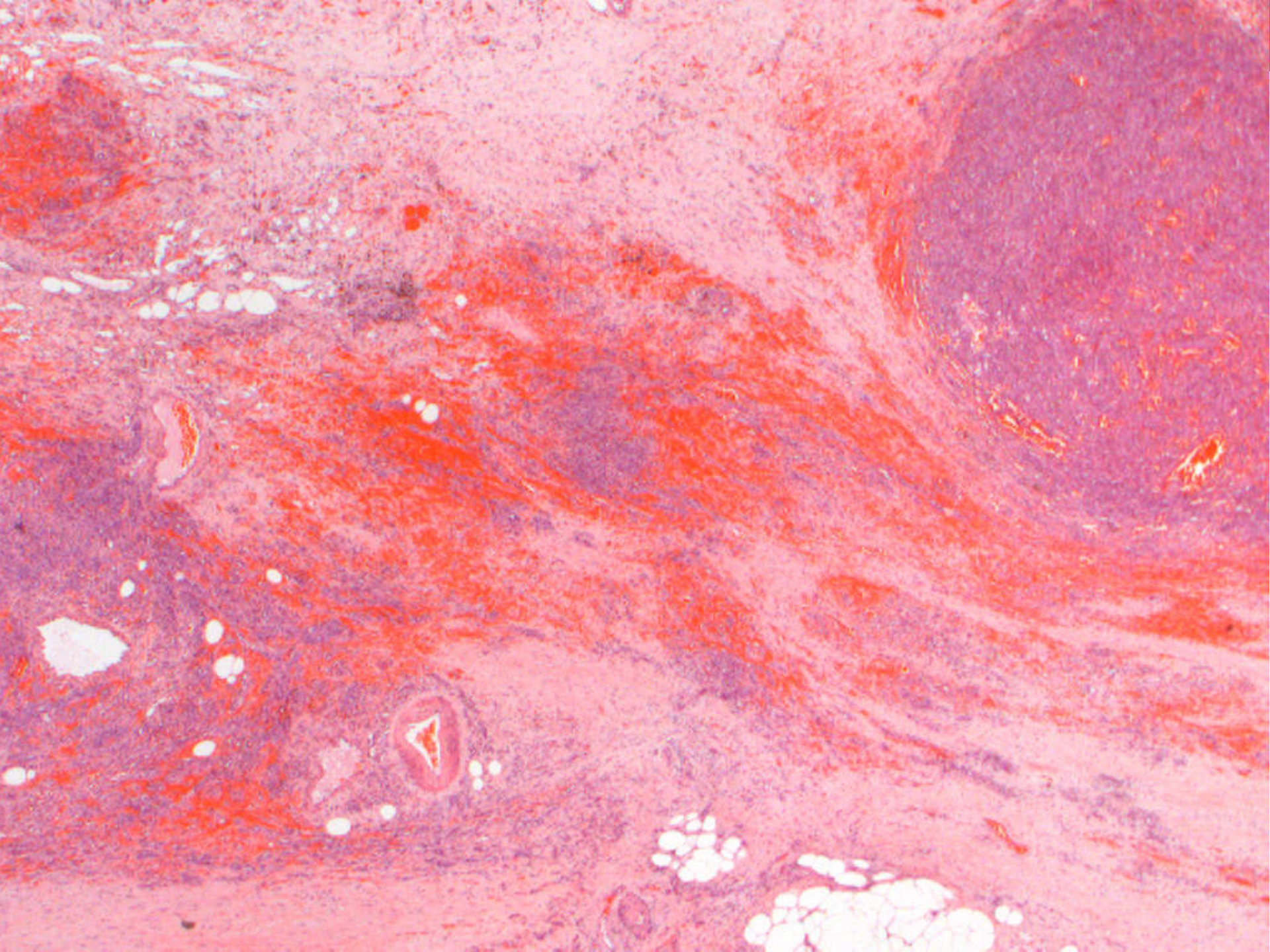
Inflammatory myofibroblastic tumour

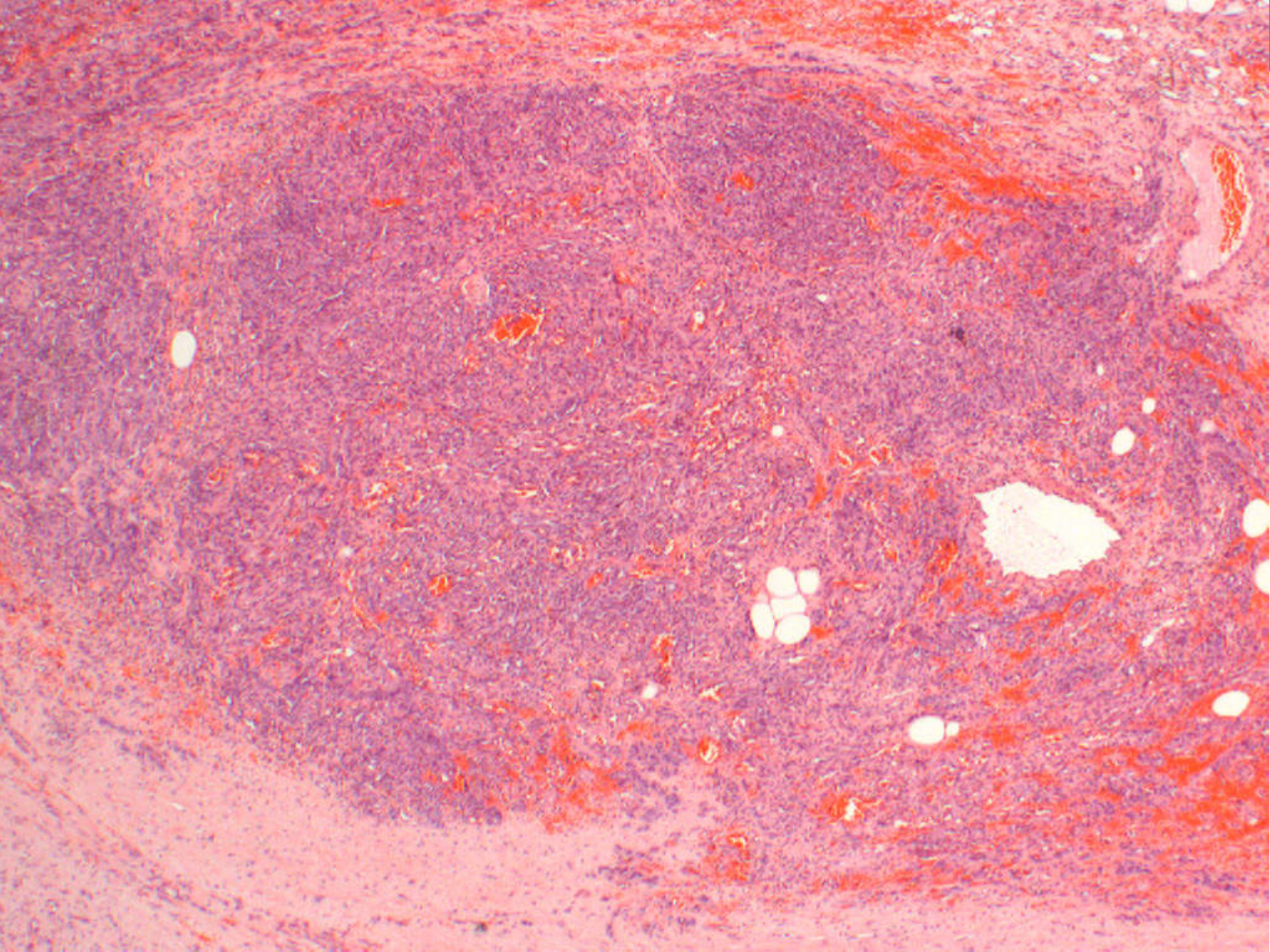
- (Don't confuse with myxoinflammatory fibroblastic sarcoma)
- Distinct fibroblastic and myofibroblastic neoplasm accompanied by a mixed, prominent inflammatory infiltrate
- Most common in soft tissue and viscera of young adults
- Variable staining for SMA, desmin and keratin
- Cytoplasmic reactivity for ALK present in 50-60% and correlates with rearrangement of *ALK* gene

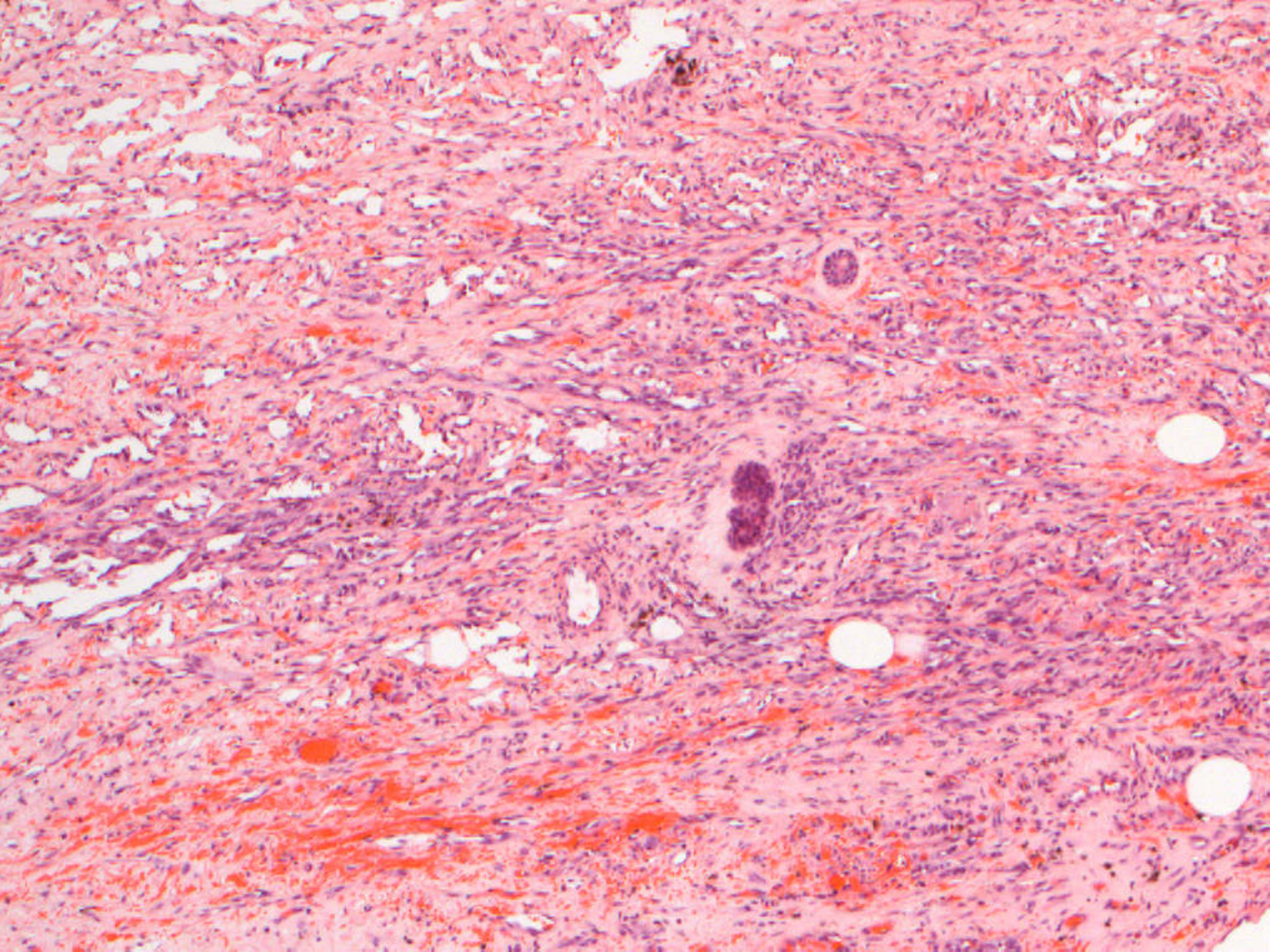
CLINICAL INFORMATION 24

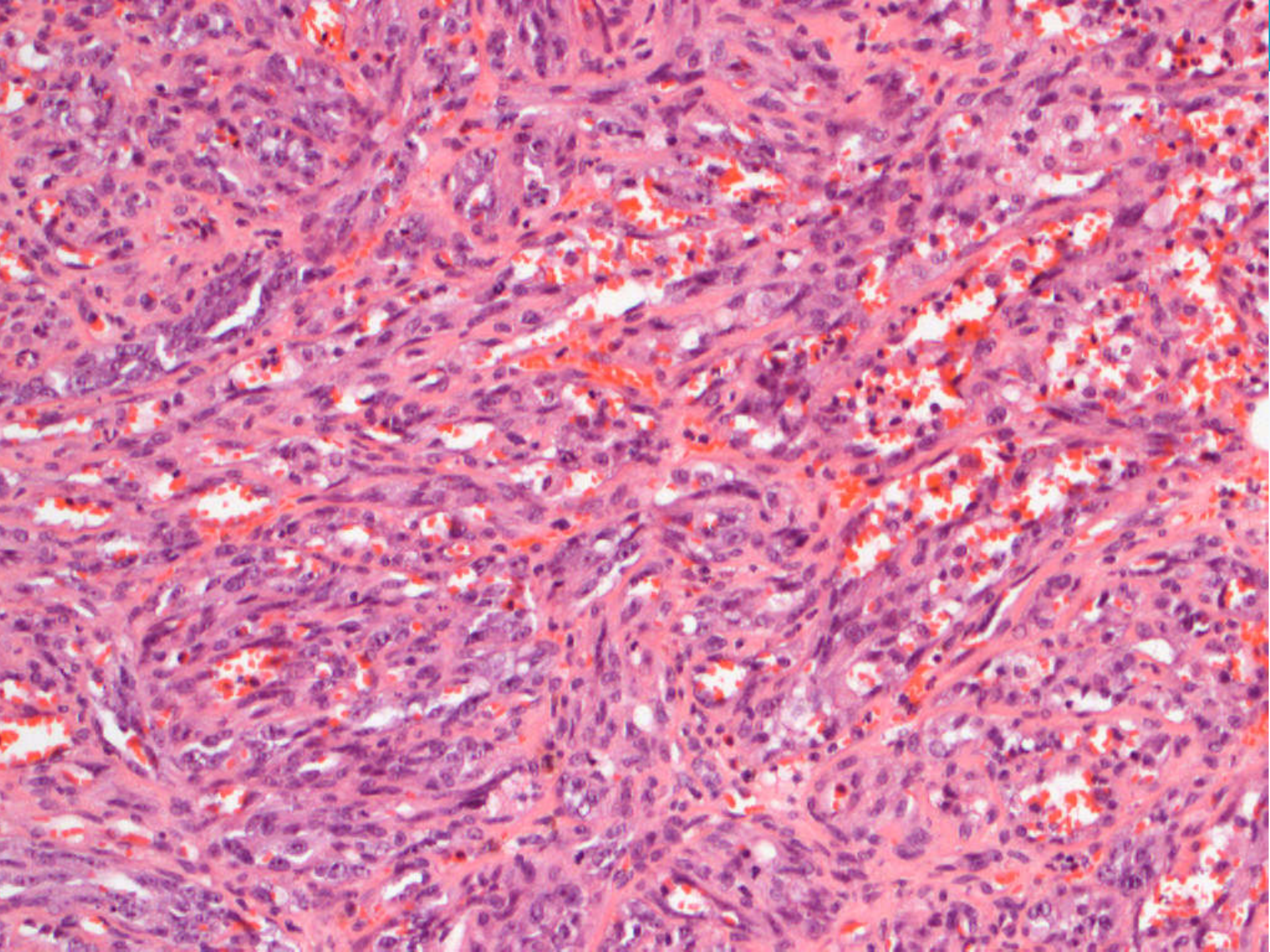
- Male, 67
- Soft tissue mass in lower leg, [80mm maximum dimension].

