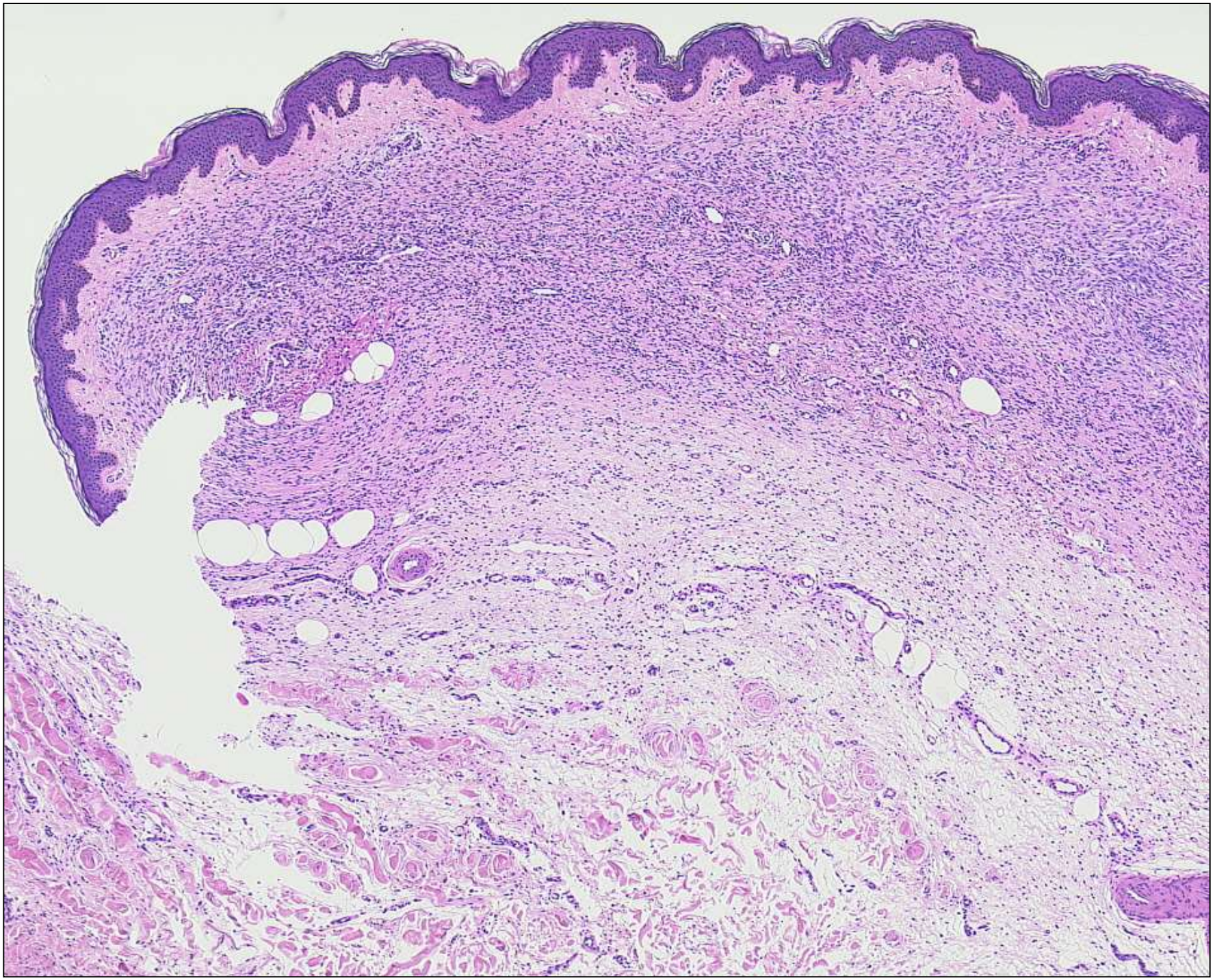
