Meeting – Alep

December 08th, 2007

Myxofibrosarcoma, fibromyxoid sarcoma, or myxofibro-*something*

Refinement or redundancy in soft tissue tumor pathology ?

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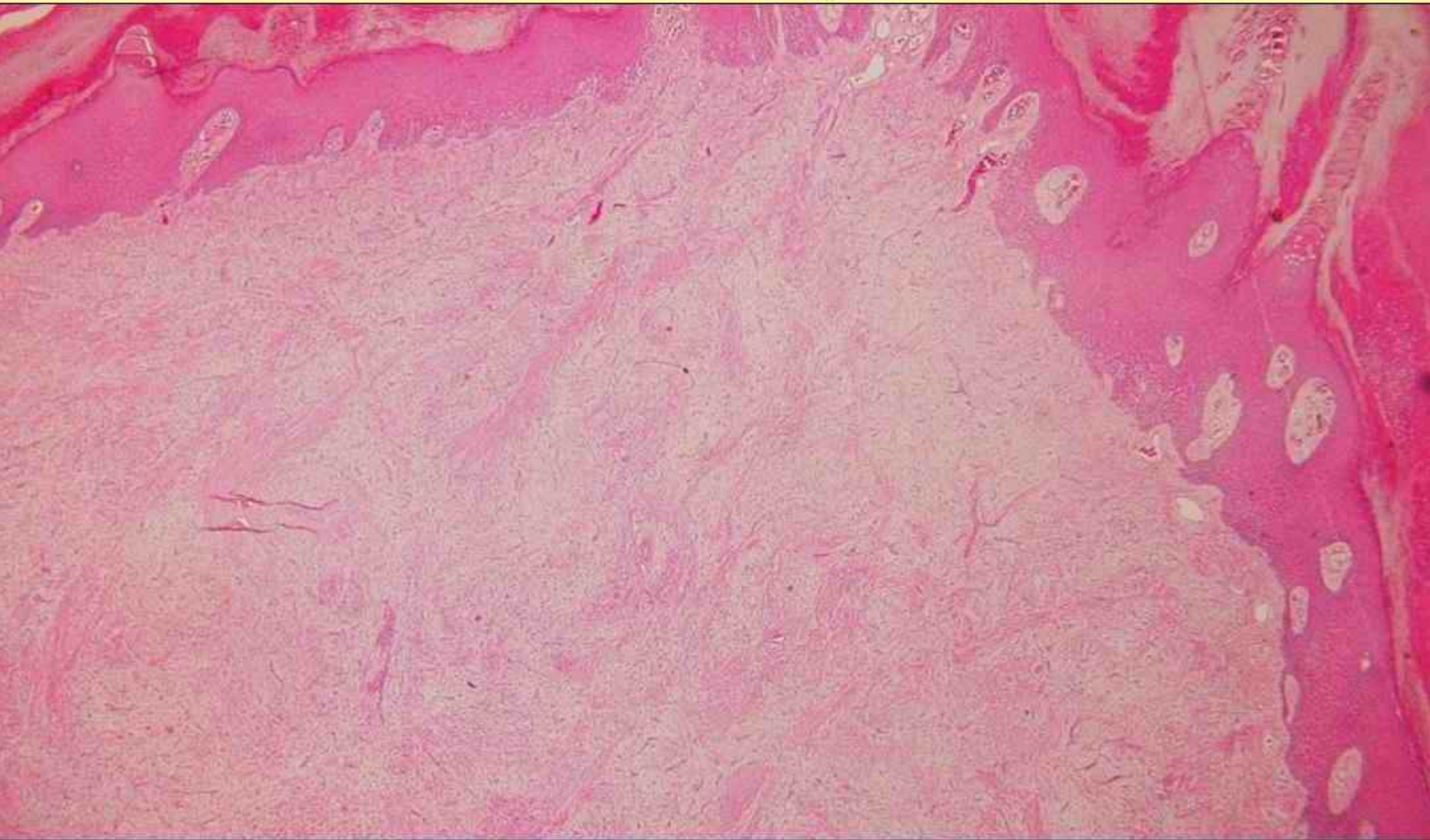
Outline

- Quiz !
- Mesenchymal lesions with a « myxo-fibro » appearance
- Clinicopathologic features of the most relevant « myxo-fibro» entities
- Differential diagnostic approach
- Conclusions, take home messages
- Quiz (results)…..

QUIZ !

QUIZ 1: 1.5 cm nodule developing in close vicinity to the nail of the 4th digit in a 40 year-old male



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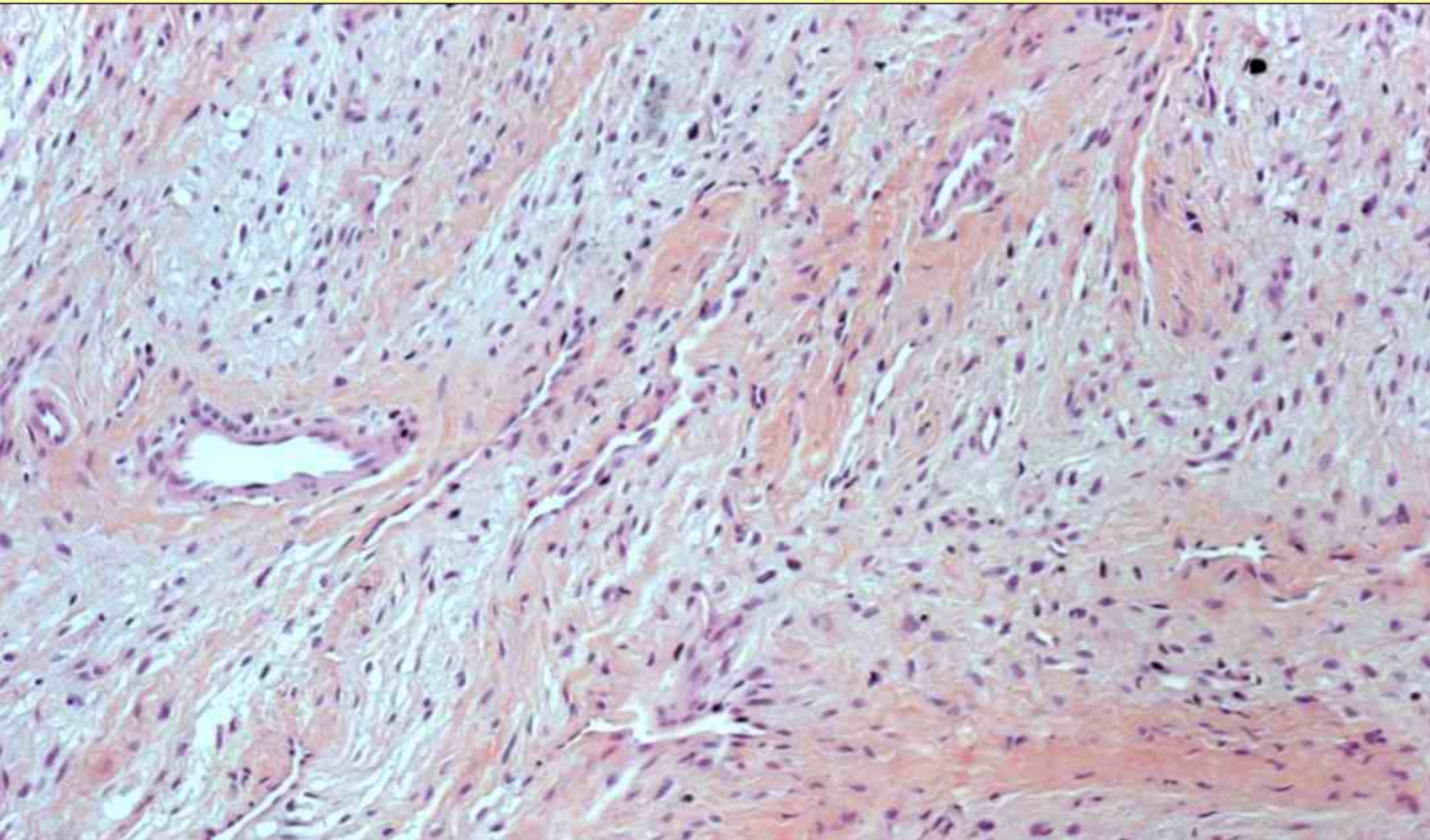

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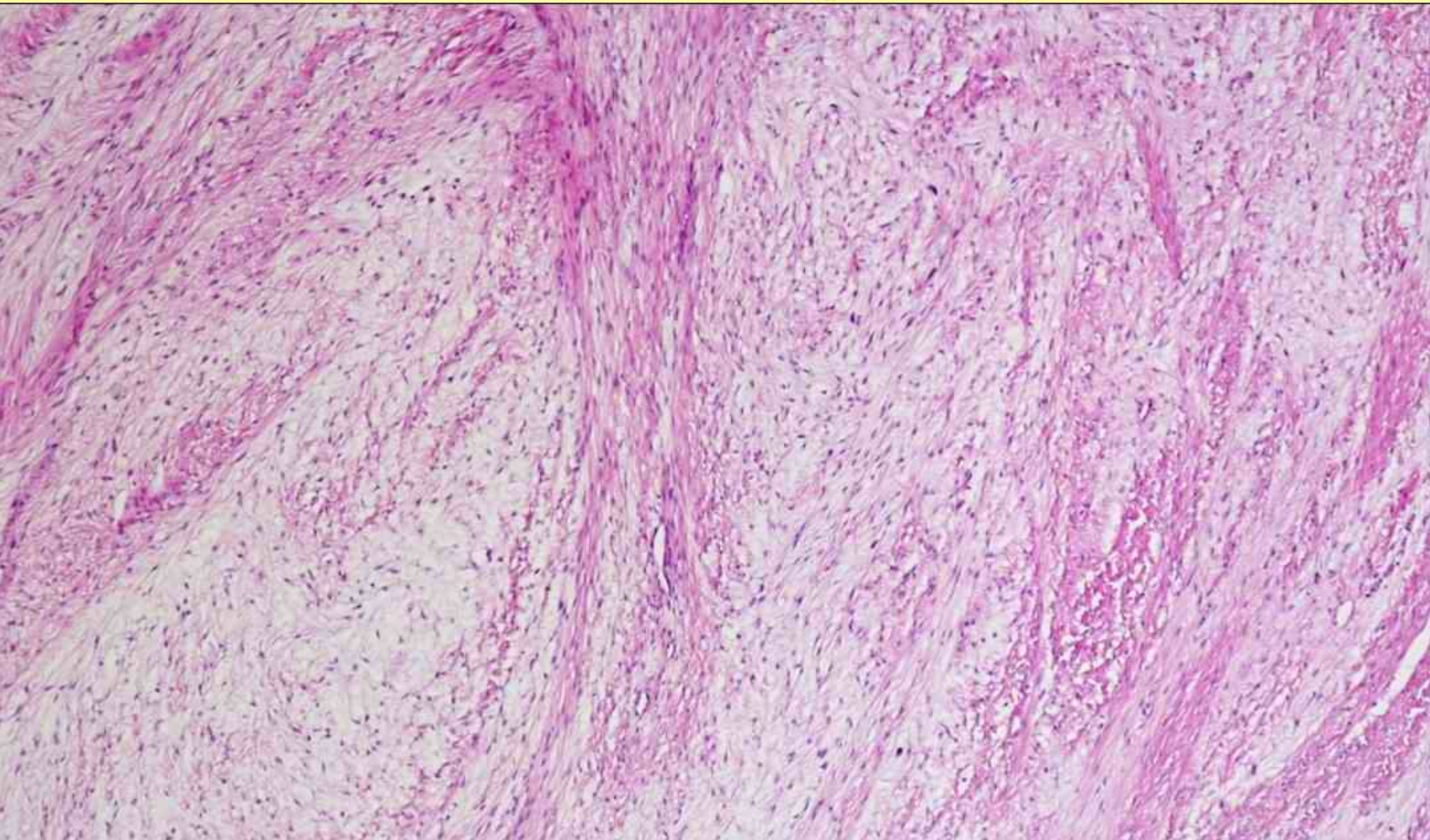

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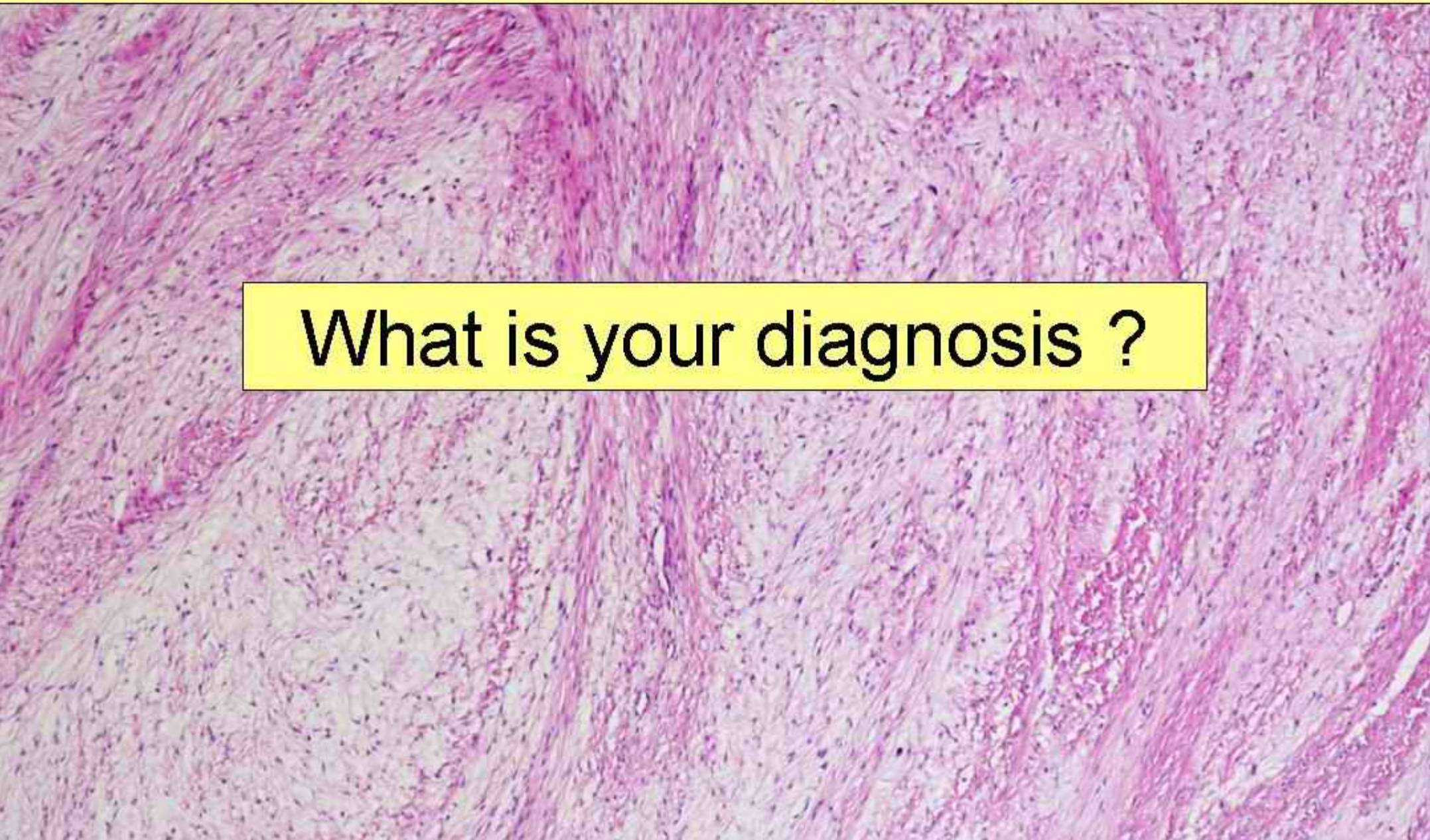
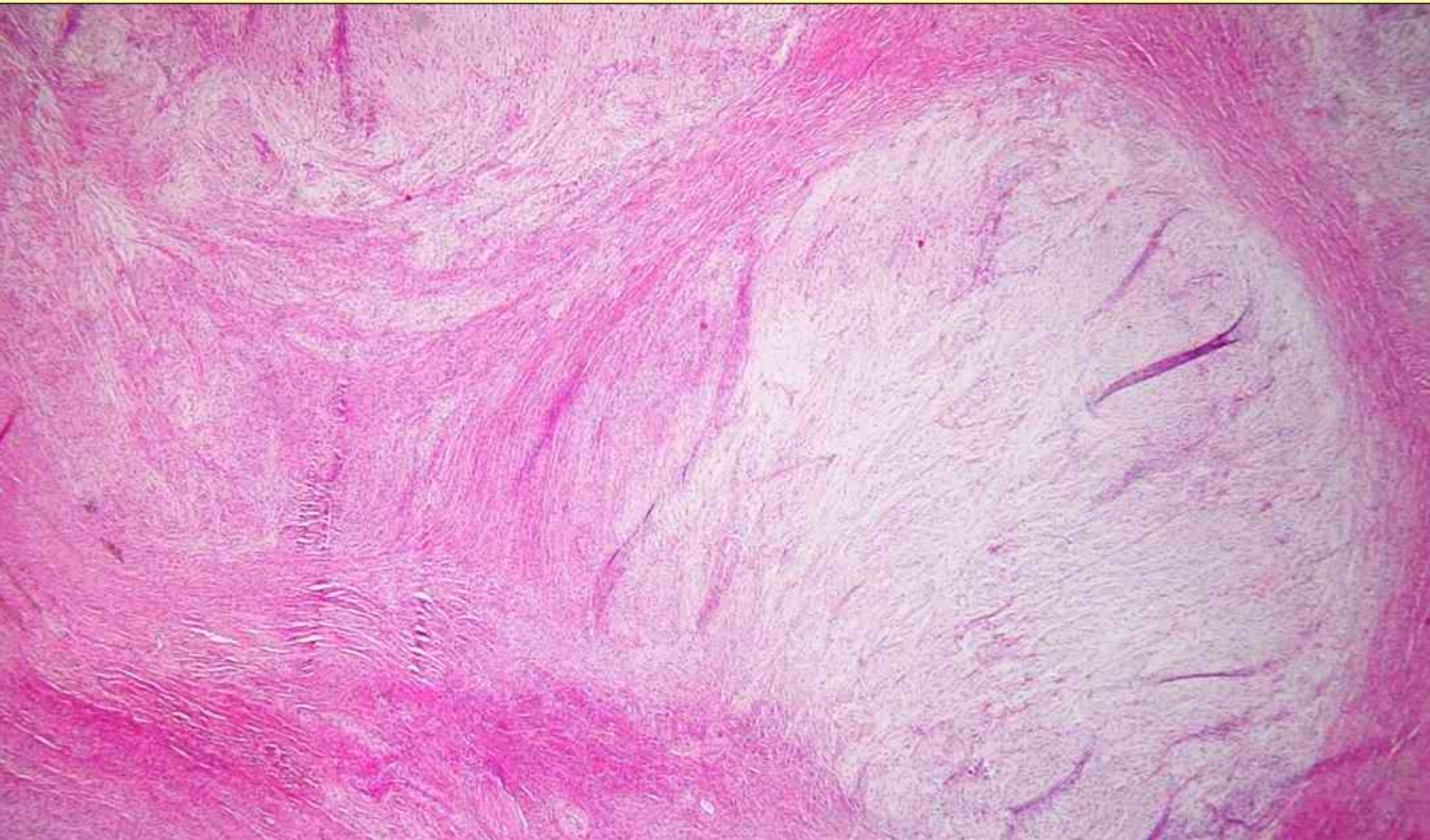


QUIZ 2: 7 cm, well-demarcated, slowly-growing, intramuscular mass in the thigh of a 32 year-old male



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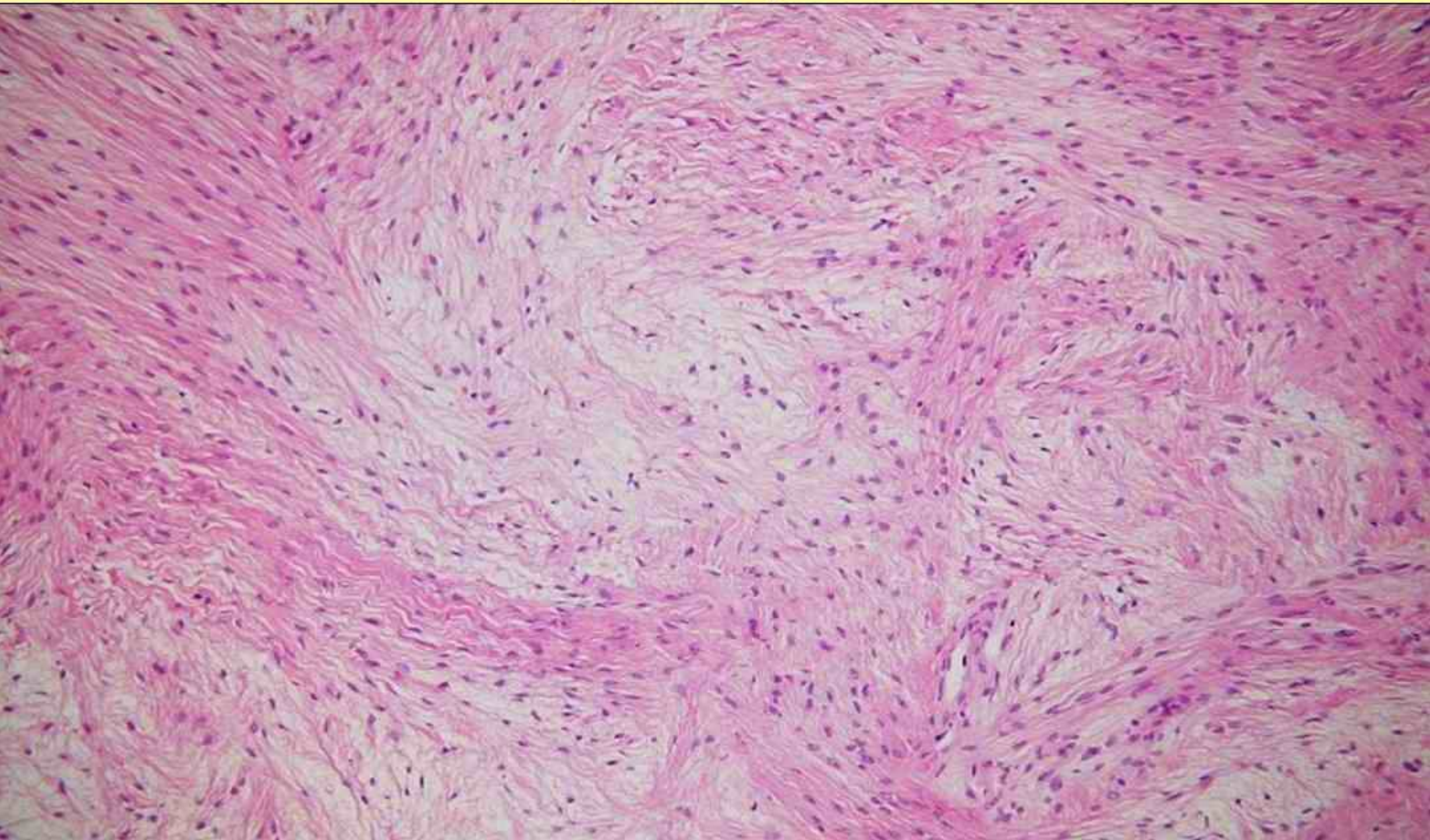

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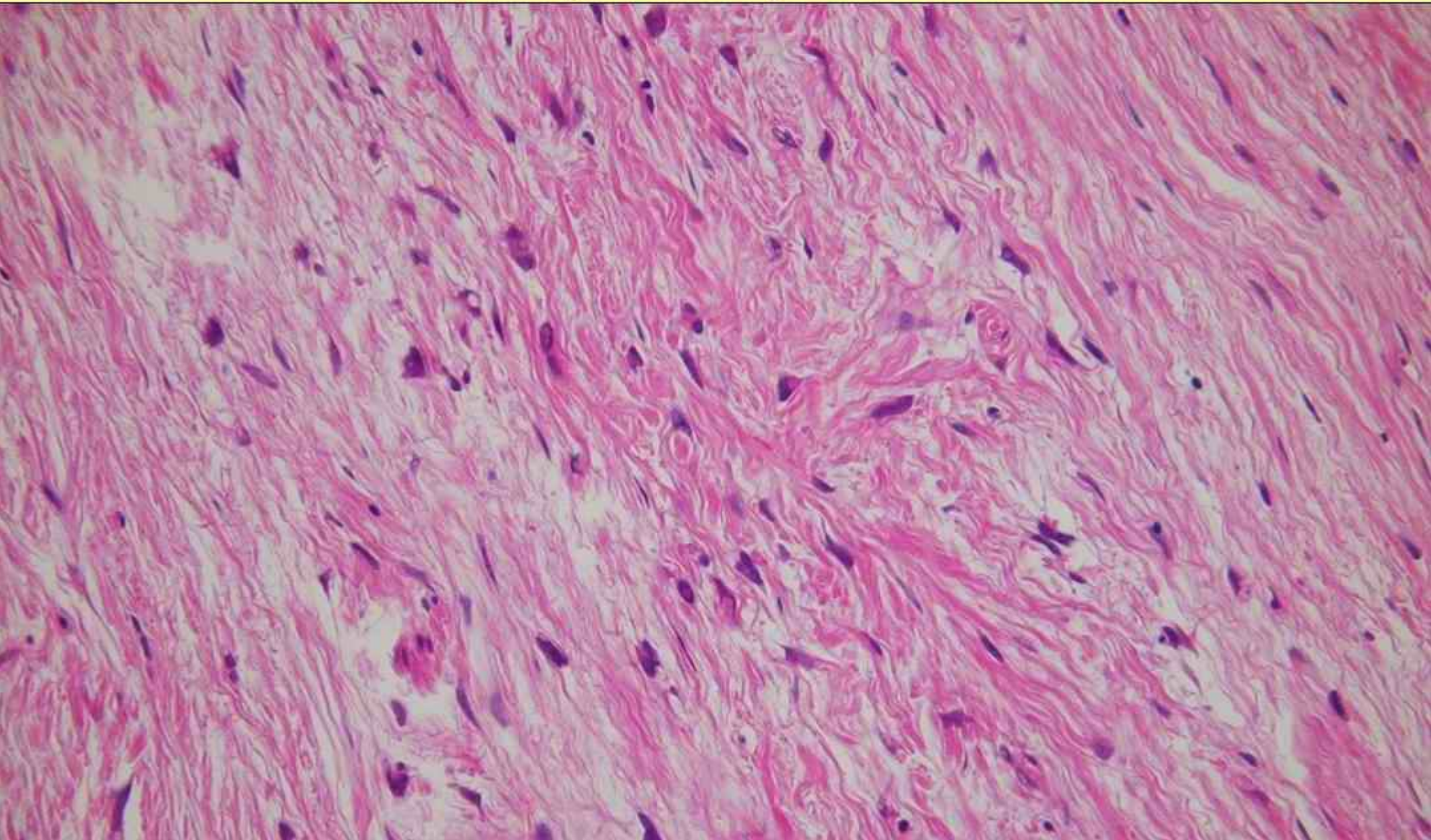

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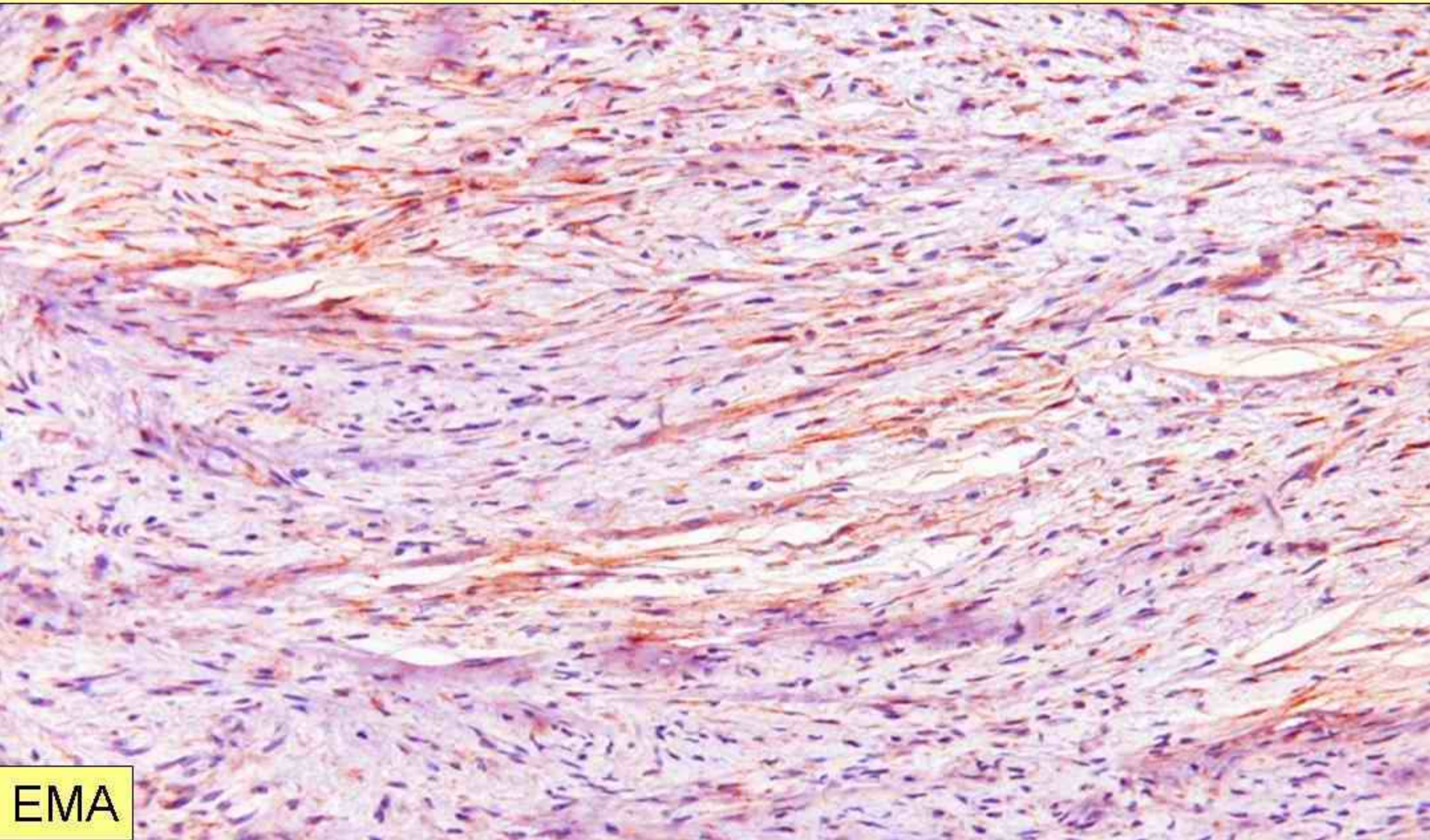
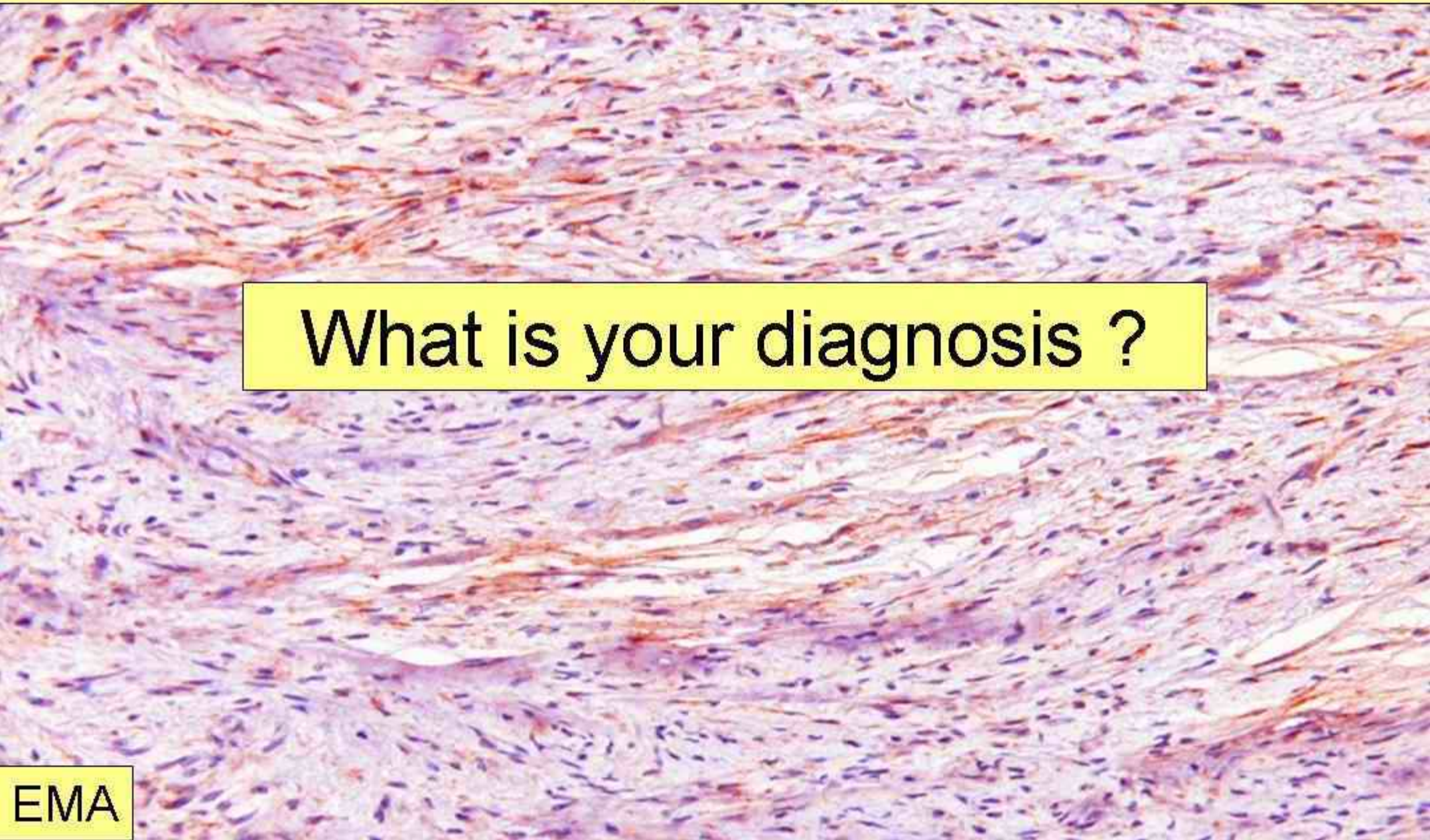
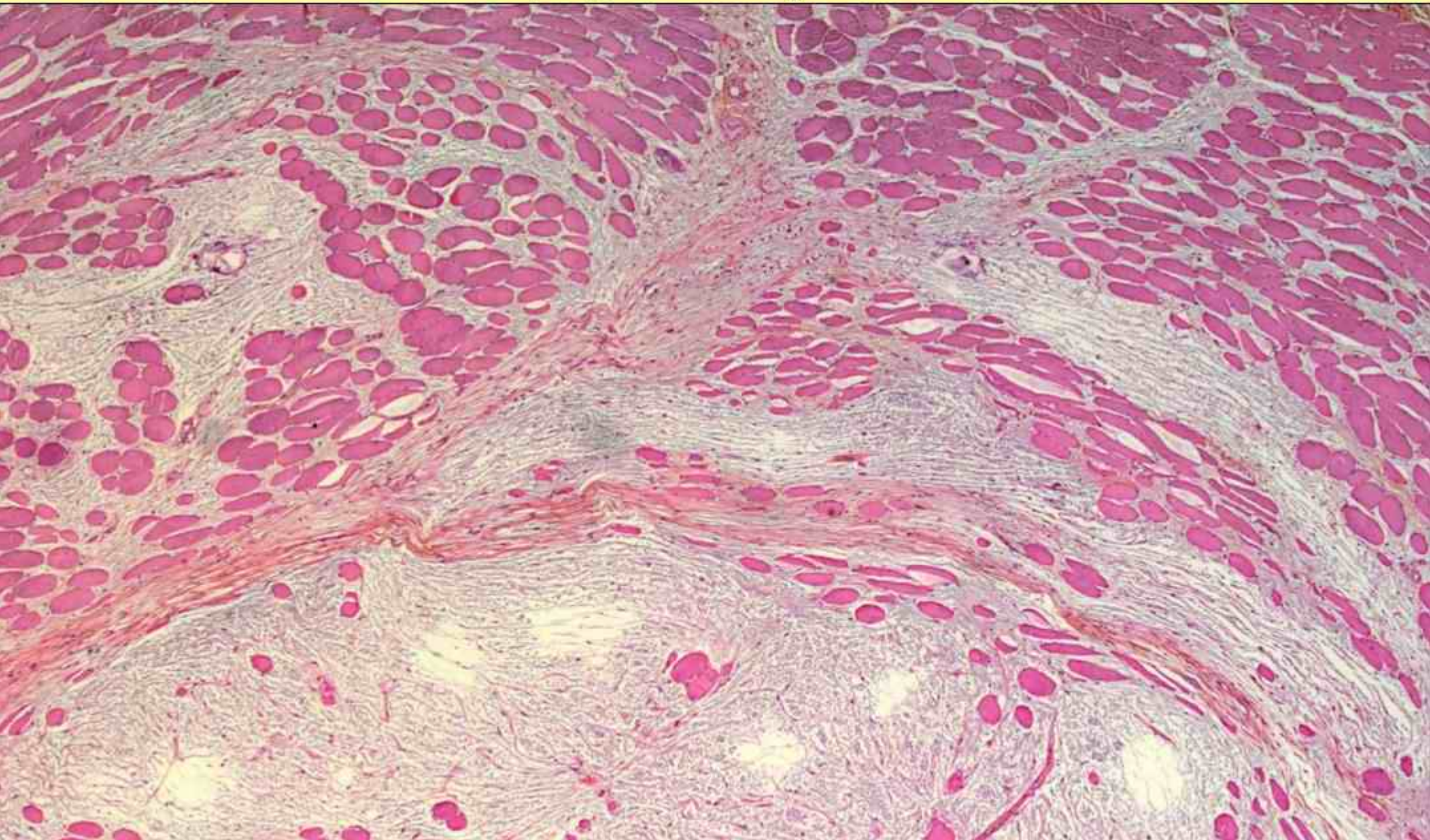