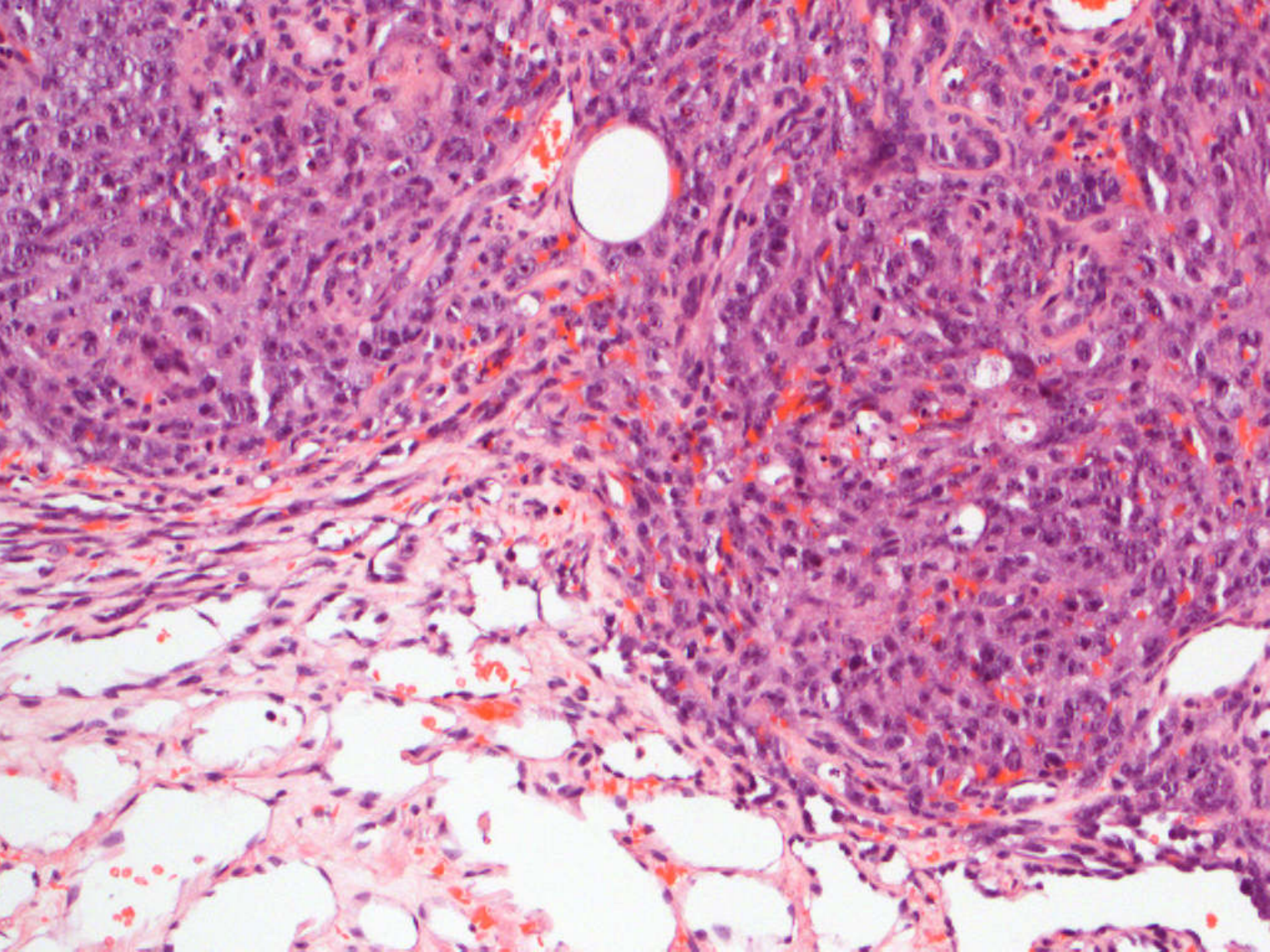


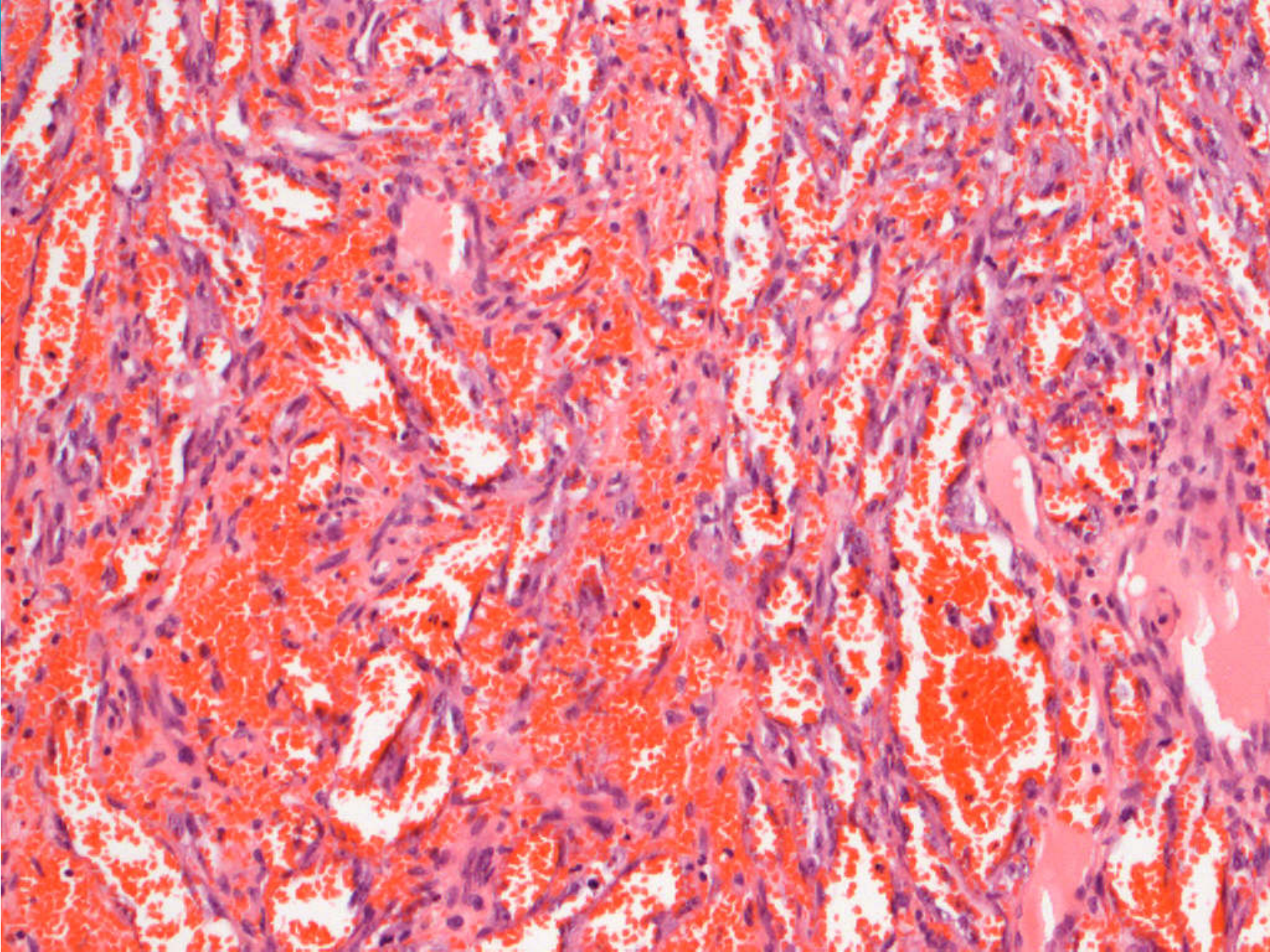












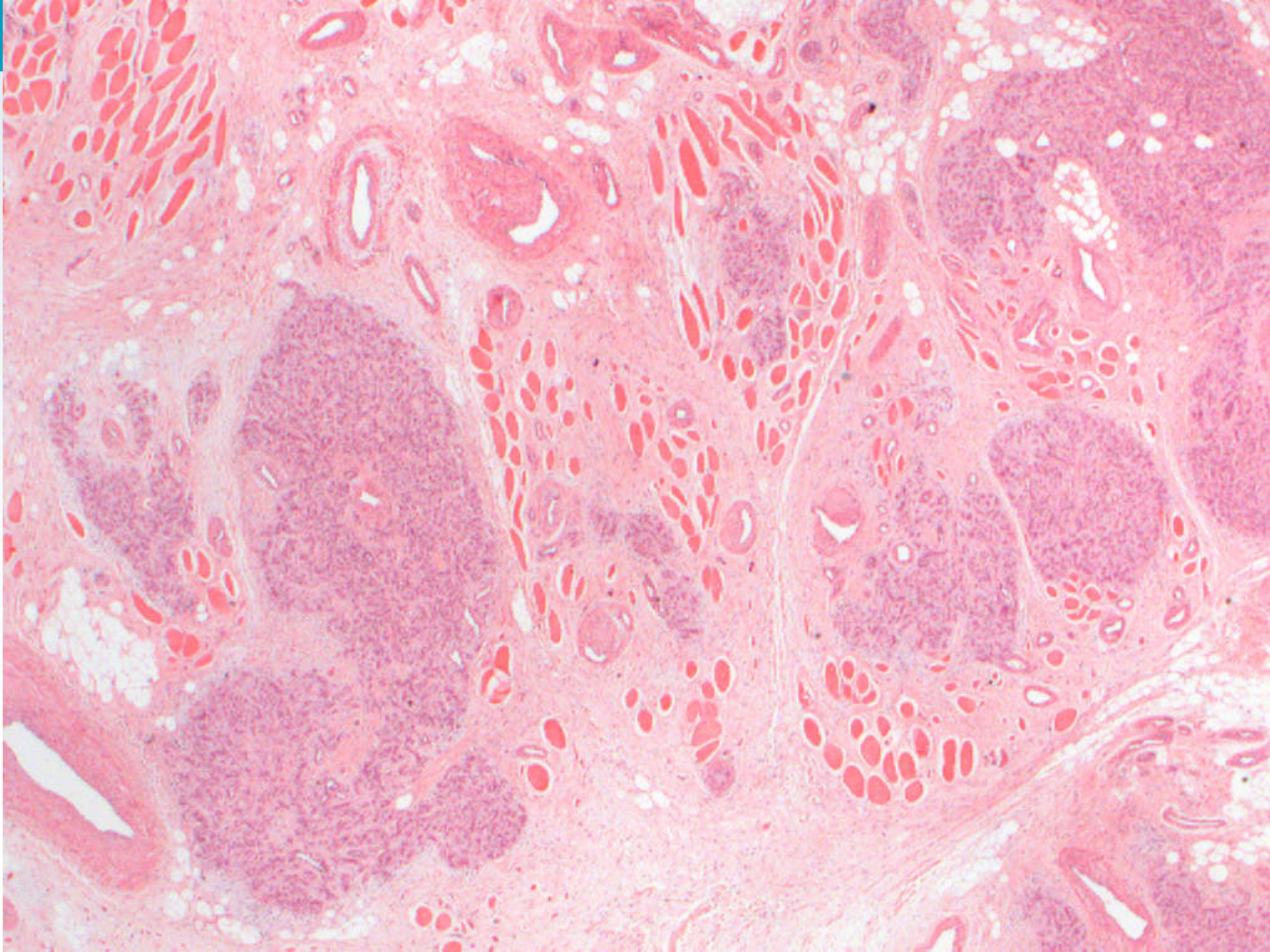
DX: Soft Tissue 24 Adv Path Course

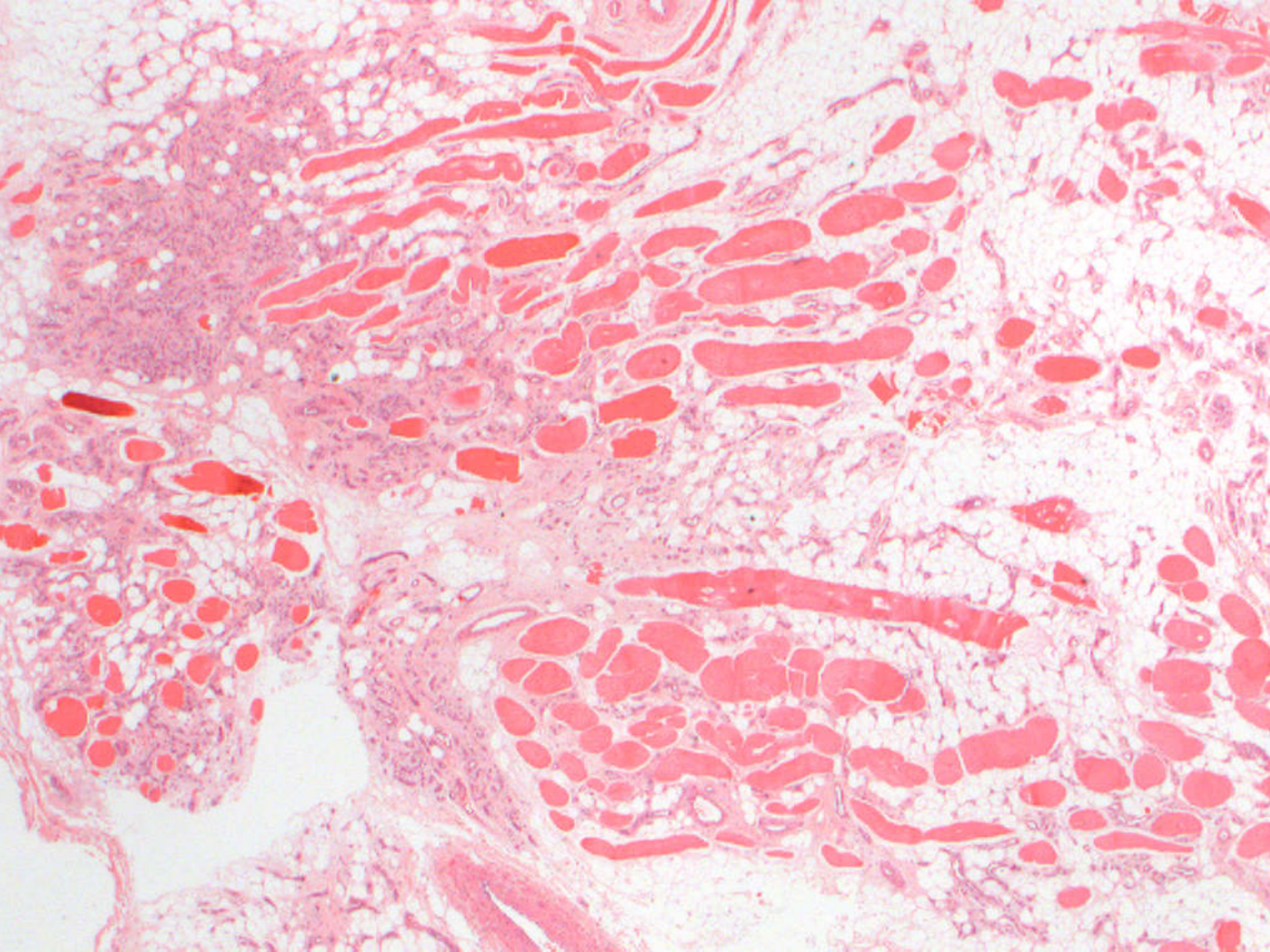
Angiosarcoma

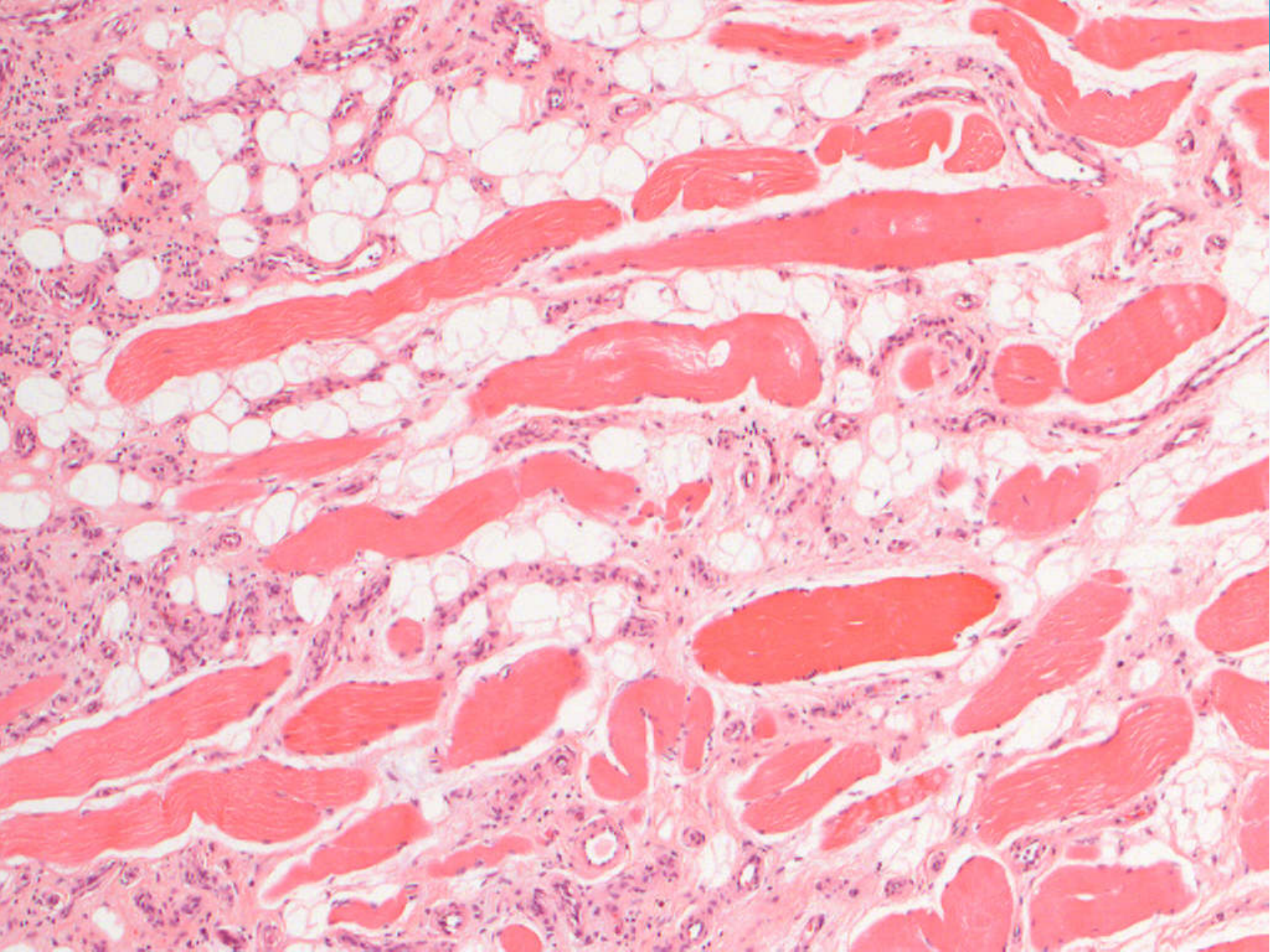
- Malignant vasoformative tumour, can be seen in all ages
- Wide morphological appearance- well-formed anastomosing vessels to solid sheets. Either spindled or epithelioid. Haemmorhage may be extensive.
- DDx includes Kaposi sarcoma (HHV8+) and carcinoma
- Vascular markers CD34, CD31, ERG and Fli1 typically +
- EMA and keratins often co-expressed in epithelioid variant
- High level amplification of MYC is a hallmark of radiation-induced or lymphoedema-associated cases