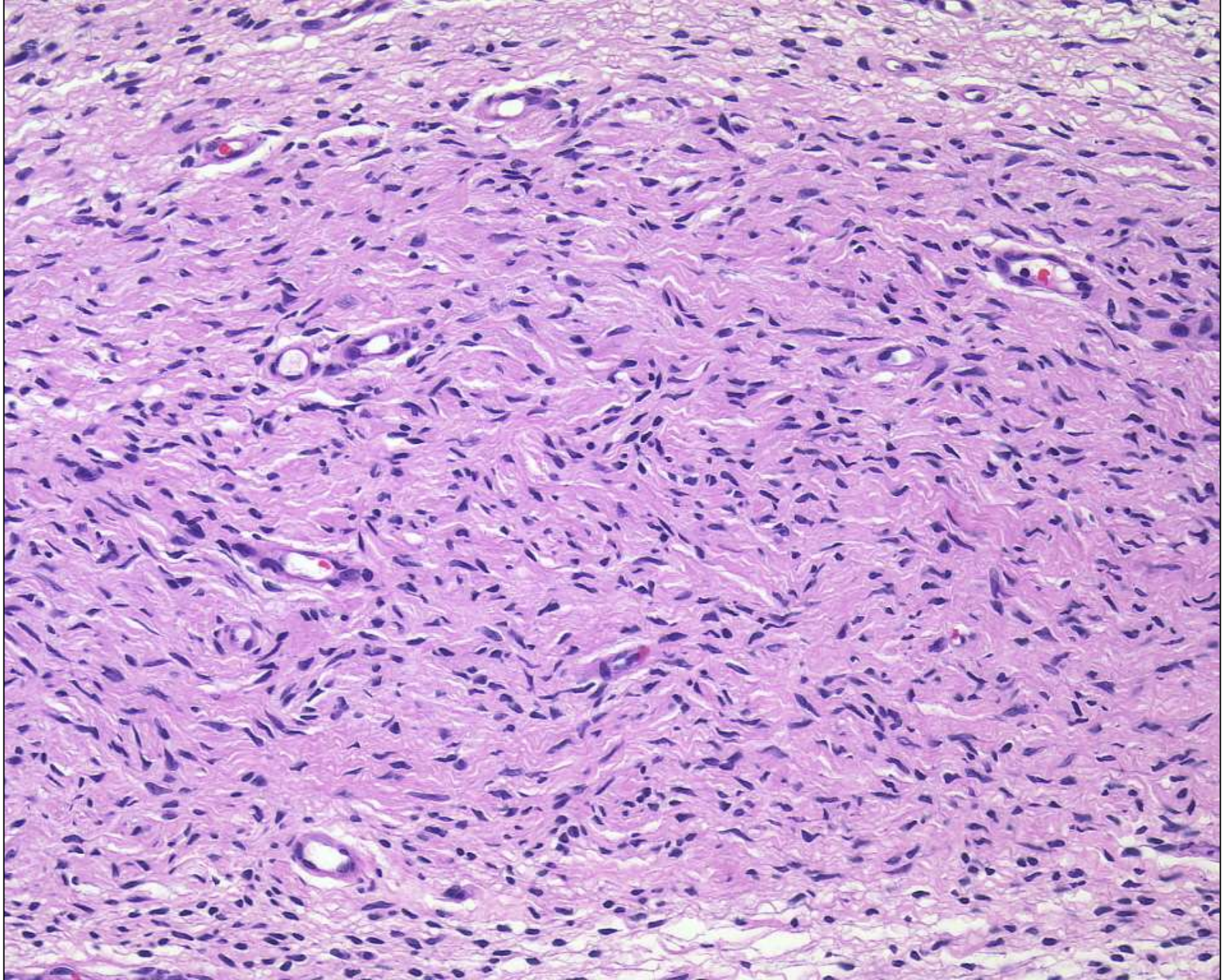
Mesenchymal Tumours of the Skin
Part 2