QUIZ 2: 7 cm, well-demarcated, slowly-growing, intramuscular mass sitting in the thigh of a 32 year-old male



QUIZ 3: 6 cm, slowly-growing, intramuscular mass developing in the thigh of a 50 year-old female



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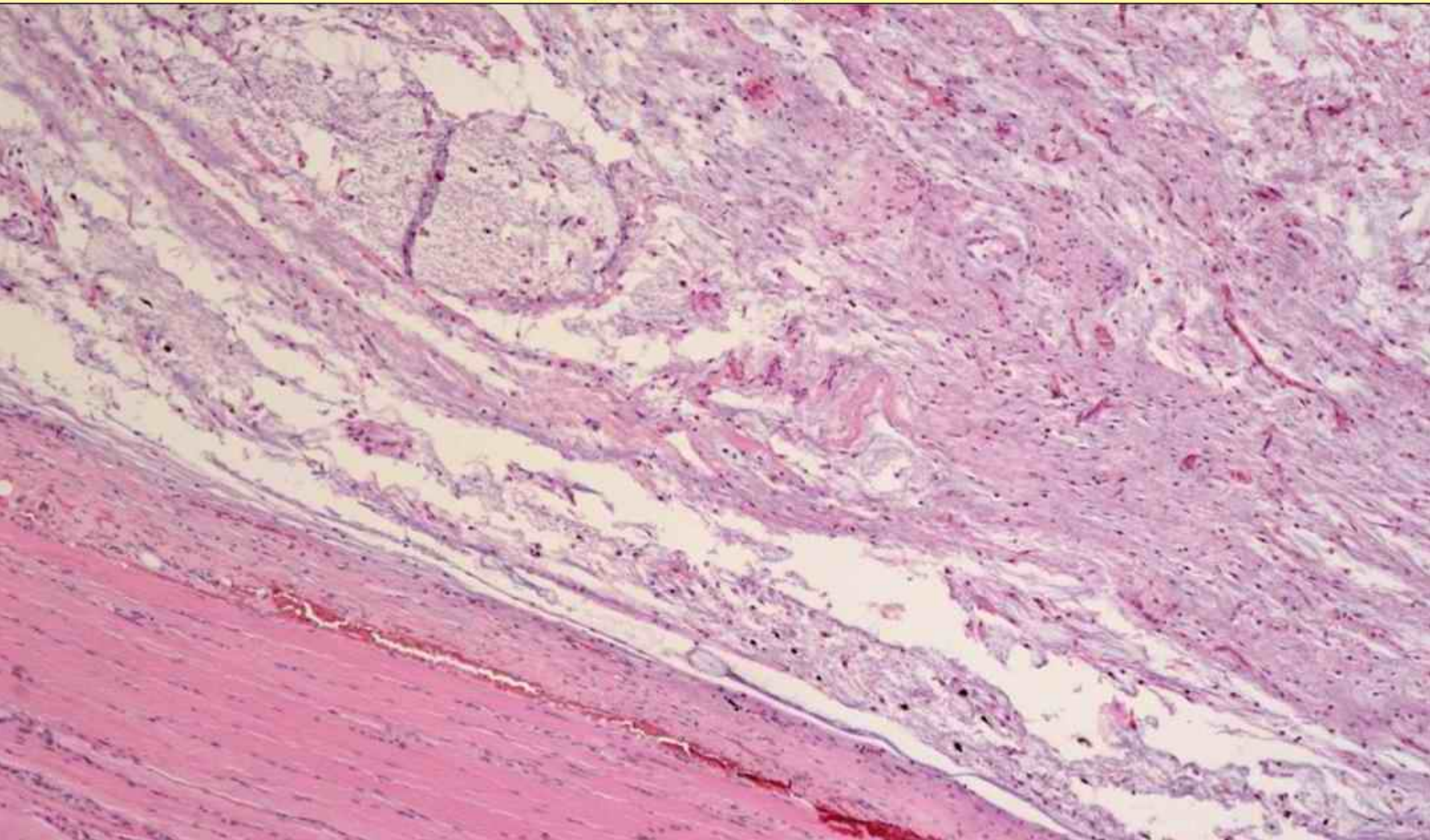

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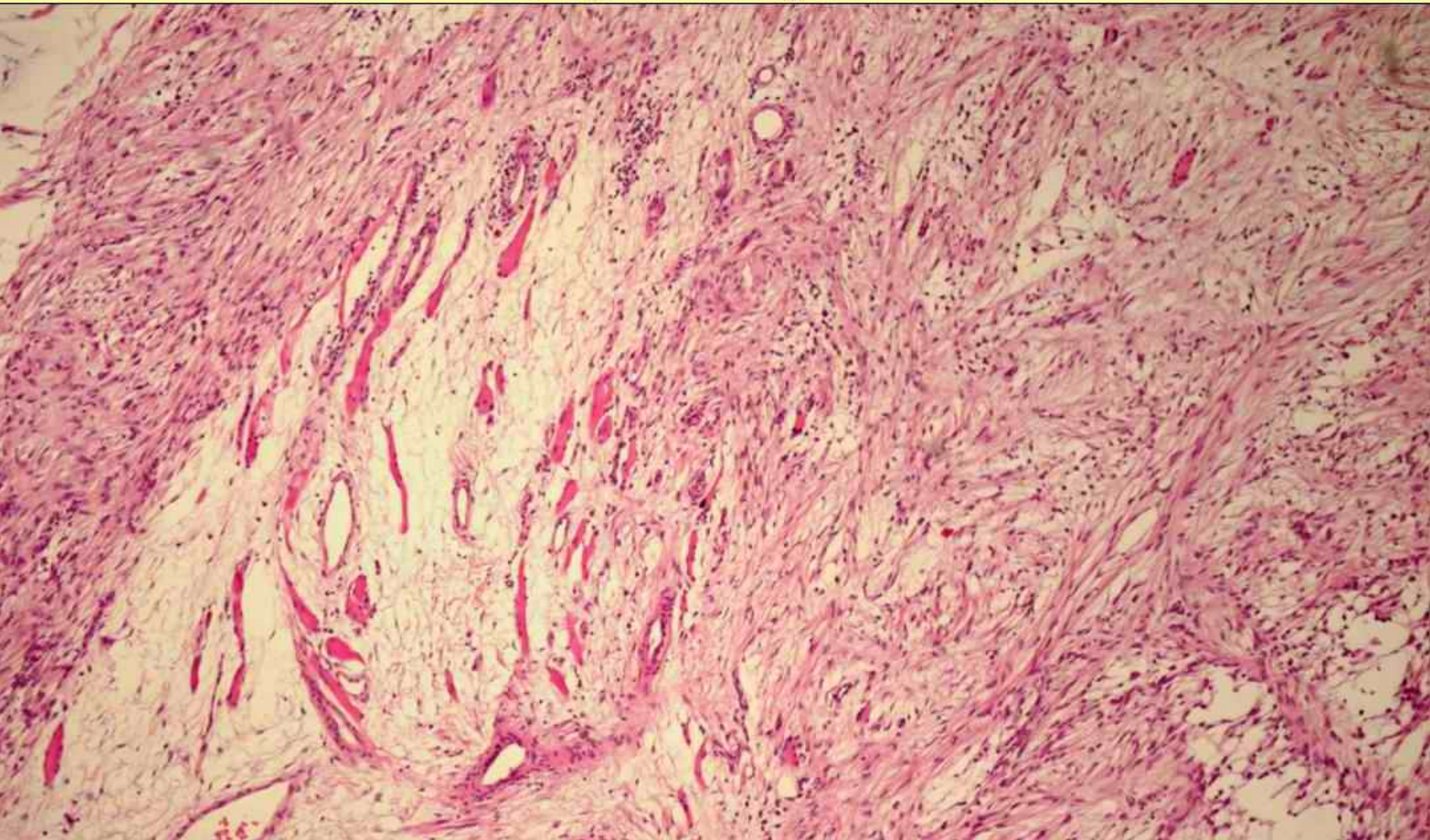

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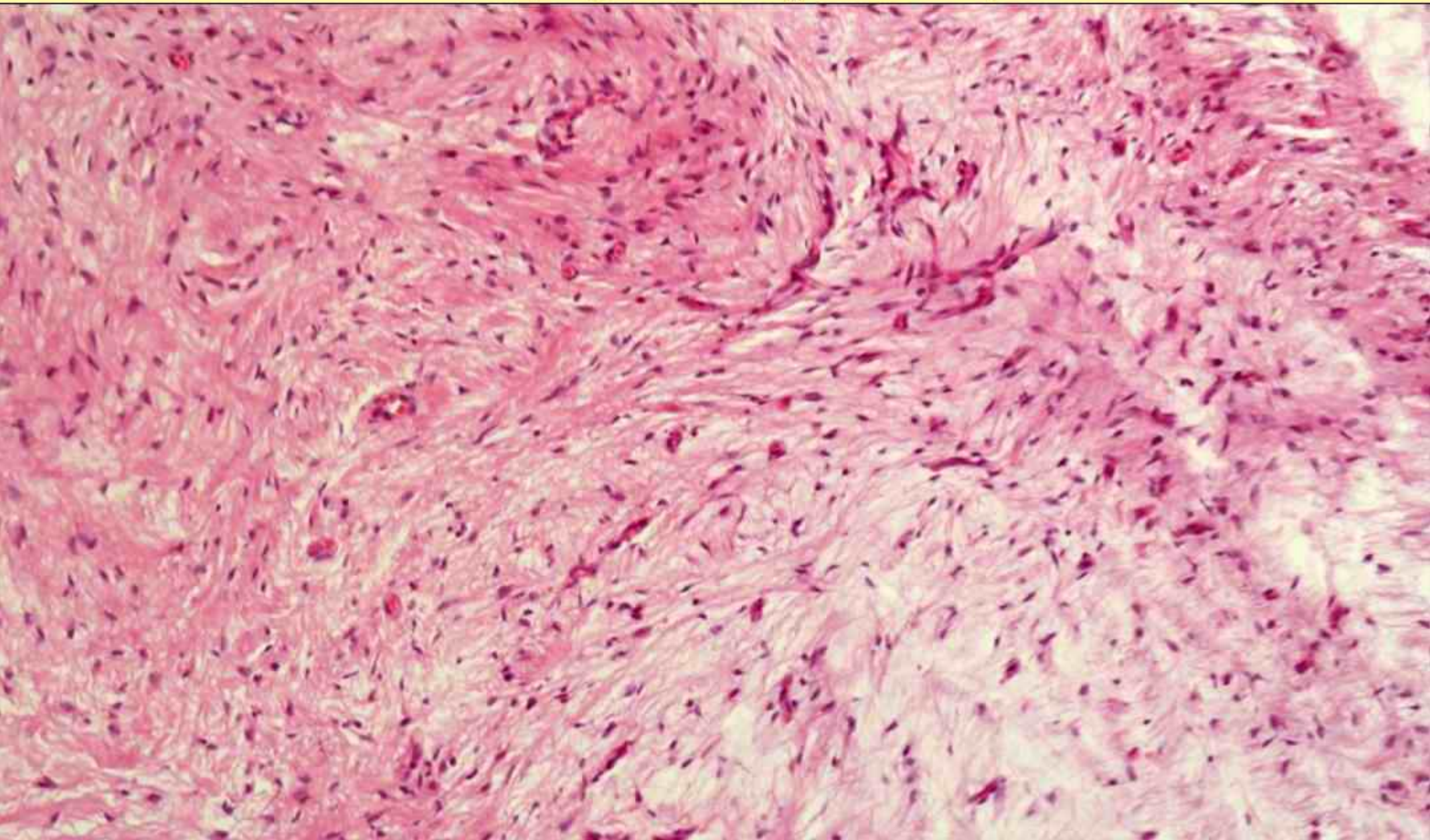

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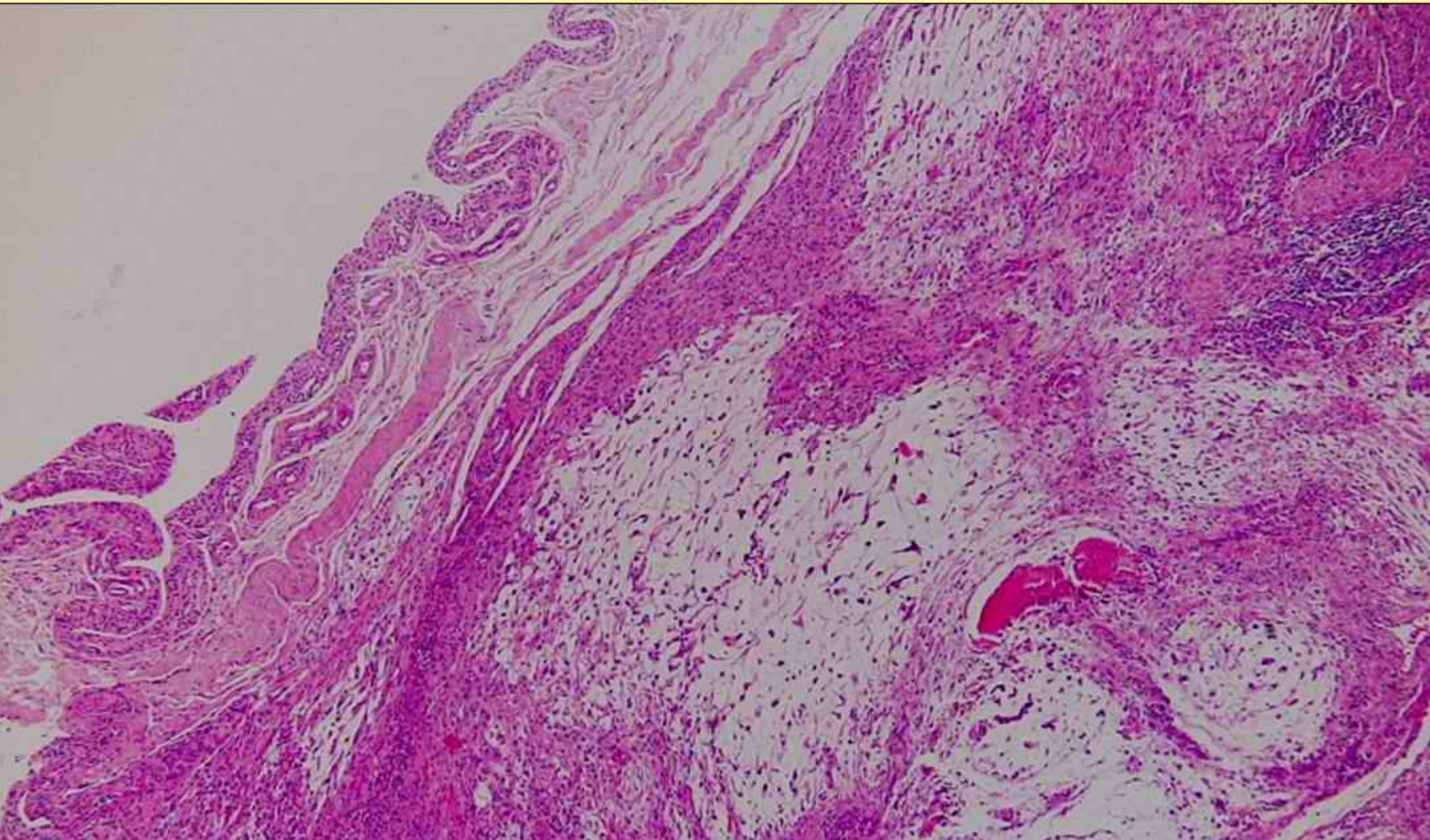
QUIZ 4: 4 cm, gelatinous, ill-defined mass of the 2nd left digit in a 45 year-old male



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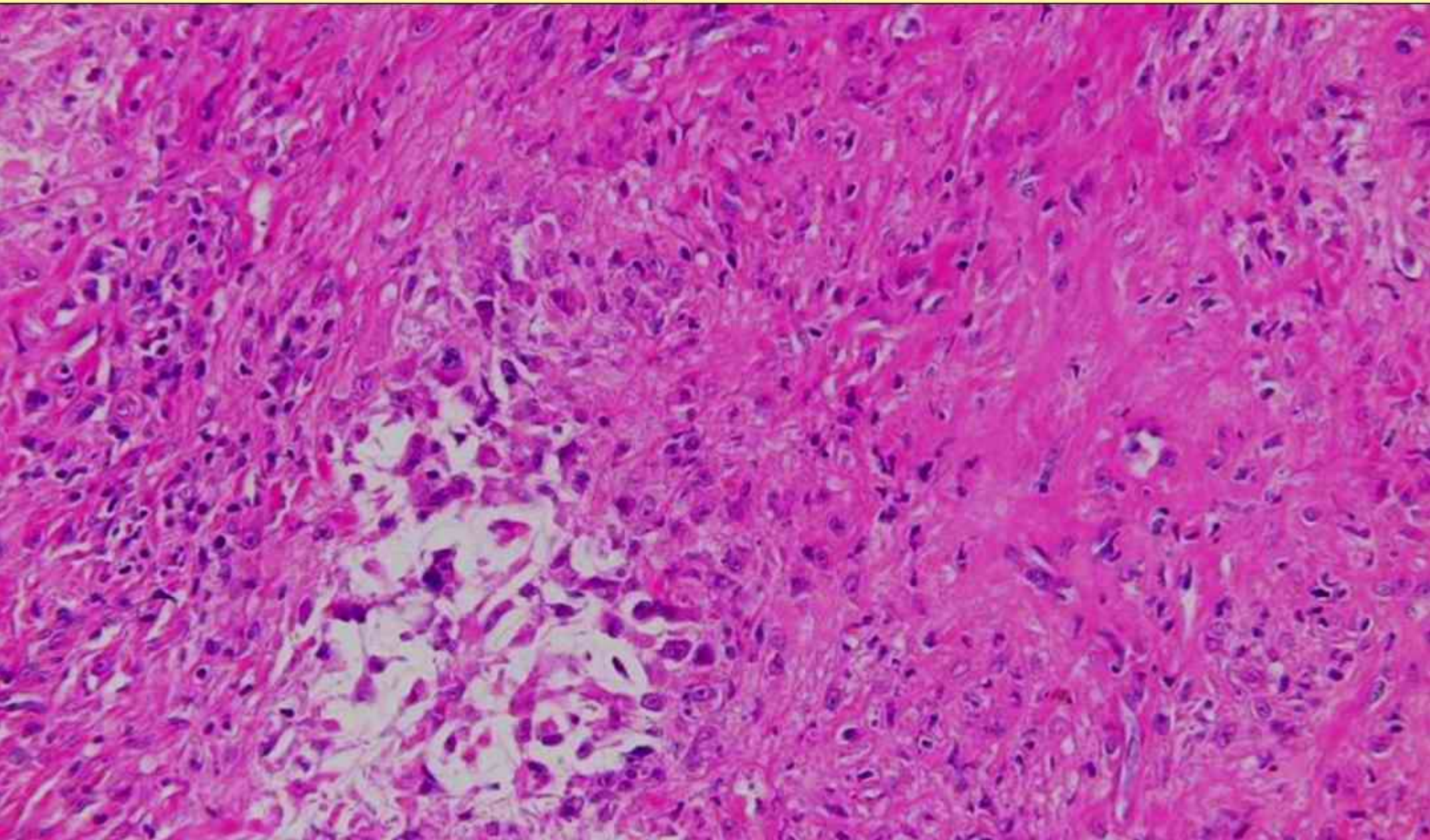

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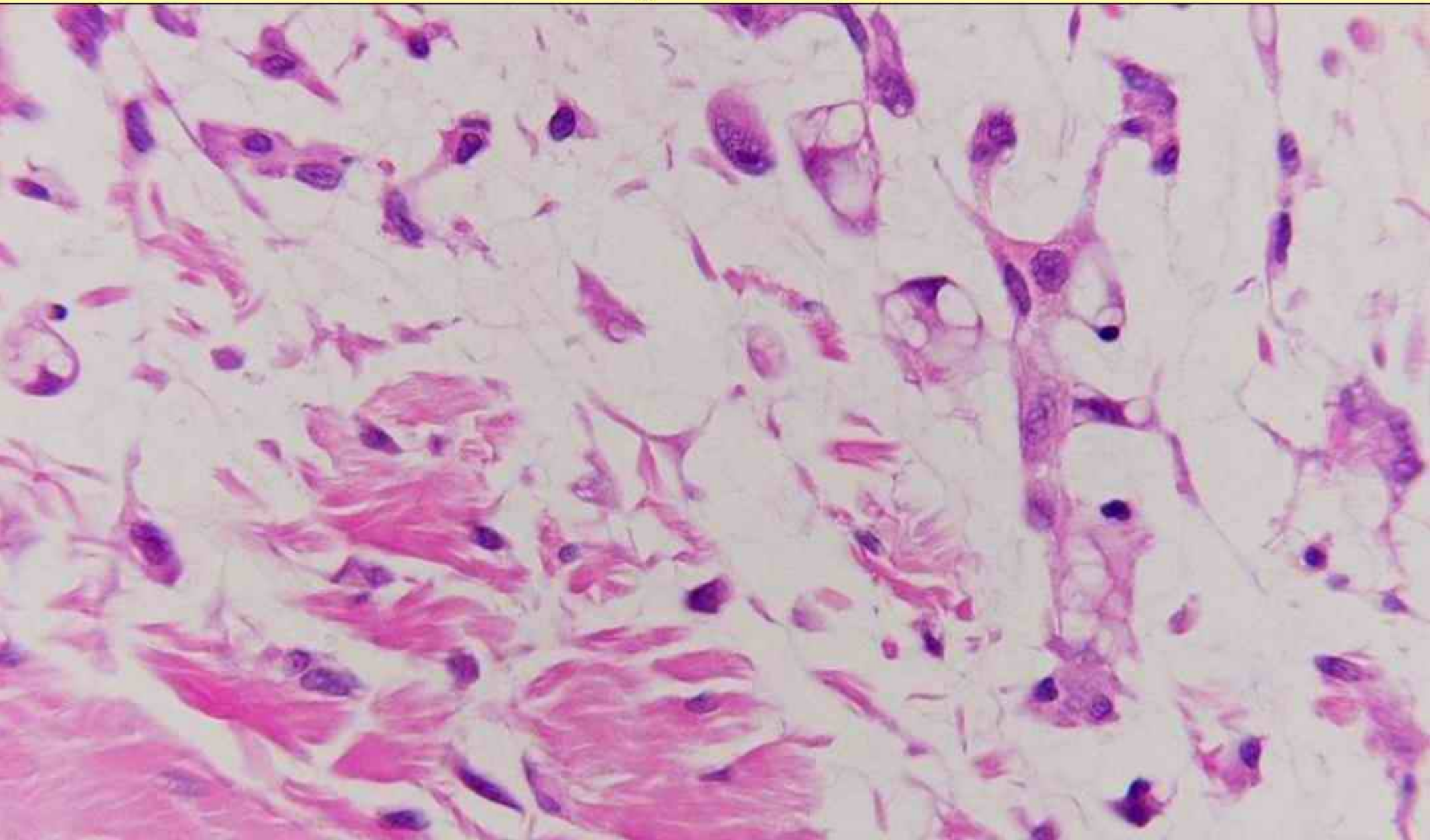

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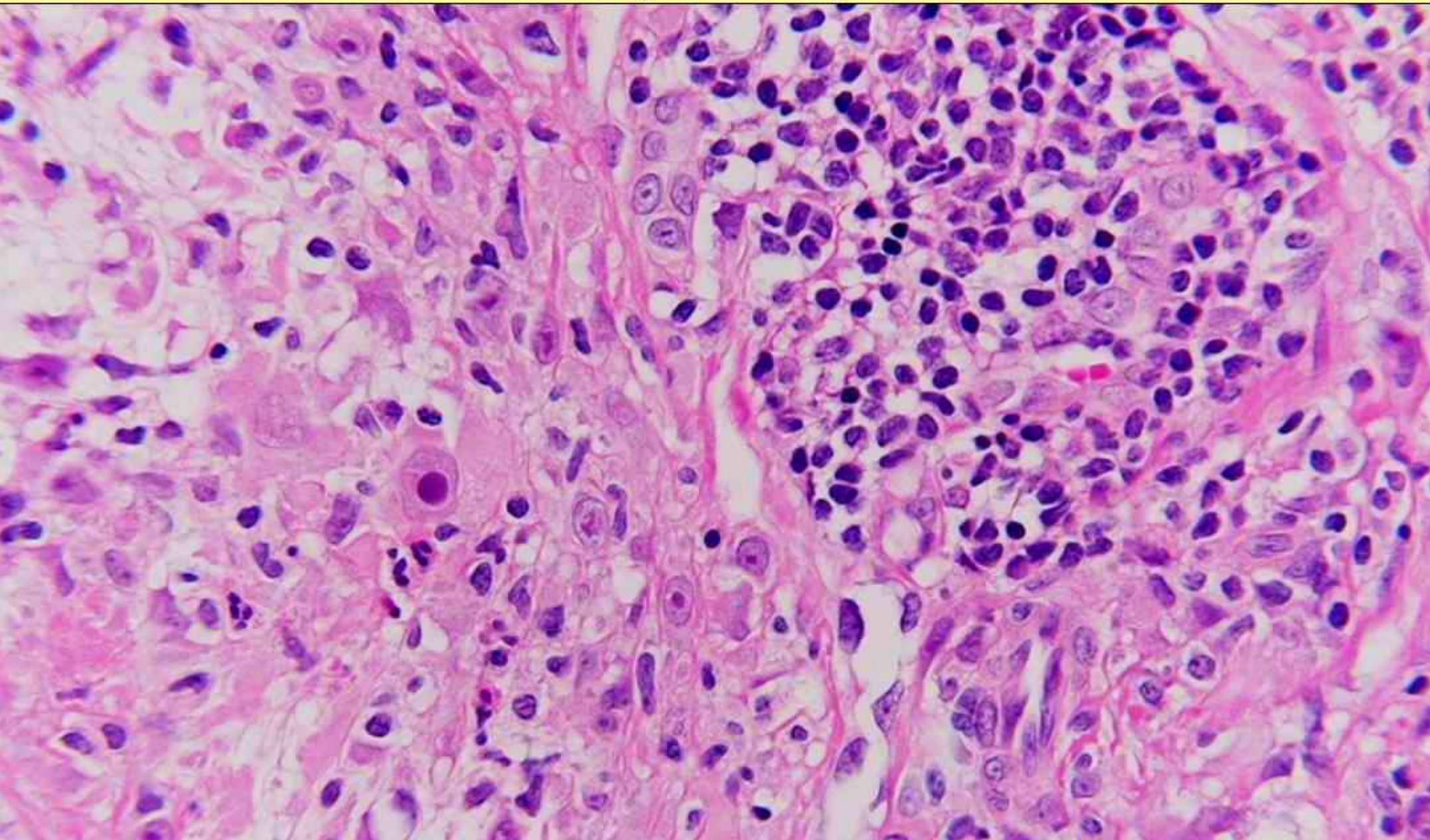

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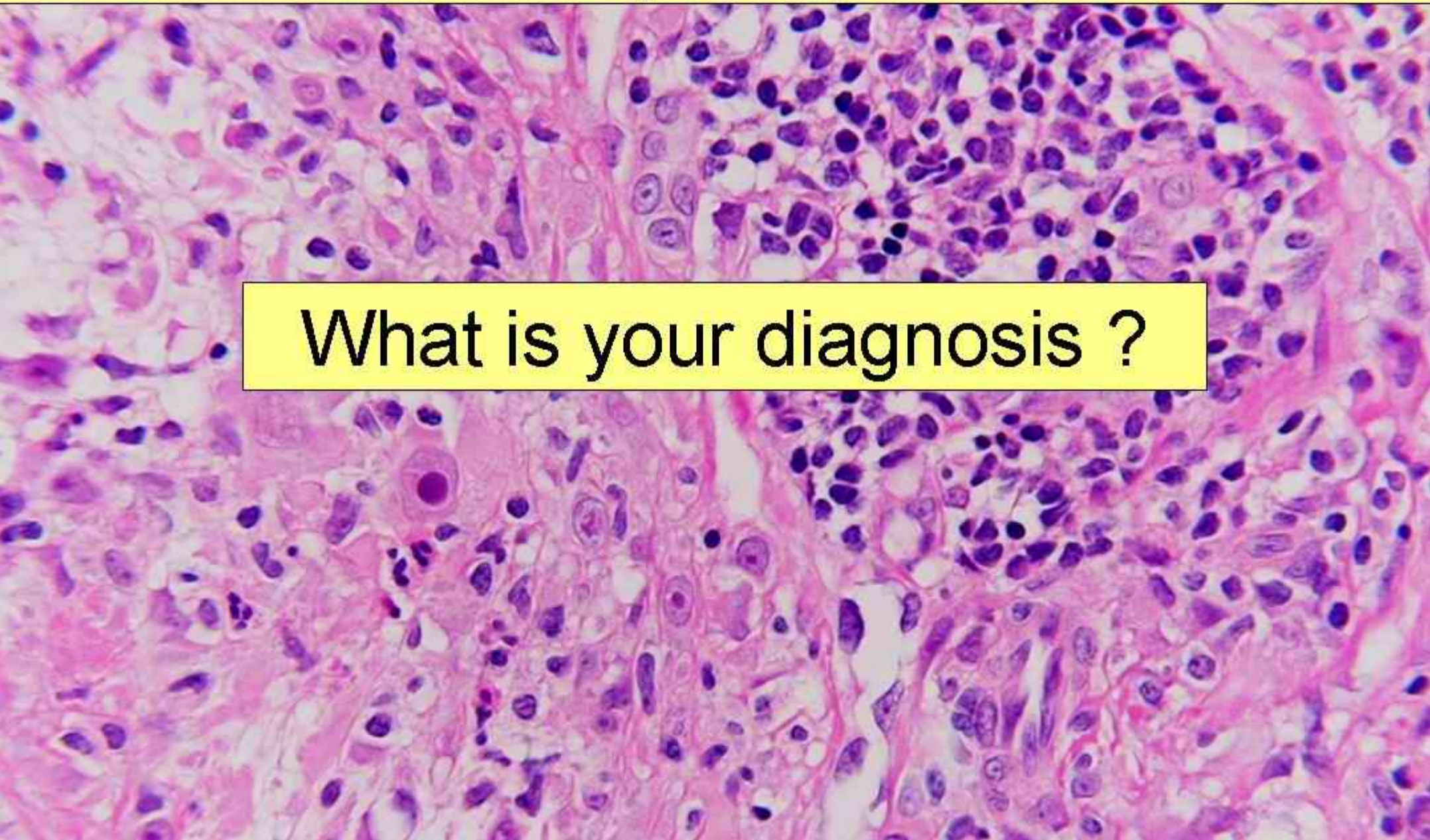


Mesenchymal lesions with a « myxofibro » appearance

« Myxofibro » areas observed frequently

- Superficial acral fibromyxoma
- Cutaneous myxoma / Superficial angiomyxoma
- Cellular myxoma / Juxtaarticular myxoma
- Ossifying fibromyxoid tumor
- Myxofibrosarcoma (low- & intermediate grade variants)
- Low-grade fibromyxoid sarcoma / hyalinizing spindle cell tumor with giant rosettes
- Inflammatory myxohyaline tumor (myxoinflammatory fibroblastic sarcoma)

Mesenchymal lesions with a « myxofibro » appearance

« Myxofibro » areas observed occasionally

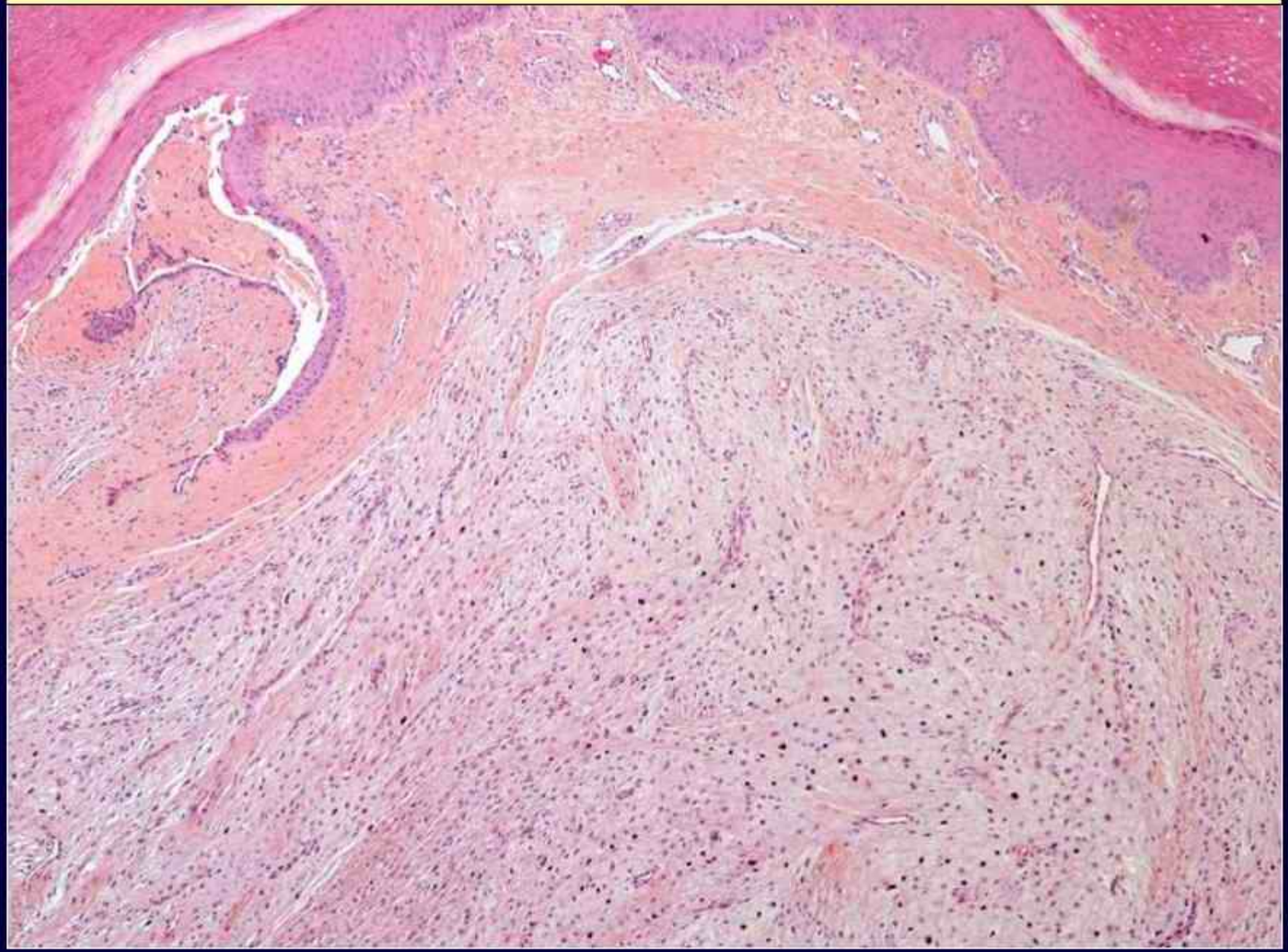
- Soft tissue perineurioma (myxoid variant)
- Desmoplastic fibroblastoma (collagenous fibroma)
- Myxoid neurofibroma
- Myxoid spindle cell lipoma (dendritic fibromyxolipoma)
- Ancient fibrohyalinized nodular fasciitis
- Giant cell fibroblastoma
- Deep « aggressive » angiomyxoma
- Desmoid tumor
- Solitary fibrous tumor (myxoid variant)
- Low-grade malignant peripheral nerve sheath tumor
- Dedifferentiated liposarcoma
- Pleomorphic liposarcoma
- Sclerosing epithelioid fibrosarcoma

Salient clinicopathologic features of the most relevant entities

Superficial Acral Fibromyxoma

- Key features
  - Described in 2001 by Fetsch *et al.* *(Hum Pathol)*
  - Middle-aged adults
  - Sites:
    - Superficial soft tissues of distal extremities (fingers, palm, toes)
    - Tends to involve the nail region
  - Size: 1-2 cm
  - Benign lesion. Recurrence rate <5%