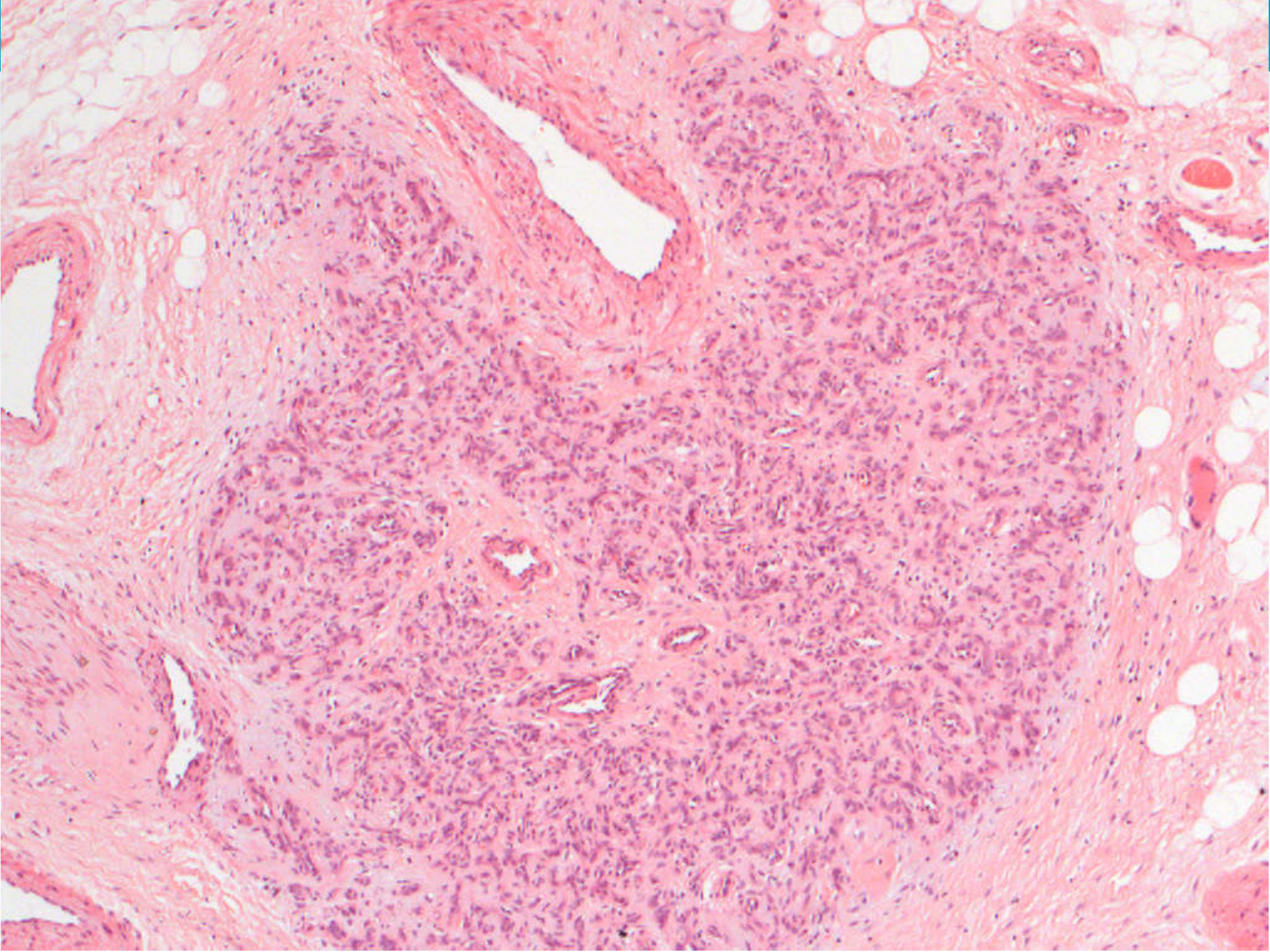
CLINICAL INFORMATION 25

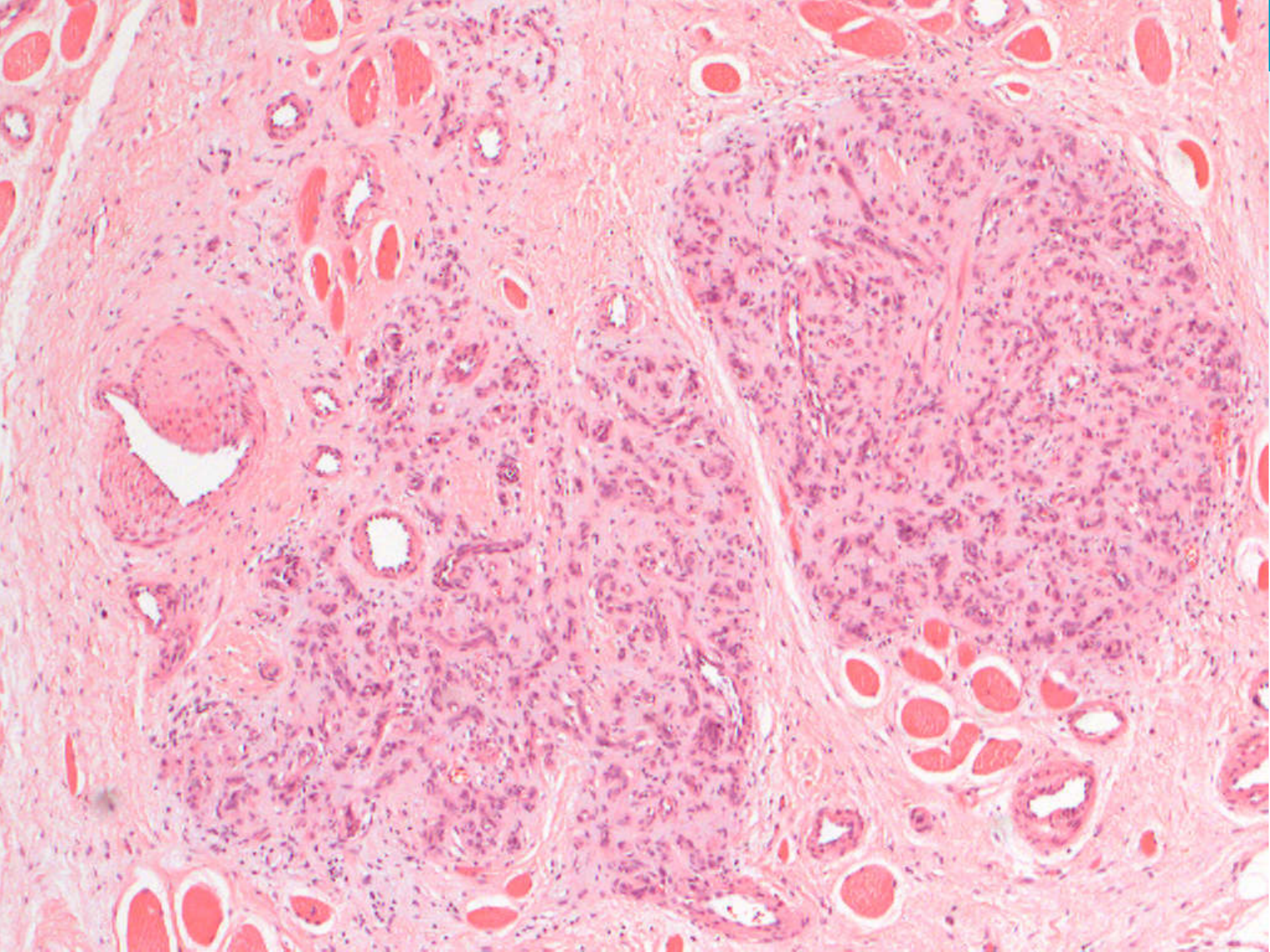
- Female, 28
- Soft tissue intramuscular lump [55mm maximum dimension].
- Right forearm.

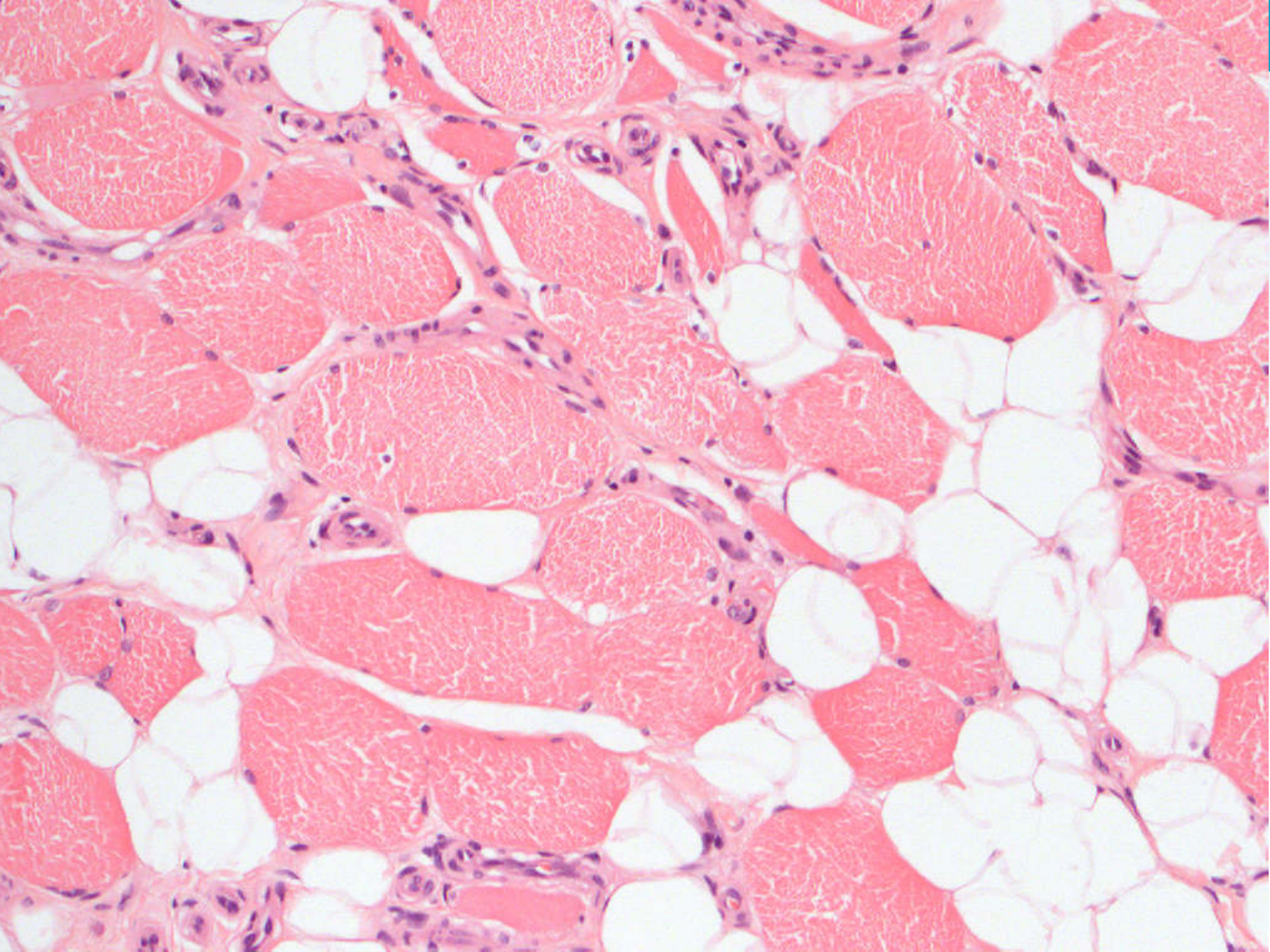












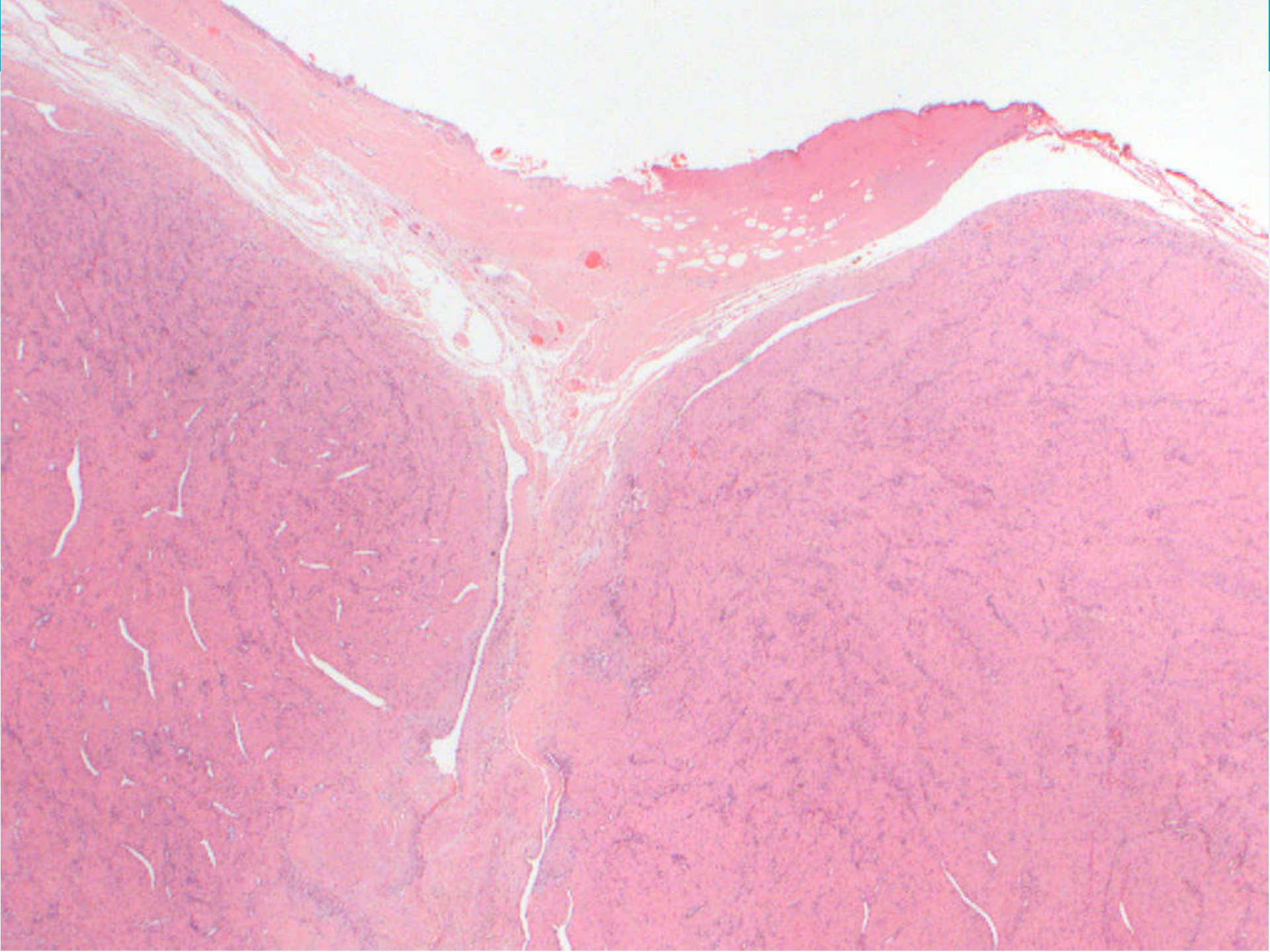
DX: Soft Tissue 25 Adv Path Course

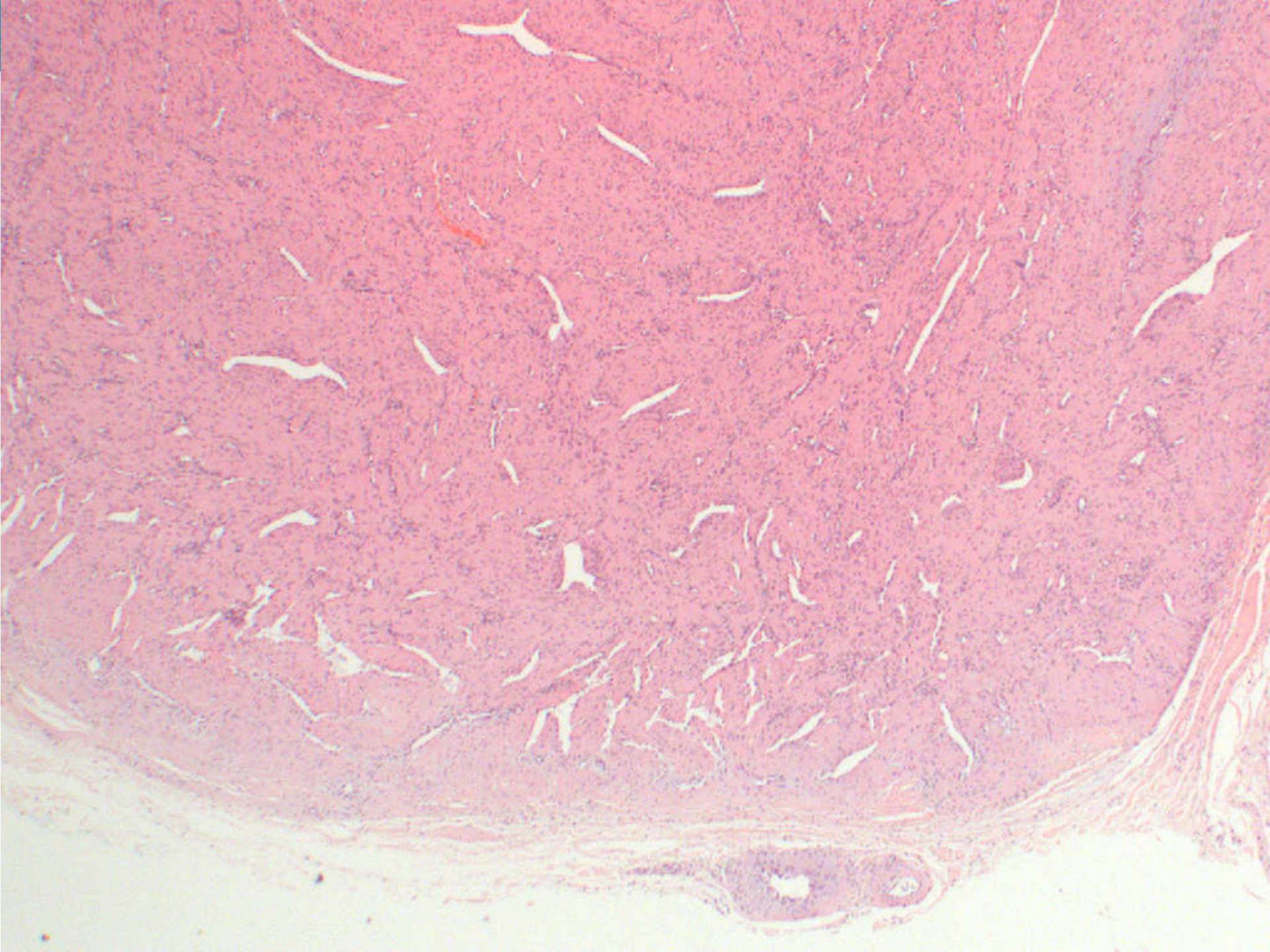
Haemangioma with diffuse fatty change

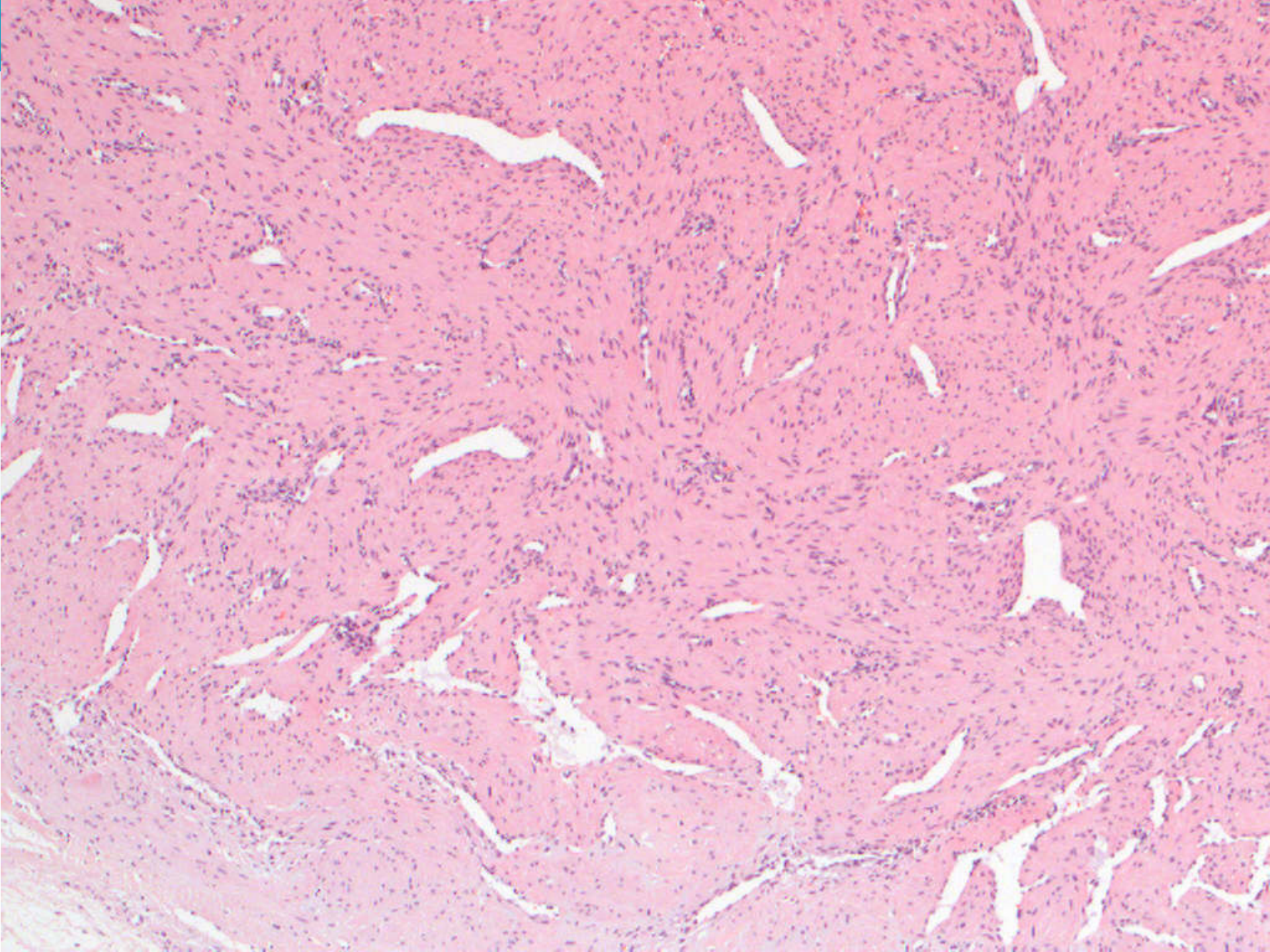
- Intramuscular angioma/haemangioma shows proliferation of benign vascular channels associated with variable amounts of mature adipose tissue
- May be small (capillary) large (cavernous) or mixed
- 30-50% show local recurrence
- May show infiltration of skeletal muscle but tumours lack atypia, mitoses and necrosis