Thomas Mentzel, Friedrichshafen, Germany

Case 6: Clinical Findings

- F, 30 years
- left lateral thigh
- dermatofibroma was suspected





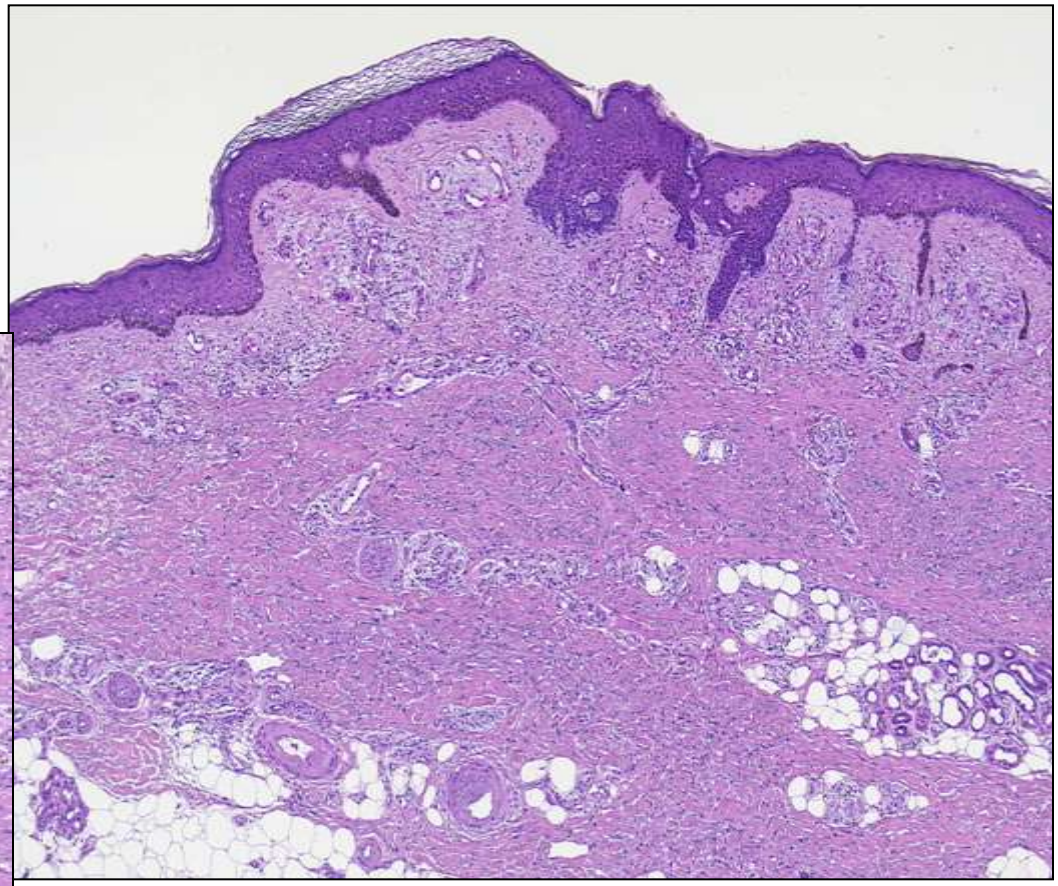
Differential Diagnosis Case 6

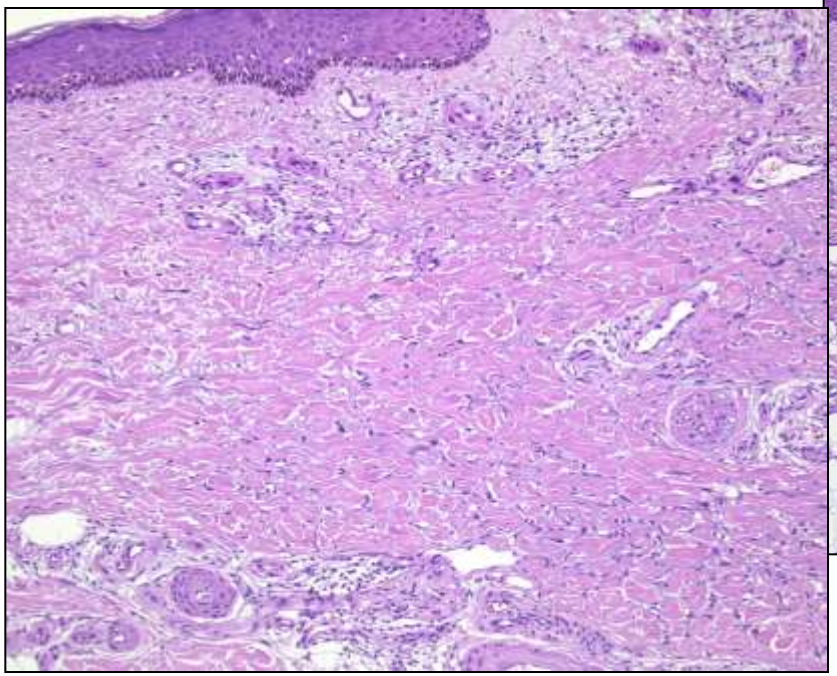
plaque-like, spindle cell, dermal neoplasm (no atypia, no mitoses, no necrosis)