Superficial acral fibromyxoma



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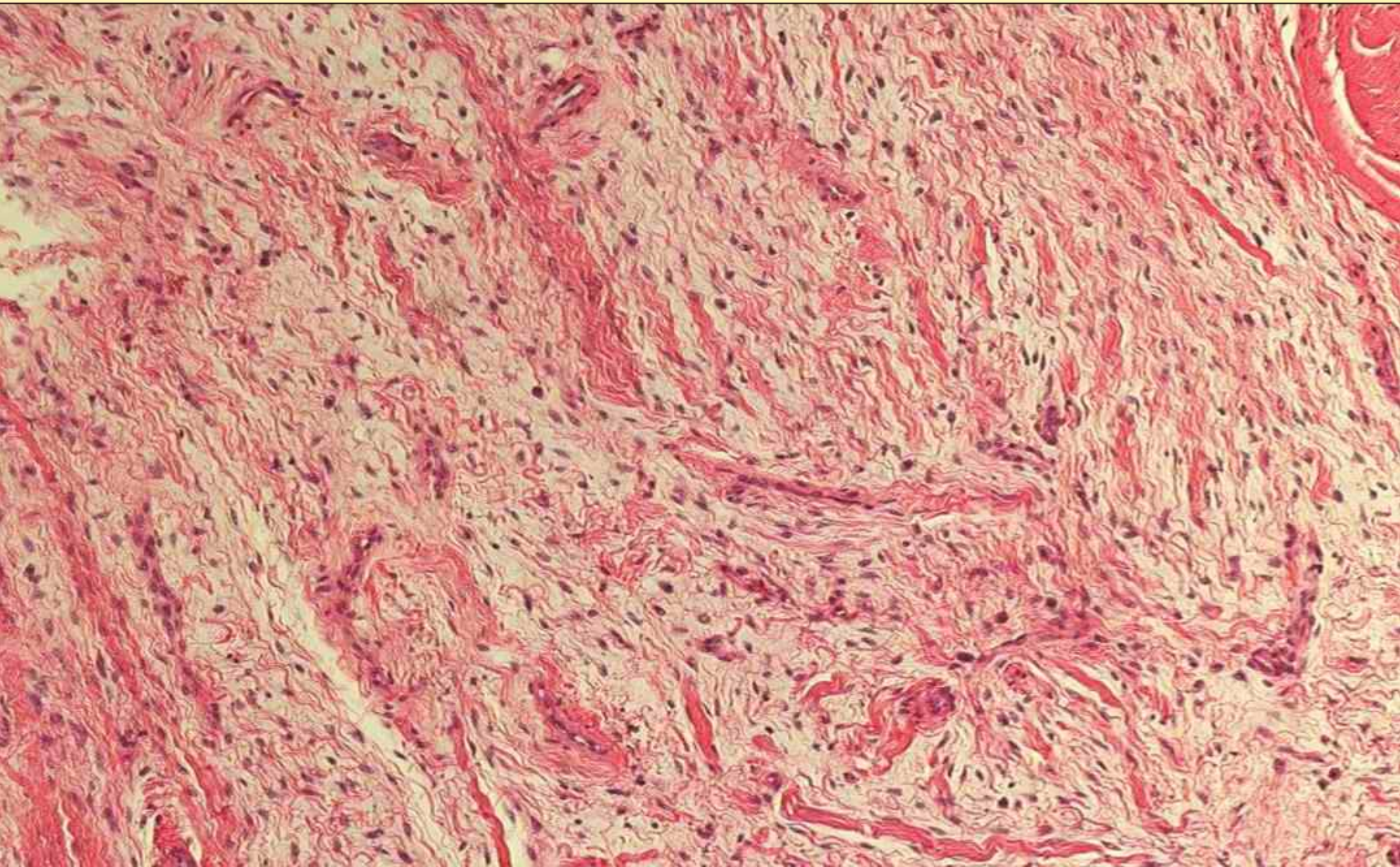

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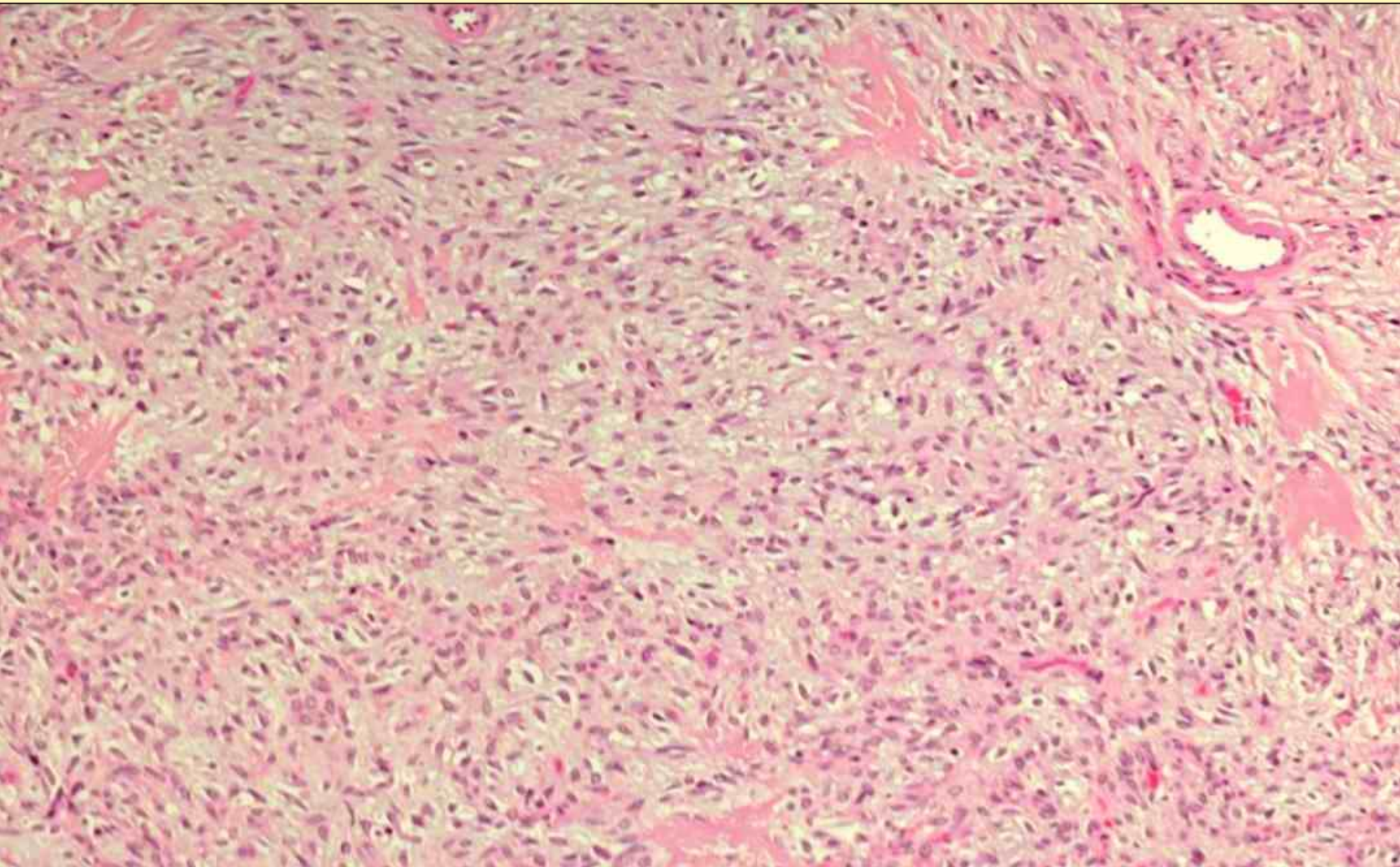
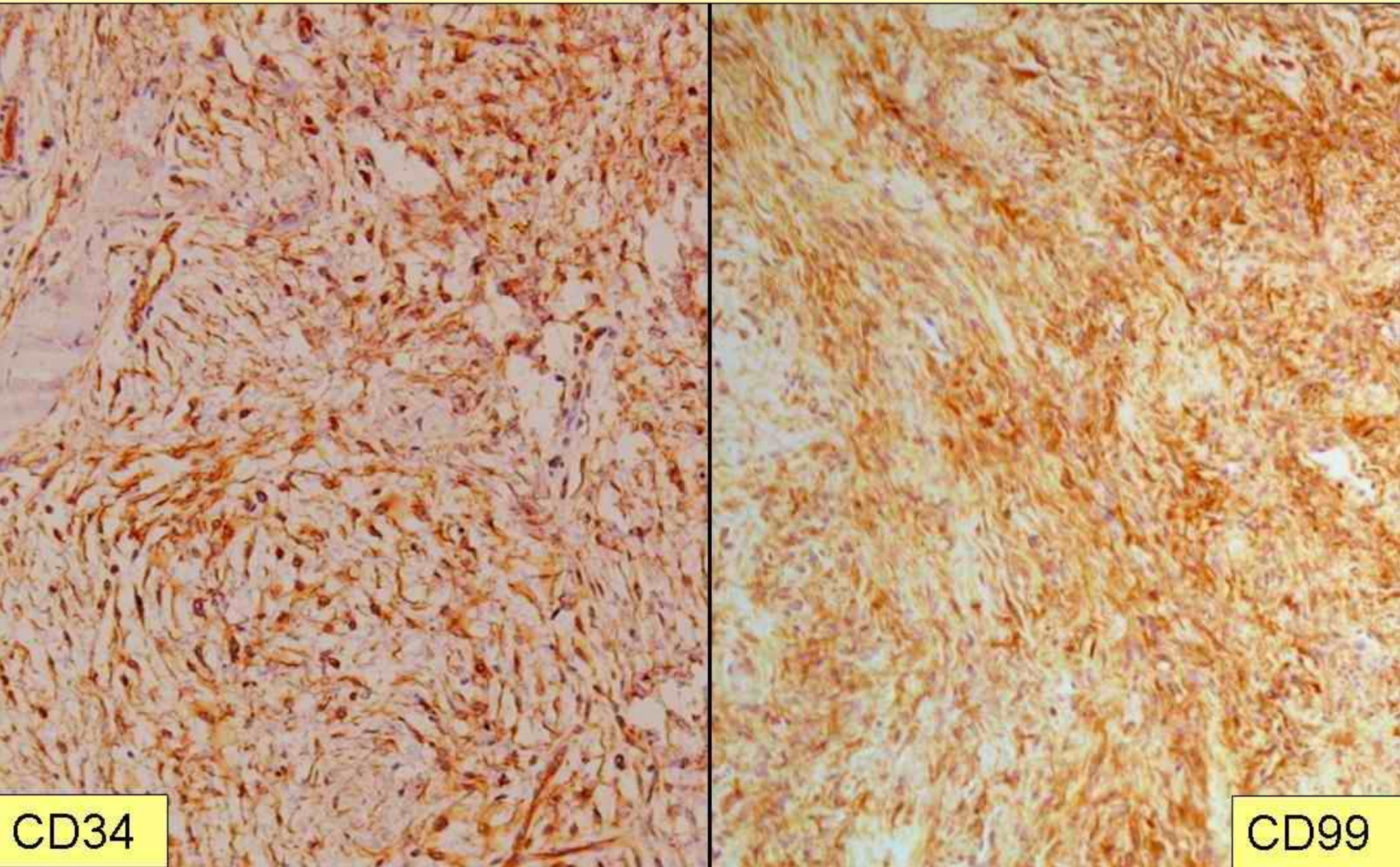


Superficial Acral Fibromyxoma

- Immunohistochemistry
  - CD34 positivity (90% of cases)
  - CD99 + (80%)
  - EMA + (70%)
  - Usually negative for smooth muscle actin, desmin, keratins, and S100 protein

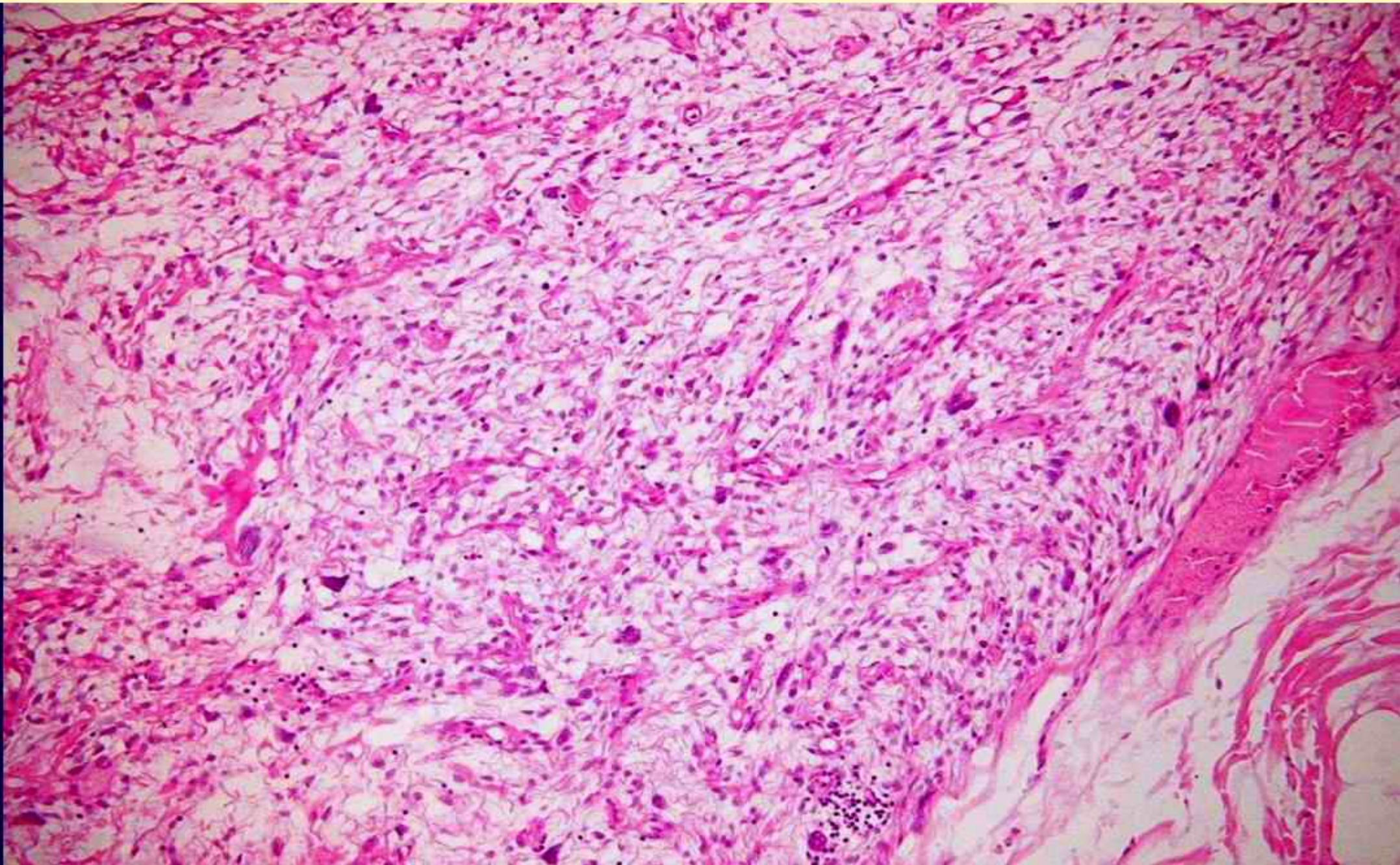
Superficial acral fibromyxoma



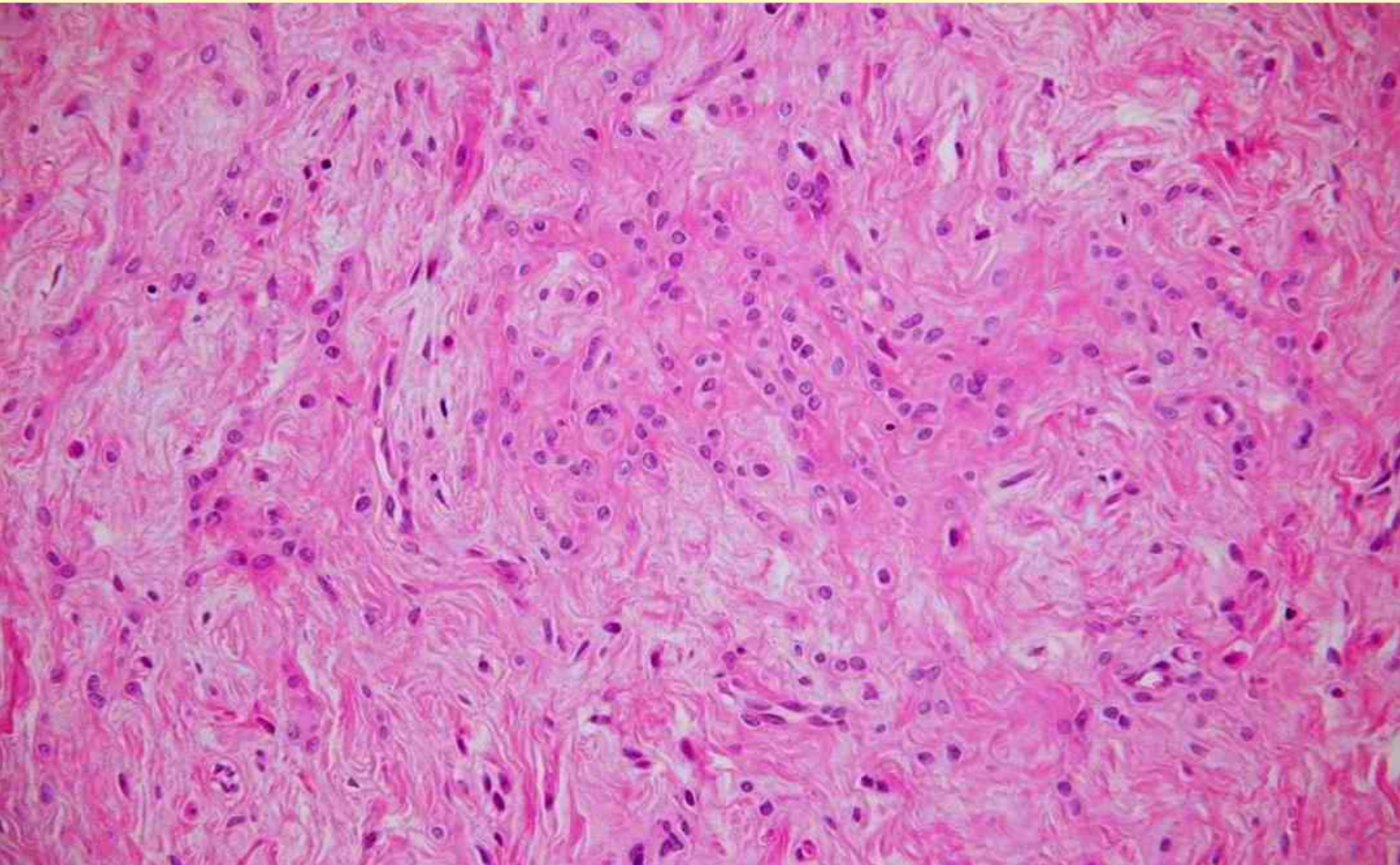
Superficial Acral Fibromyxoma

- Differential diagnosis
  - Low-grade sarcomas +++
    - Low to intermediate-grade myxofibrosarcoma
    - Low-grade fibromyxoid sarcoma
    - Low-grade MPNST
    - Acral myxoinflammatory fibroblastic sarcoma
    - Myxoid variant of dermatofibrosarcoma protuberans
  - Benign lesions
    - Sclerosing perineurioma, Periungueal fibrokeratoma, Myxoid fibrous histiocytoma, Cutaneous myxoma, Superficial angiomyxoma

Intermediate-grade myxofibrosarcoma



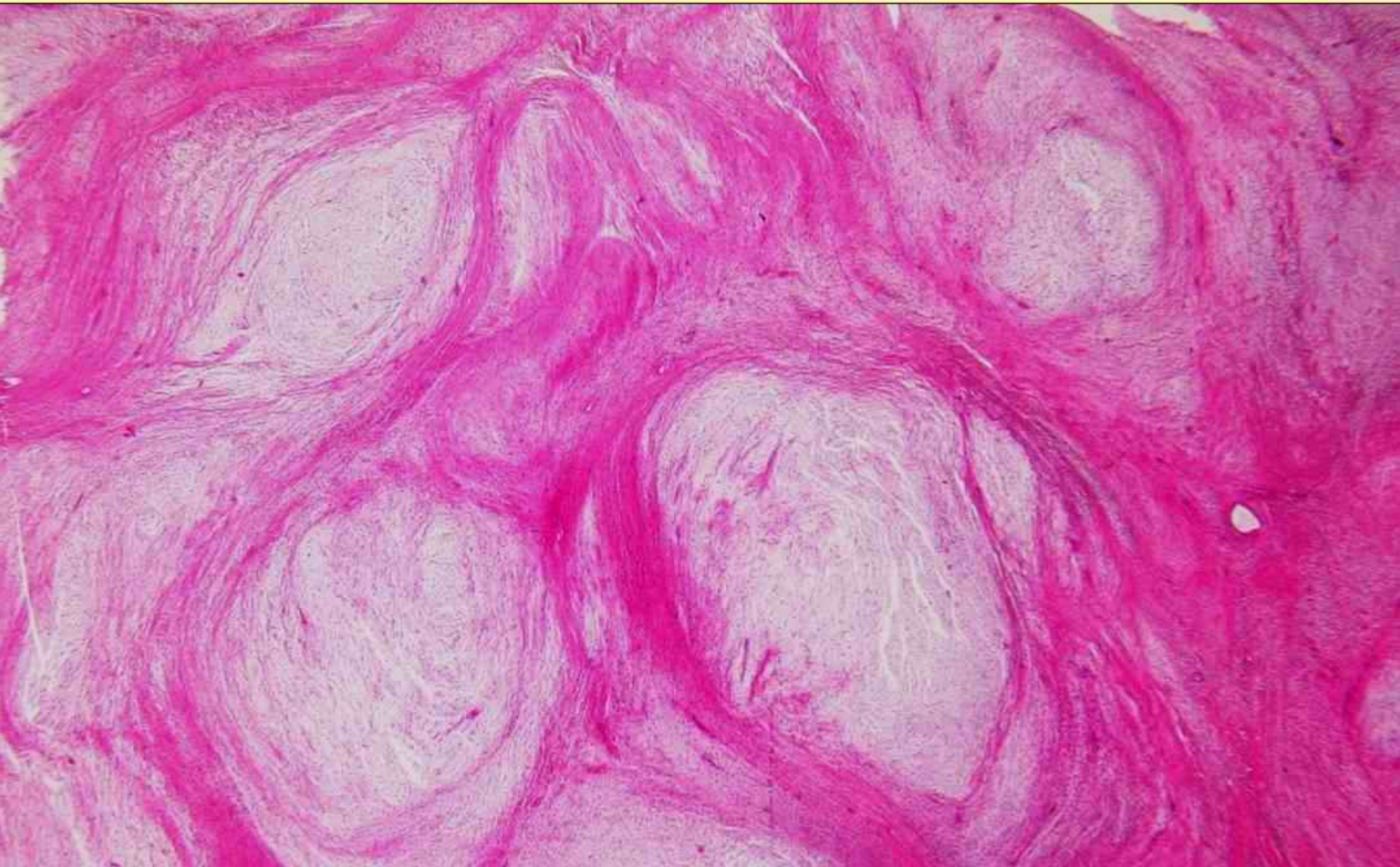
Sclerosing/myxoid perineurioma



Low-grade fibromyxoid sarcoma

- Key features
  - Described in 1987 by Harry Evans
  - Young adults (median 35 yrs); M>F
  - Long-standing, painless mass
  - Deep soft tissue of limbs (thigh +++), limb girdles, trunk
  - Cytogenetics: t(7;16) (q33;p11) FUS/CREB3L2 (90%) or t(11;16) (p11;p11) FUS/CREB3L1 (10%)
  - Local recurrence: 10% (if the lesion is correctly excised *ab initio*)
  - Metastatic rate: 5-10% (lungs, pleura, bone) if F-U <5 years, 70% if F-U > 8-10 years

Low-grade fibromyxoid sarcoma



Low-grade fibromyxoid sarcoma

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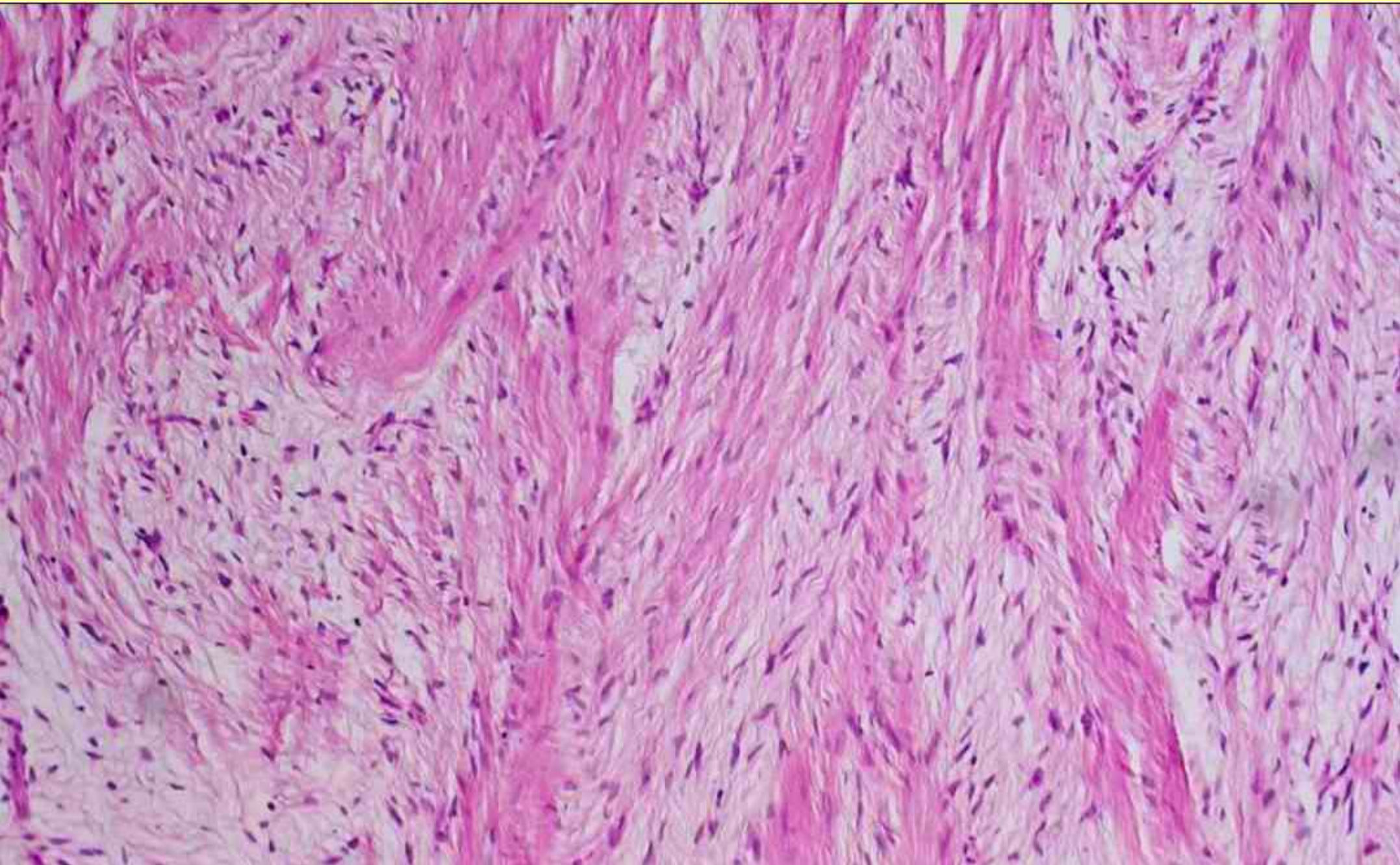

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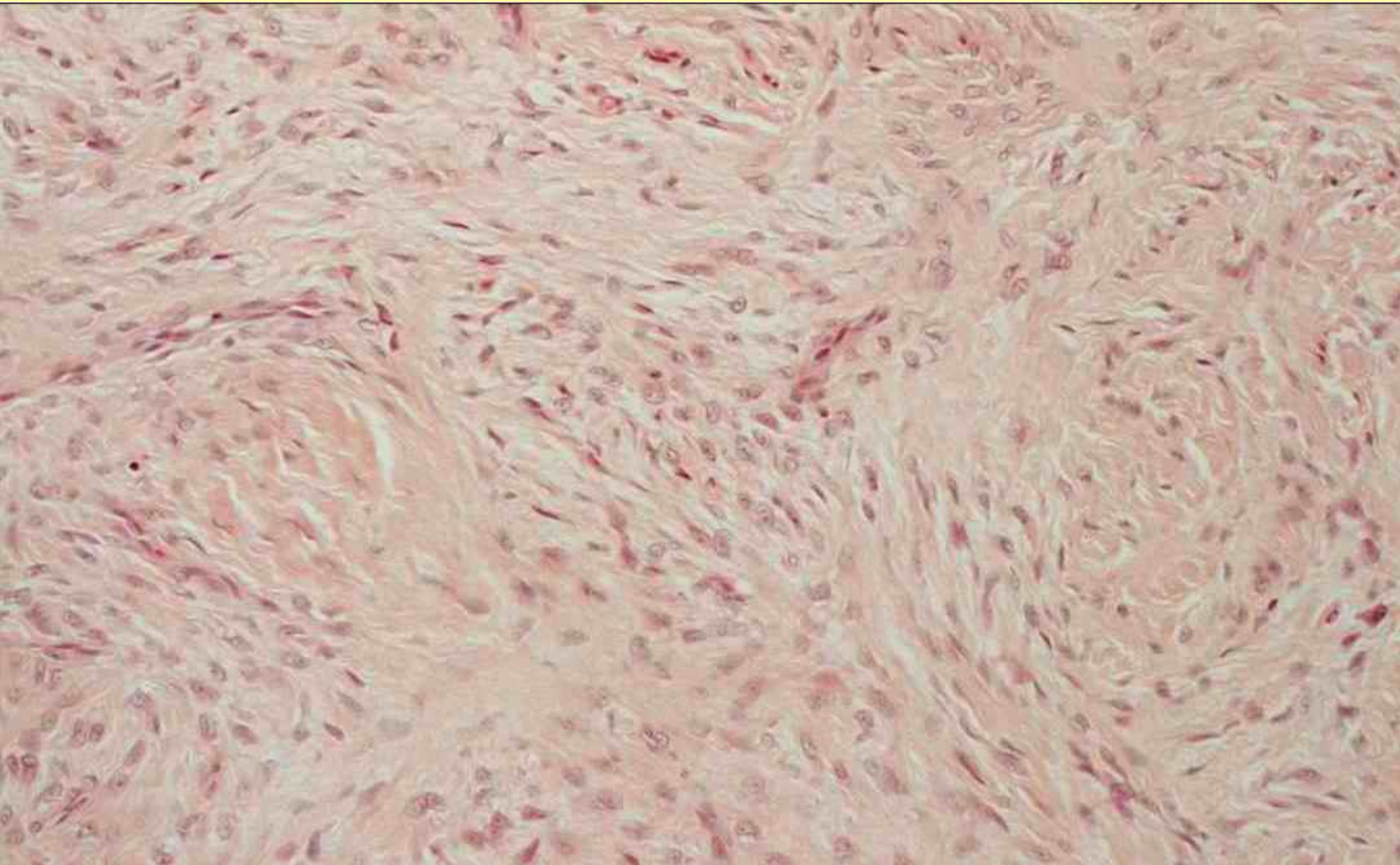

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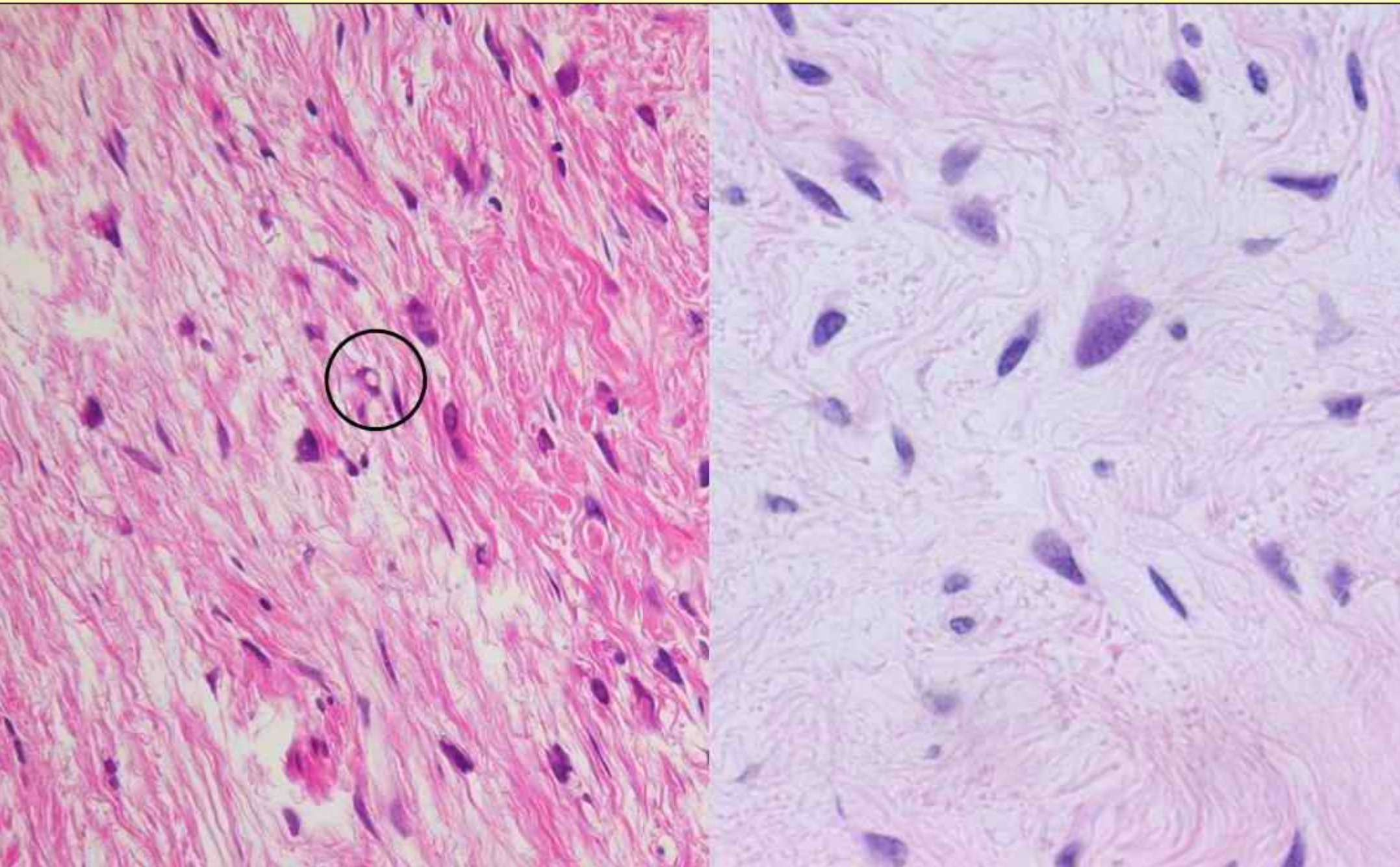
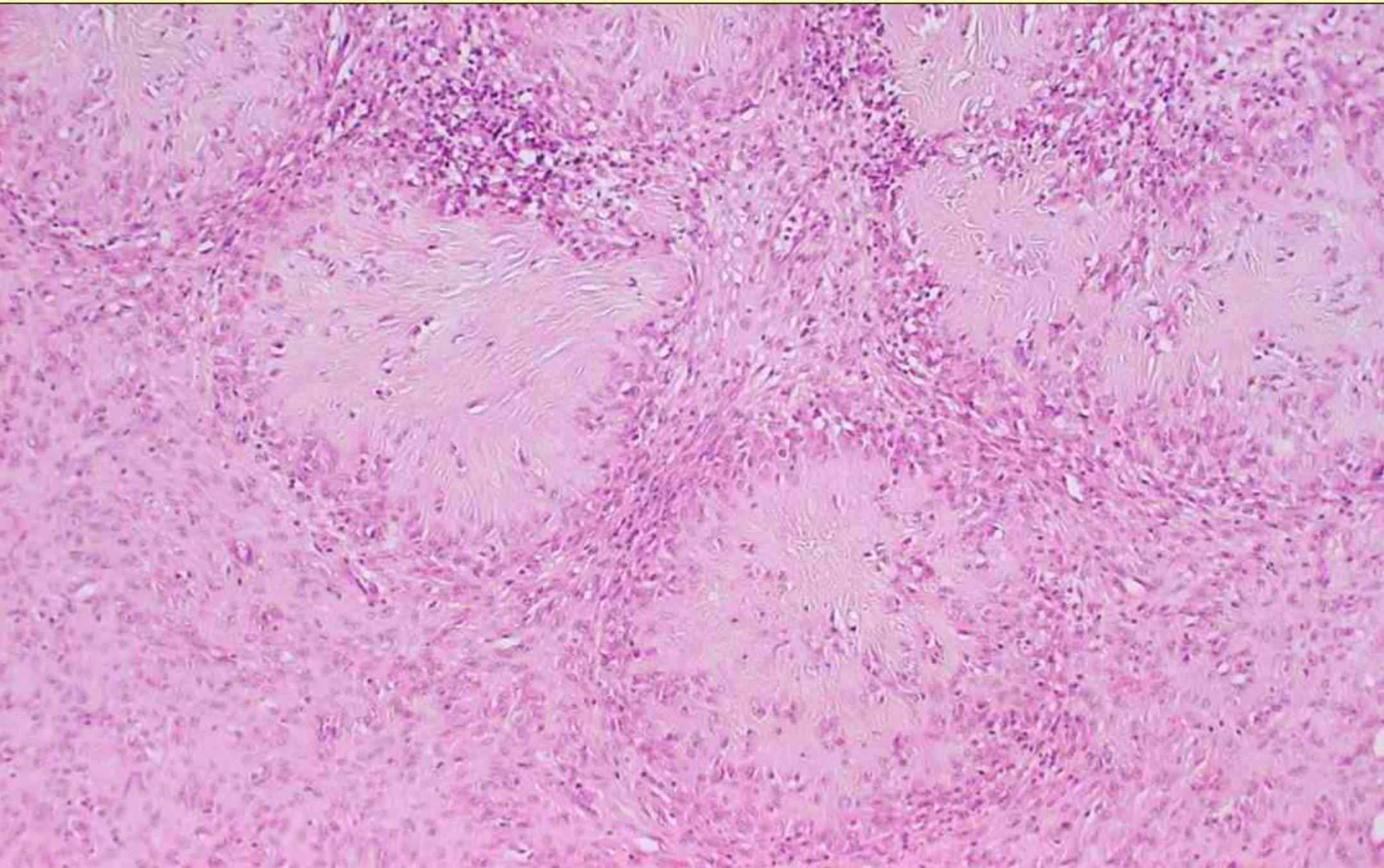
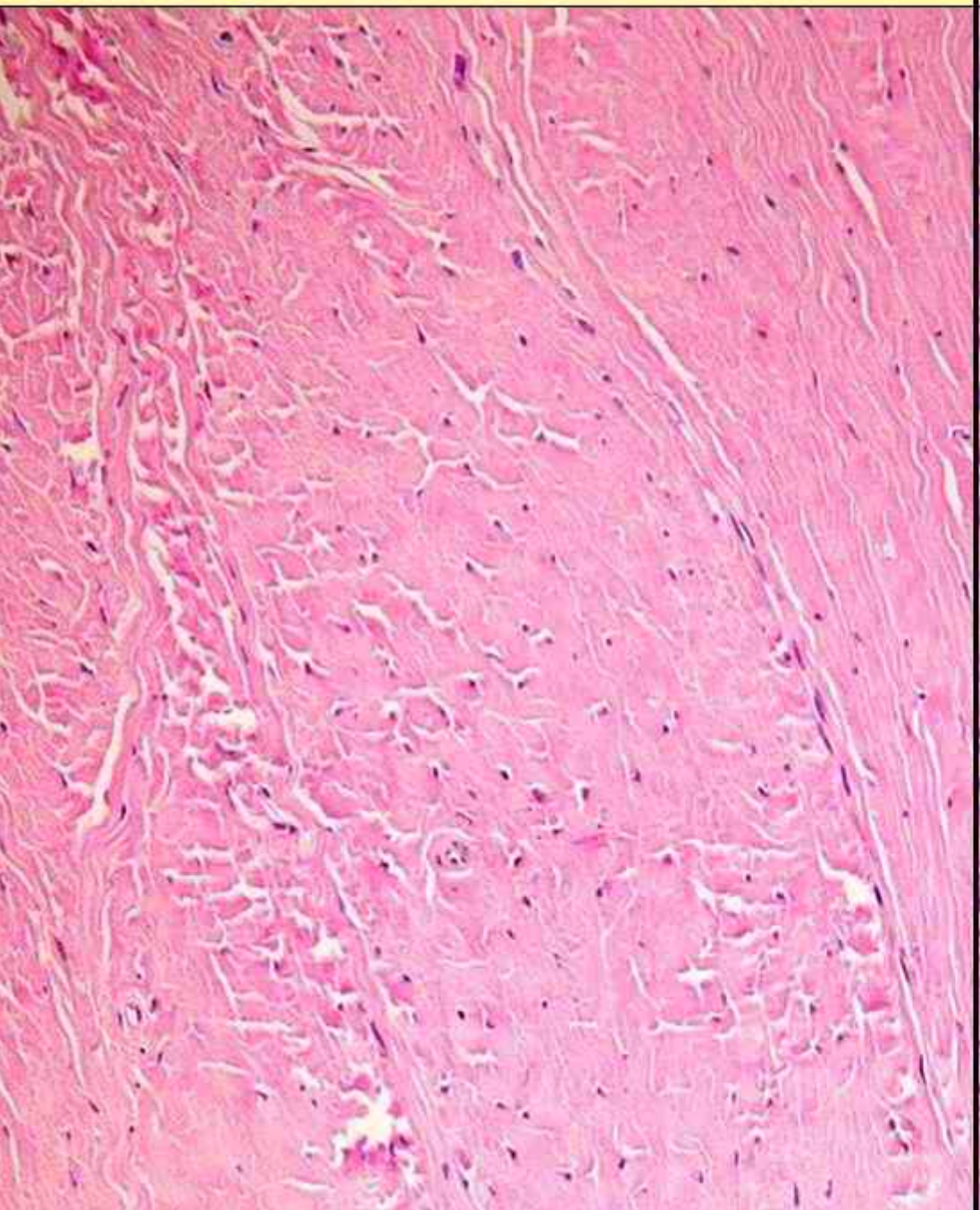