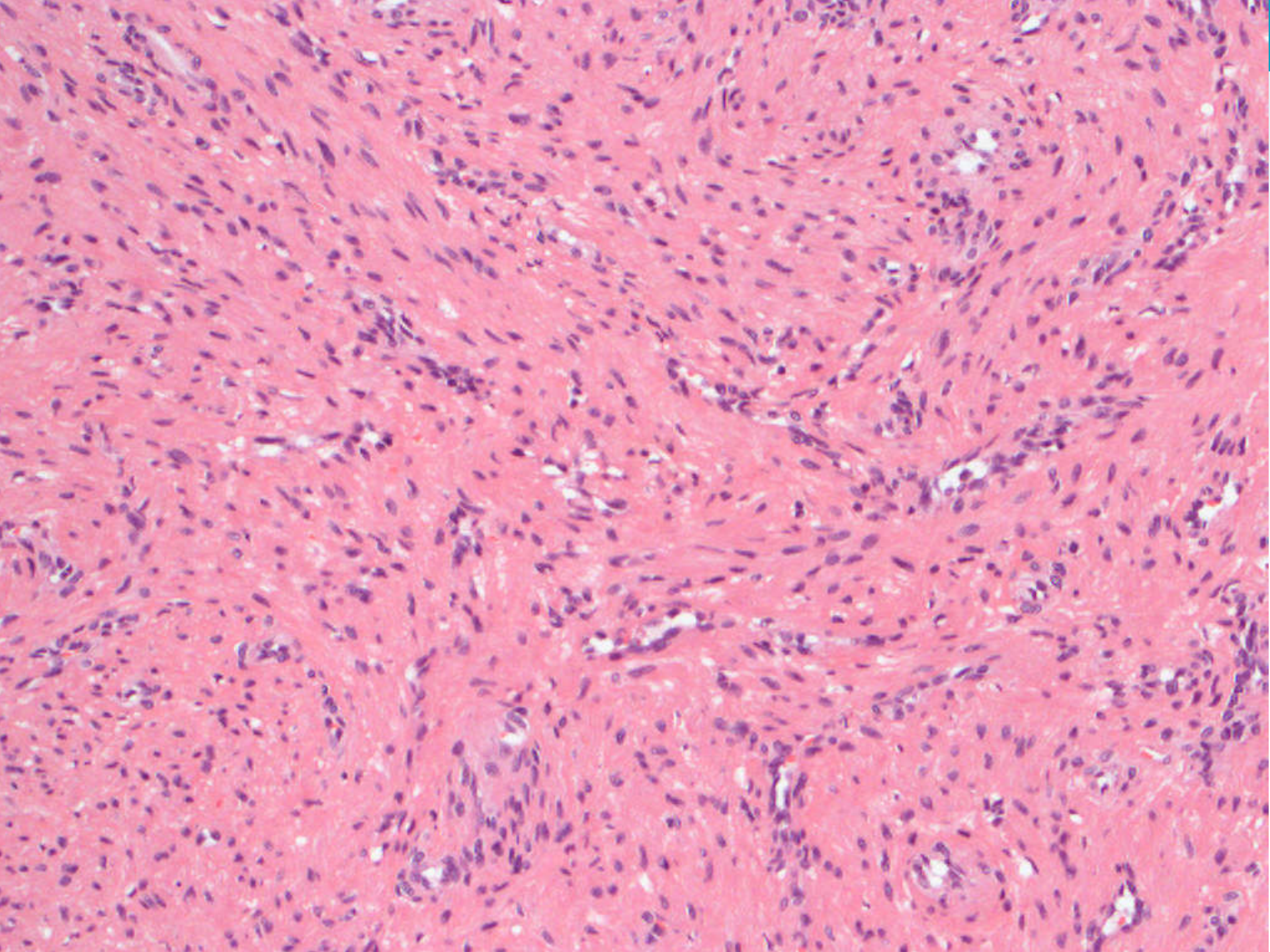
CLINICAL INFORMATION 26

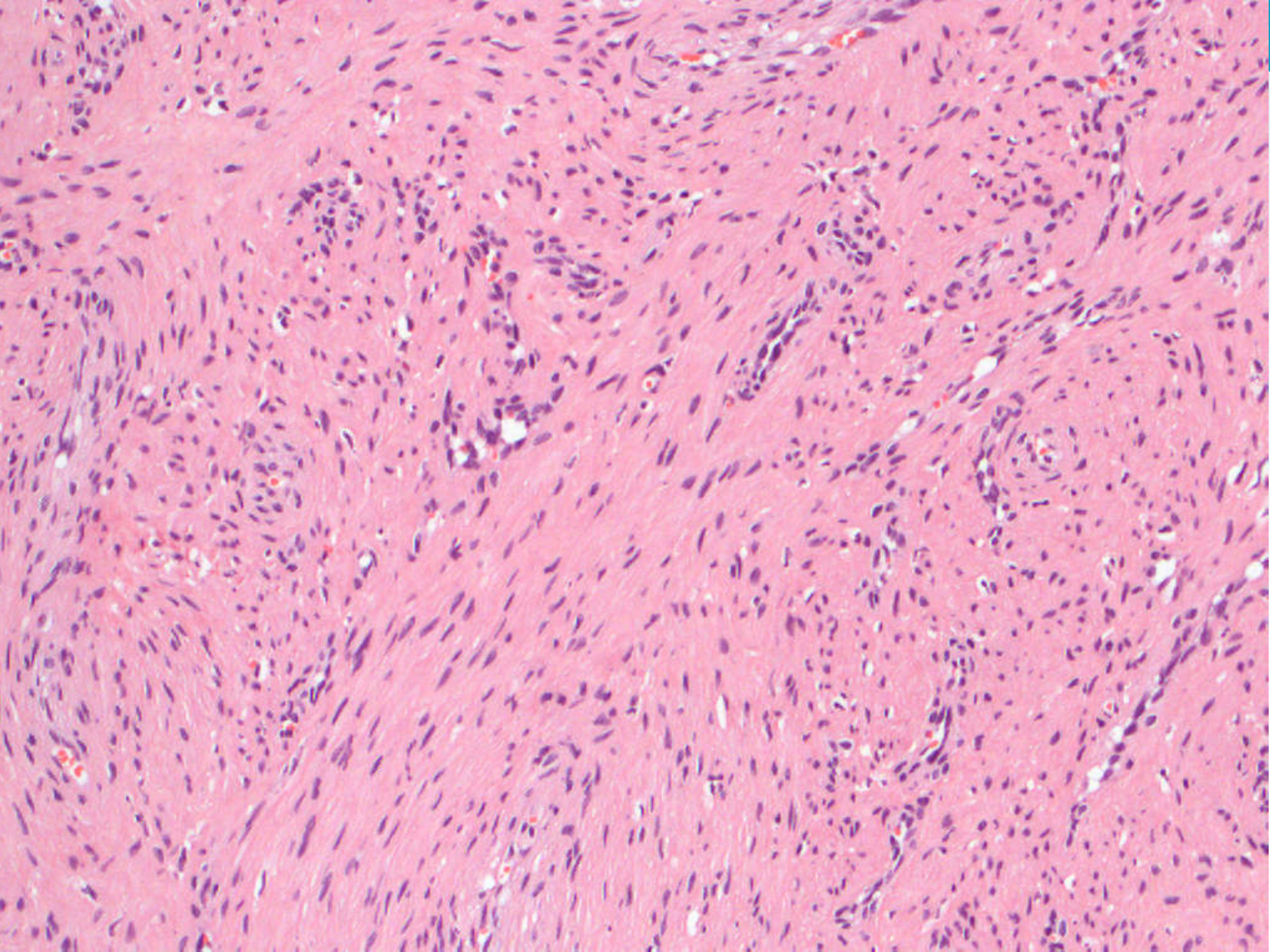
- Male, 53
- Soft tissue lesion around knee [40mm maximum dimension].