- flat dermatofibroma
- neurofibroma
- dermatomyofibroma
- plaque-like CD34-positive dermal fibroma
- plaque-stage DFSP

flat, atrophic Dermatofibroma

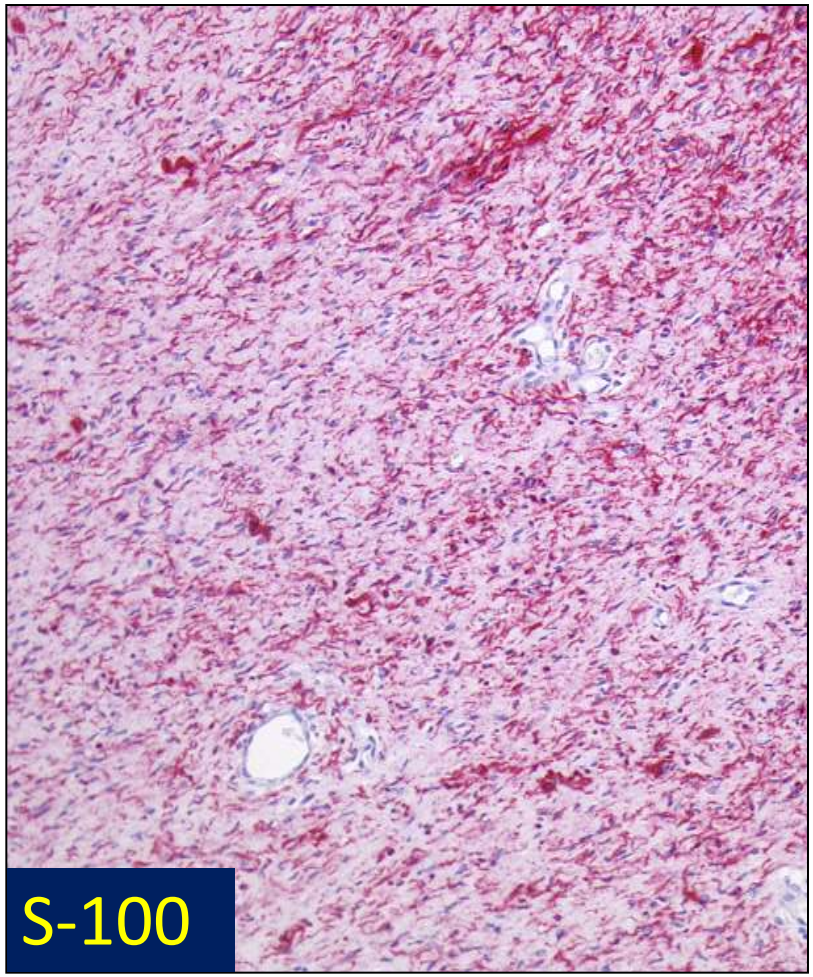
- hyperplasia of the epidermis
- plump spindled tumour cells
- hyalinised collagenous fibres (entrapment)
- CD34 -