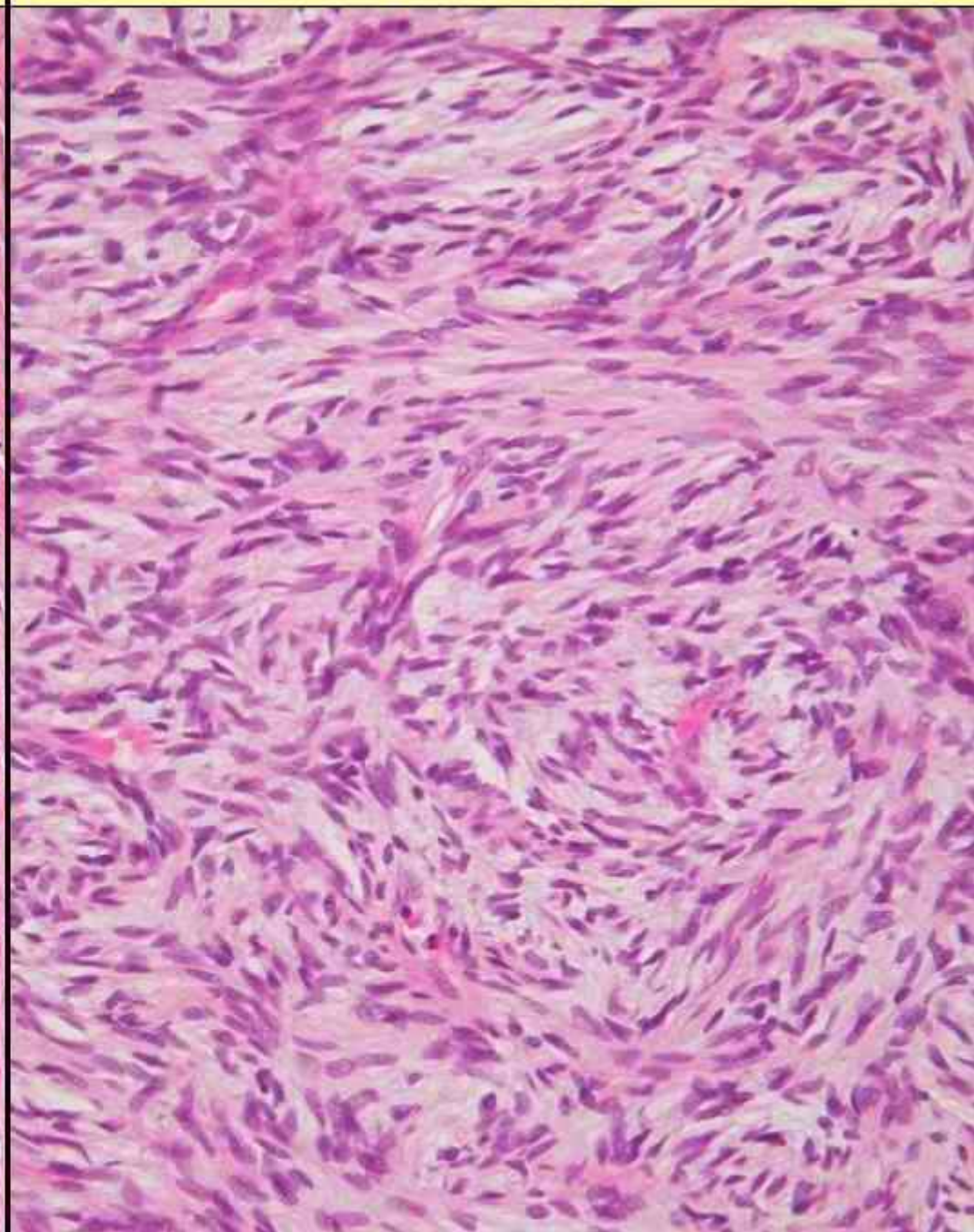
Hyalinizing spindle cell tumor with giant rosettes: a variant of LGFMS



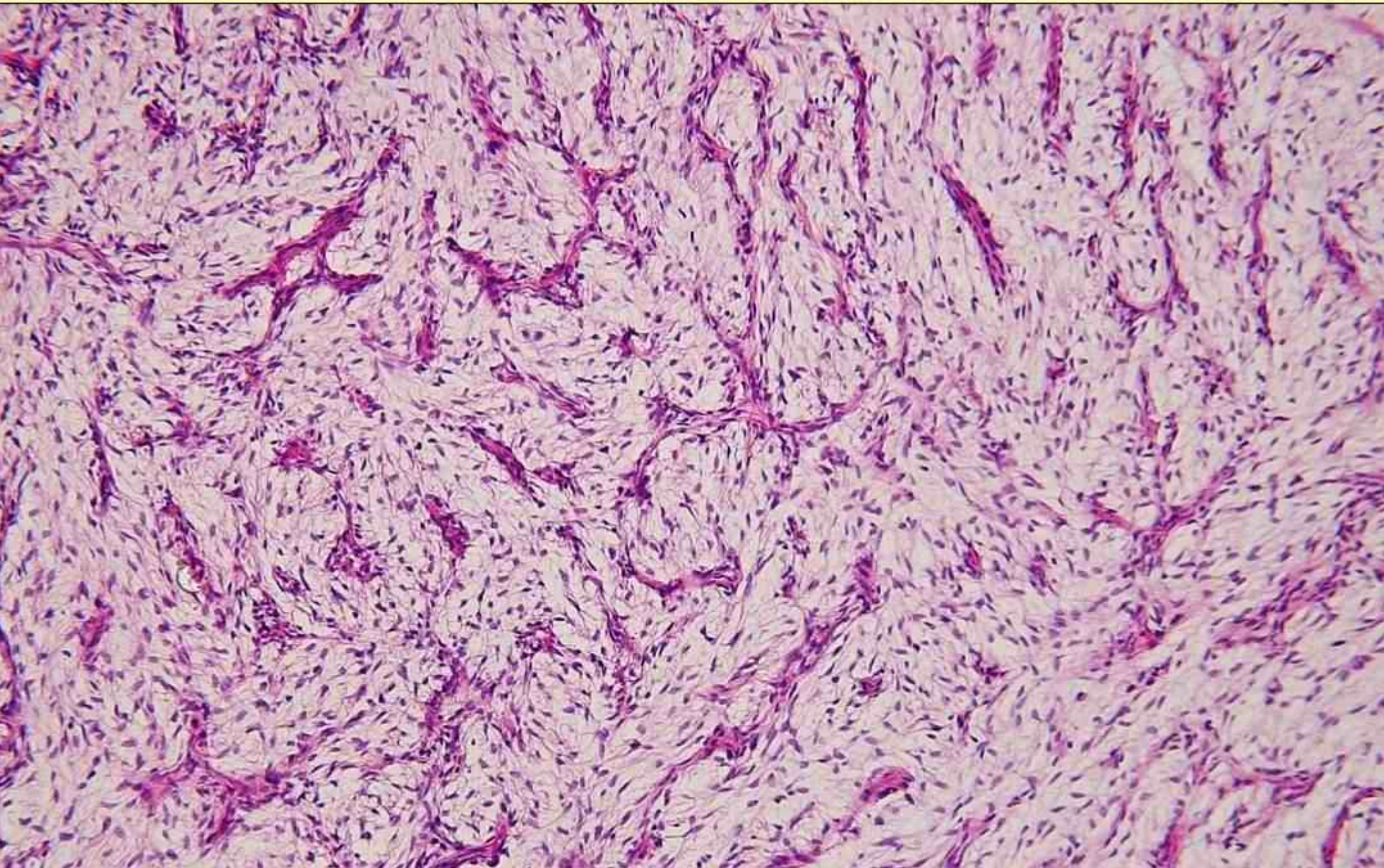
LGFMS, fibroma-like variant



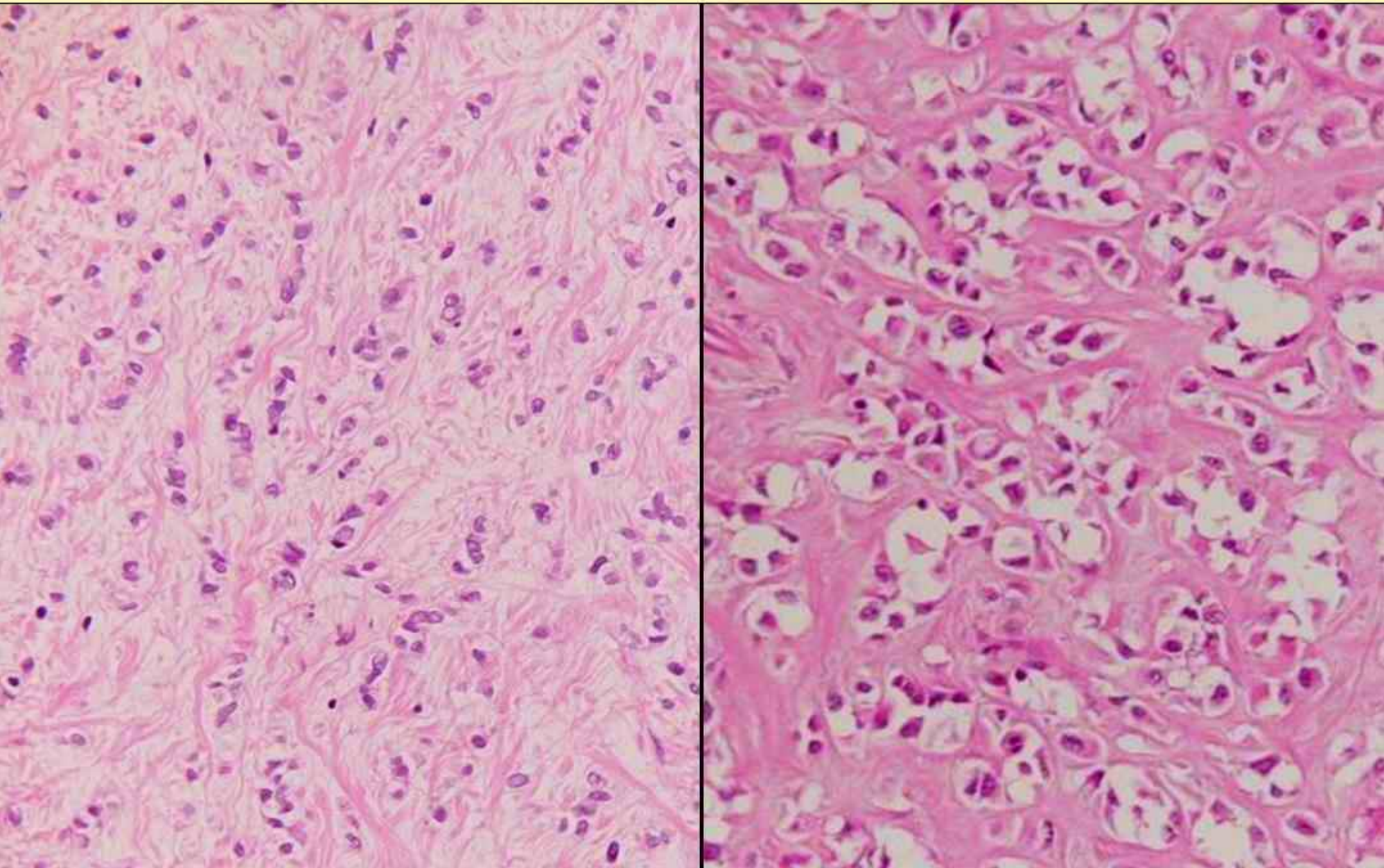
LGFMS, cellular variant



LGFMS resembling a low-grade myxofibrosarcoma



LGFMS with epithelioid features, resembling sclerosing epith. fibrosarcoma

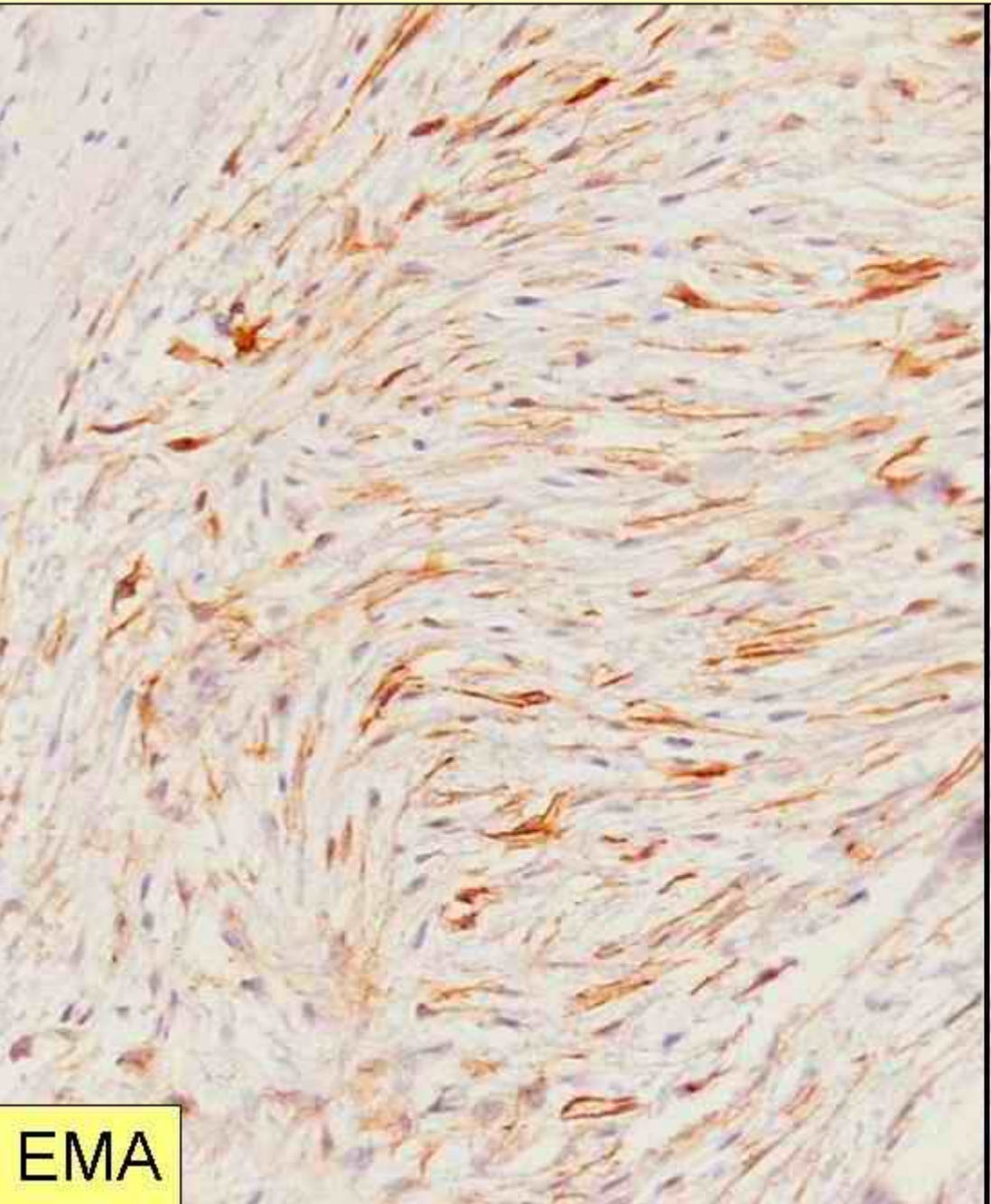


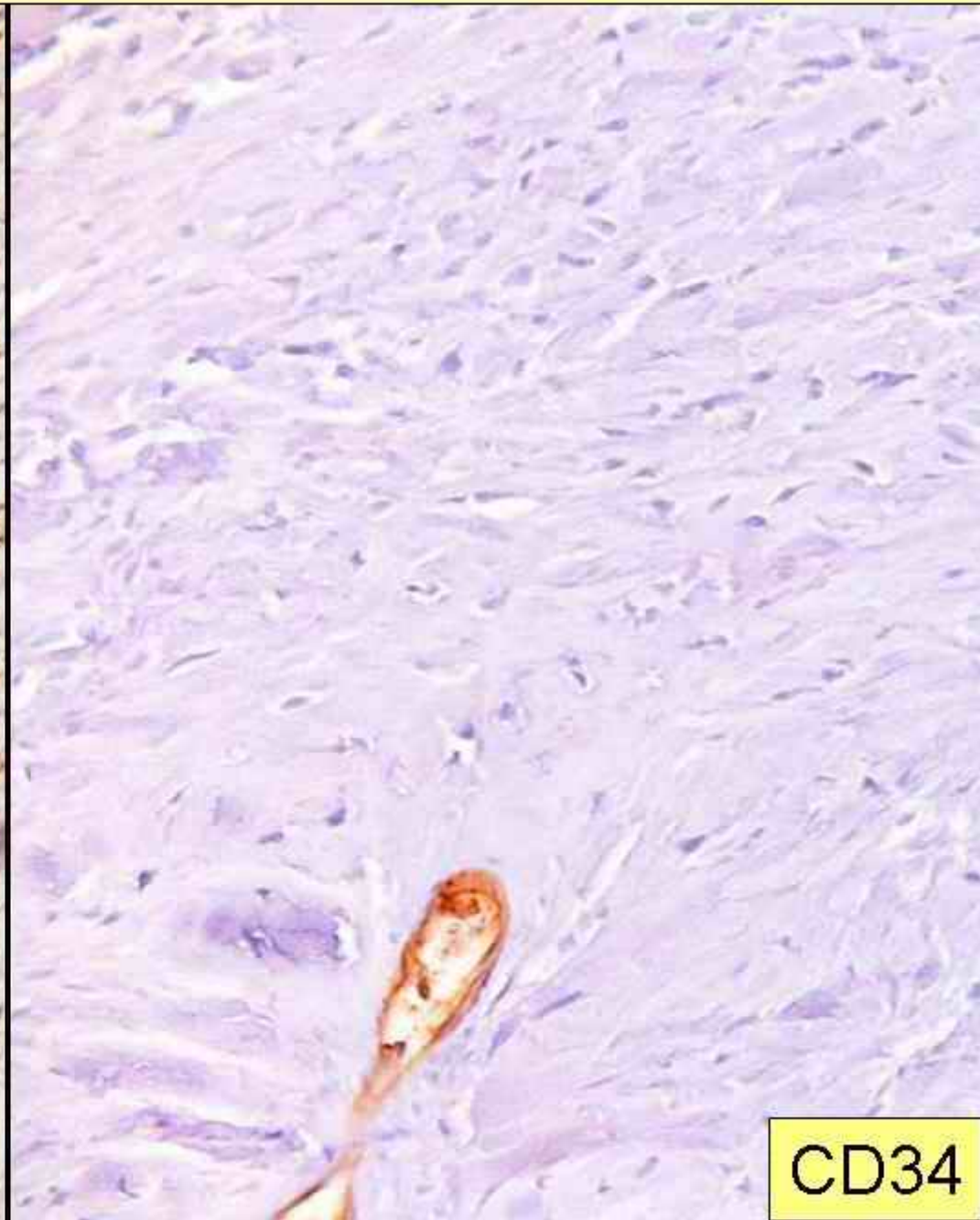
Low-grade fibromyxoid sarcoma

- Immunohistochemistry
  - EMA + : 80%
  - CD99 + : 80%
  - Bcl-2 + : 80%

  - CD34: negative
  - S100: negative
  - SMA: negative
  - Desmin: negative
  - Keratins: negative

Low-grade fibromyxoid sarcoma

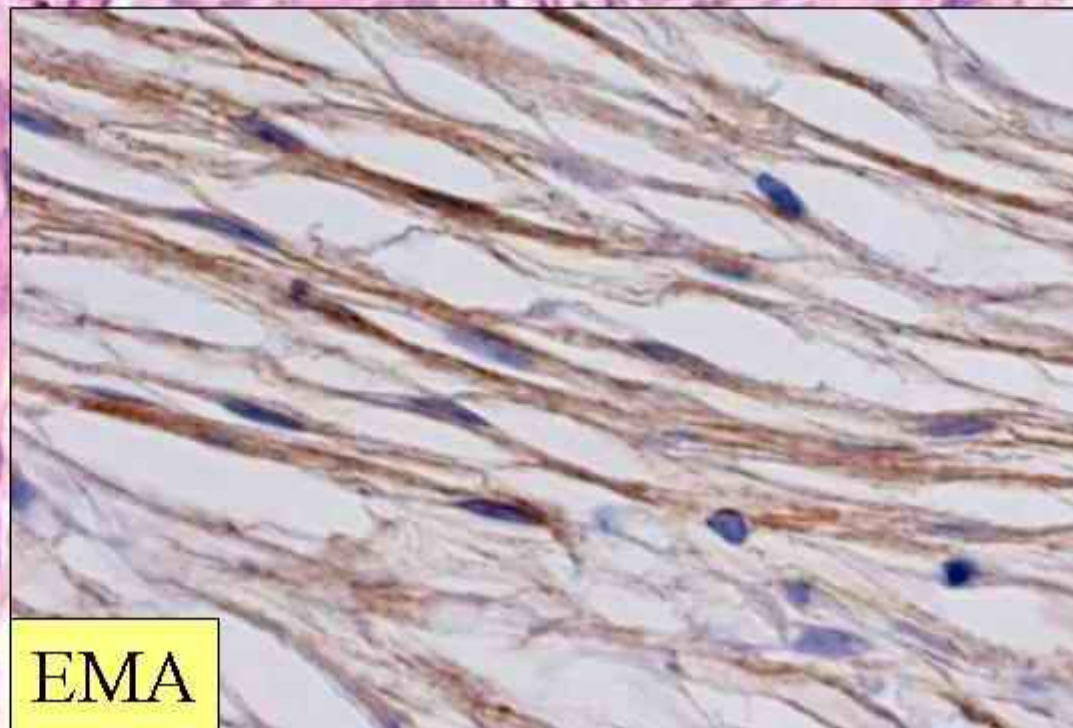




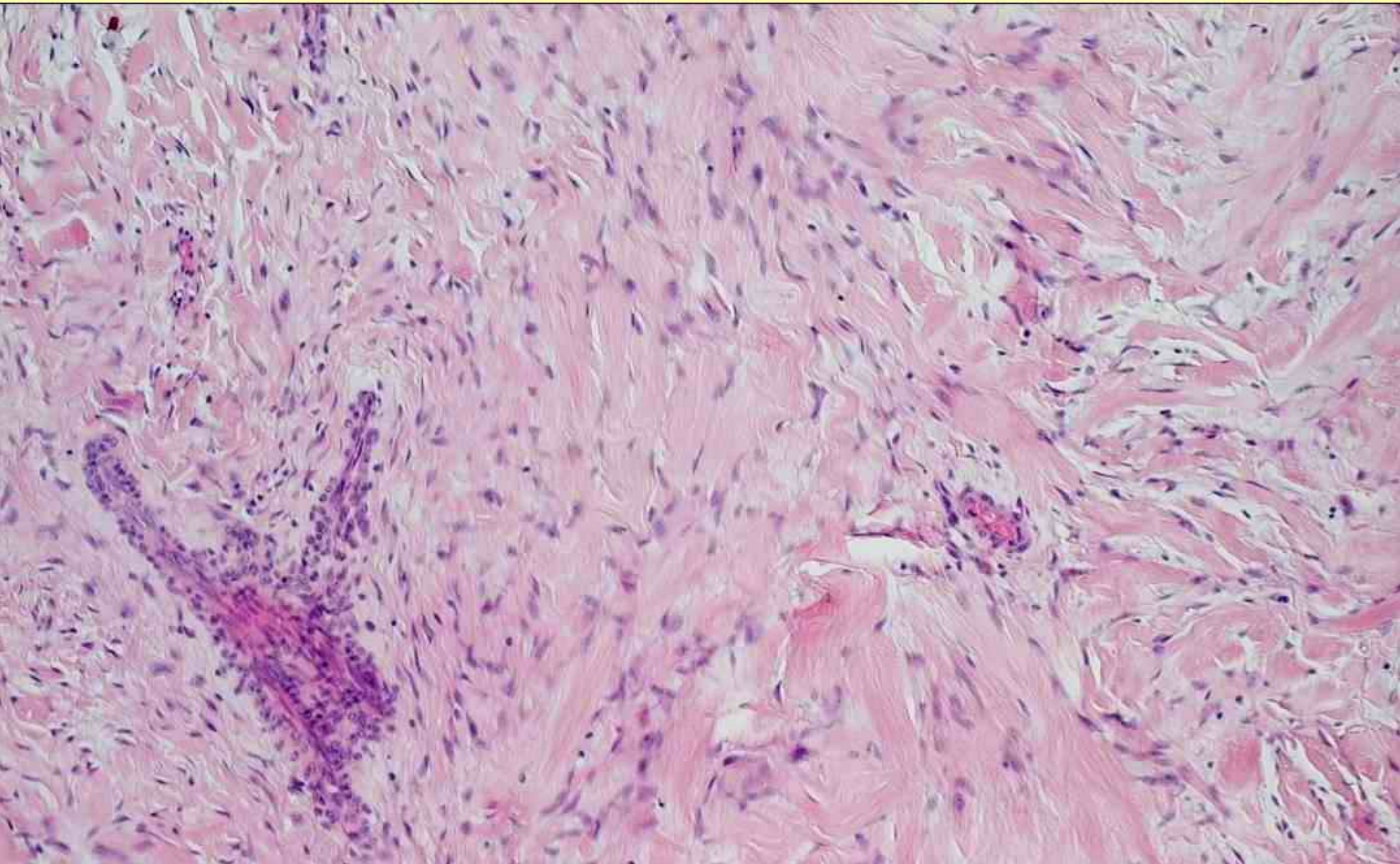
Low-grade fibromyxoid sarcoma

- Differential diagnosis
  - Perineurioma +++ , fibroma, neurofibroma
  - Desmoid tumor +++
  - Low-grade myxofibrosarcoma +++
  - Low-grade MPNST +++
  - Cellular myxoma (for predominantly myxoid lesions) ++
  - Sclerosing epithelioid fibrosarcoma (for predominantly epithelioid lesions)
  - Leiomyoma & metastatic low-grade endometrial stromal sarcoma (if giant rosettes present)

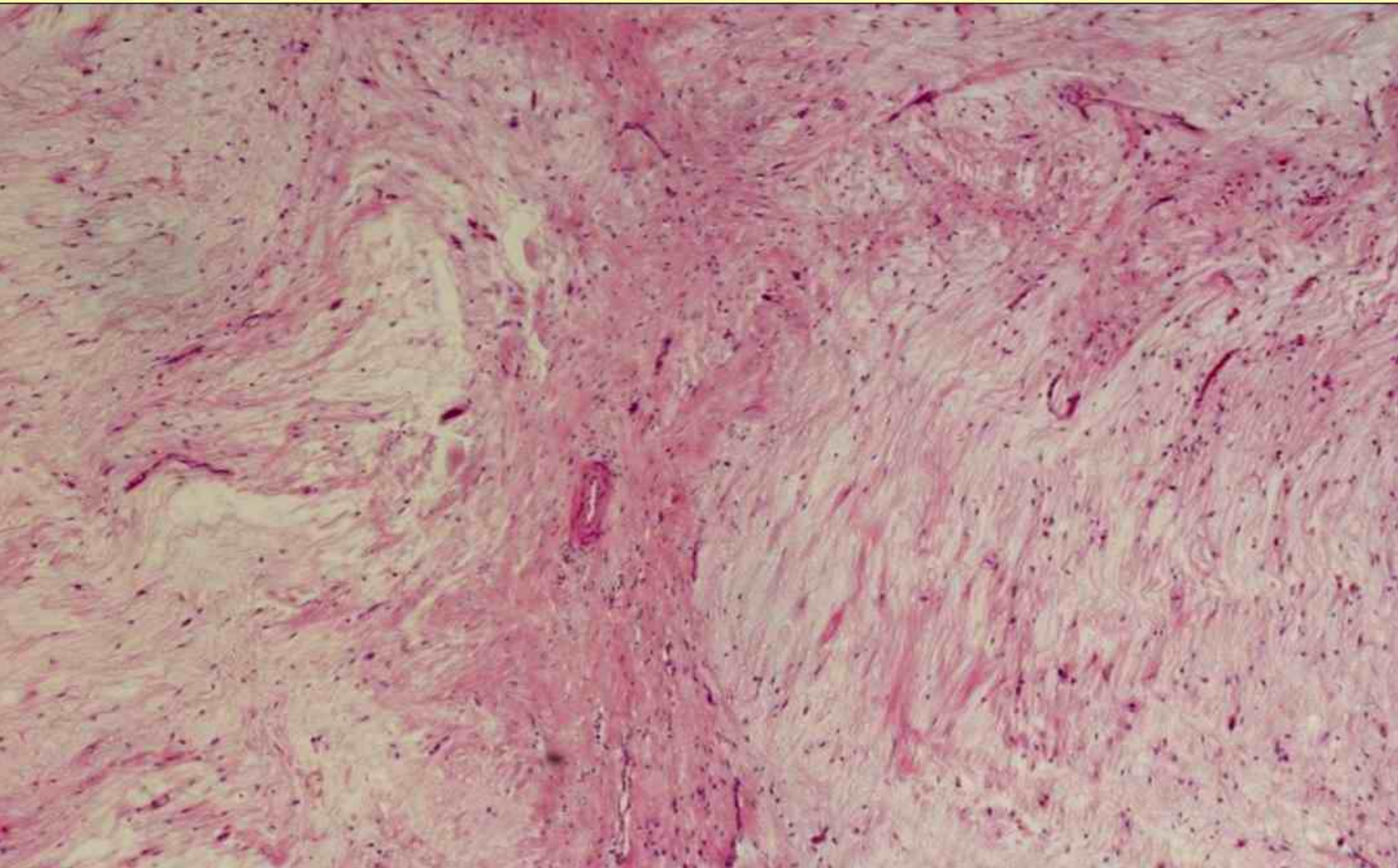
Soft tissue perineurioma



Desmoid tumor



Cellular myxoma



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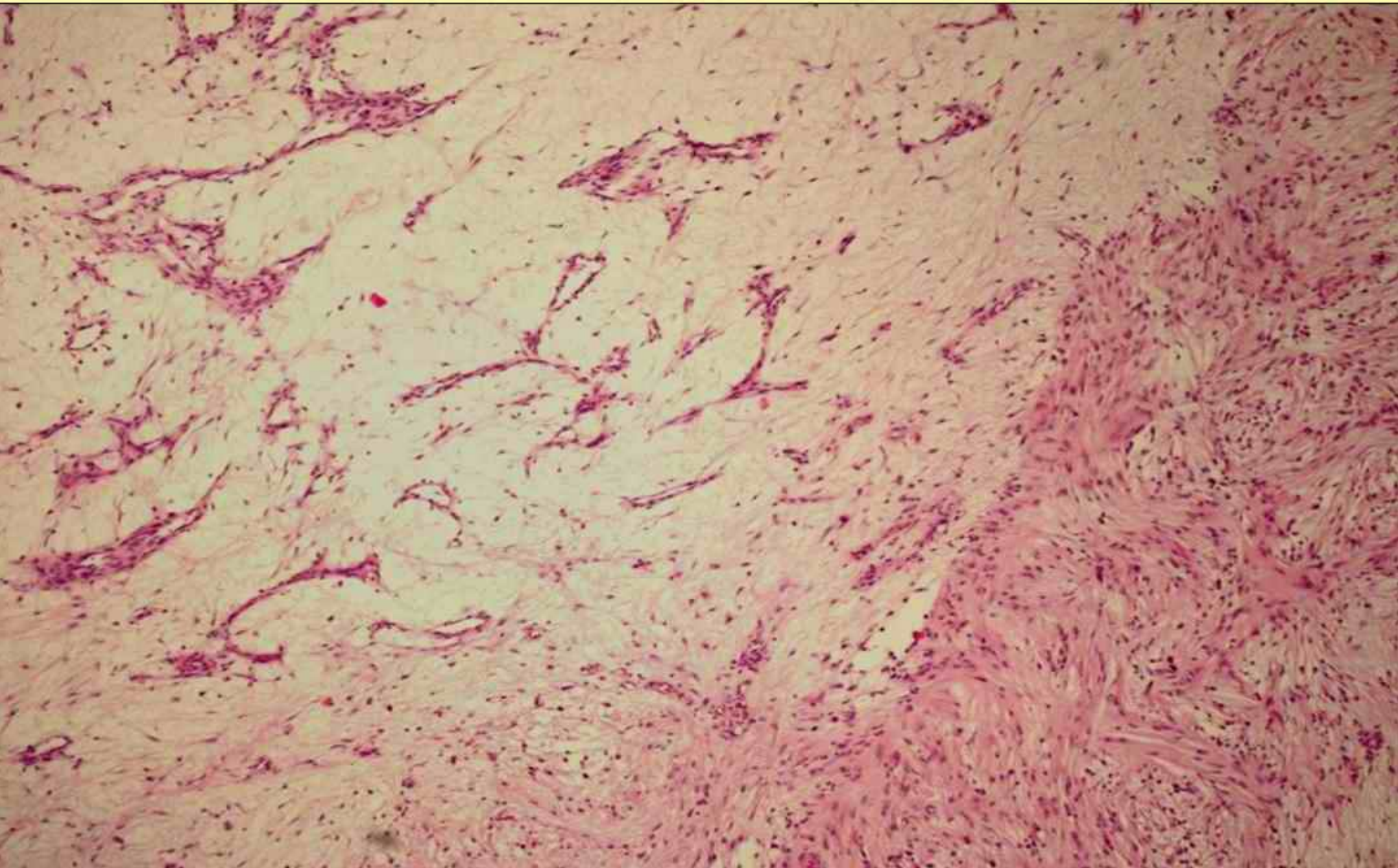