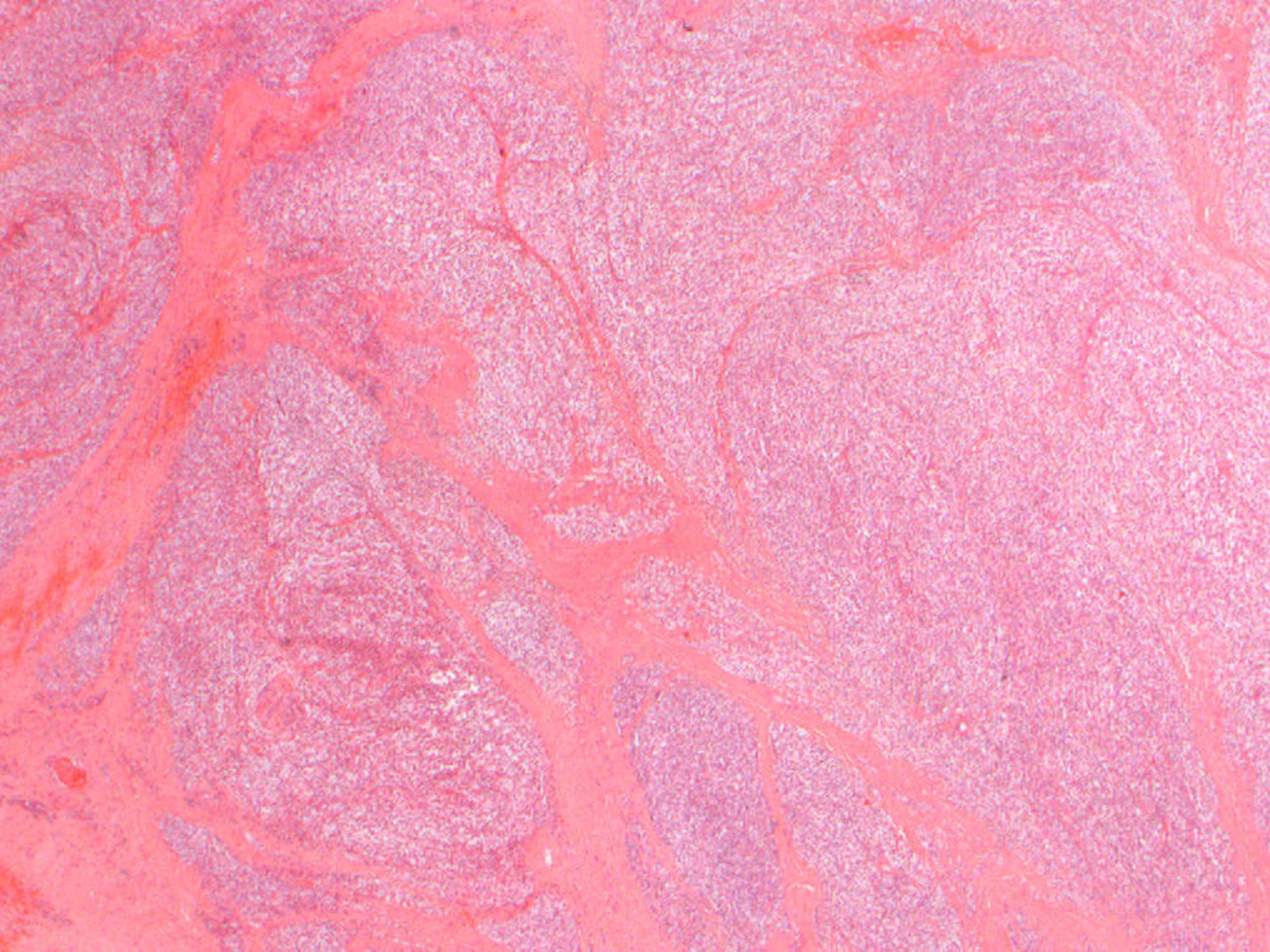
DX: Soft Tissue 26 Adv Path Course

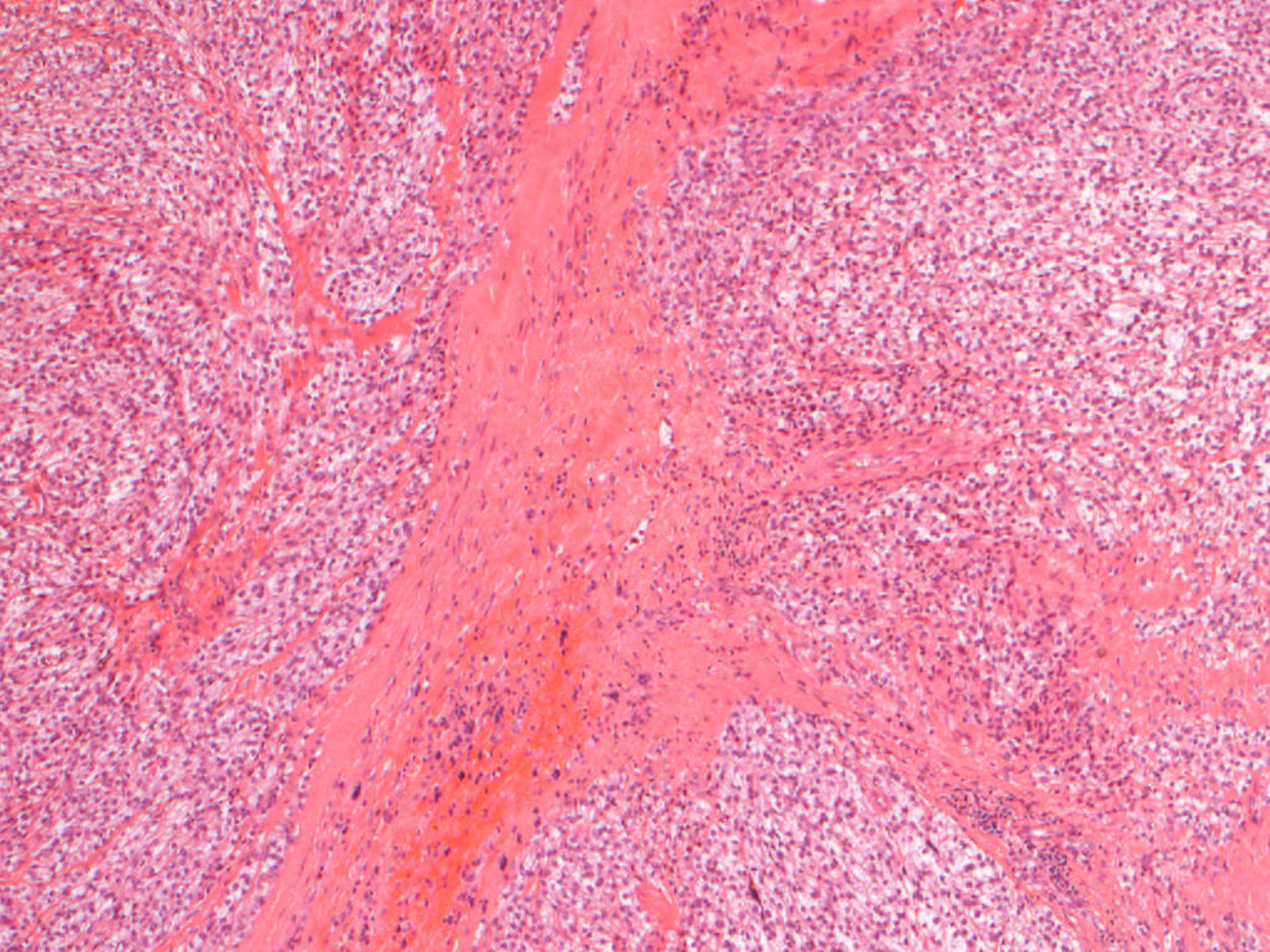
Angioleiomyoma / myopericytoma

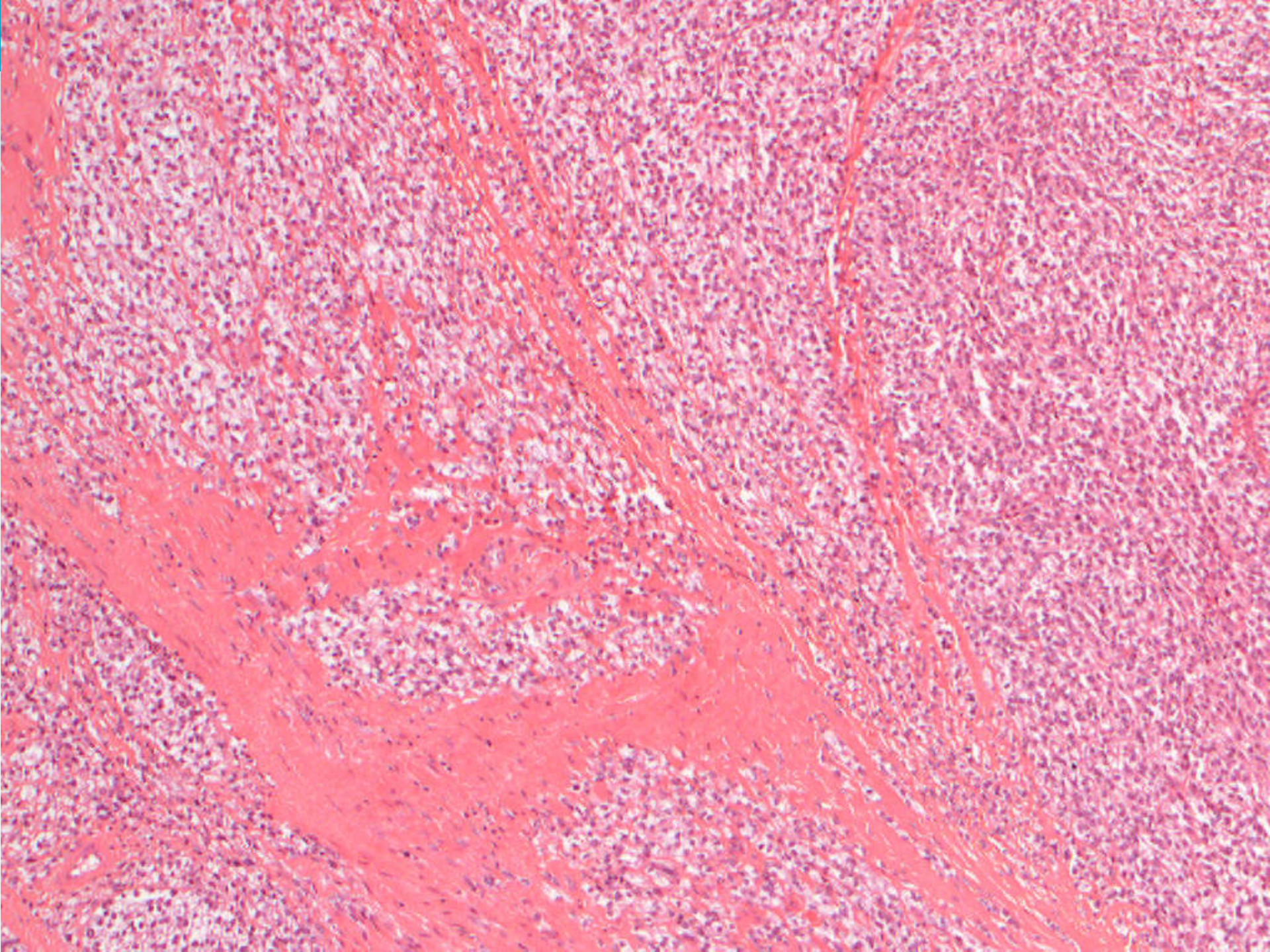
- Benign lesion of smooth muscle cells surrounding thin vascular channels.
- A morphological continuum exists between angioleiomyoma and myopericytoma
- Etiology largely unknown, commonly painful
- Variations include solid, venous and cavernous types
- Perivascular concentric arrangement of smooth muscle typically seen in myopericytoma

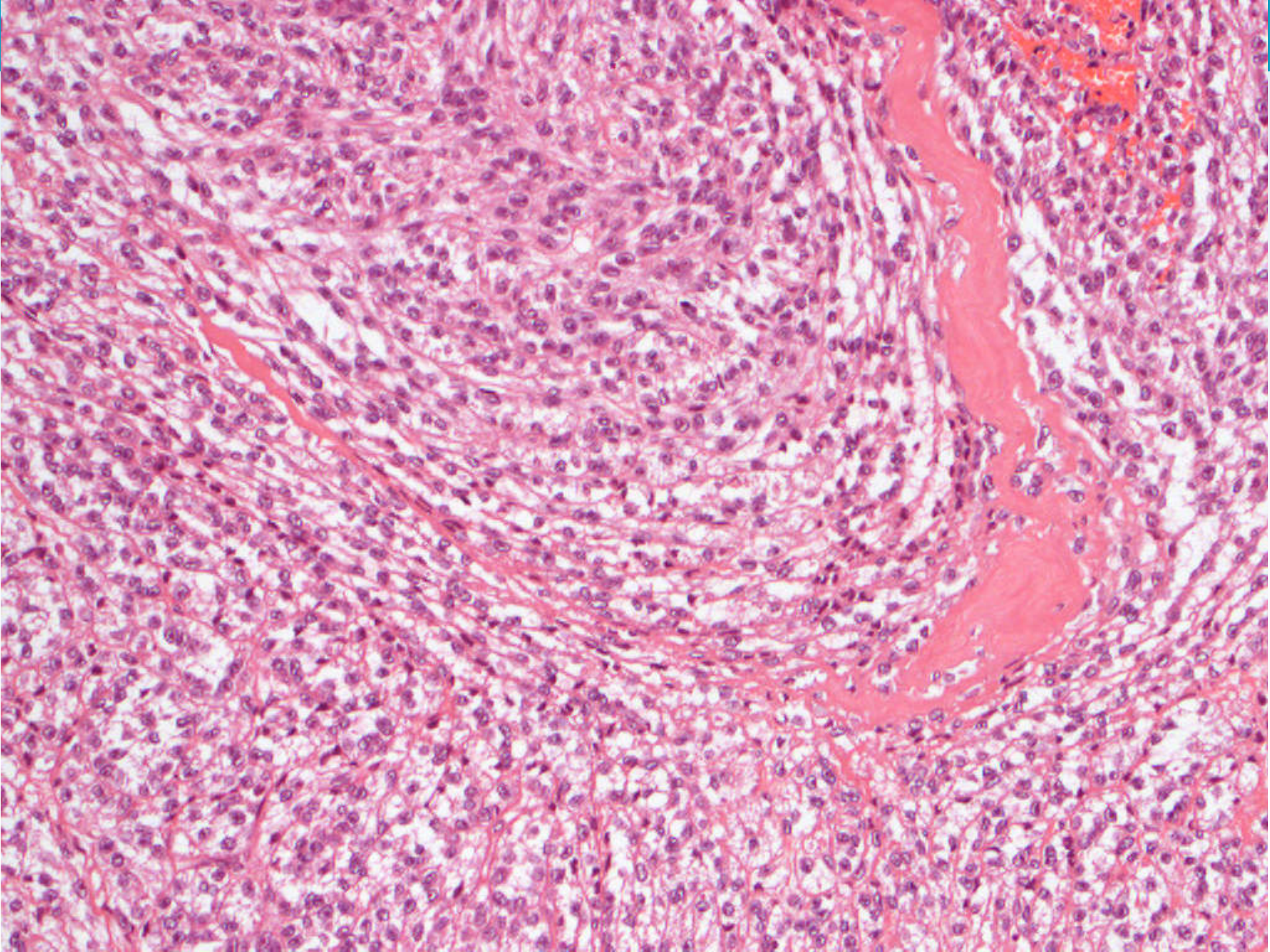
CLINICAL INFORMATION 27

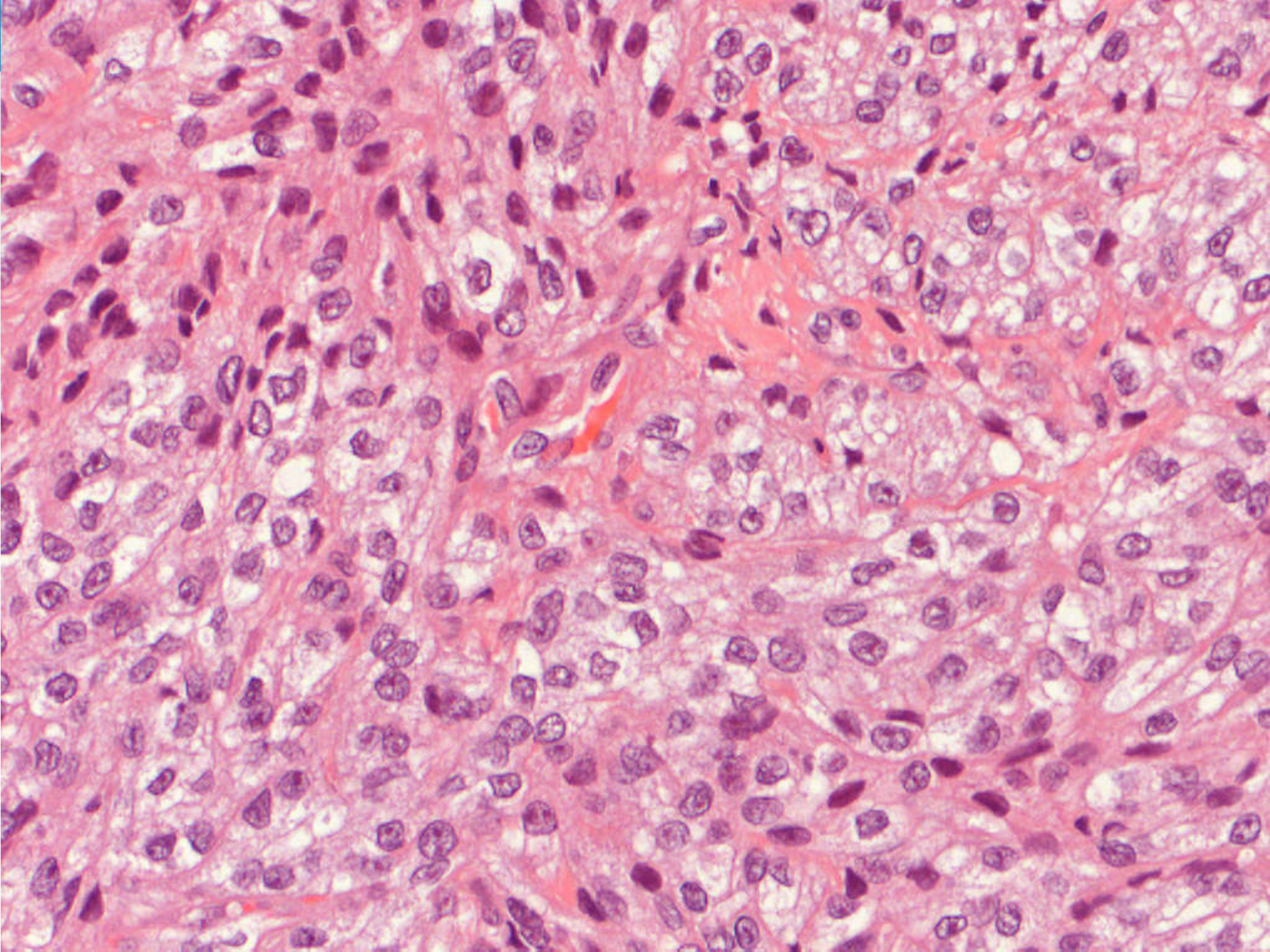
- Female, 33
- Soft tissue mass on volar aspect of hand [50mm maximum dimension].