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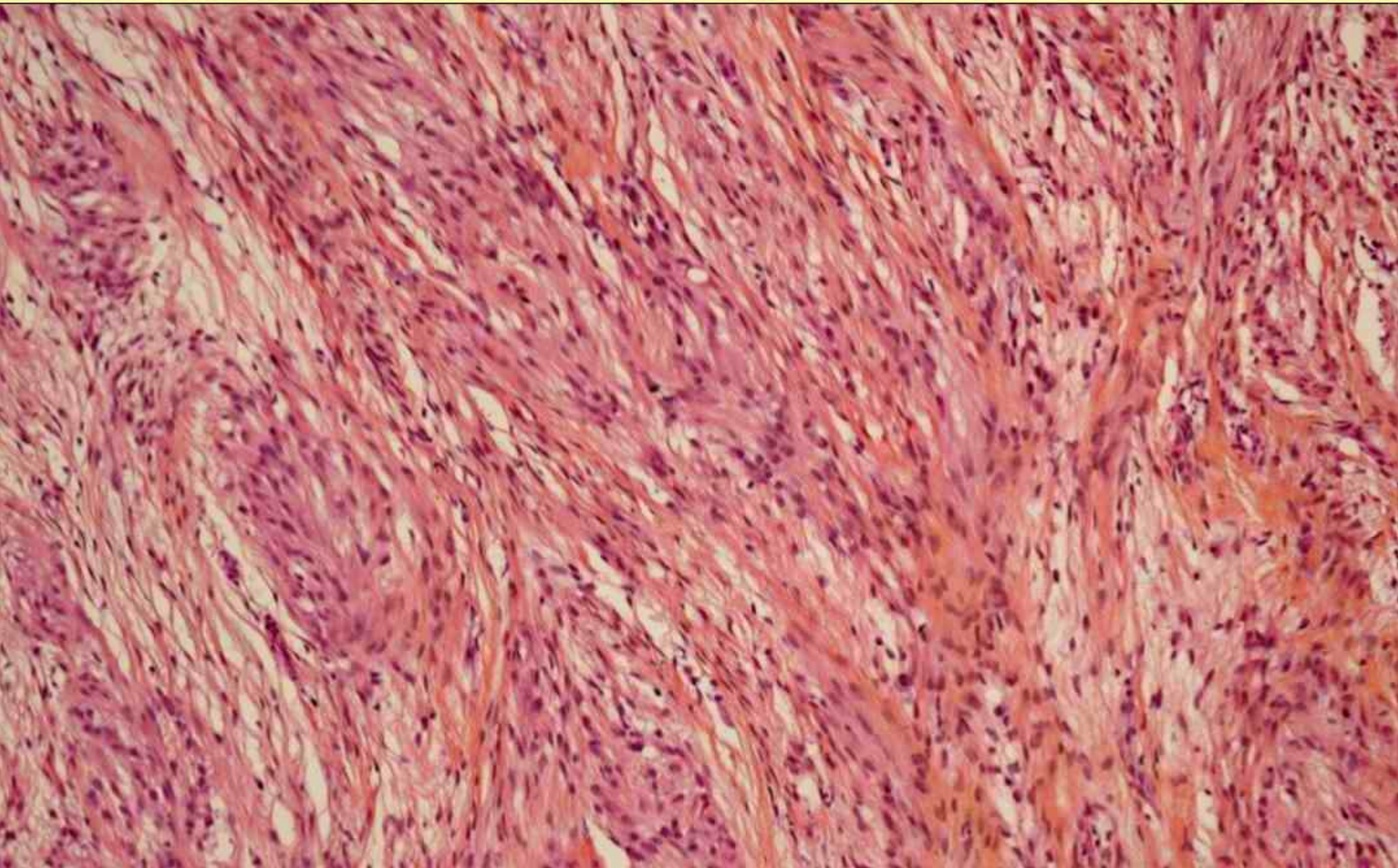

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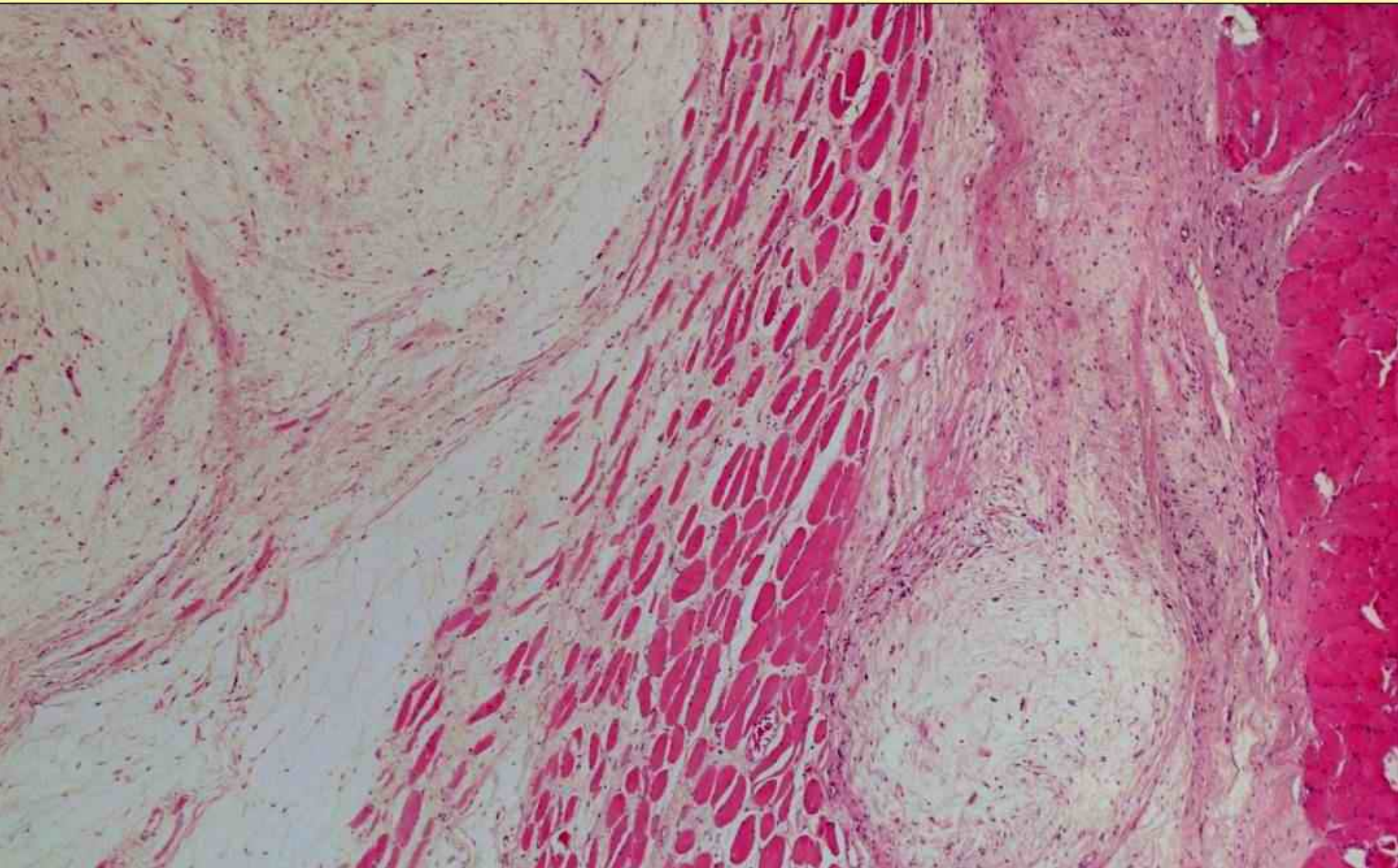

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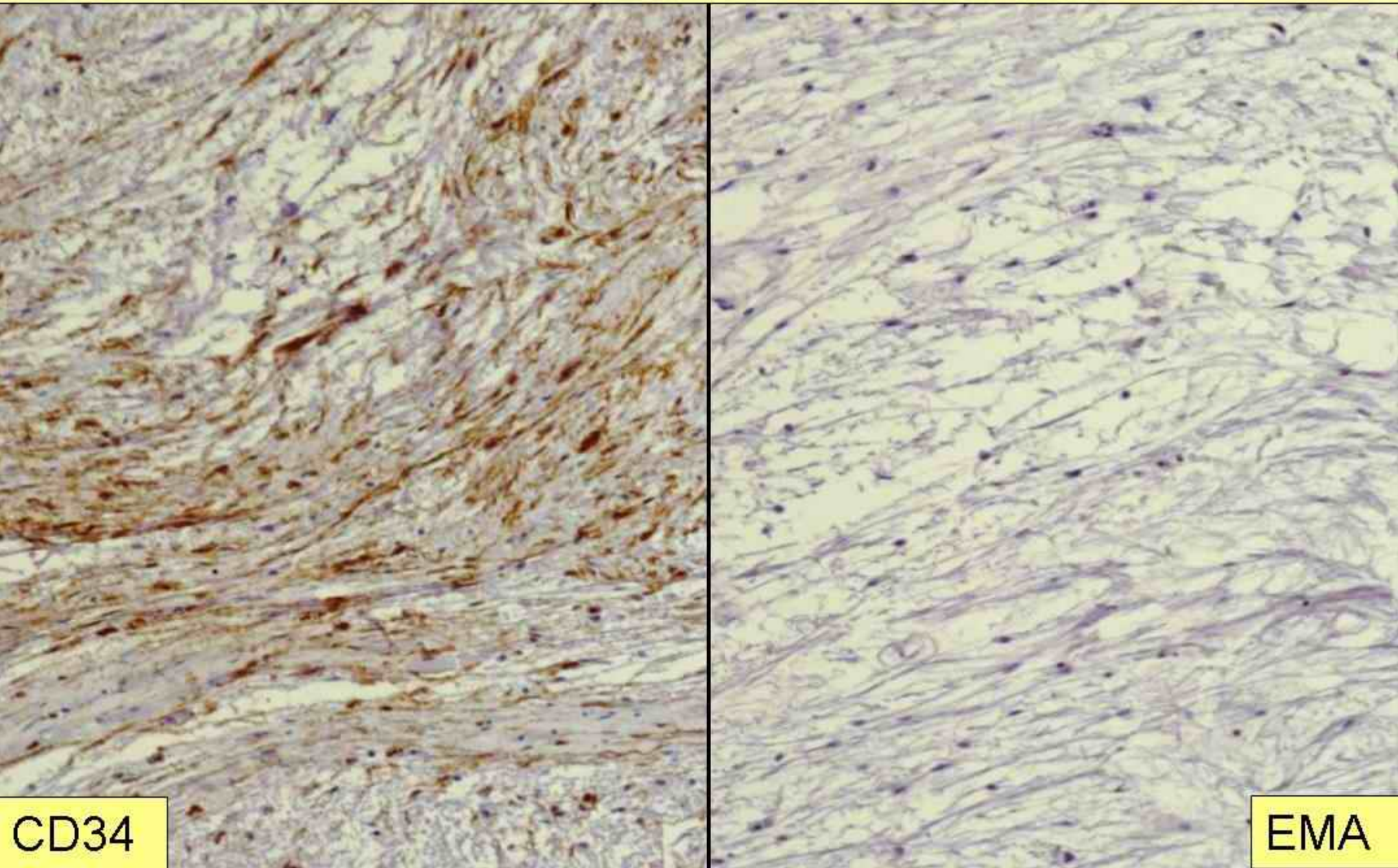
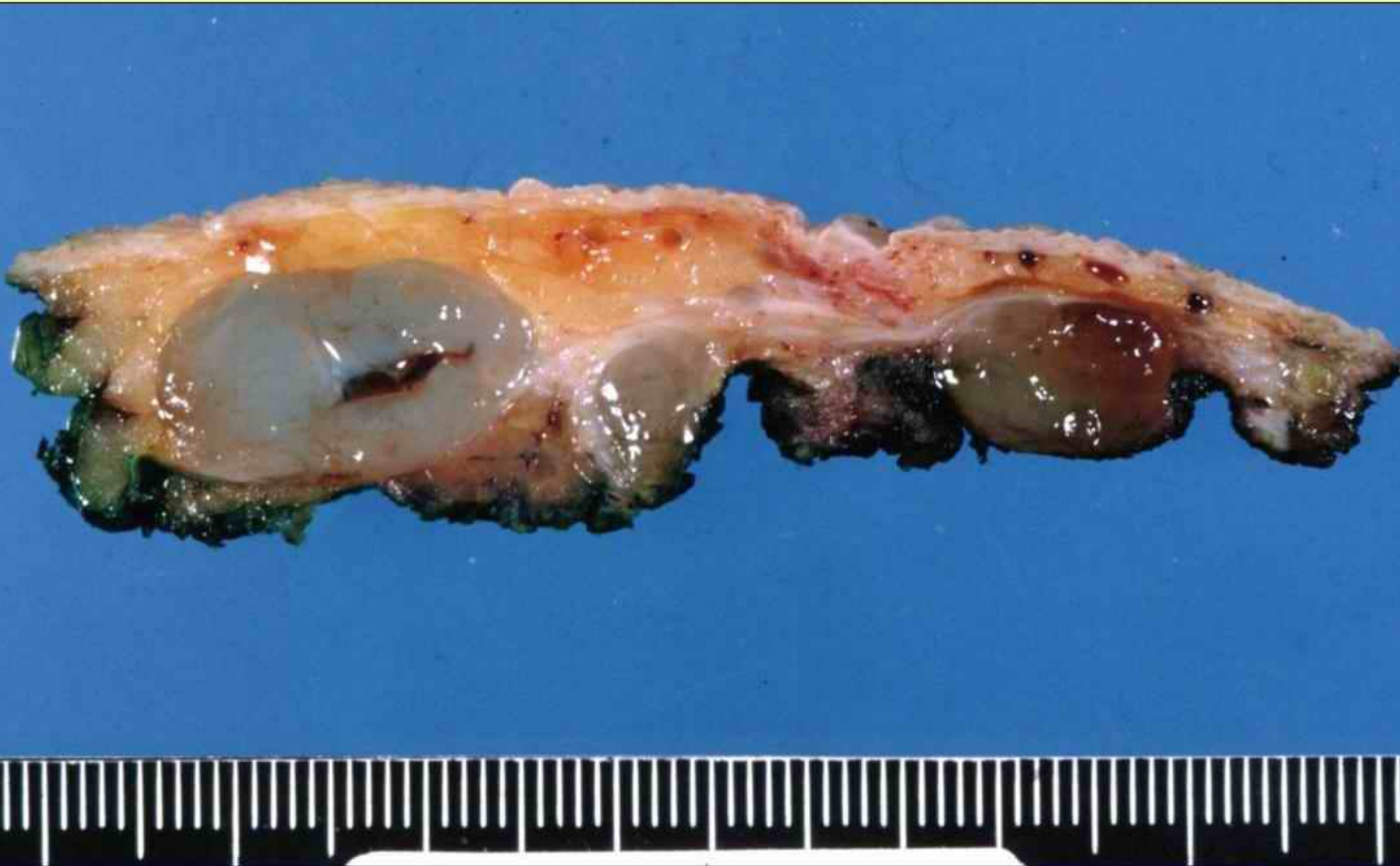


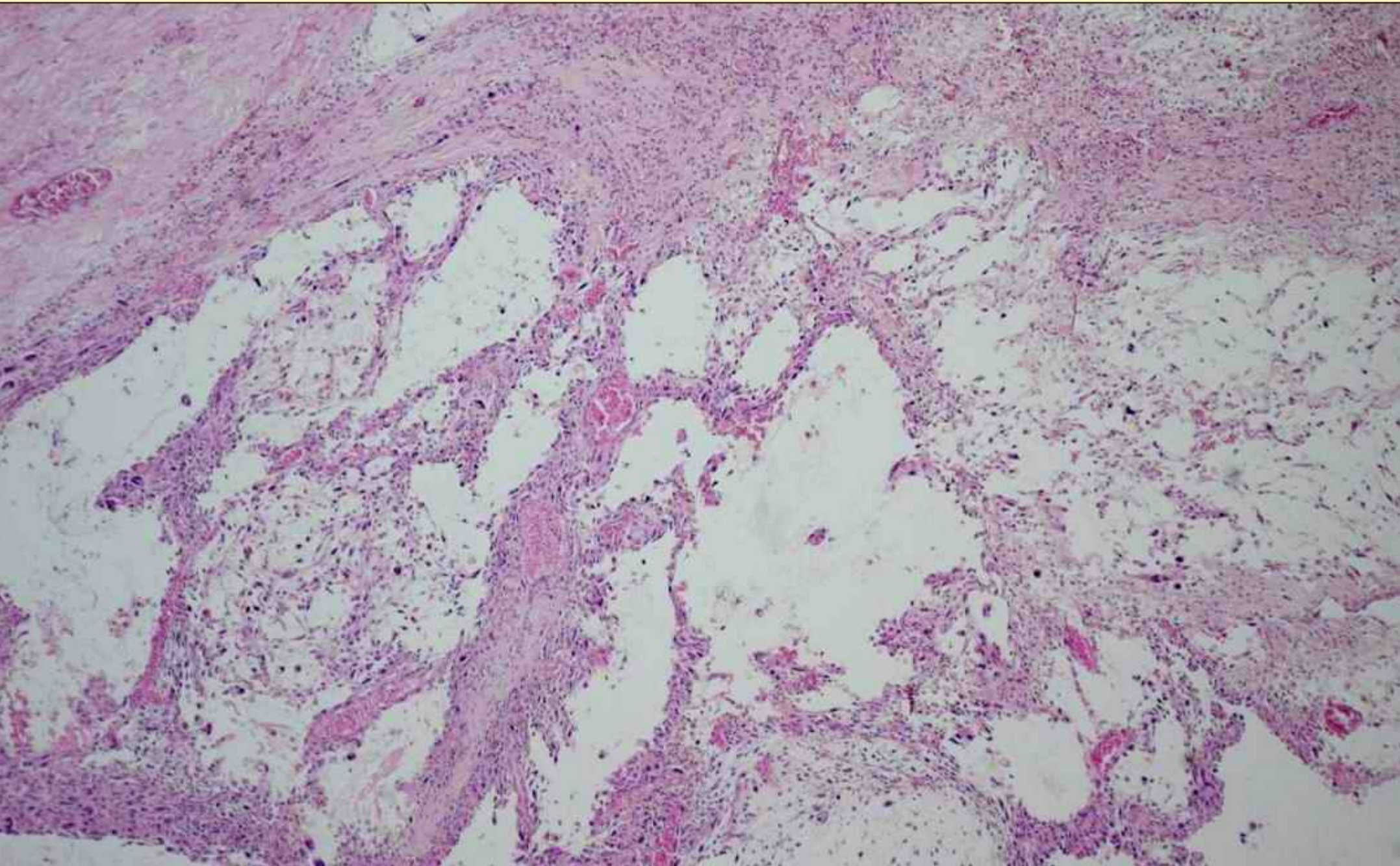
Low- and intermediate-grade myxofibrosarcoma

- Key features
  - Previously called « myxoid MFH »
  - Elderly (median 60 yrs); M>F
  - Superficial : 60%
  - Sites: limbs (lower extrem. +++), limb girdles
  - Size: 5-7 cm
  - Behavior: depends on histologic grade and extent of resection
  - Recurrence rate: 50% (often due to inadequate excisions) – upgrading possible in recurrences
  - Metastases rare in low-grade lesions (lungs, bone): 5-15% , often ocurring after multiple recurrences
  - 5-yr disease specific survival rate: >95%

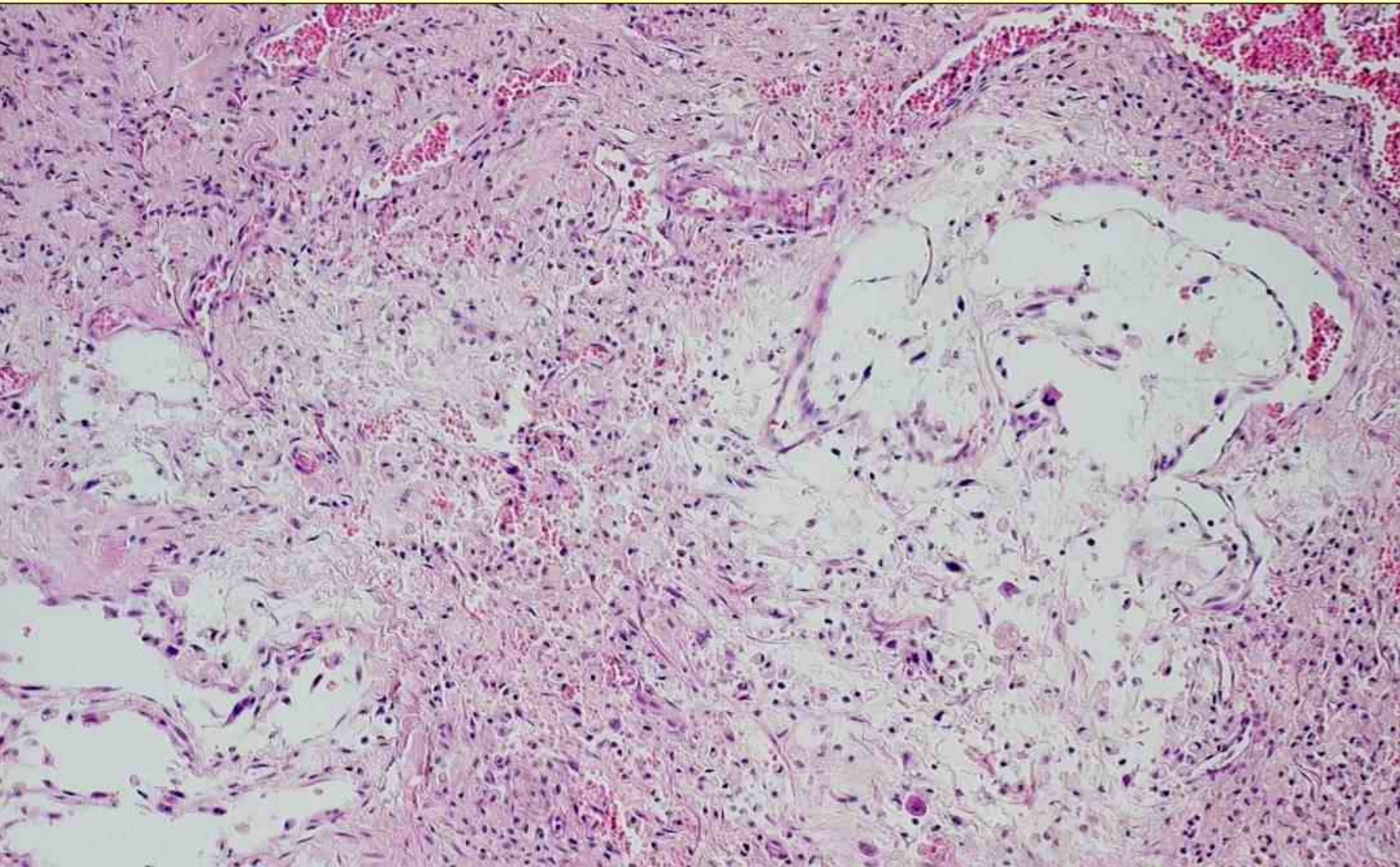
Low-grade myxofibrosarcoma



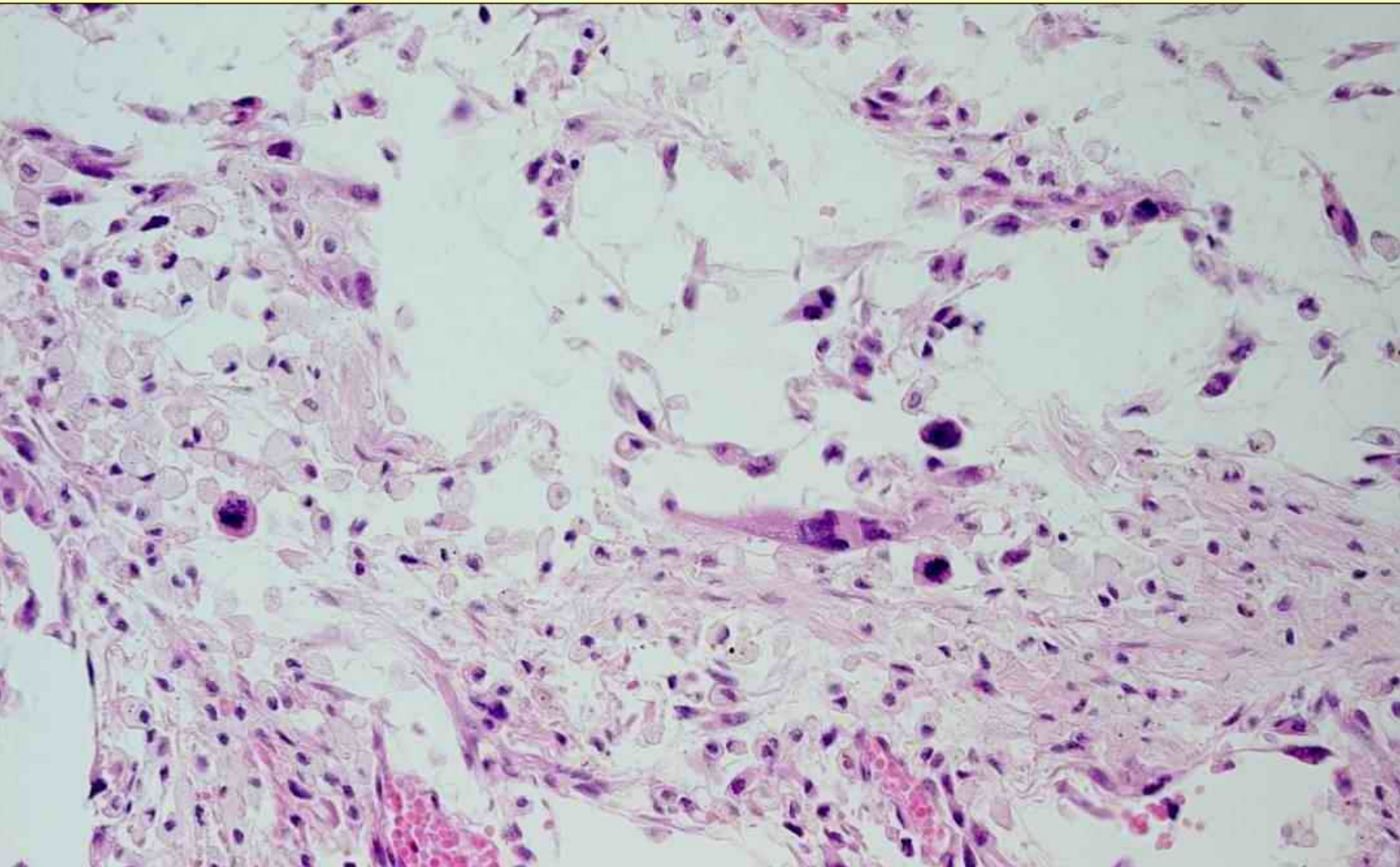
Low to intermediate-grade myxofibrosarcoma



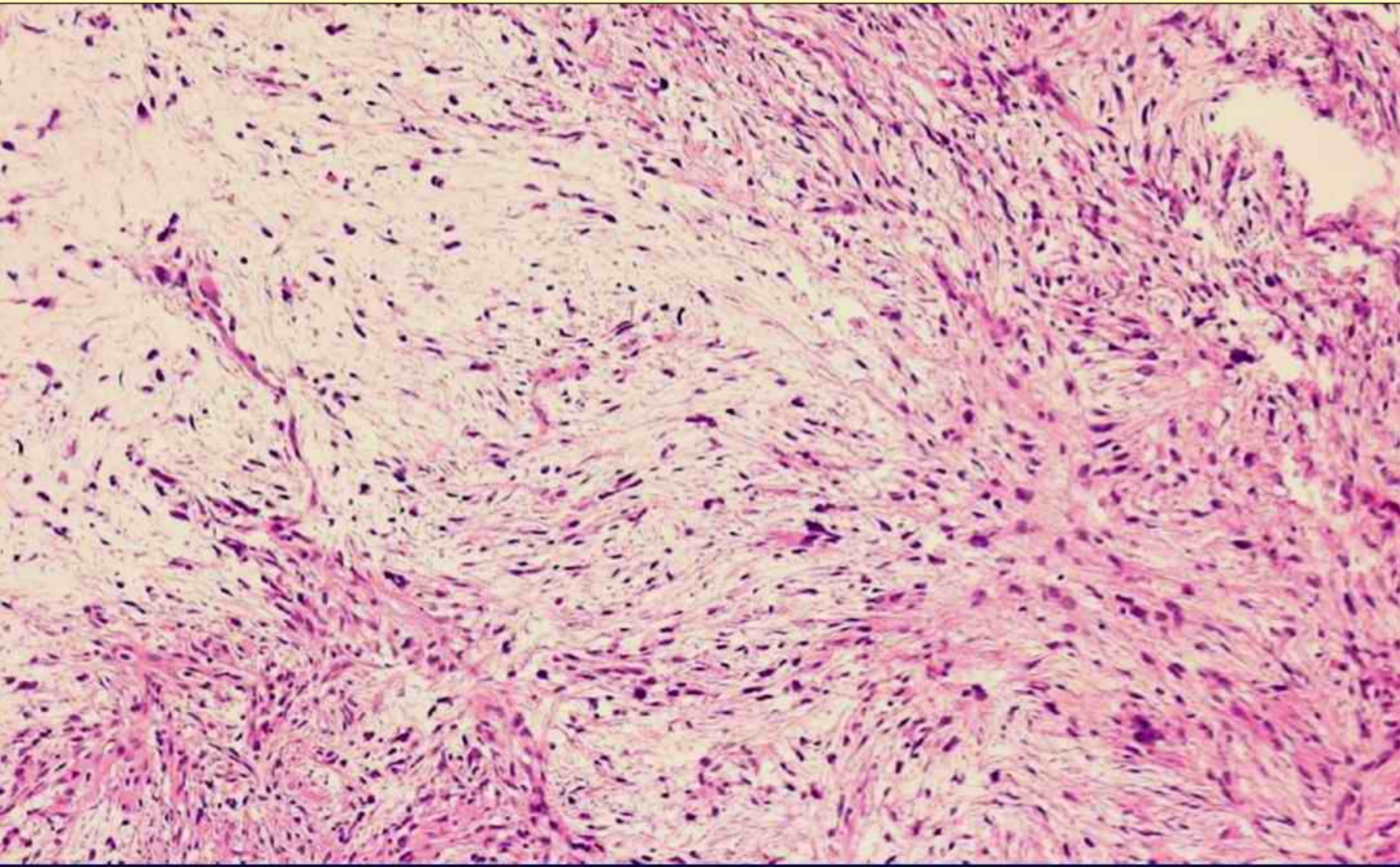
Low to intermediate-grade myxofibrosarcoma



Low-grade myxofibrosarcoma



Intermediate-grade myxofibrosarcoma



Low- and intermediate-grade myxofibrosarcoma

- Immunohistochemistry

  Of no help !

Low- and intermediate-grade myxofibrosarcoma

- Differential diagnosis
  - Myxoma / Cellular myxoma
  - Nodular fasciitis (myxoid variant)
  - Low-grade fibromyxoid sarcoma
  - Myxoid liposarcoma (if plexiform vessels numerous)

Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

- Recognized as a distinct entity in 1998 by two different teams who coined two different terms :
  - Inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg-like cells: a distinctive lesion with features simulating inflammatory conditions, Hodgkin's disease, and various sarcomas. Montgomery EA, et al. Mod Pathol, 1998, 11: 384-391.
  - Acral myxoinflammatory fibroblastic sarcoma: a low-grade tumor of the hands and feet. Meis-Kindblom JM, Kindblom LG. Am J Surg Pathol, 1998, 22: 911-924.

Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

- Key features
  - Adults
  - Distal extremities (hand, wrist, foot, ankle). Upper extremites, especially fingers and hands, more frequently affected
  - Often mistaken clinically for a ganglion cyst or tenosynovitis
  - Tumor size: 3-4 cm on average with a gelatinous, multinodular gross appearance
  - Situation: subcutis or deep soft tissues, involving tendon sheaths and the synovium of adjacent joints

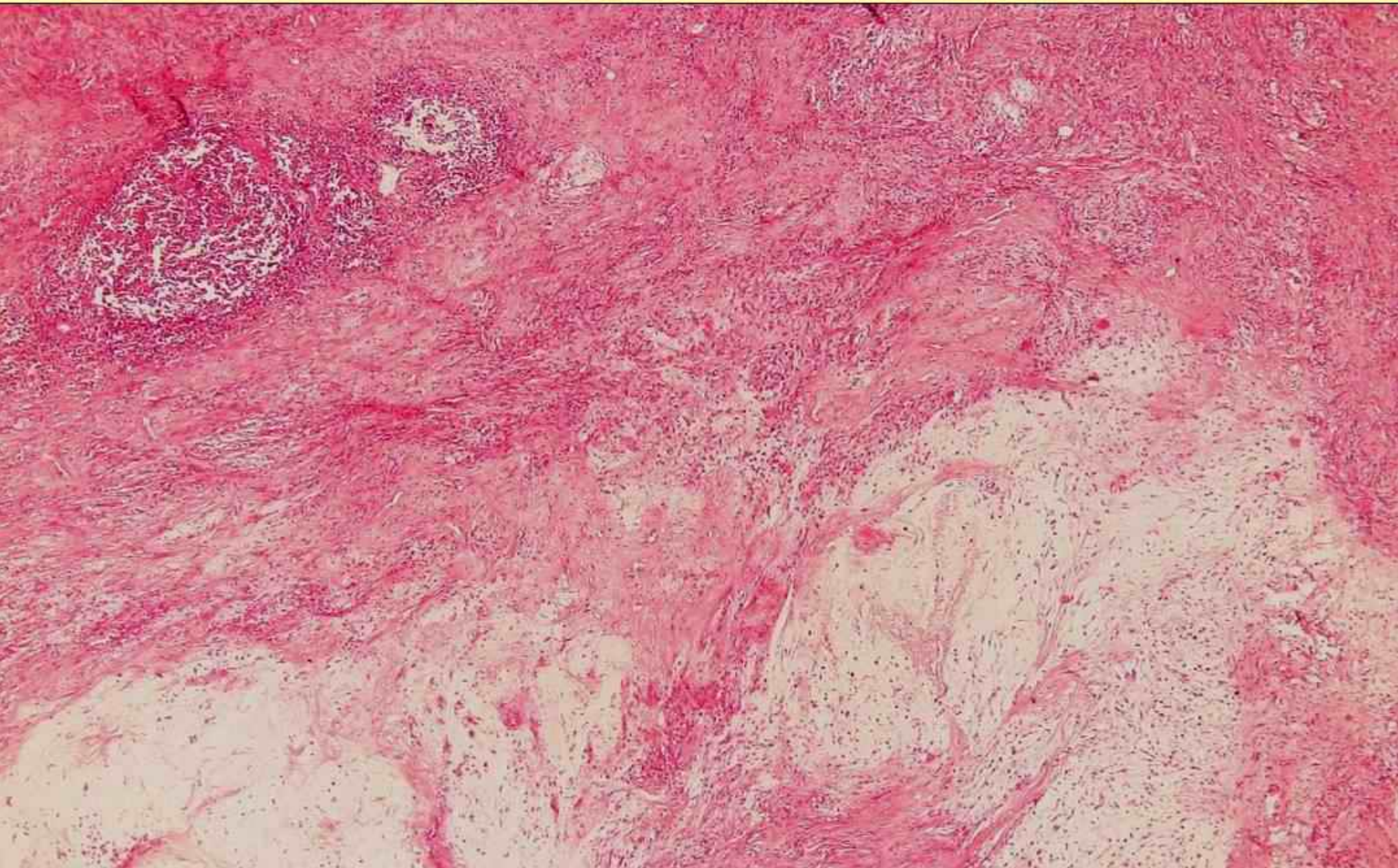
Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

- Key features (continued)
  - Recurs in about 20% of cases

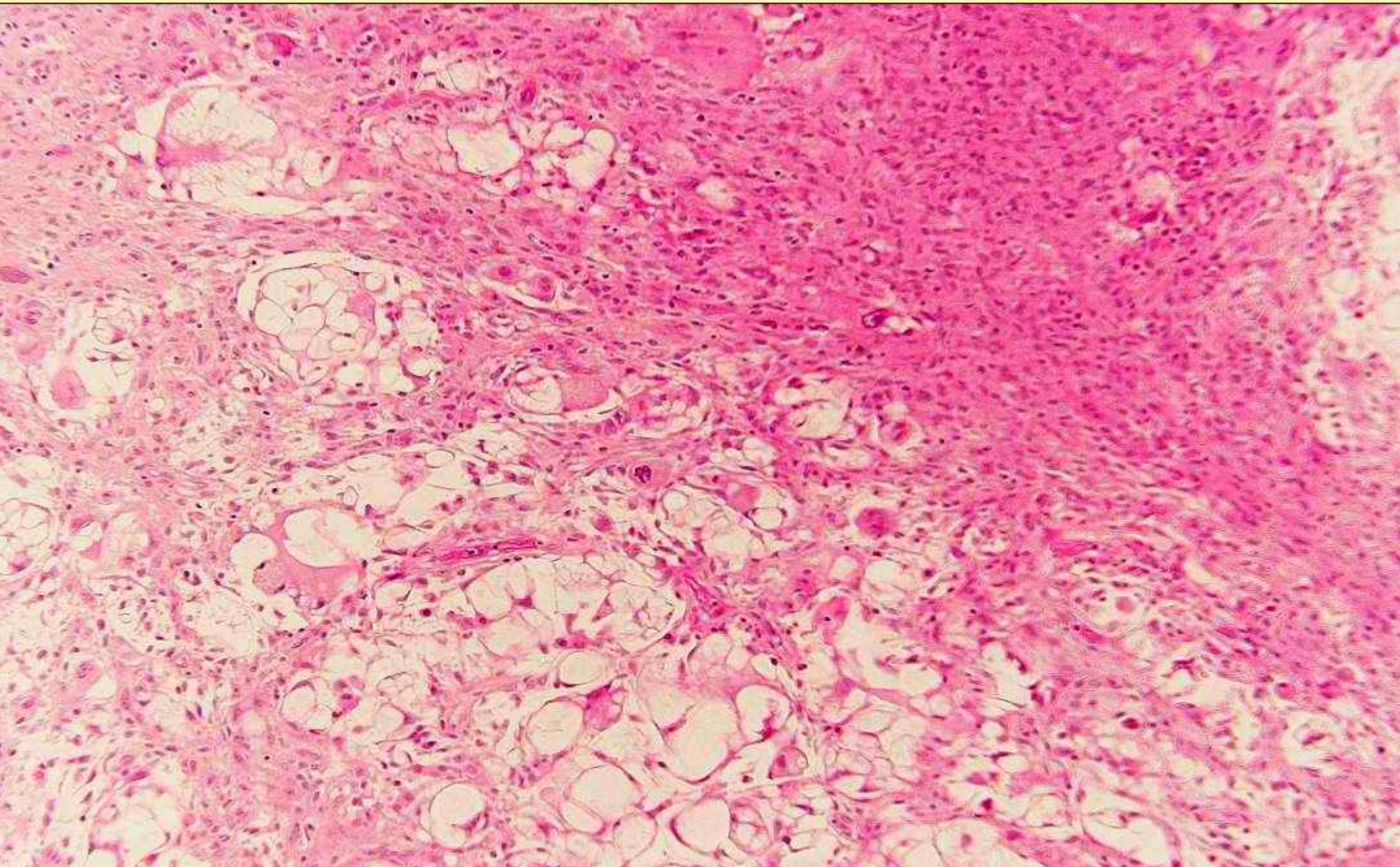
    The high proportion - 67% - of recurrent cases reported by Meis-Kindblom et al. is probably related to incomplete excisions due to erroneous diagnoses of benignity