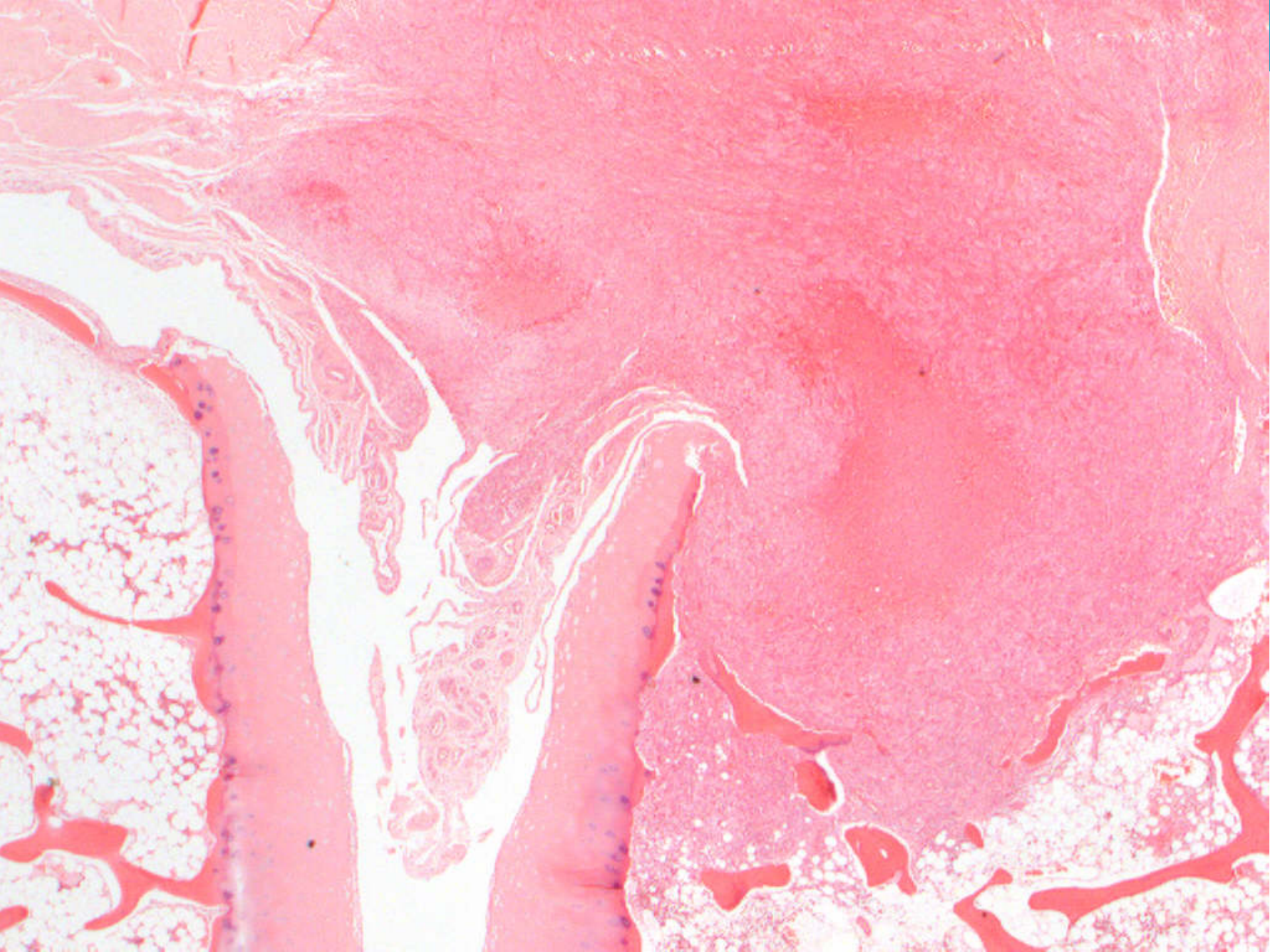
DX: Soft Tissue 27 Adv Path Course

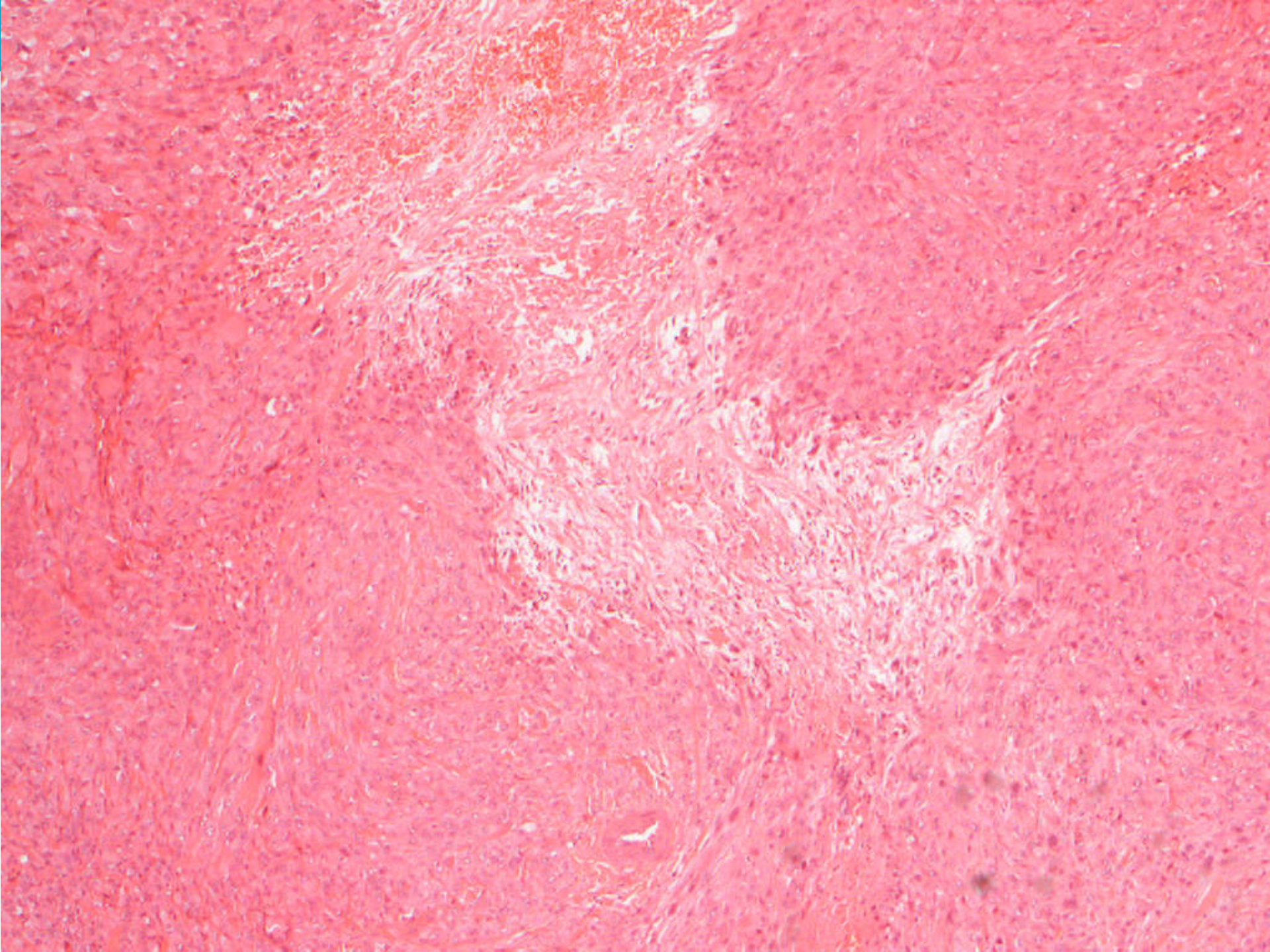
Clear cell sarcoma

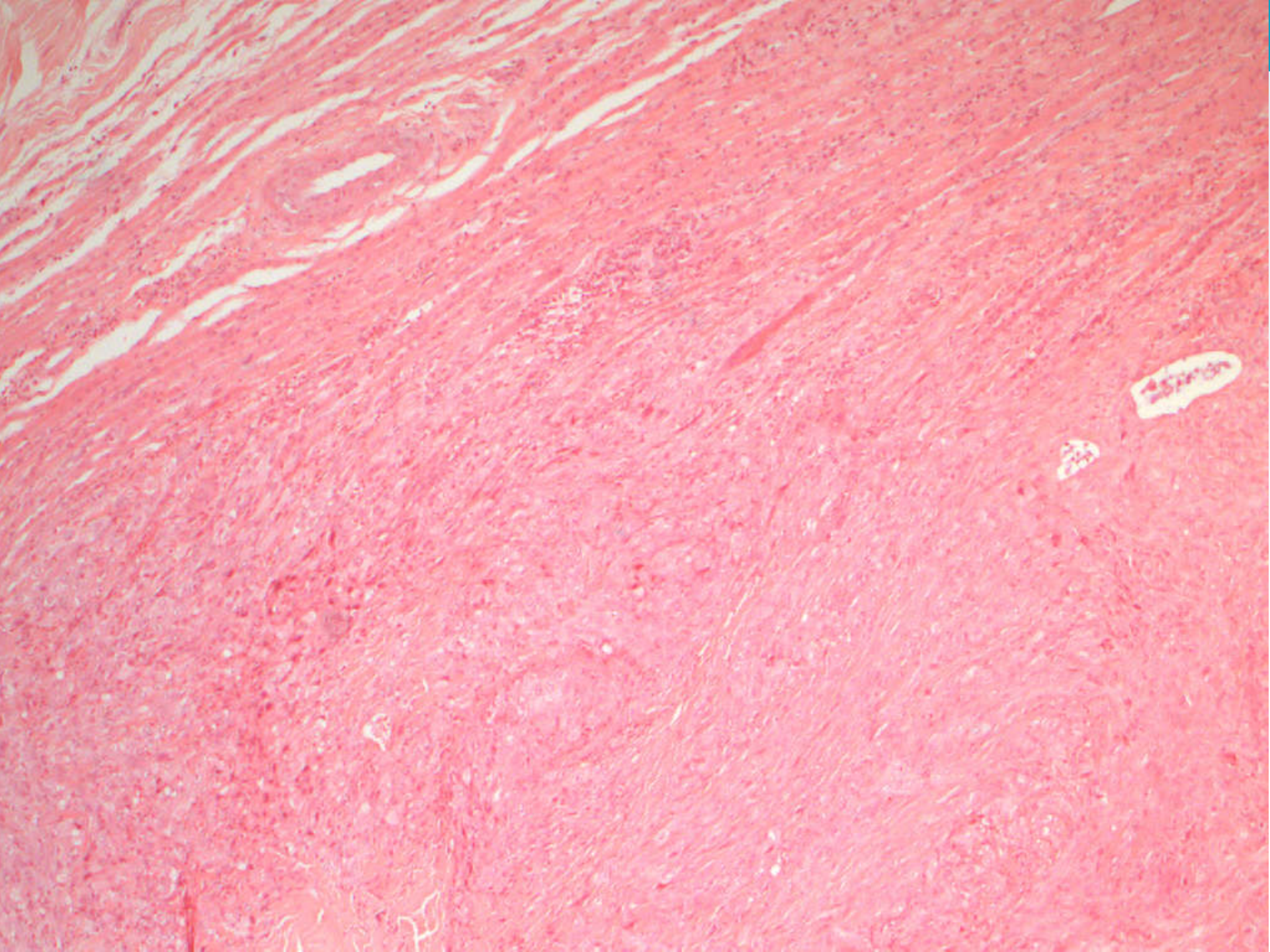
- Deep soft tissue of the extremities, in close proximity to tendons and aponeurotic structures.
- Consistent melanocytic differentiation and nested growth pattern
- Cells generally epithelioid, and despite name have eosinophilic or amphophilic cytoplasm
- Strong and diffuse S100, HMB45, melanA
- Melanin often absent on H&E but highlighted by Fontana
- *EWSR1-ATF1* fusion in >90%

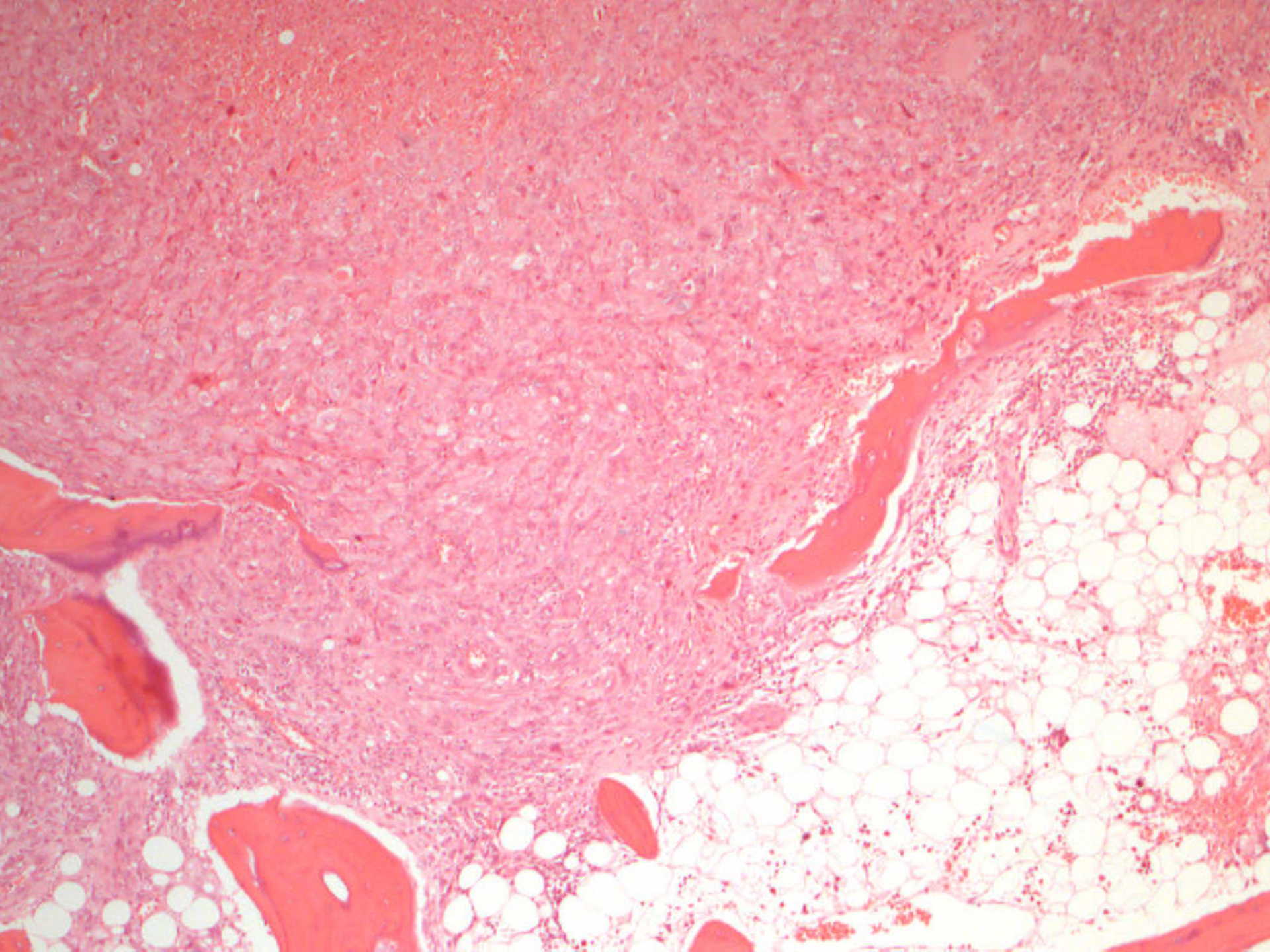
CLINICAL INFORMATION 28

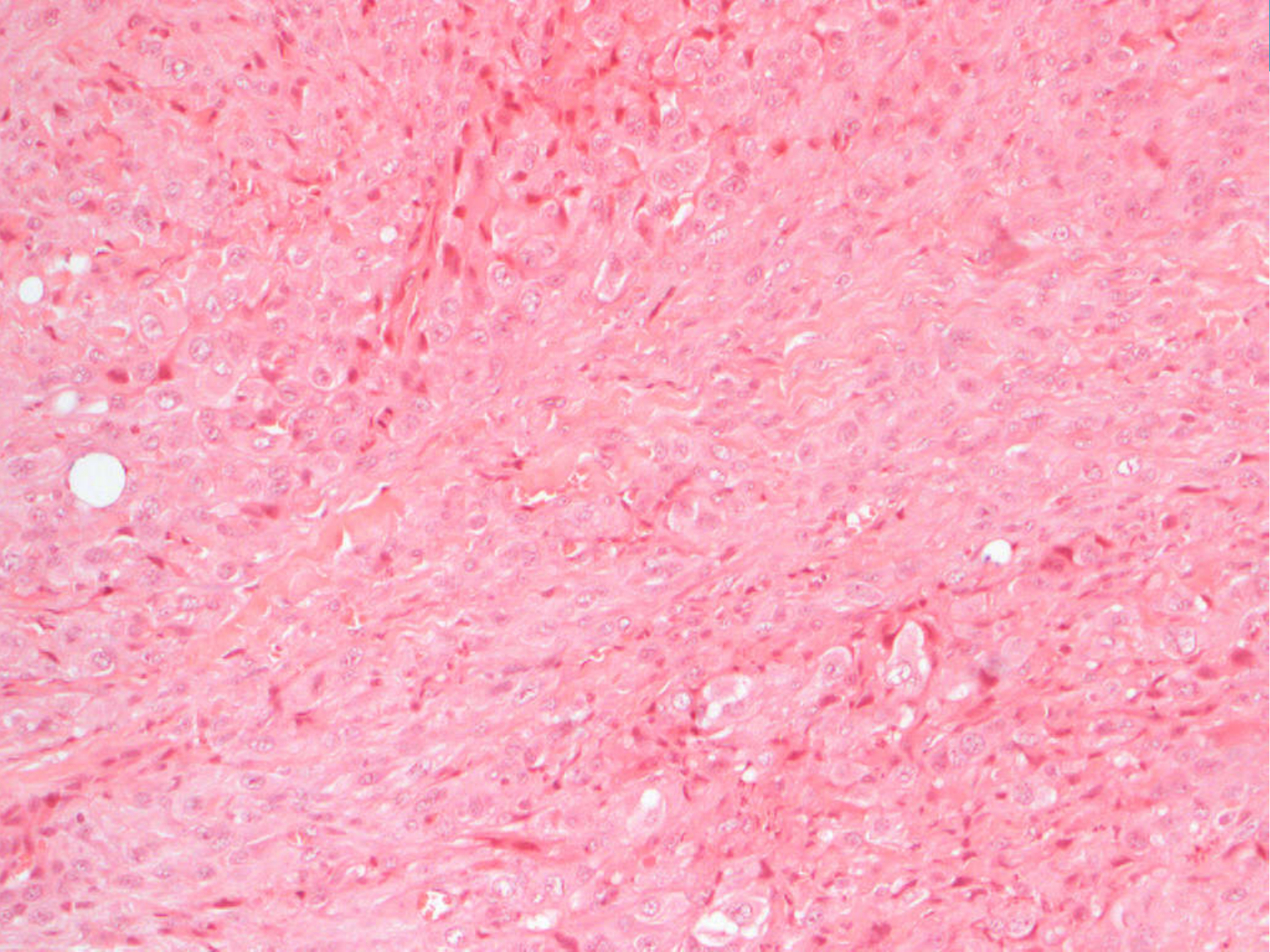
- Male, 24
- Disarticulation of left hand at wrist.
- Soft tissue mass. [approx. 50mm maximum dimension].
- Lesion erodes bone.