  - Metastasizes in less than 5% of cases

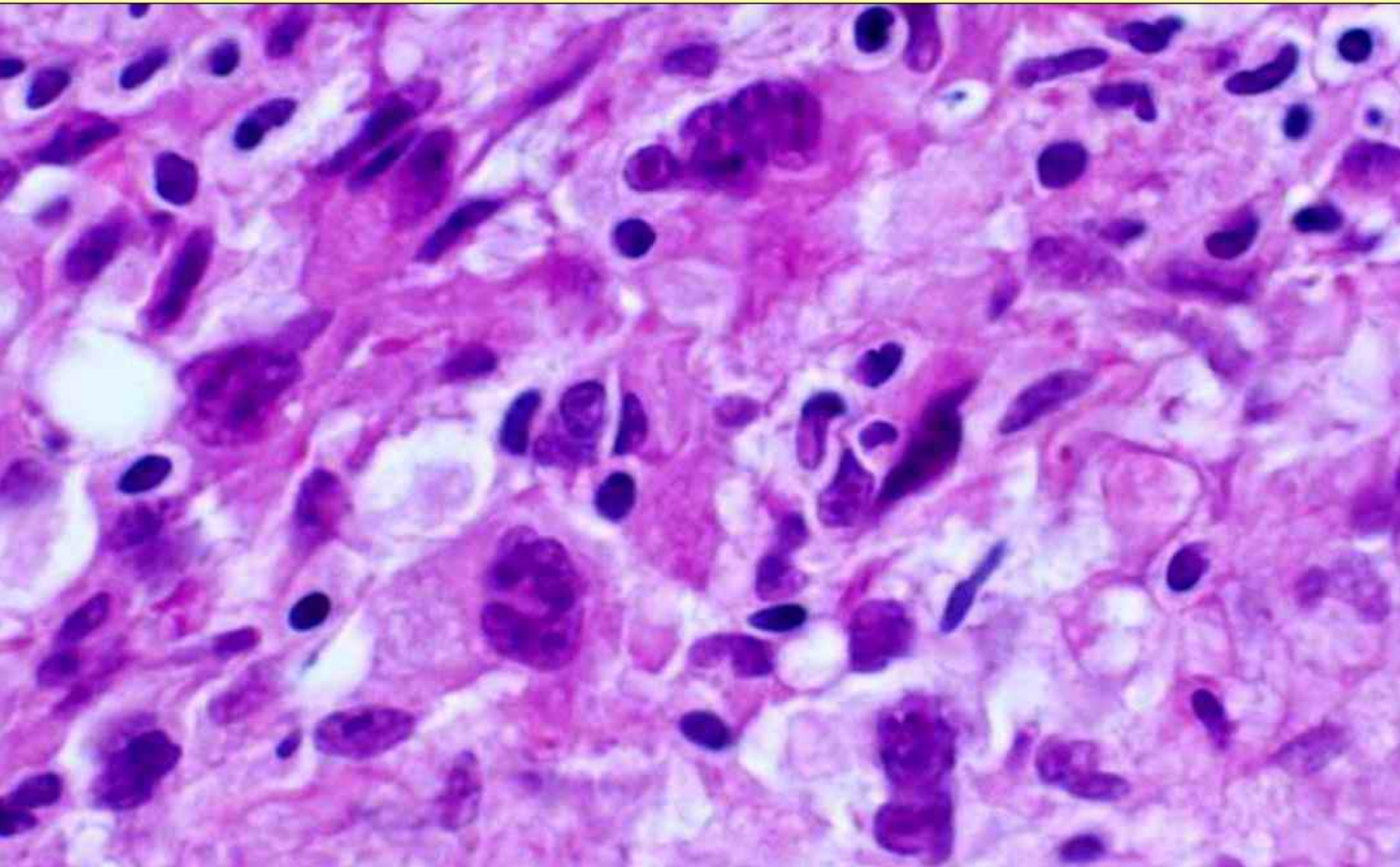
Inflammatory myxohyaline tumor



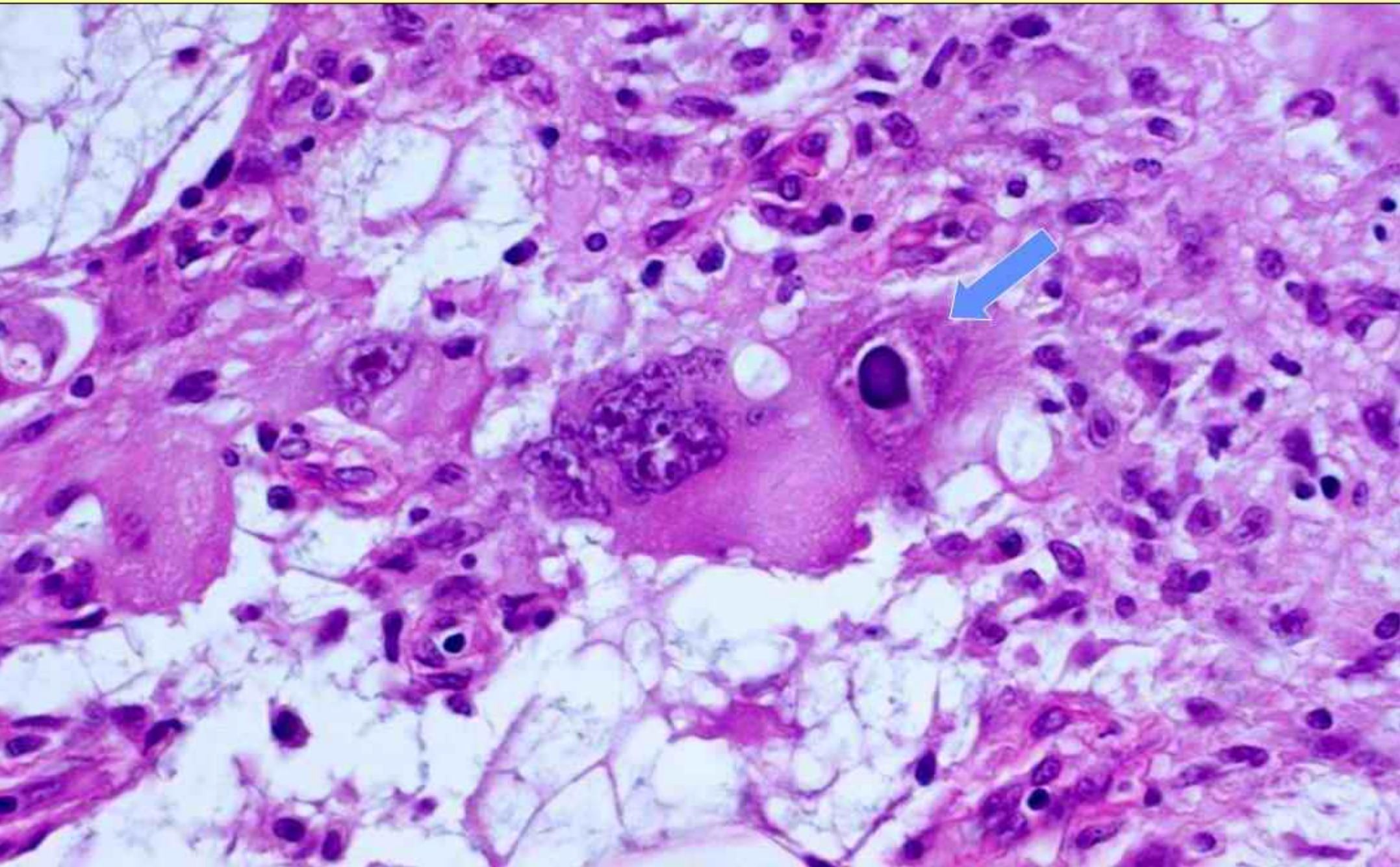
Inflammatory myxohyaline tumor



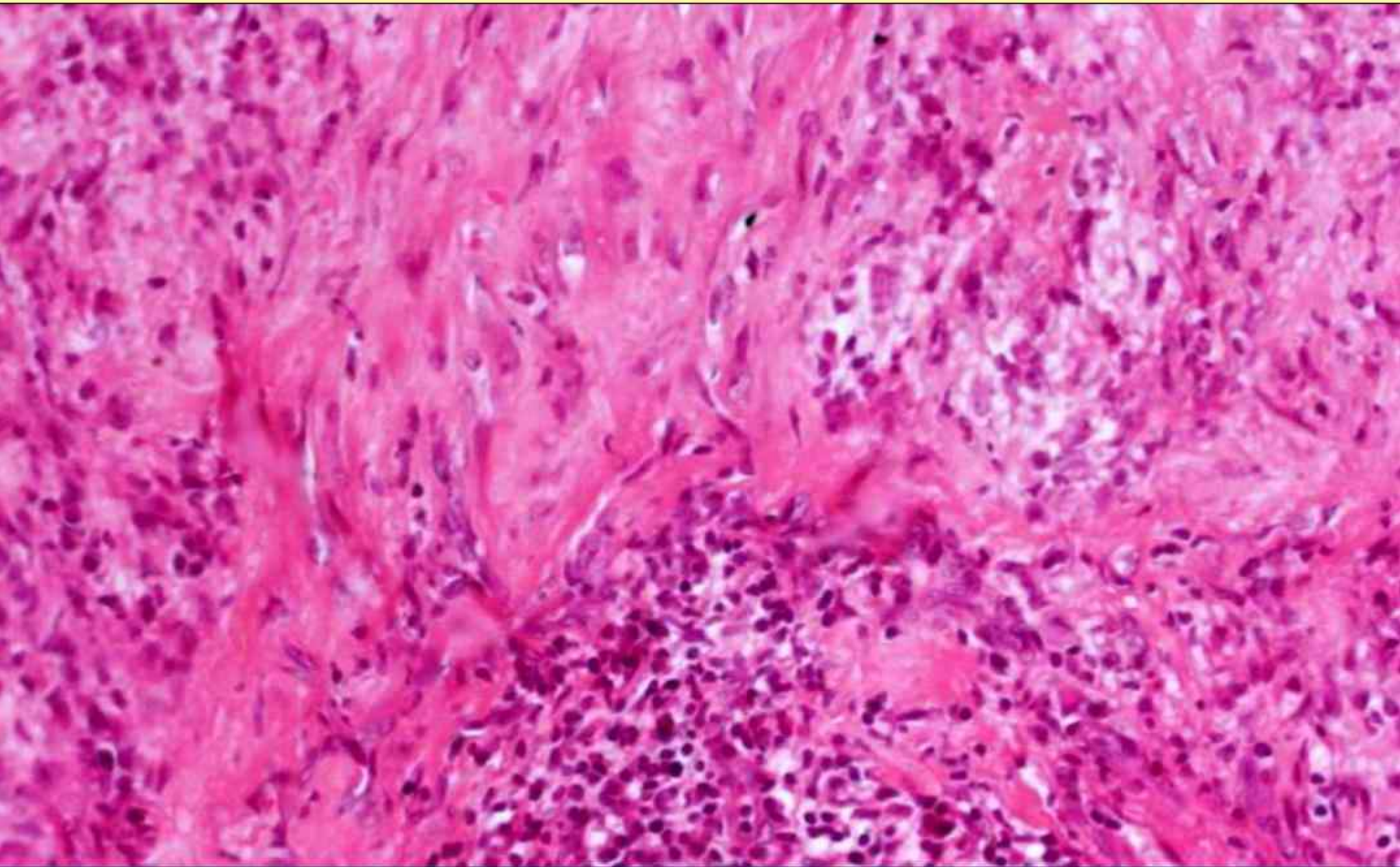
Inflammatory myxohyaline tumor



Inflammatory myxohyaline tumor

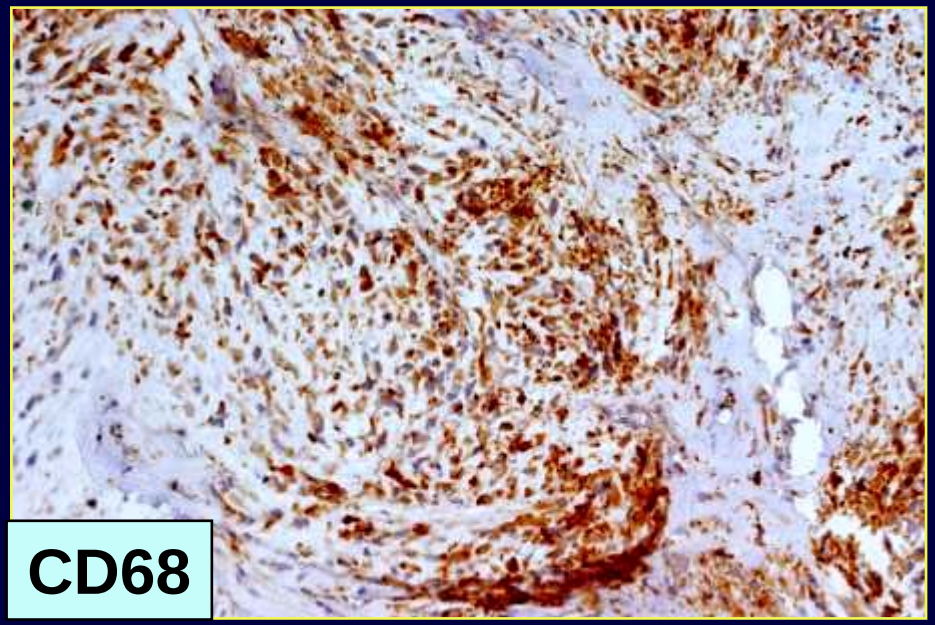


Inflammatory myxohyaline tumor



Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

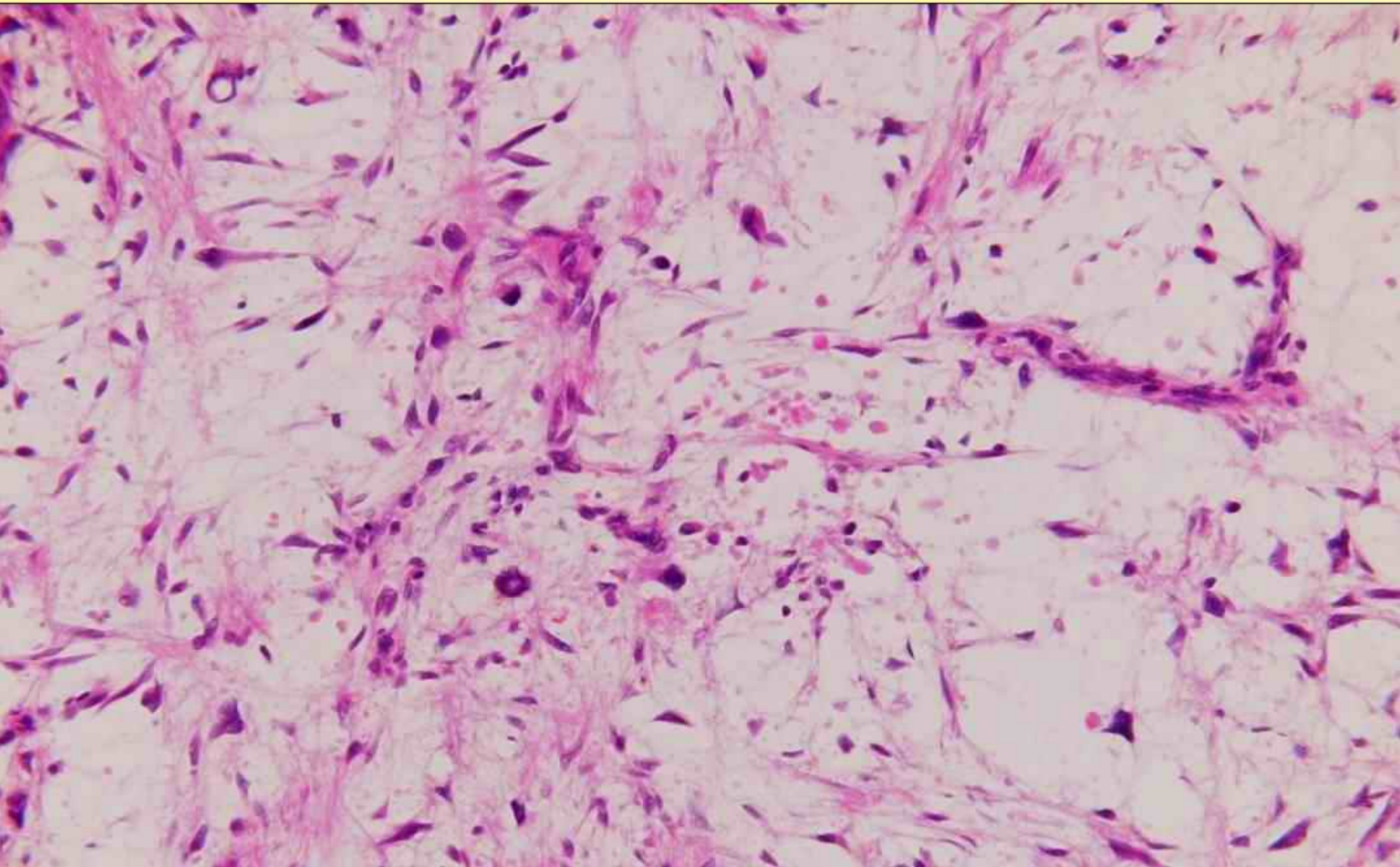
- Immunohistochemistry
  - Positivity for vimentin and CD68
  - Occasional reactivity for CD34, smooth muscle actin, and/or cytokeratin



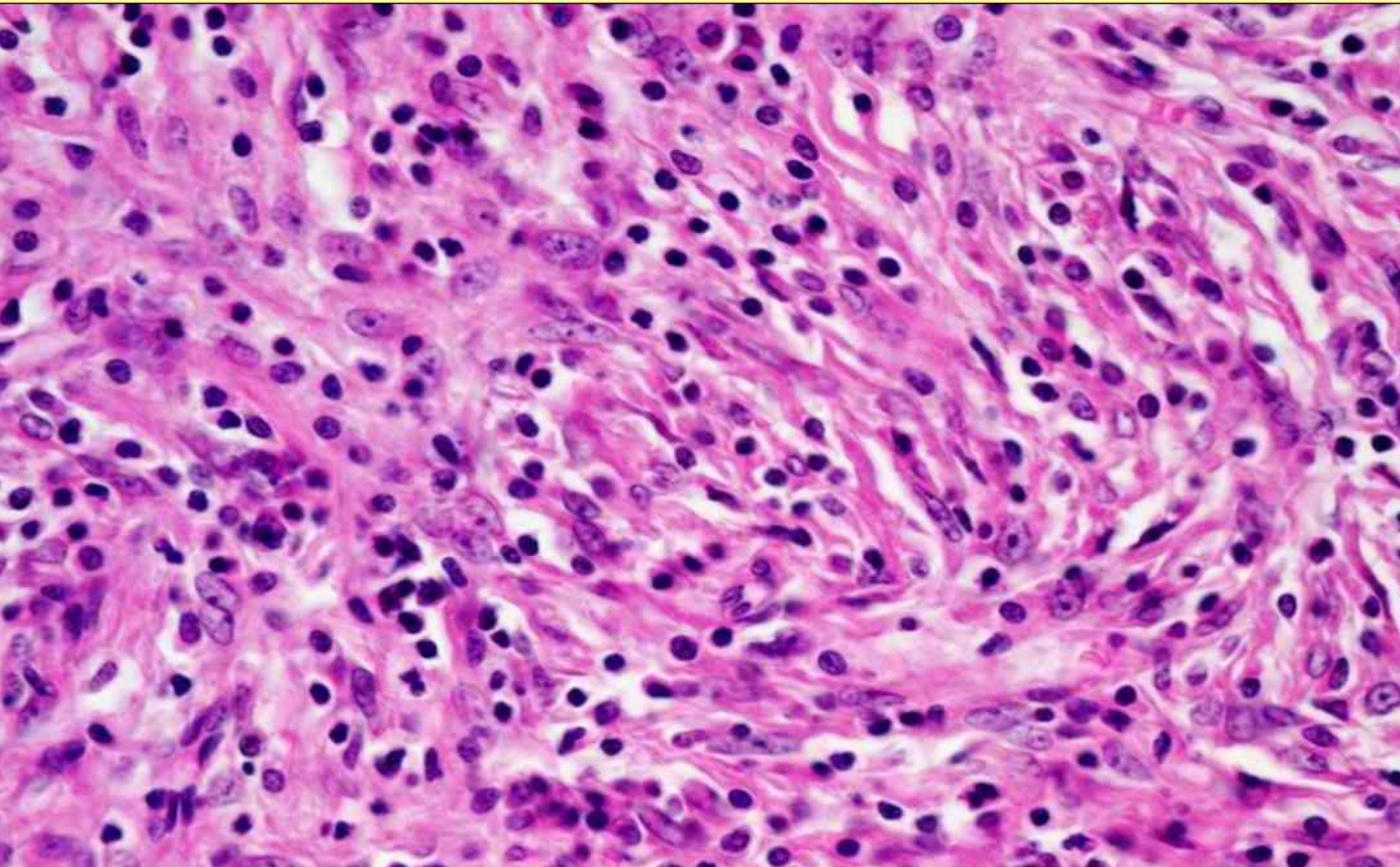
Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

- Differential diagnosis
  - if the inflammation predominates inflammatory processes such as chronic tenosynovitis, inflammatory pseudotumor, mucoid pseudocyst with superimposed inflammatory changes
  - if multinucleated giant cells are numerous giant cell tumor of tendon sheath
  - if cellular atypia predominate malignant tumors such as myxofibrosarcoma (myxoid malignant fibrous histiocytoma), pleomorphic liposarcoma (owing to the presence of pseudolipoblastic cells), and inflammatory fibrosarcoma

Low-grade myxofibrosarcoma (myxoid MFH)



Inflammatory myofibroblastic tumor

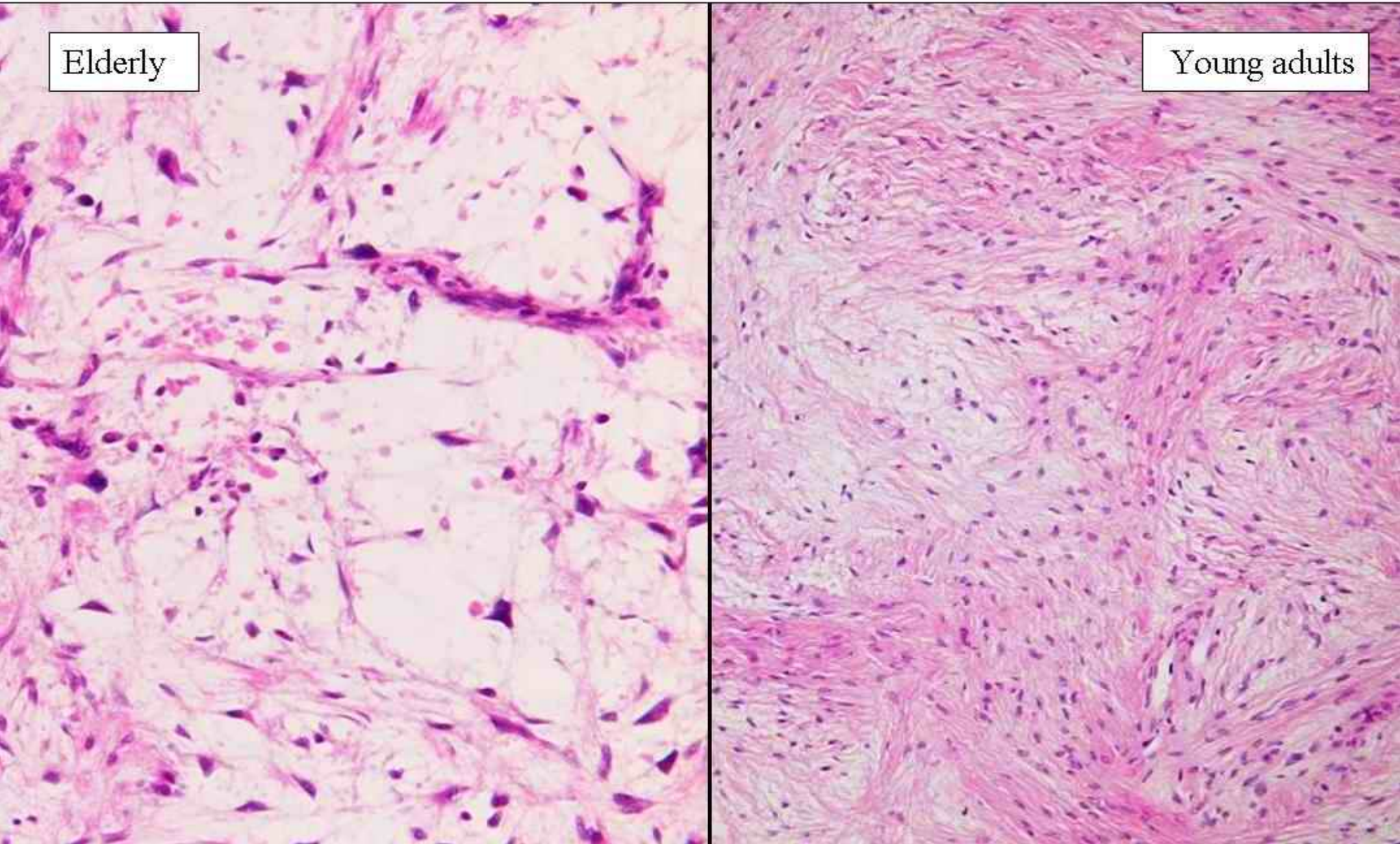


Helpful clues in the differential diagnostic approach

Low-grade myxofibrosarcoma (LG-MFS) *vs* Low-grade fibromyxoid sarcoma (LGFMS)

- Question
  - is it clinically relevant to distinguish low-grade myxofibrosarcoma (LG-MFS) from low-grade fibromyxoid sarcoma (LGFMS) ?
- Yes !
  - LG-MFS: 50% recurrences; 5-15% mets.
  - LGFMS: 10% recurrences; 10%-70% mets.

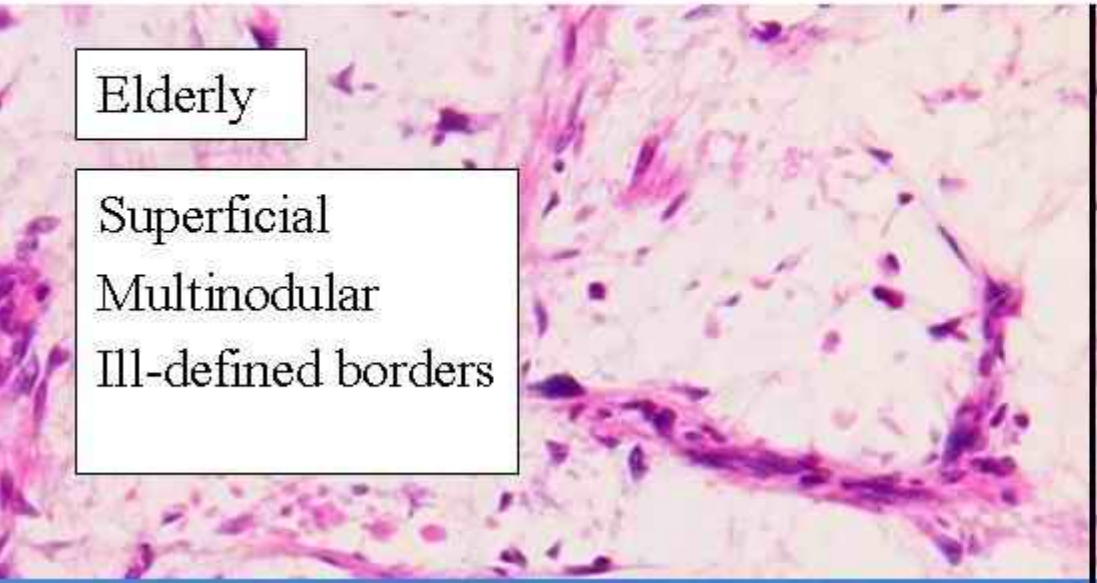
LG-Myxofibrosarcoma *vs* LGFMS

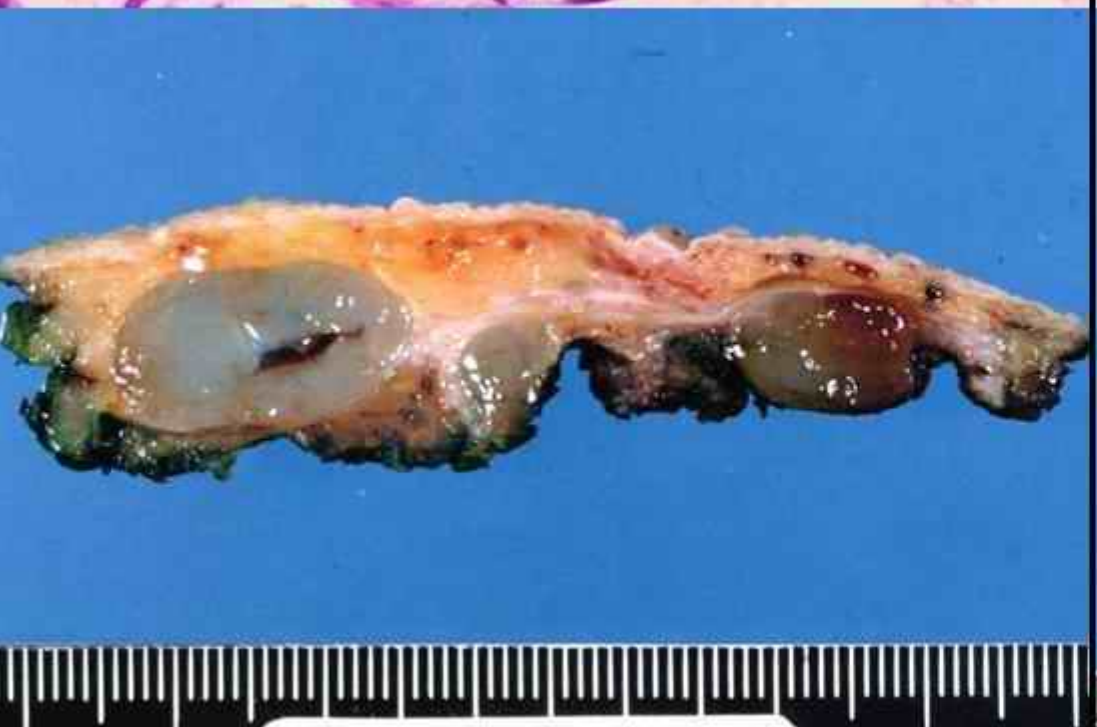


LG-Myxofibrosarcoma *vs* LGFMS

Elderly

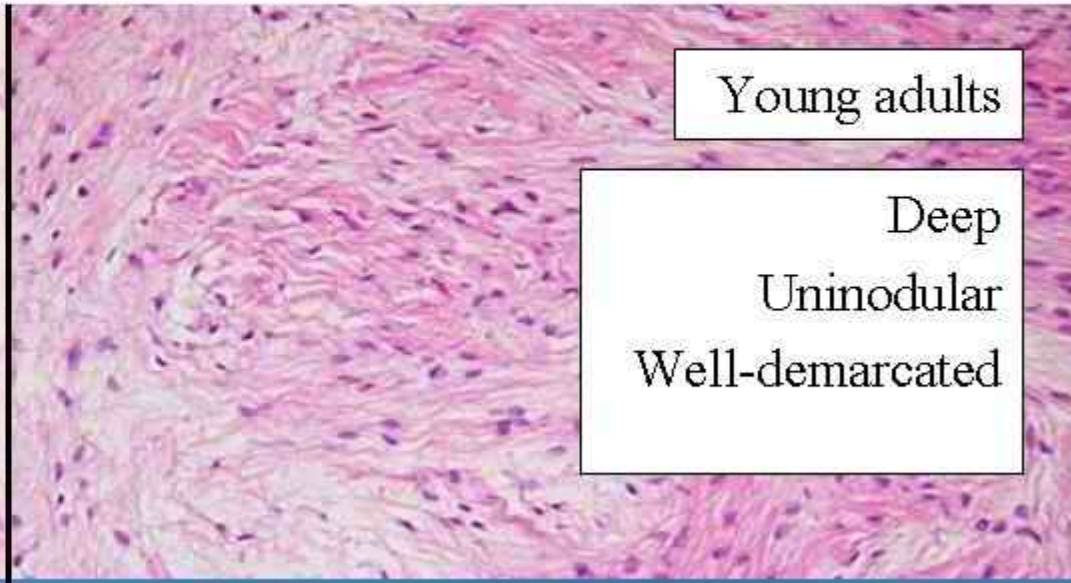
Superficial
Multinodular
Ill-defined borders

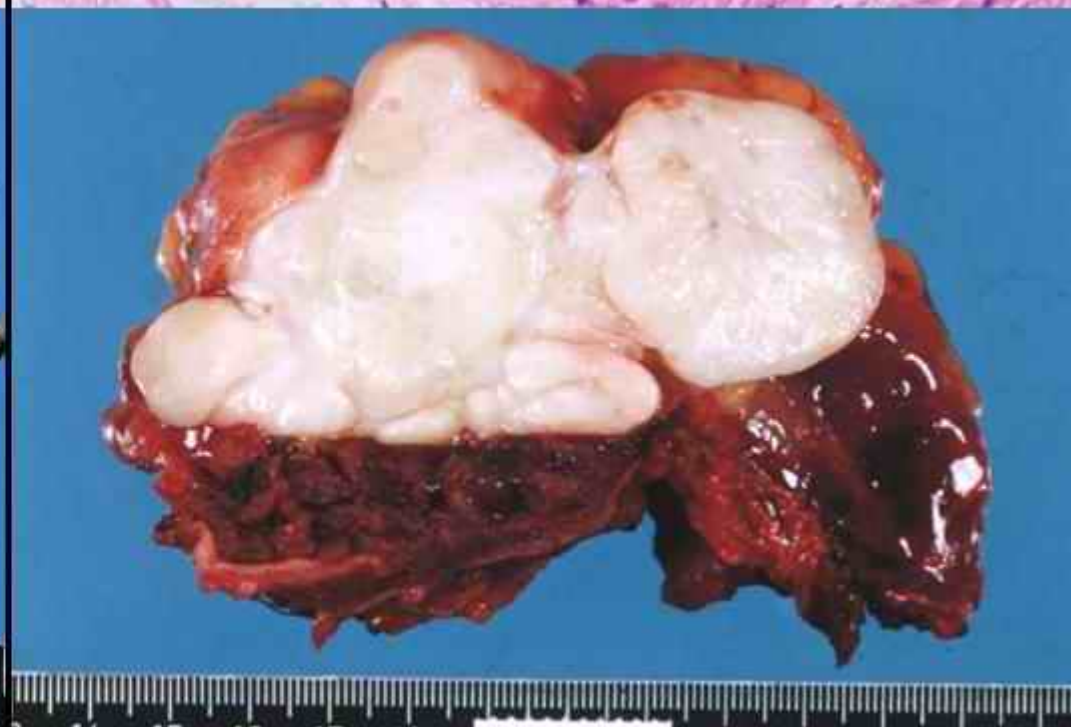




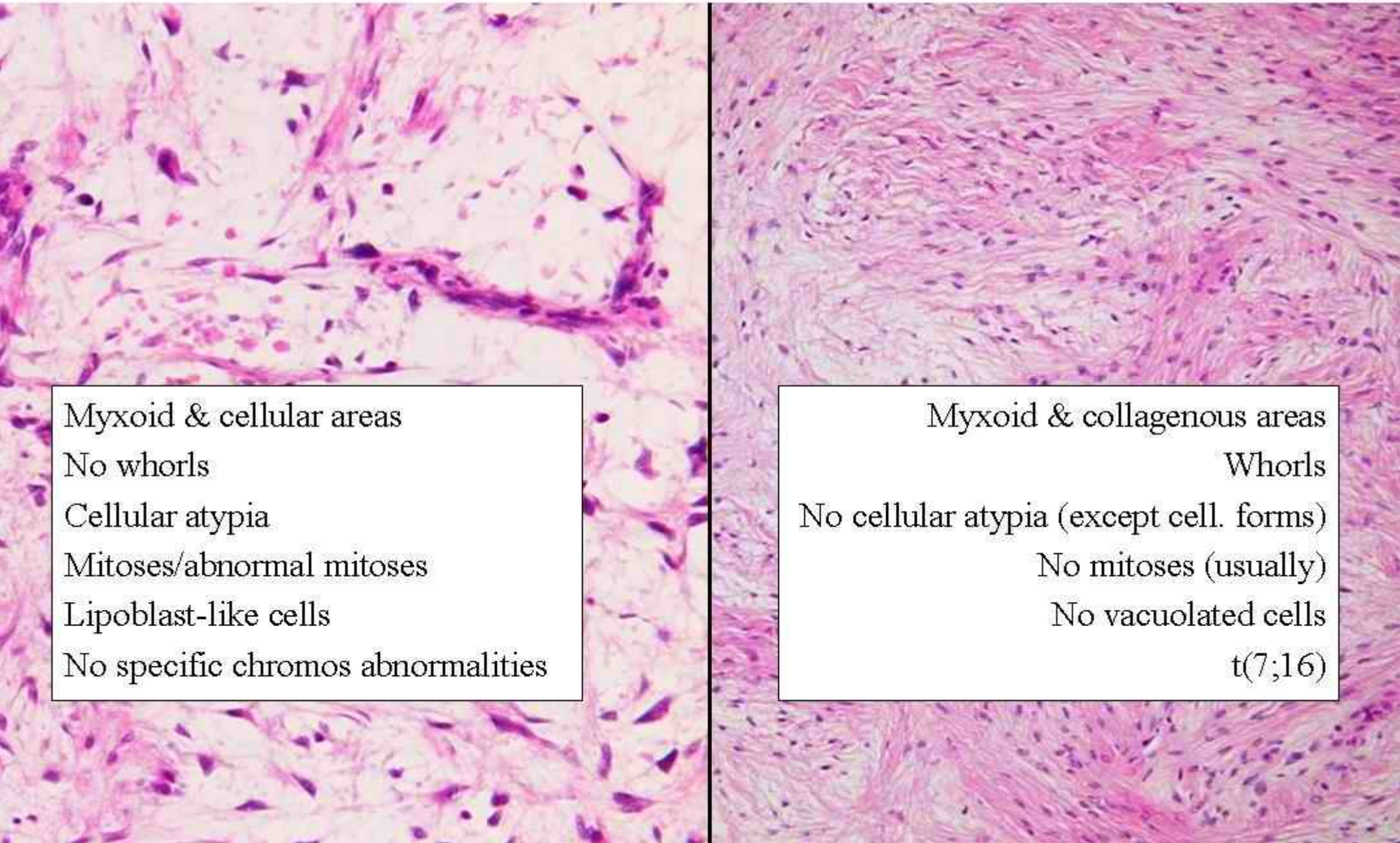
Young adults

Deep
Uninodular
Well-demarcated





LG-Myxofibrosarcoma *vs* LGFMS



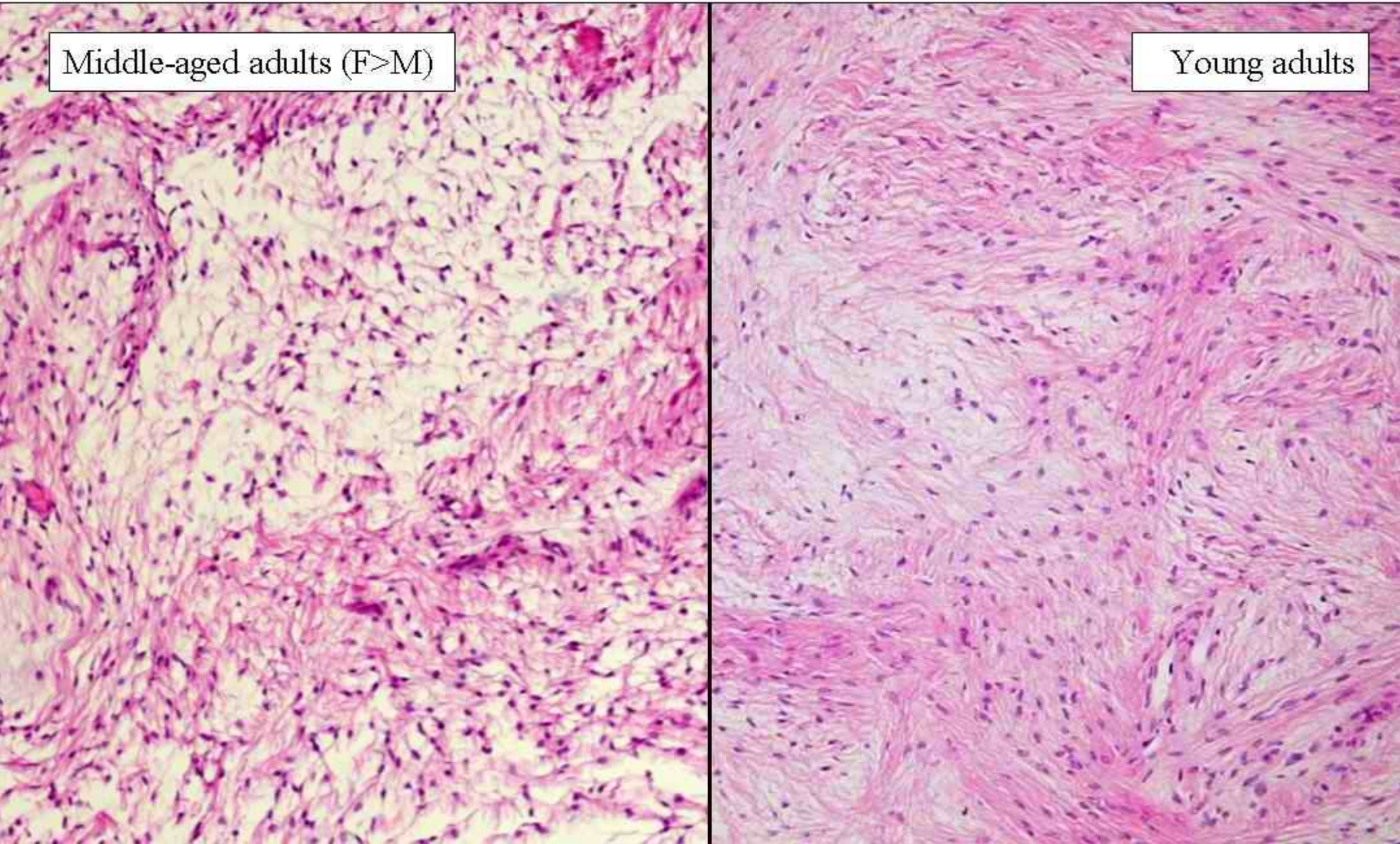
Myxoid & cellular areas
No whorls
Cellular atypia
Mitoses/abnormal mitoses
Lipoblast-like cells
No specific chromos abnormalities