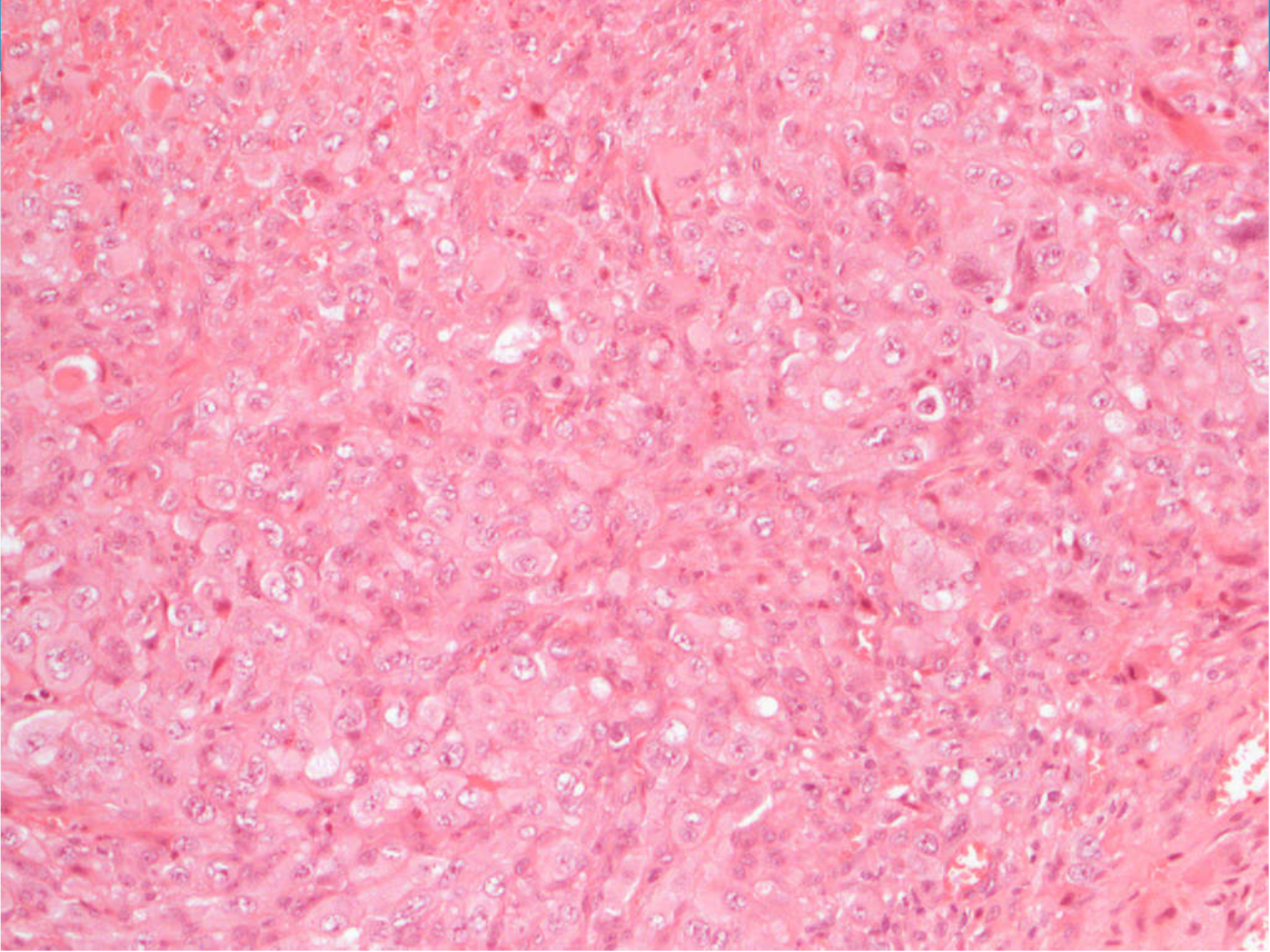












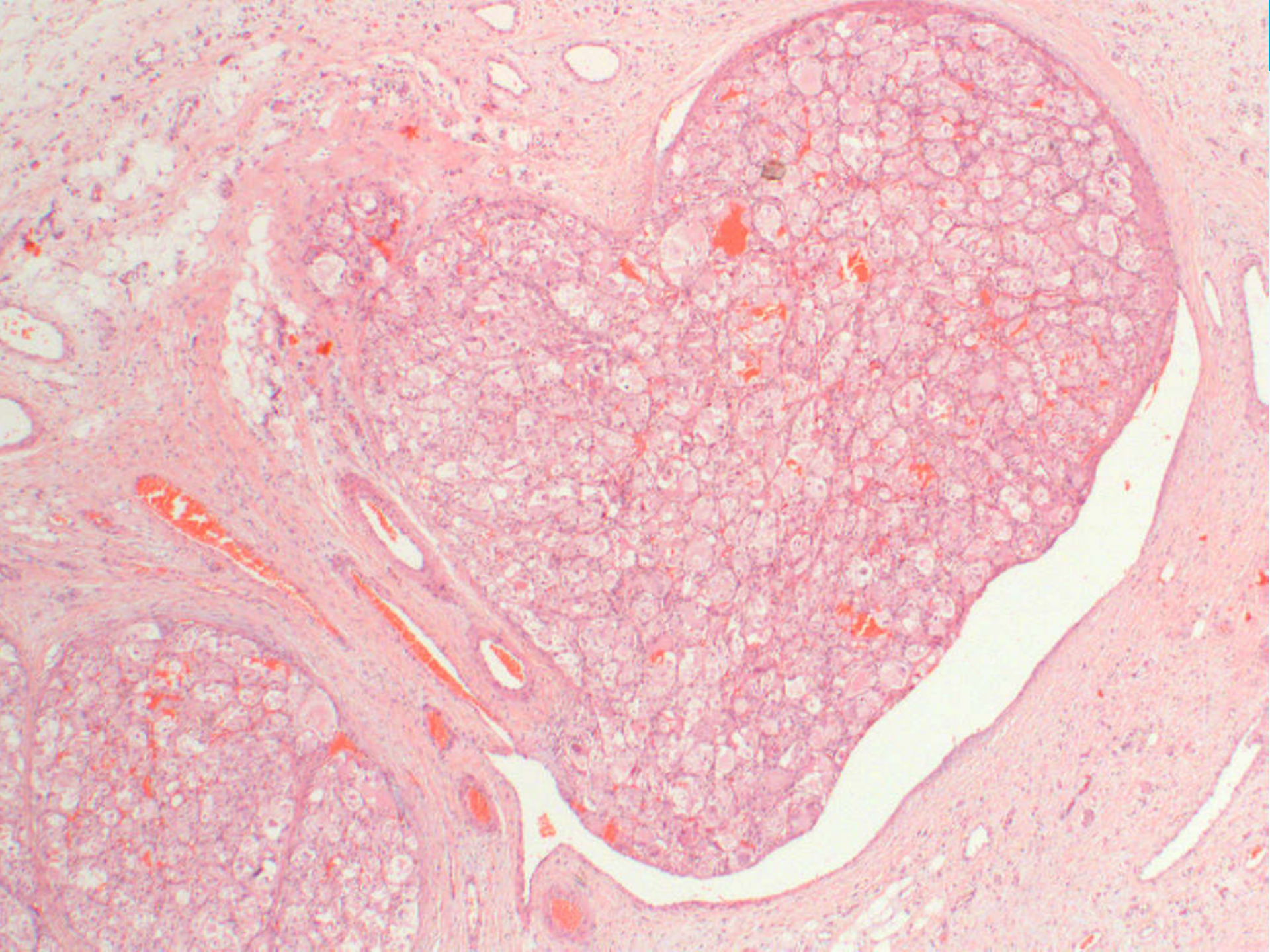
DX: Soft Tissue 28 Adv Path Course

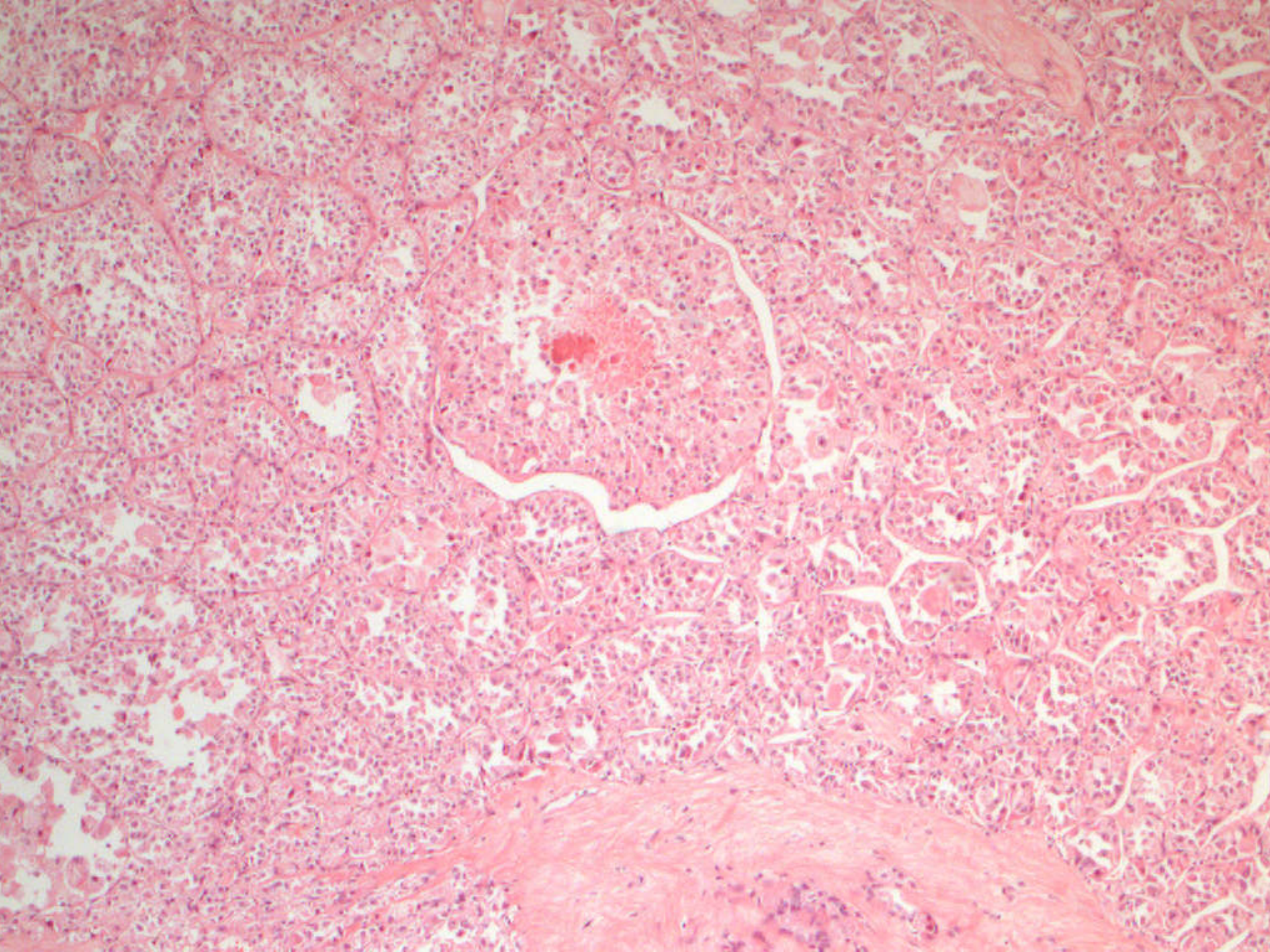
Epithelioid sarcoma

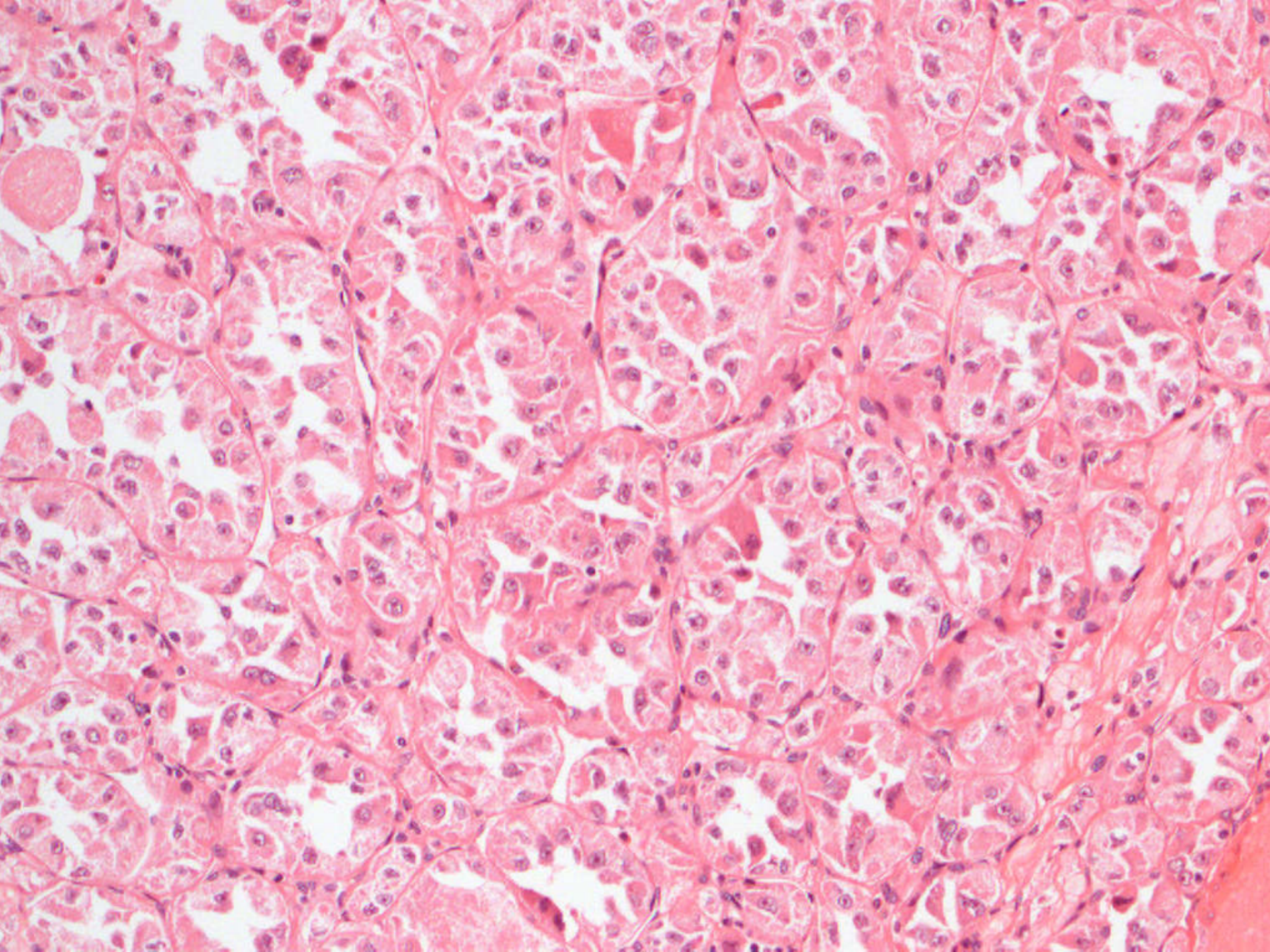
- Malignant mesenchymal neoplasm with predominantly epithelioid phenotype
  - Classic or conventional “distal” type- acral site and pseudogranulomatous growth
  - Proximal “large-cell” type- proximal/truncal site and sheets of large epithelioid cells
- Both types positive for epithelial markers and show loss of SMARCB1 (INI1)
- Rare variants include angiomatoid, fibroma-like and myxoid
- Beware mis-diagnosing granuloma annulare at proximal sites

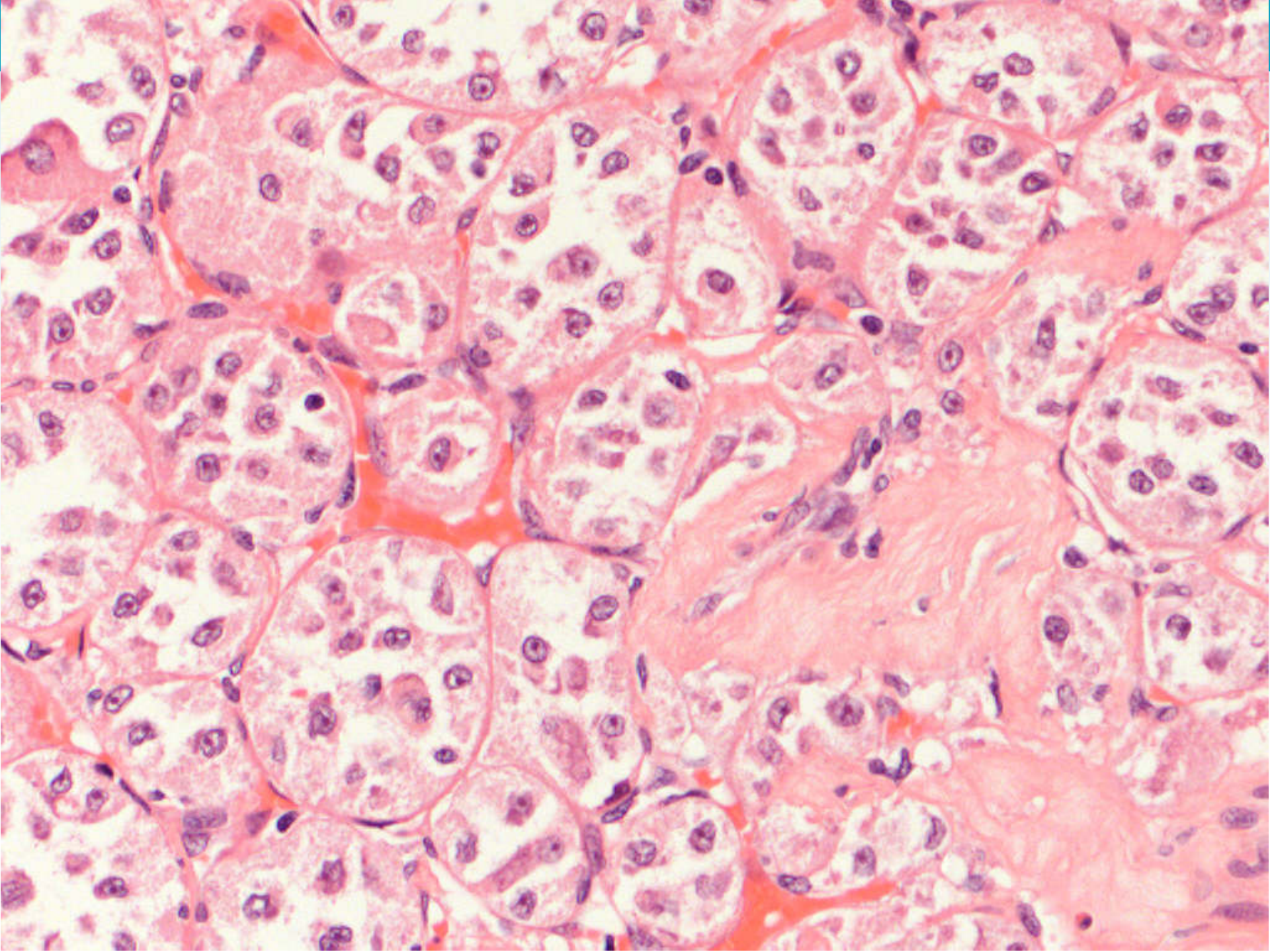
CLINICAL INFORMATION 29

- Male, 23
- Soft tissue mass on right medial aspect of distal thigh [50mm maximum dimension].