Myxoid & collagenous areas
Whorls
No cellular atypia (except cell. forms)
No mitoses (usually)
No vacuolated cells
t(7;16)

Cellular myxoma
vs
Low-grade fibromyxoid sarcoma (LGFMS)

- Question
  - is it clinically relevant to distinguish cellular myxoma from low-grade fibromyxoid sarcoma and myxofibrosarcoma ?
- Yes
  - Cellular myxoma = benign. <2% recur.; no mets.
  - LGFMS = sarcoma; 10% recur.; 10%-70% mets.
  - Myxofibrosarc. = sarc.; 50% rec.; 5-15% mets

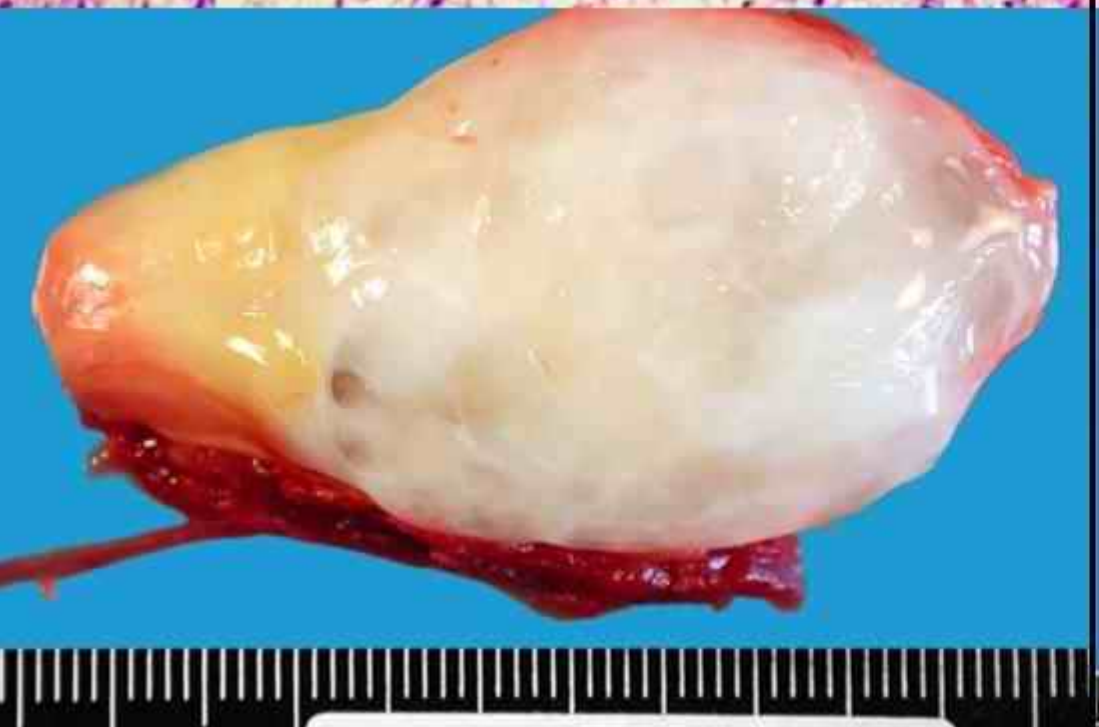
Cellular myxoma *vs* LGFMS



Cellular myxoma *vs* LGFMS

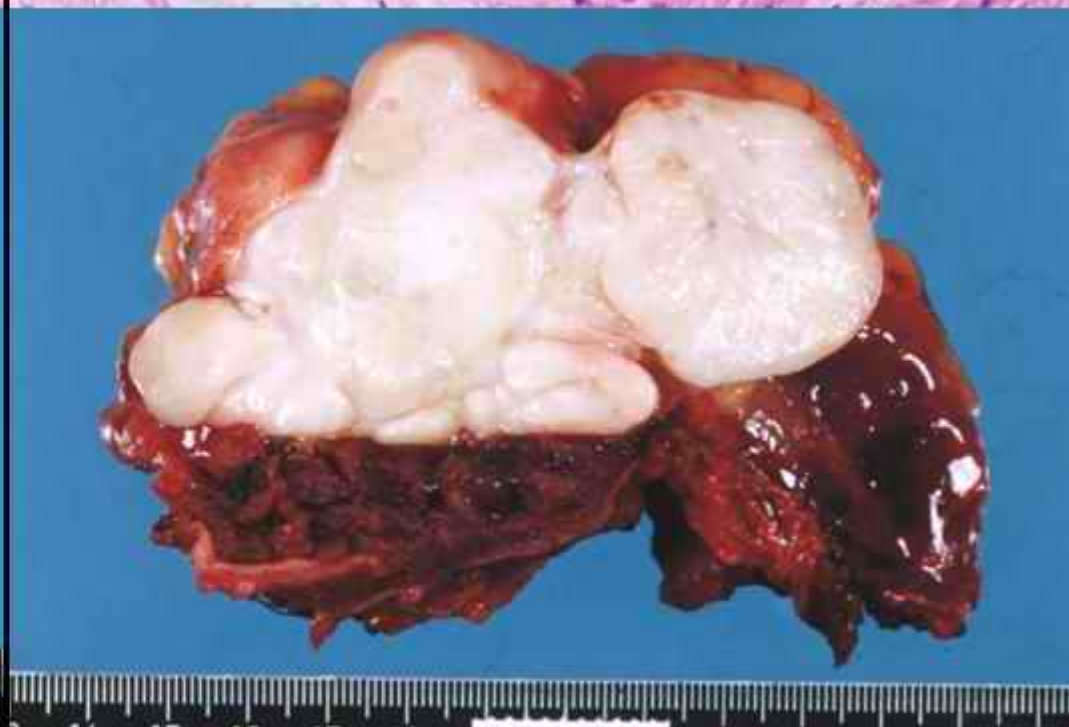
Middle-aged adults (F>M)

Ill-defined borders
Gelatinous

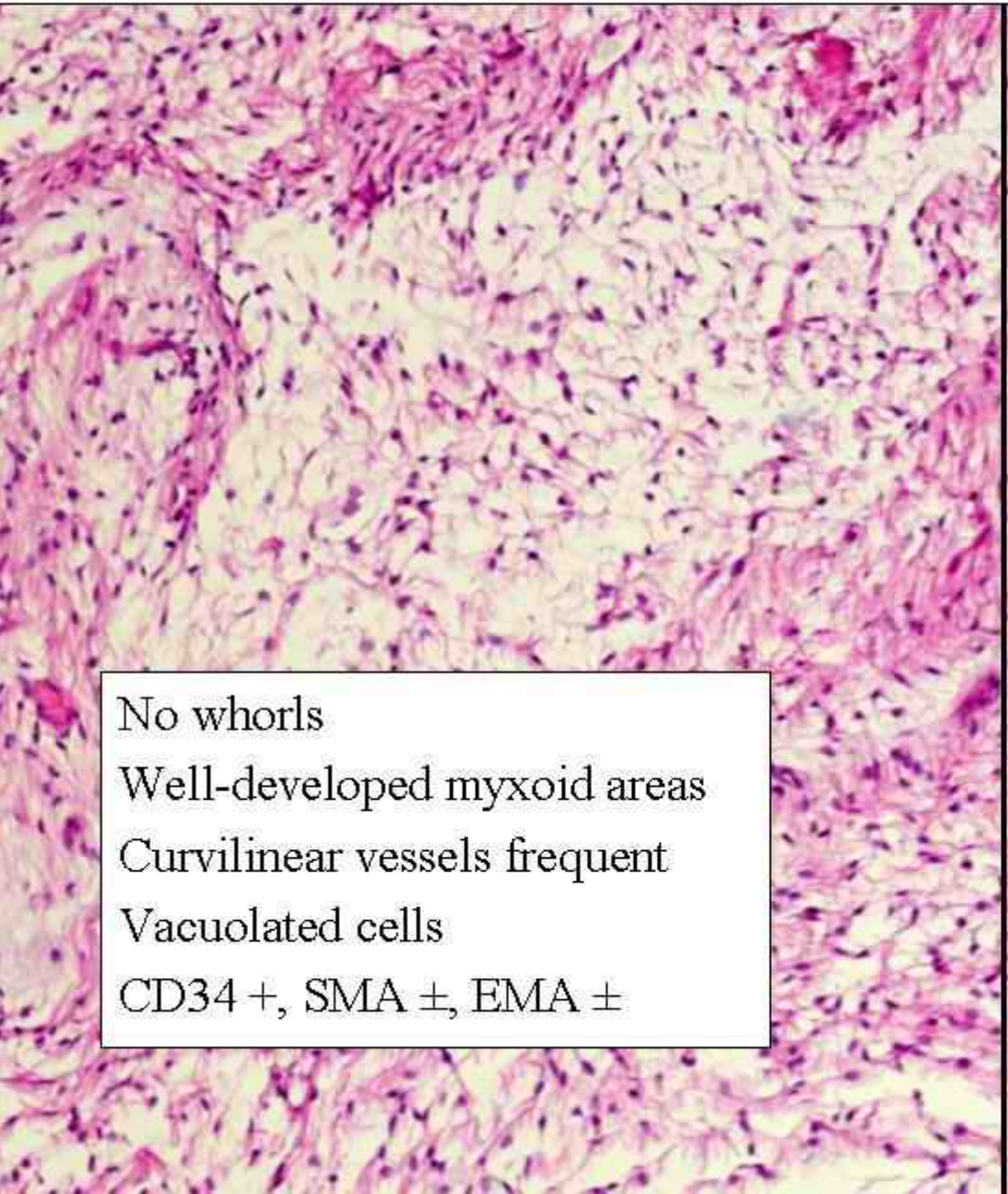


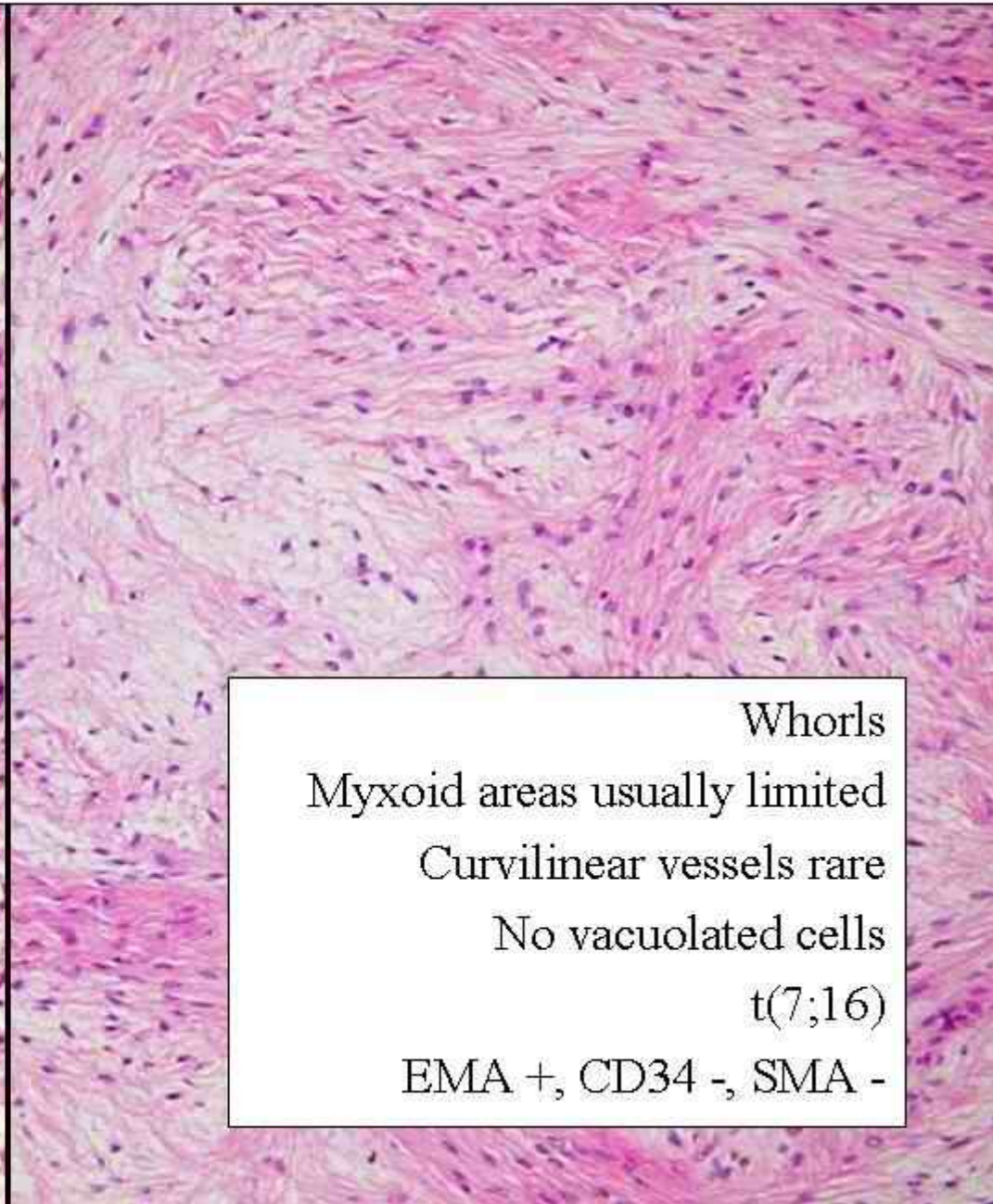
Young adults

Well-demarcated
Uninodular
Often solid and fibrous

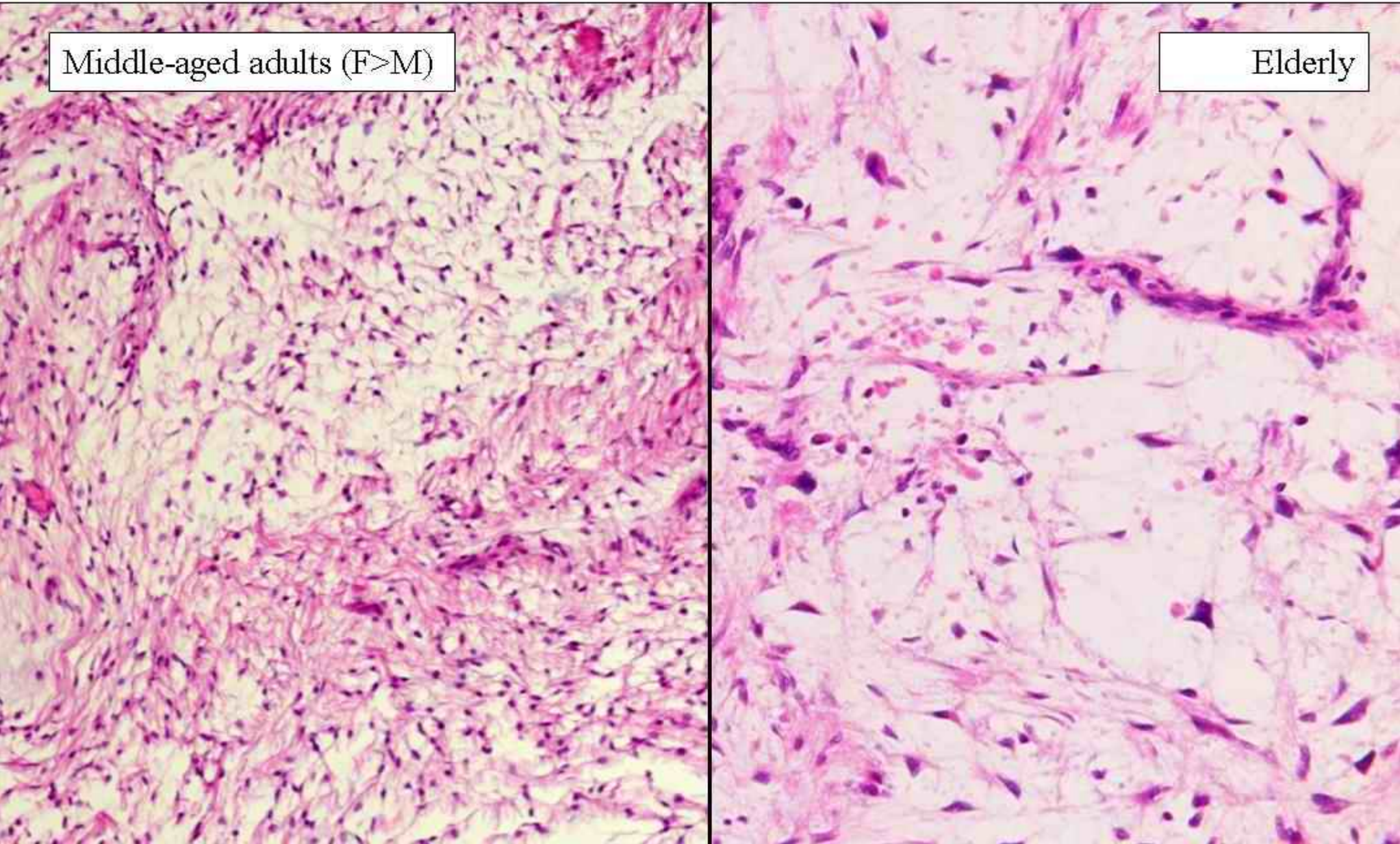


Cellular myxoma *vs* LGFMS

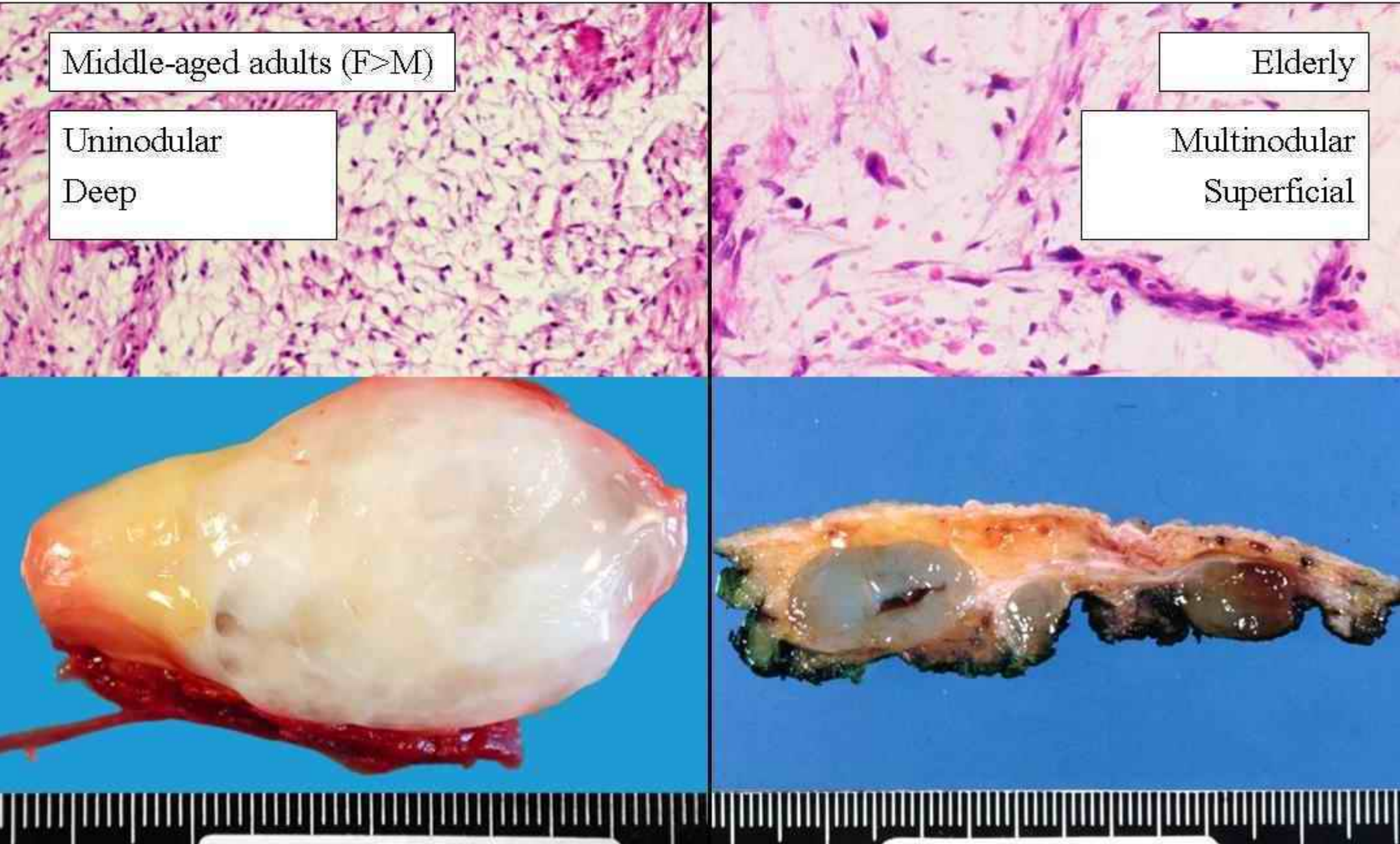




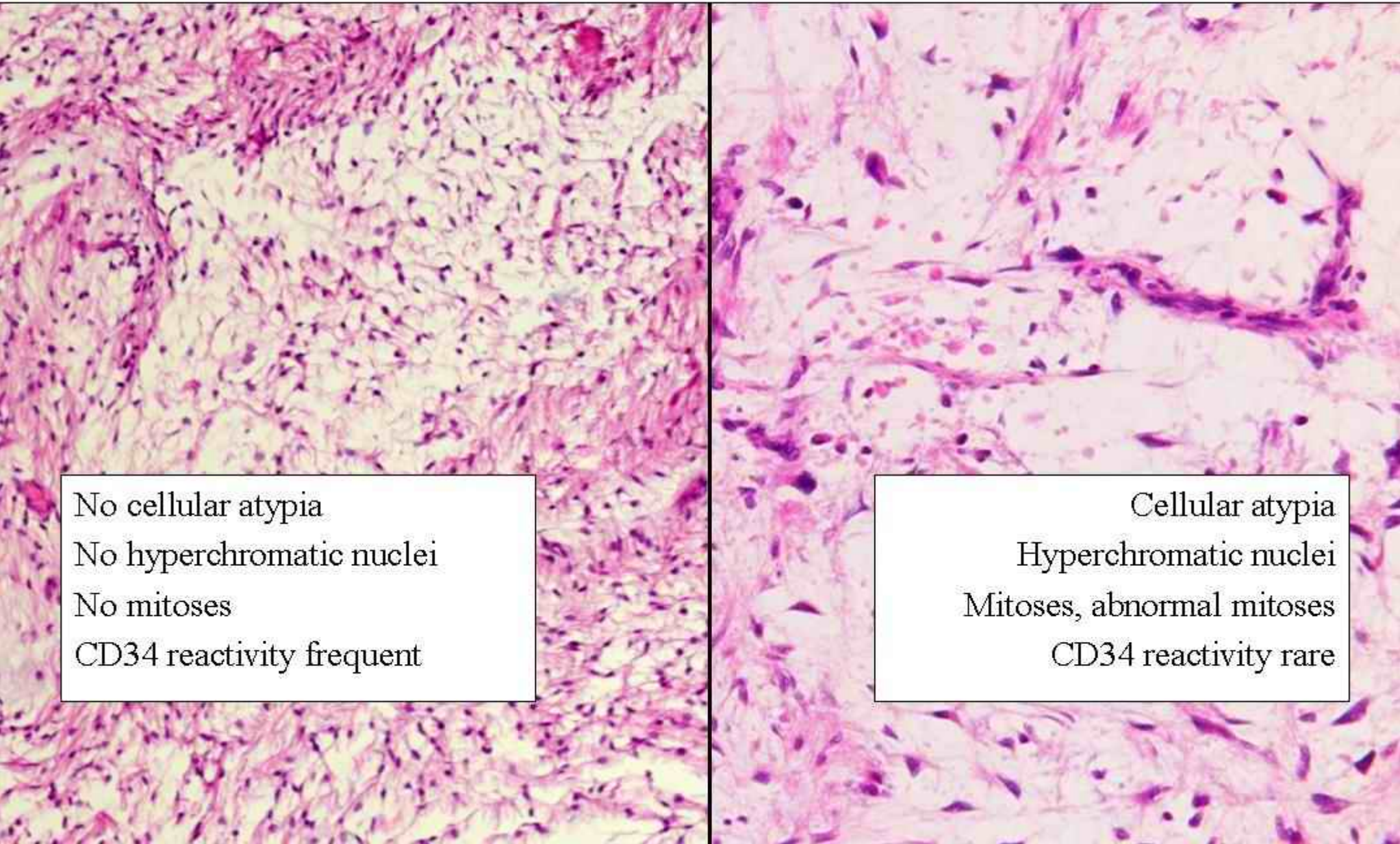
Cellular myxoma *vs* LG myxofibrosarcoma



Cellular myxoma *vs* LG myxofibrosarcoma



Cellular myxoma *vs* LG myxofibrosarcoma

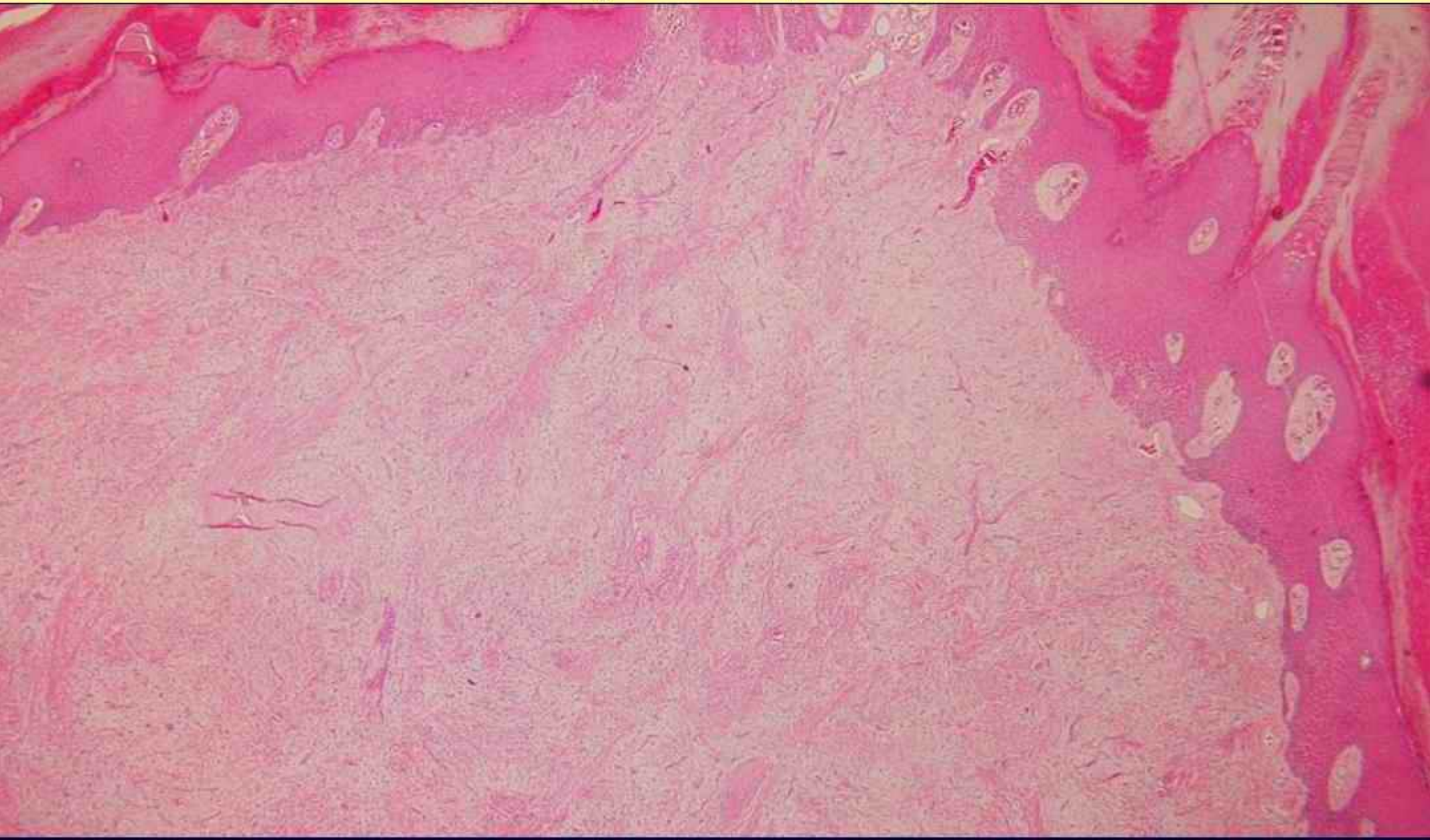


Conclusions - Take home messages

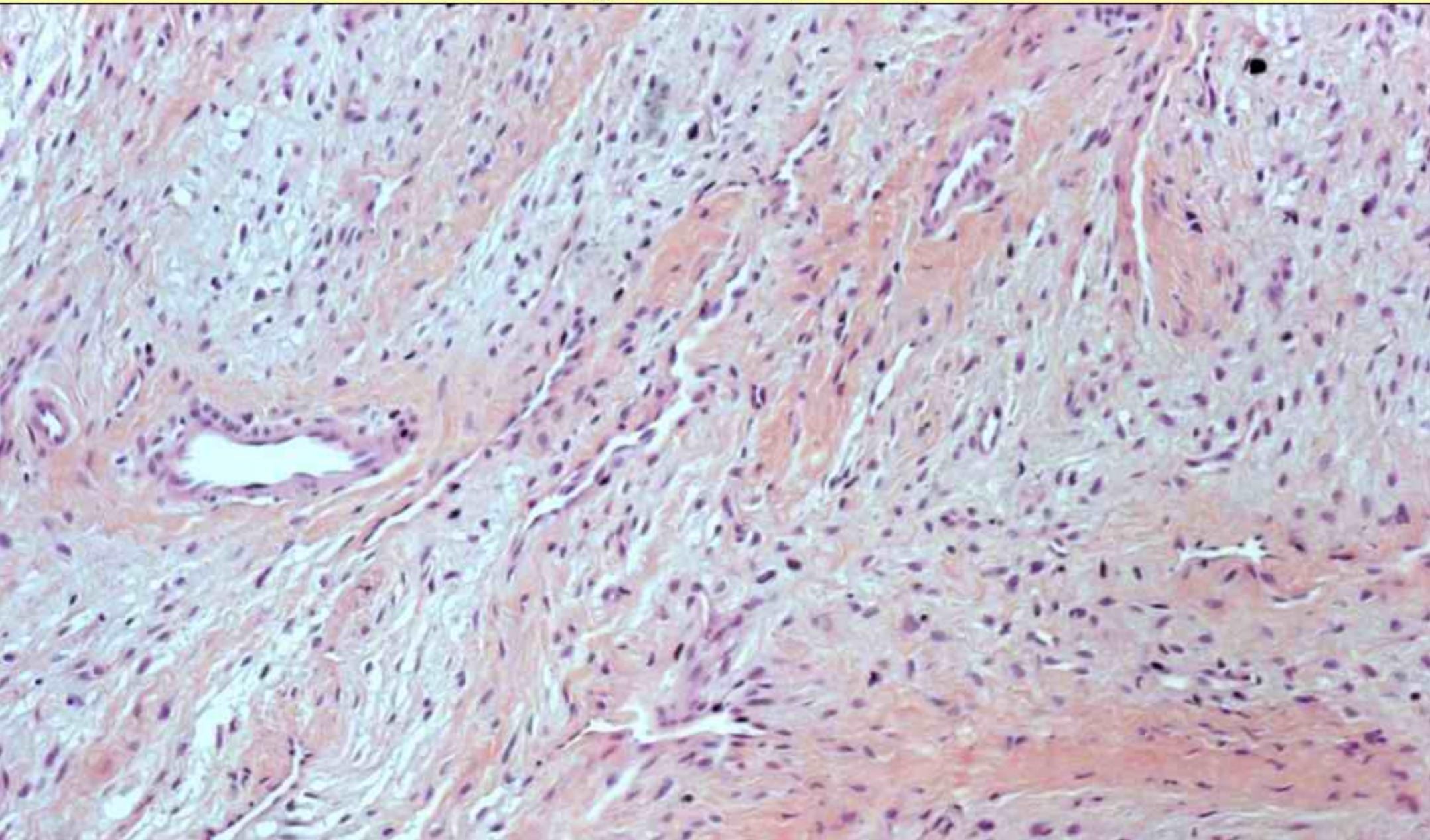
- « Myxo-fibro » mesenchymal lesions are not all the same !
- Myxofibrosarcoma and low-grade fibromyxoid sarcoma are two separate clinicopathologic entities that deserve recognition
- There is some degree of overlap between myxofibrosarcoma and inflammatory myxohyaline tumor

QUIZ: RESULTS

QUIZ 1: 1.5 cm nodule developing in close vicinity to the nail of the 4th digit in a 40 year-old male



QUIZ 1: 1.5 cm nodule developing in close vicinity to the nail of the 4th digit in a 40 year-old male



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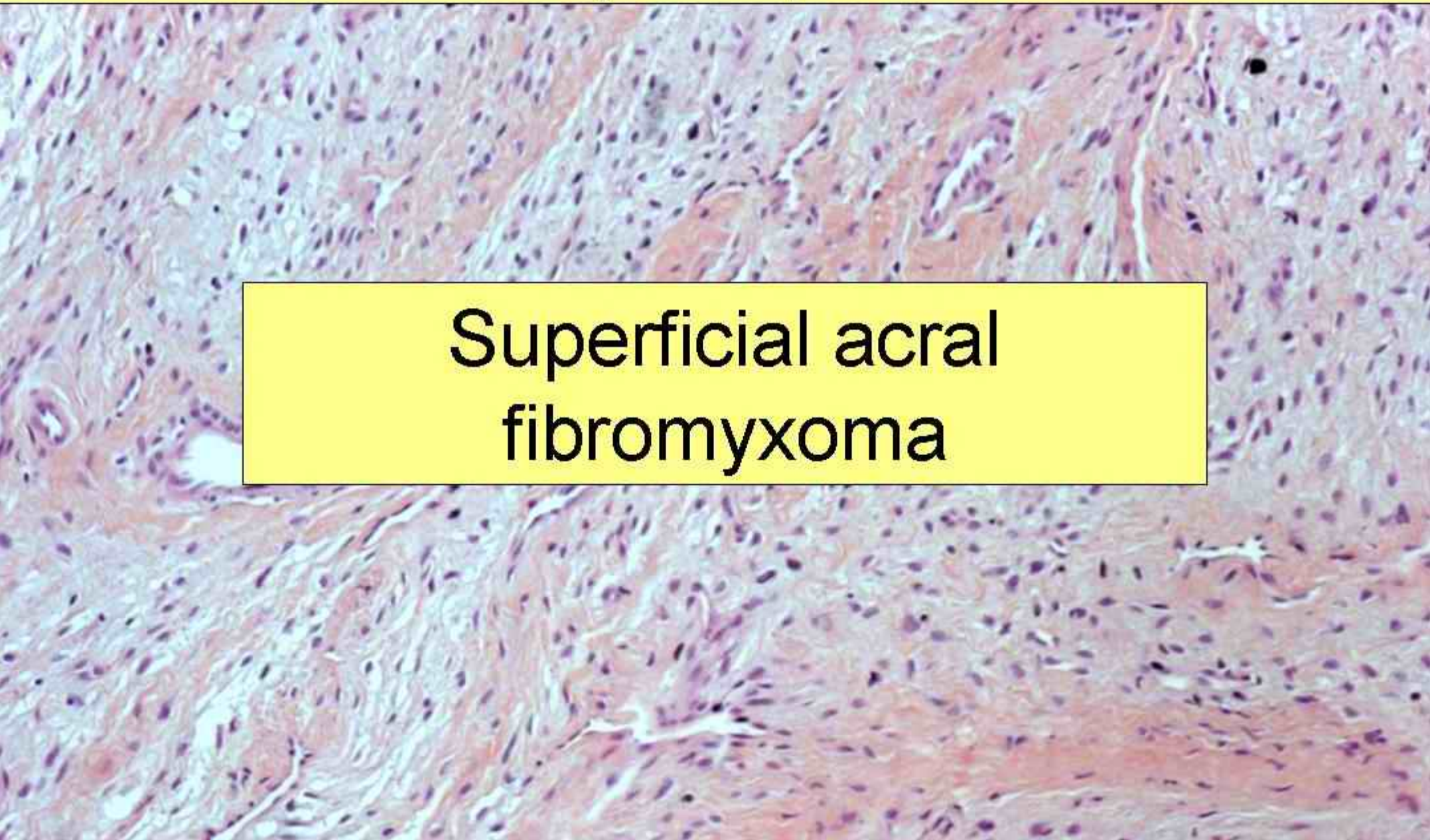
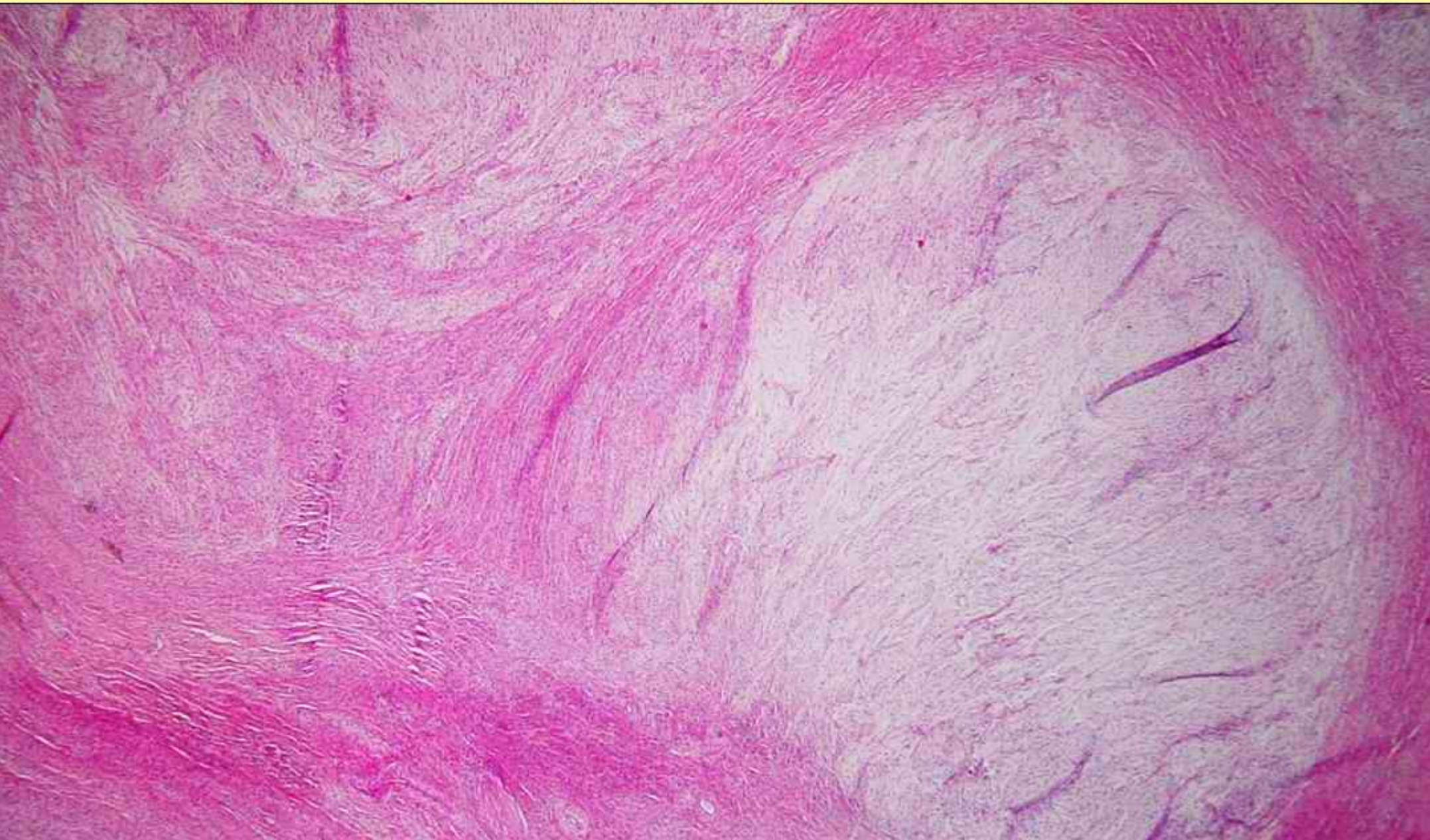
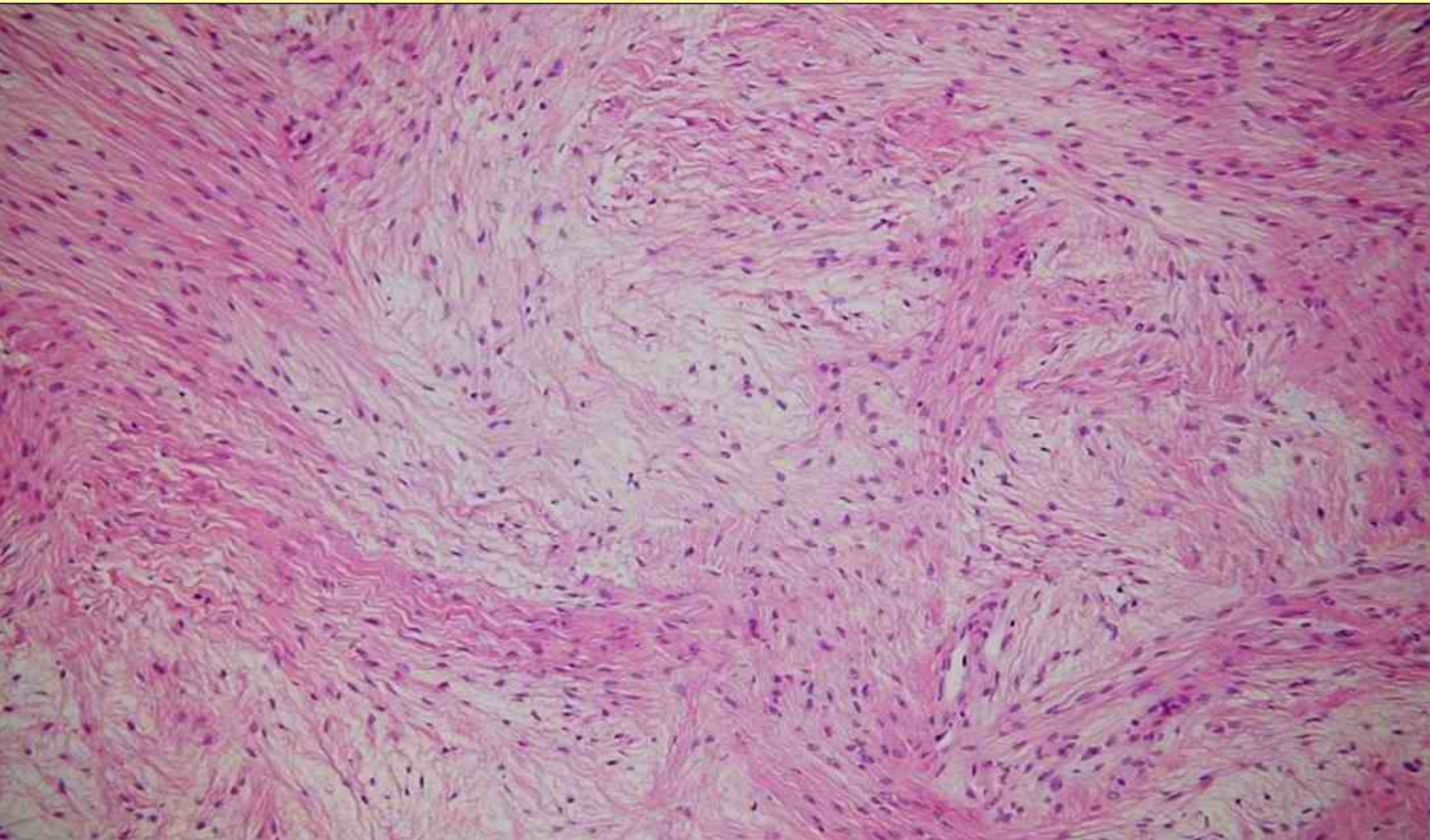


QUIZ 2: 7 cm, well-demarcated, slowly-growing, intramuscular mass in the thigh of a 32 year-old male



QUIZ 2: 7 cm, well-demarcated, slowly-growing, intramuscular mass sitting in the thigh of a 32 year-old male



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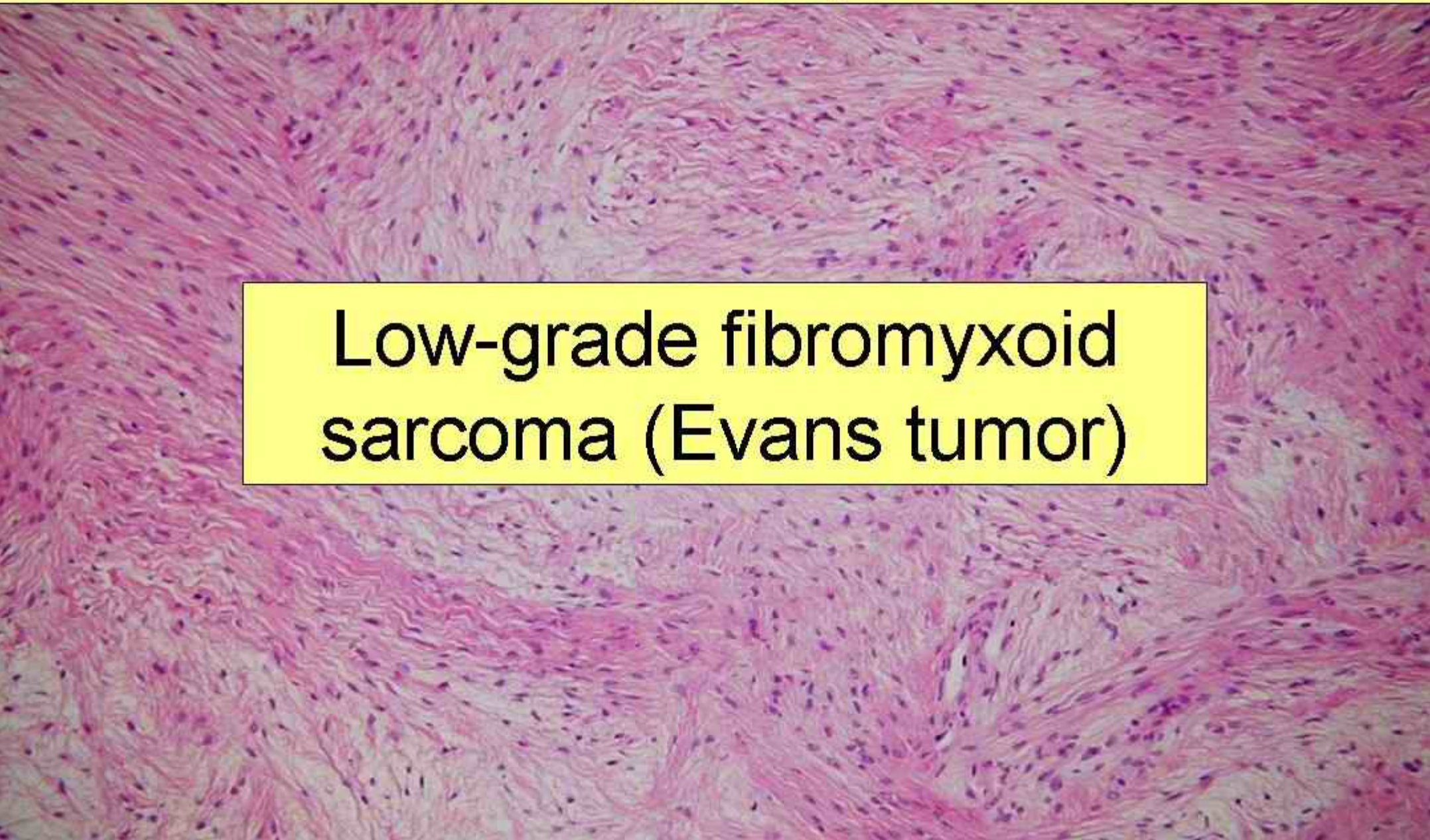
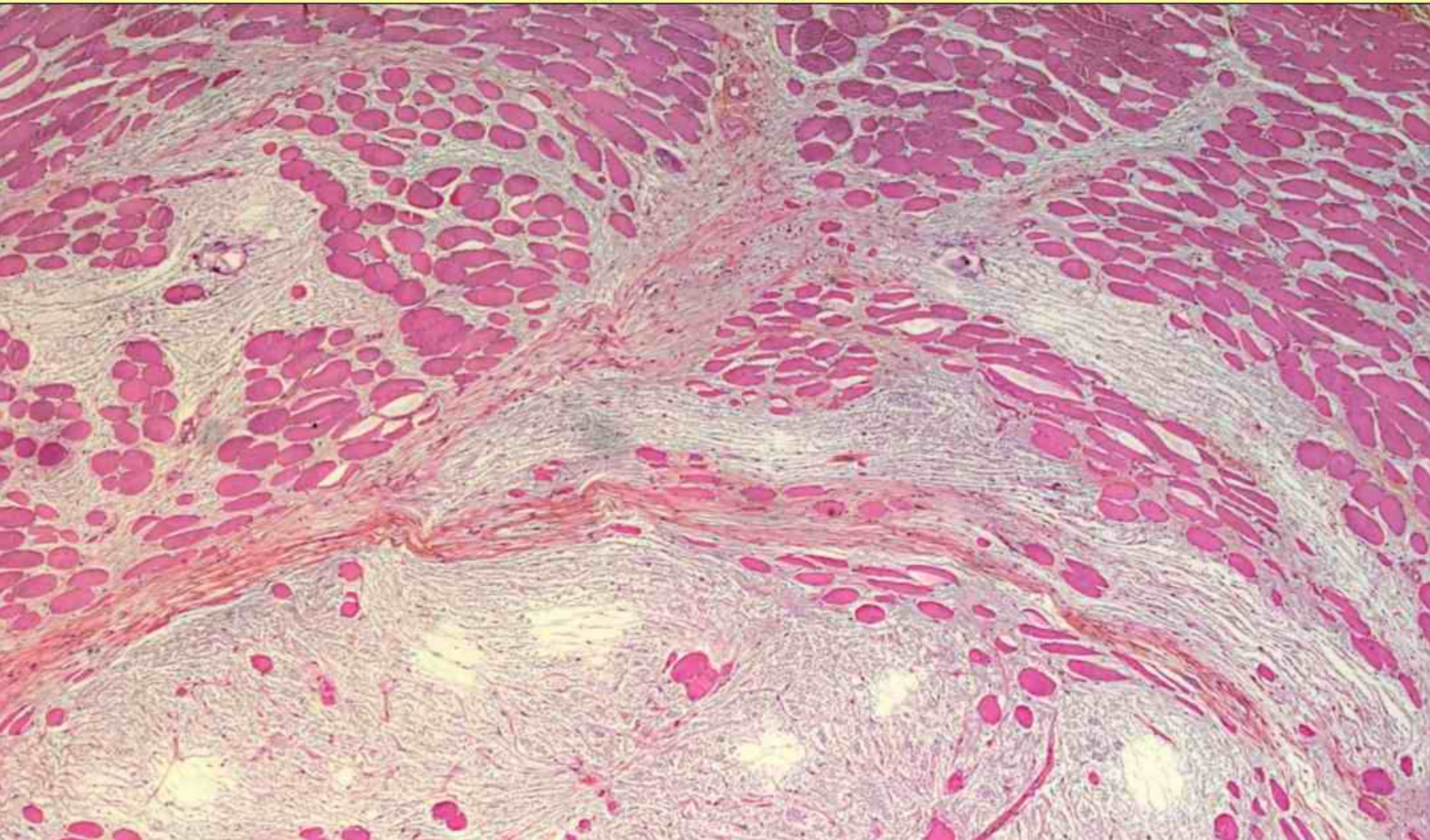


Low-grade fibromyxoid sarcoma (Evans tumor)

QUIZ 3: 6 cm, slowly-growing, intramuscular mass developing in the thigh of a 50 year-old female



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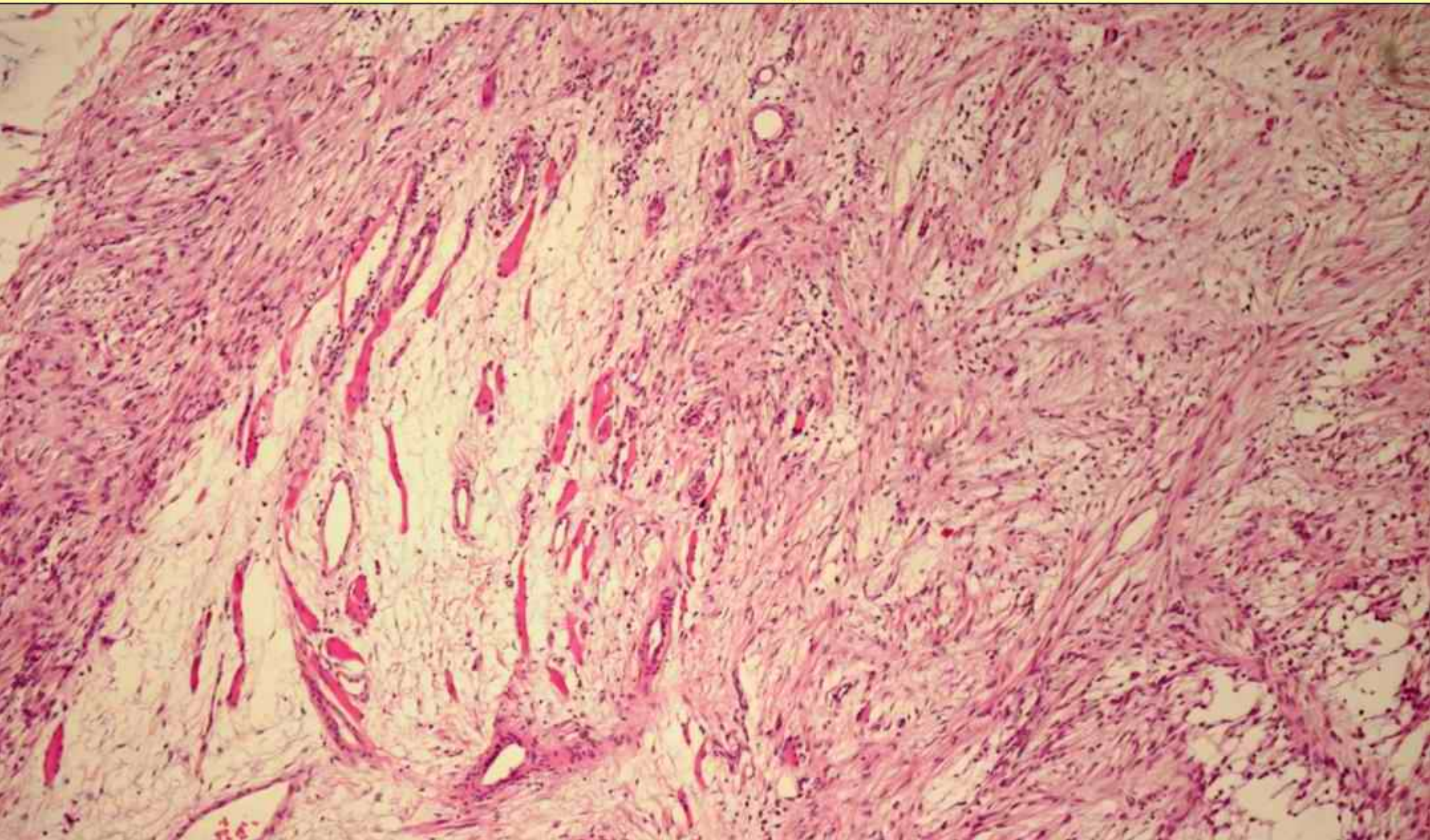

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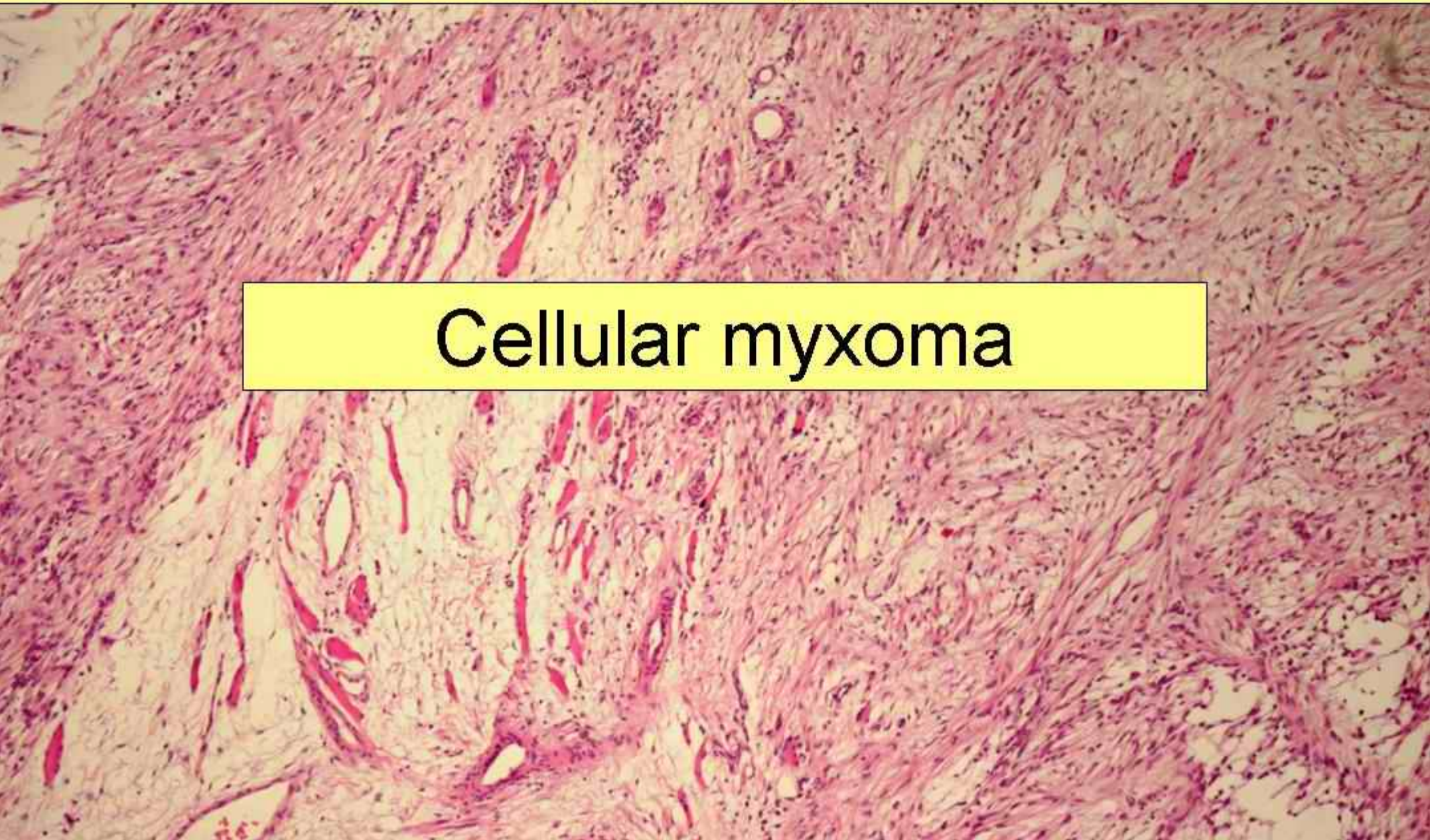
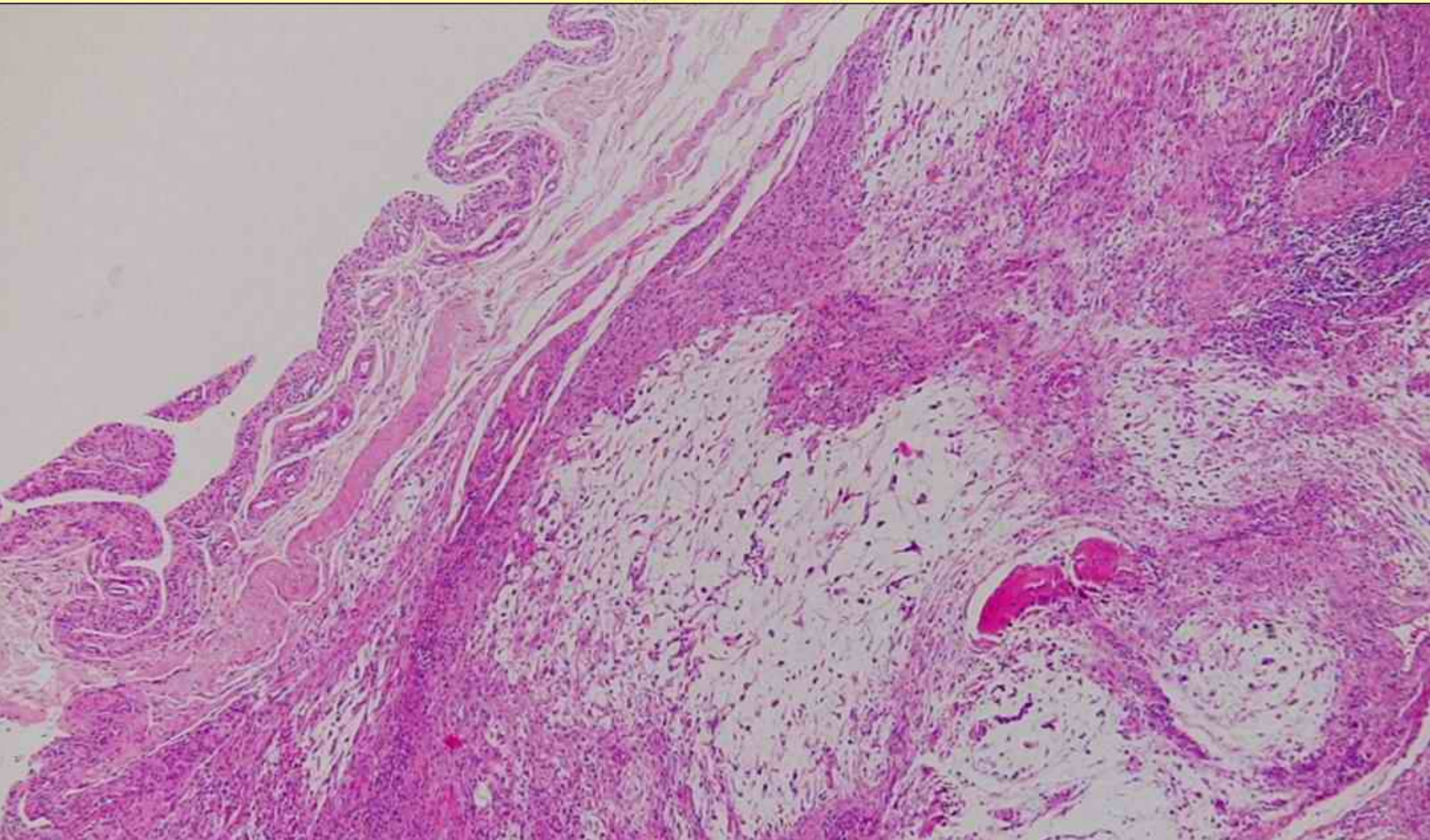


QUIZ 4: 4 cm, gelatinous, ill-defined mass of the 2nd left digit in a 45 year-old male



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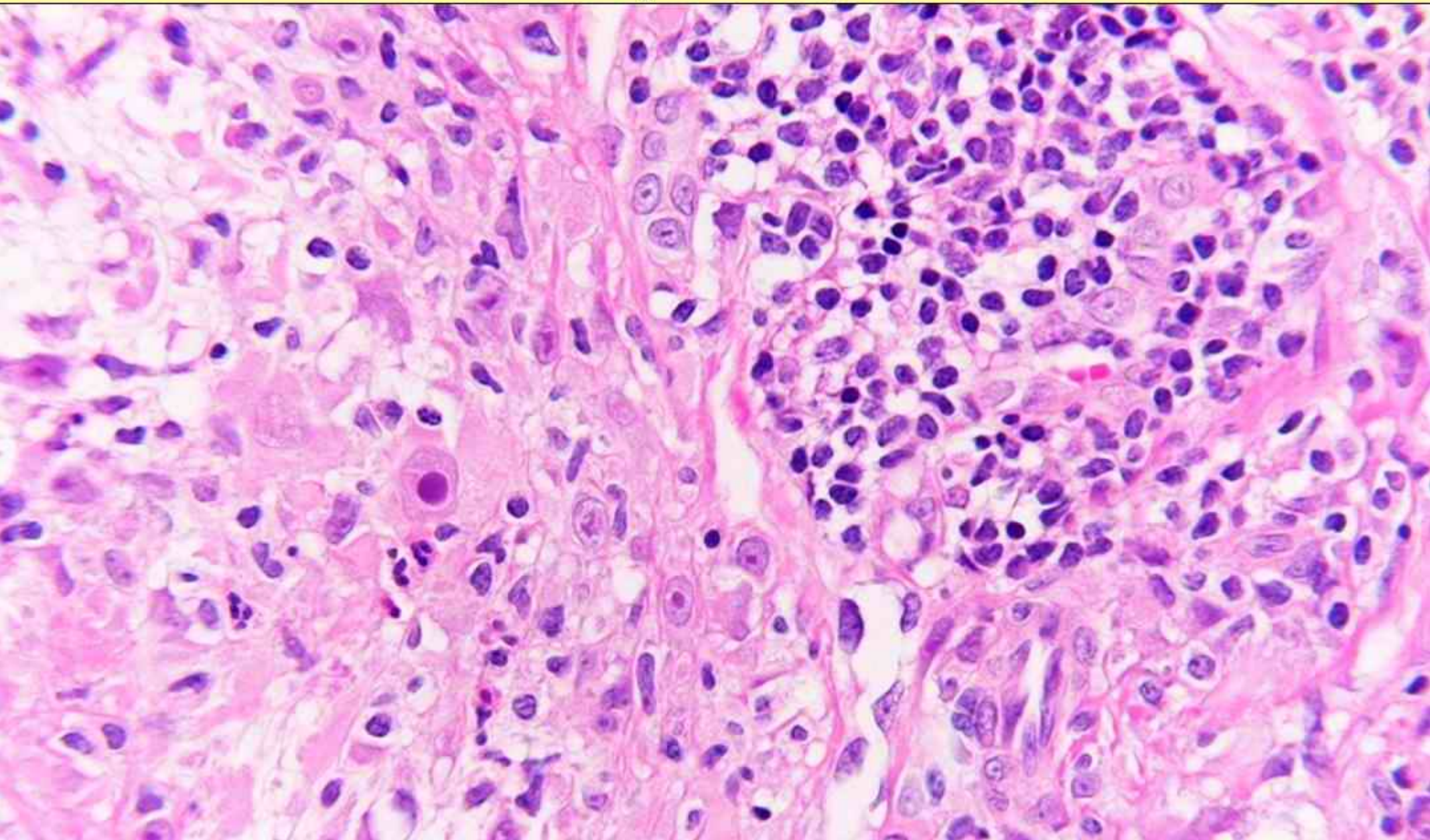

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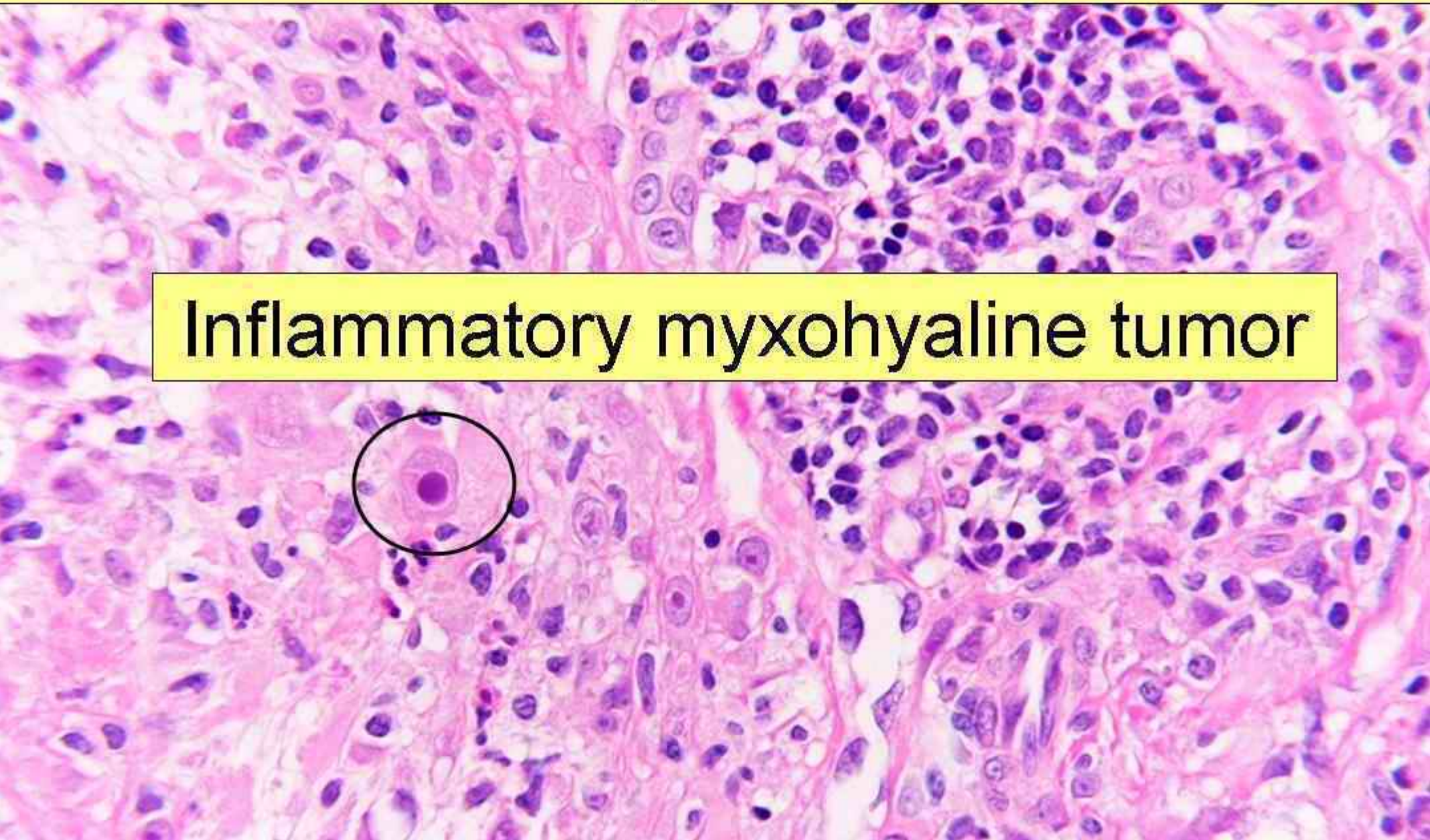

Thank you for your attention….

…..Louis Guillou