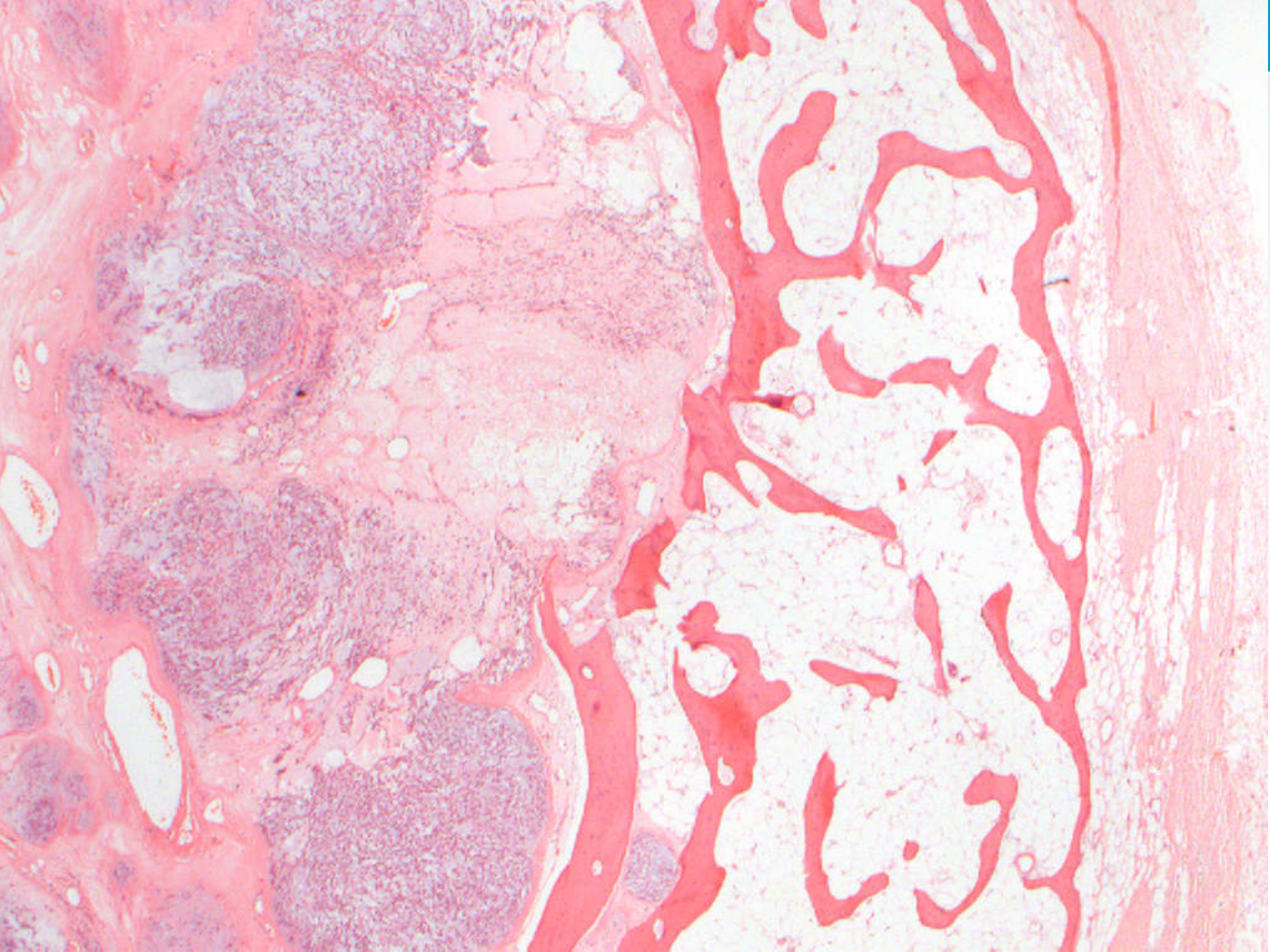
DX: Soft Tissue 29 Adv Path Course

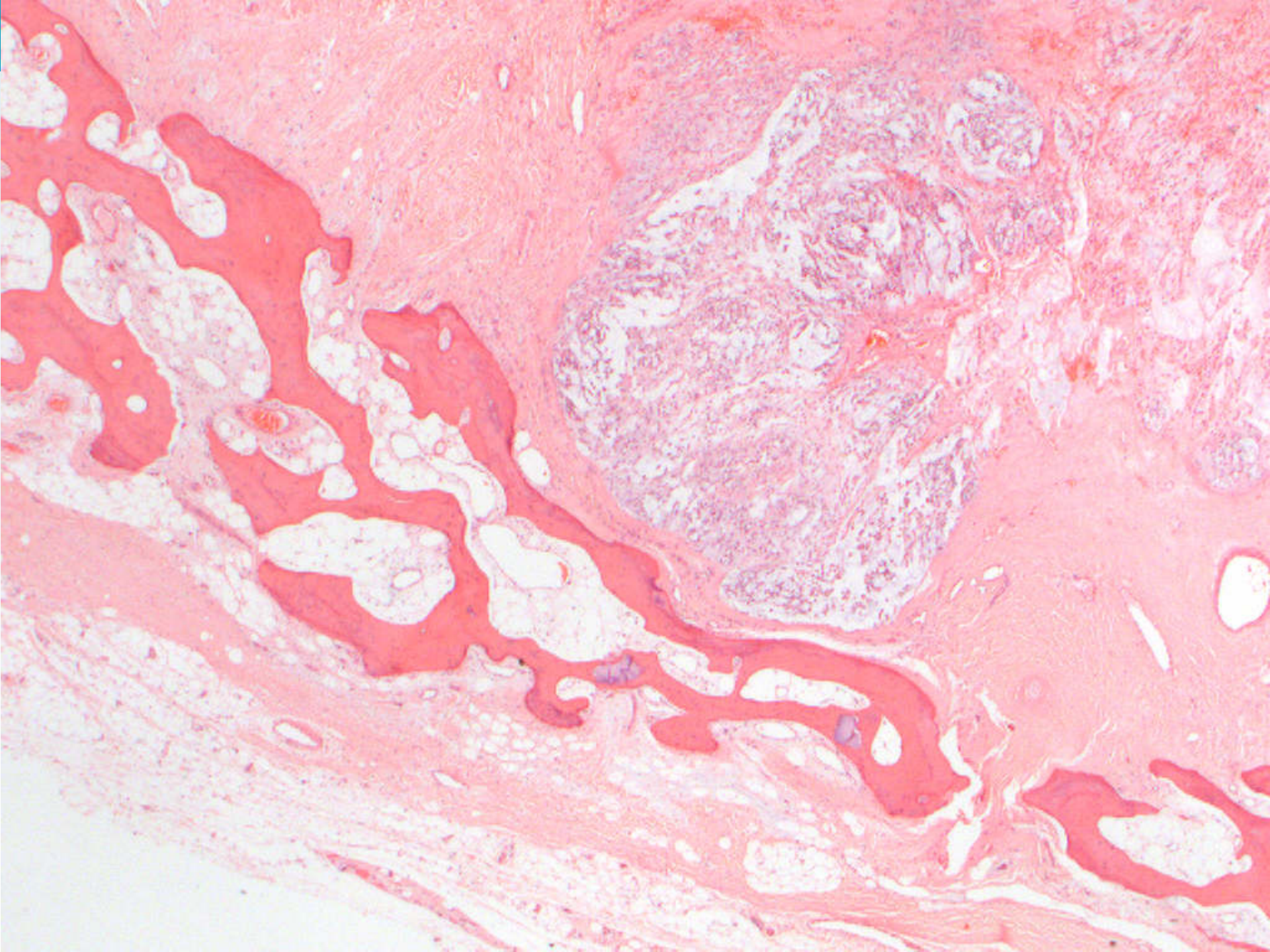
Alveolar soft part sarcoma

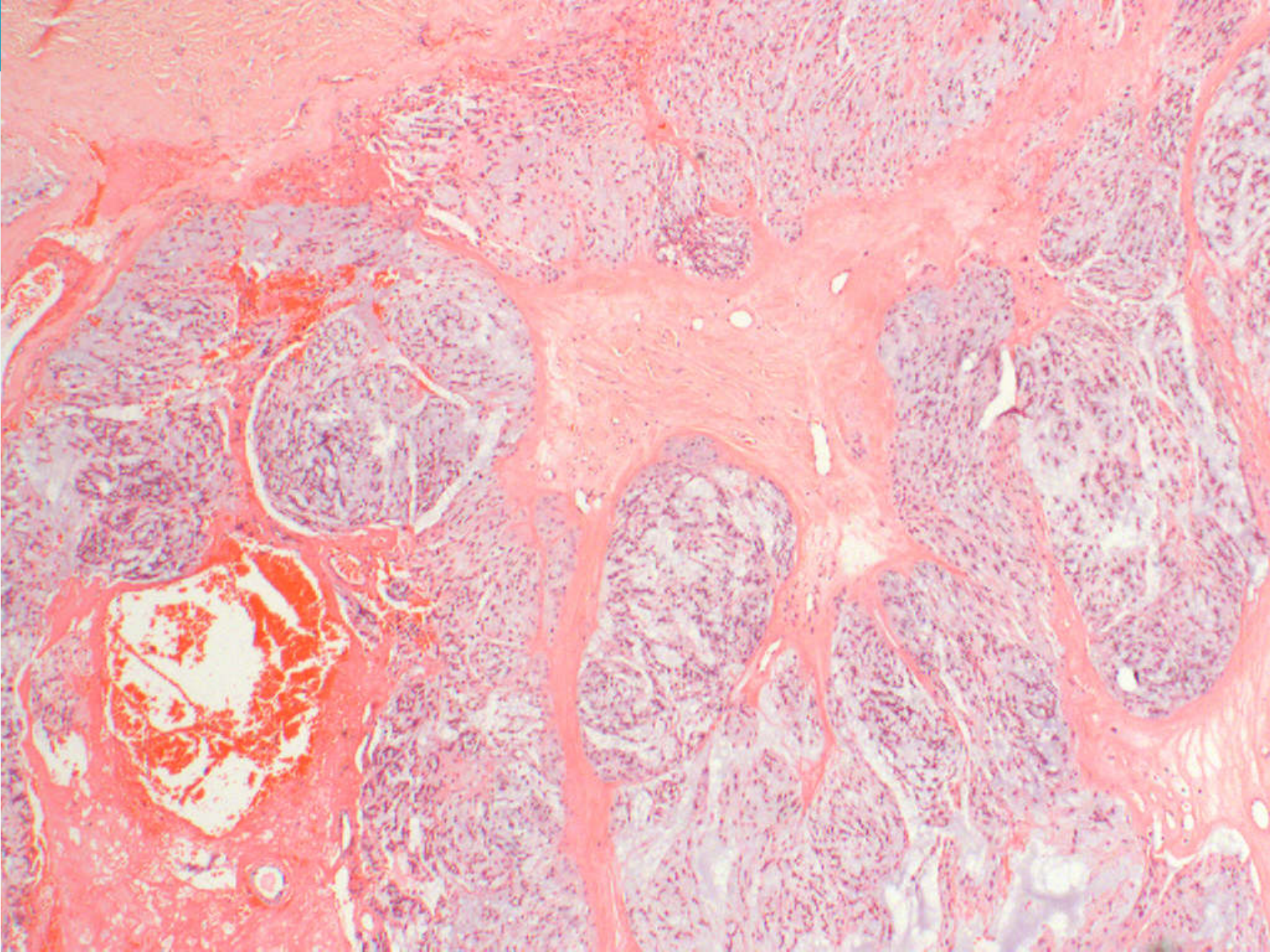
- Rare, distinctive sarcoma characterised by *ASPSCR1-TFE3* fusion
- In adults, common sites aredeep soft tissue of thigh or buttock
- In children, and infants, the head and neck (tongue and orbit)
- Nuclear staining for TFE3 common (but beware, granular cell tumours may also be TFE3+)
- 50% can show focal desmin
- Can also be S100+, but in contrast to PEComa HMB45 is negative

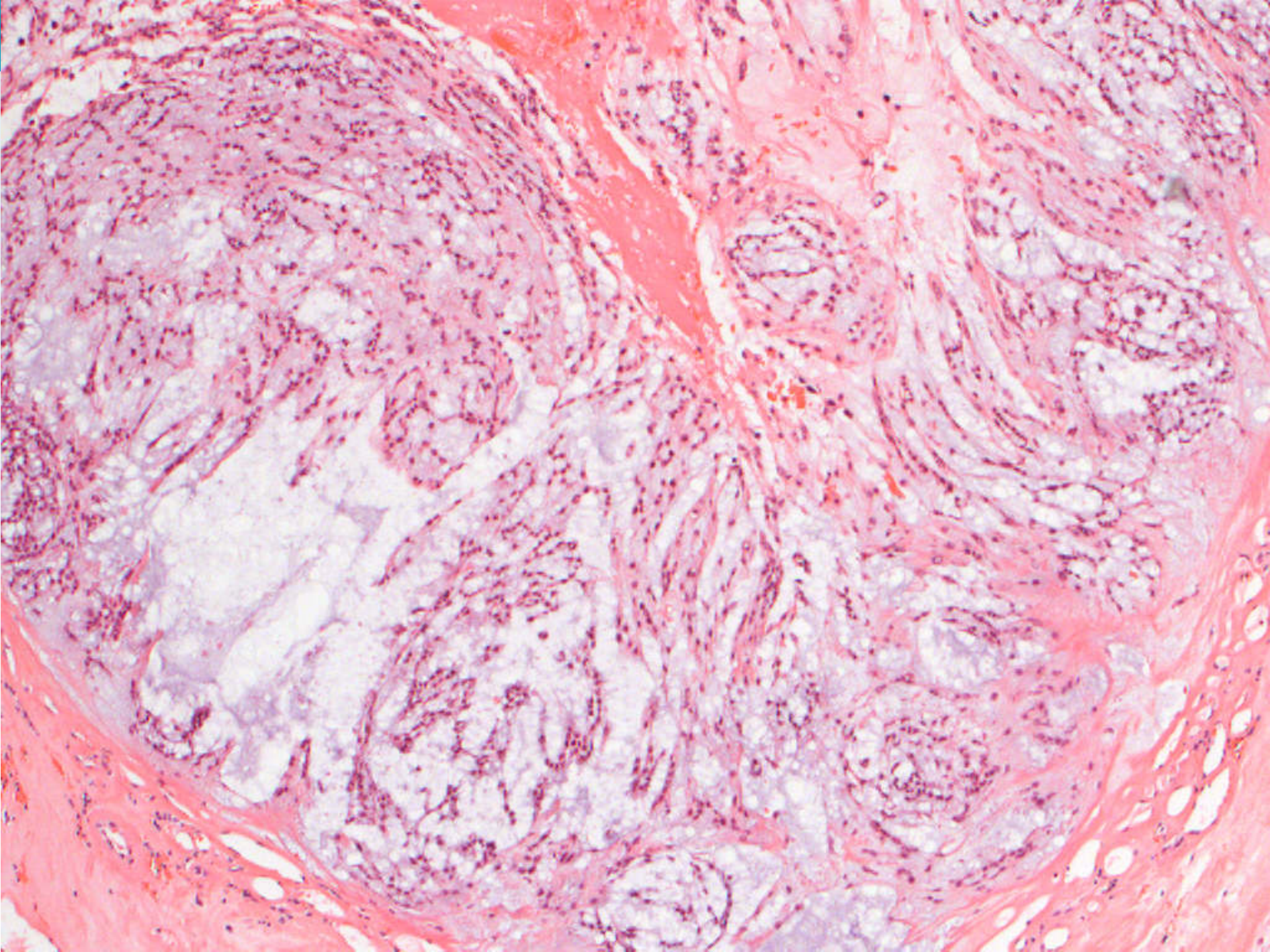
CLINICAL INFORMATION 30

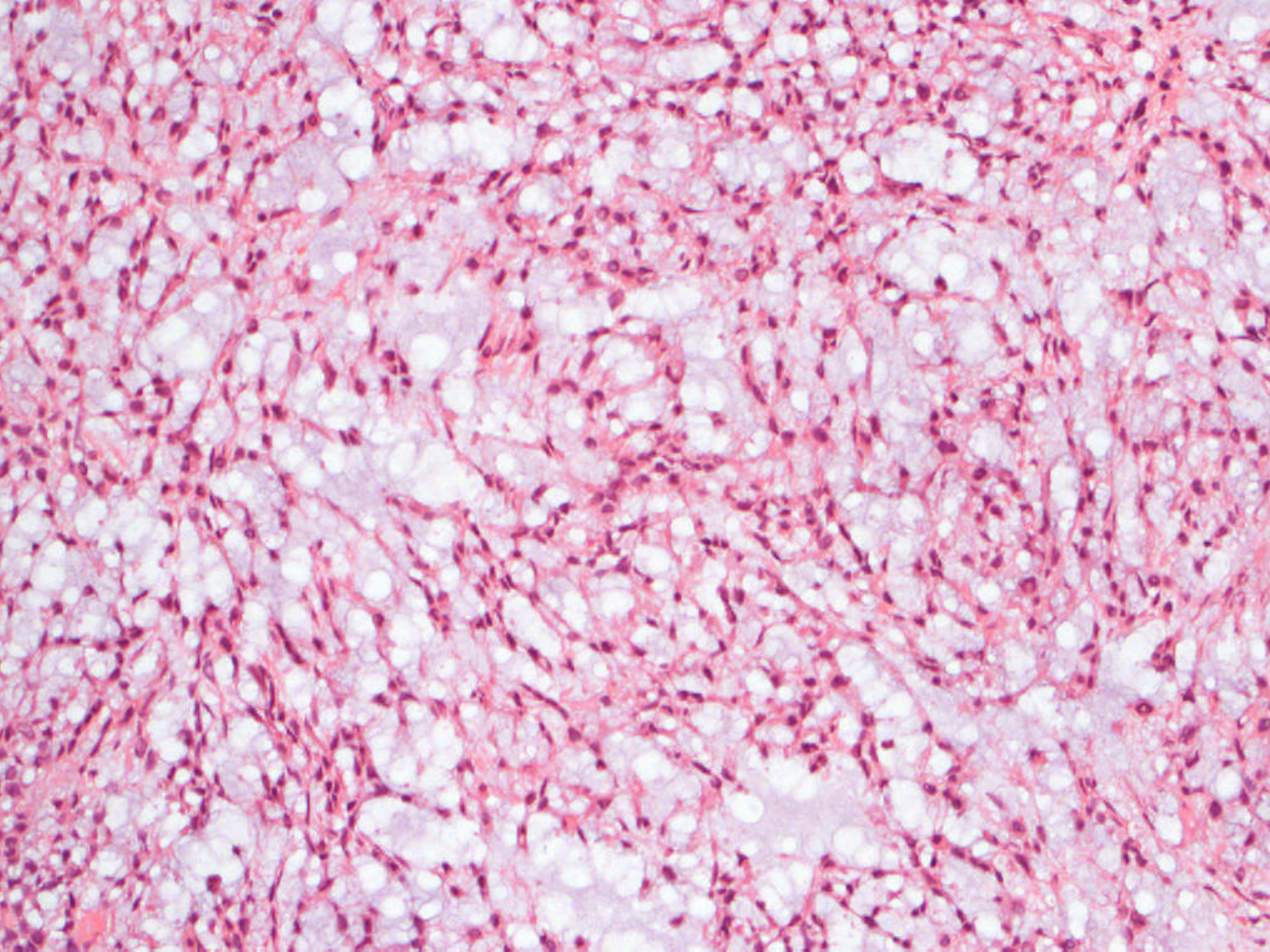
- Female, 58
- Partly ossified intramuscular mass [55mm maximum dimension].
- Upper arm.

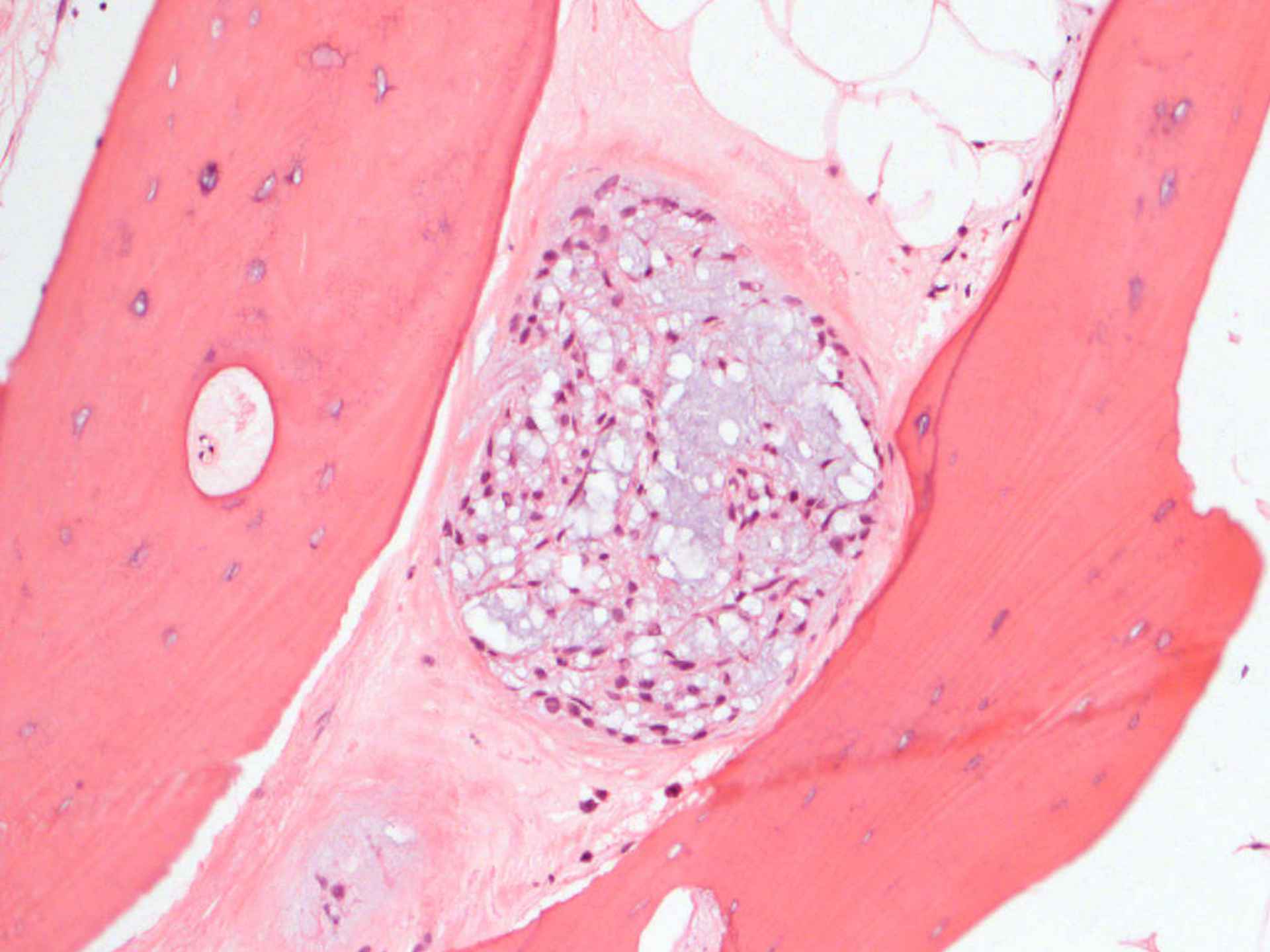












DX: Soft Tissue 30 Adv Path Course

Ossifying fibromyxoid tumour

- Rare mesenchymal tumour of uncertain lineage, composed of cords and trabeculae of ovoid cells embedded in a fibromyxoid matrix and surrounded by a peripheral partial shell of lamellar bone
- Occurs in adults of all ages, particularly in thigh, head and neck and trunk
- Extracapsular satellite nodules may occur
- >90% S100 positive
- May also express desmin, GFAP, keratins and SMA