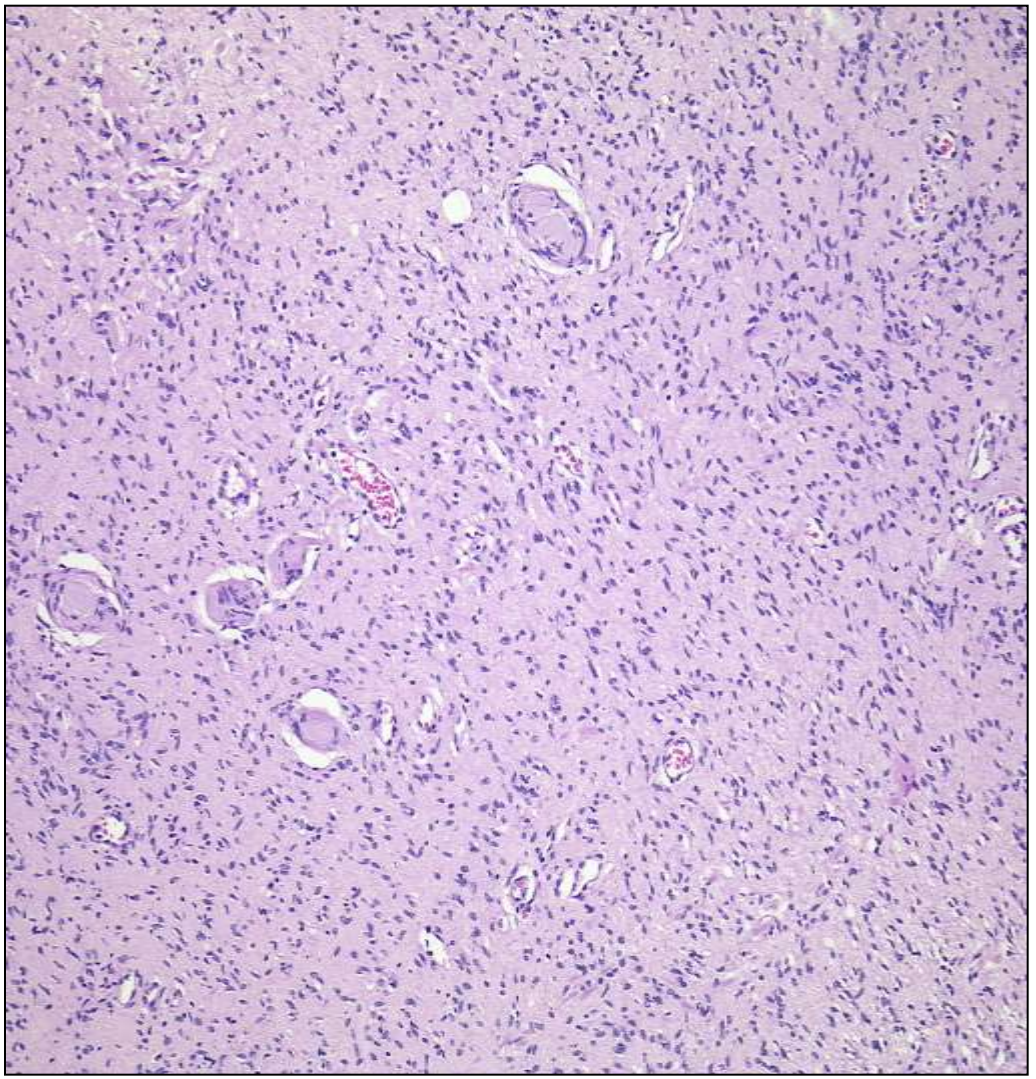




diffuse Neurofibroma

- often myxoid stroma
- scattered mast cells
- S-100 +





Dermatomyofibroma

Dermatomyofibroma: Clinicopathologic and Immunohistochemical Analysis of 56 Cases and Reappraisal of a Rare and Distinct Cutaneous Neoplasm

Thomas Mentzel, MD and Heinz Kutzner, MD

Abstract: Dermatomyofibroma represents a rare and distinct benign cutaneous mesenchymal neoplasm of fibroblastic/myofibroblastic differentiation. A series of 56 cases of dermatomyofibroma has been analyzed to further characterize the clinicopathologic spectrum of this entity. Forty patients were female and 8 were male (gender was unknown in 8 cases). Patients' age ranged from 3 to 51 years (mean 30.8 years, median 30 years). Interestingly, 6 patients were younger than 16 years, and in this age group, 3 male and 3 female patients, respectively, were noted. The shoulder (13 cases) was the anatomic site most commonly affected, followed by the upper arm (7 cases), the neck (6 cases), the thigh (6 cases), the chest wall (4 cases), the back (3 cases), the axillary fold (2 cases), the abdominal wall (2 cases), and 1 case each was seen on the forearm, the buttock, and the popliteal fossa (exact anatomic location was unknown in 10 cases). One patient presented with 2 lesions arising simultaneously on both shoulders. Histologically, an ill-defined, plaque-like dermal neoplasm of varying cellularity was seen in all cases, composed of bland spindle-shaped tumor cells often oriented parallel to the overlying epidermis. An infiltration of superficial part of the subcutis was seen in 23 cases, and in 6 cases, deeper parts of the subcutis were involved by often perpendicular growing bands of neoplastic cells. Immunohistochemically, tumor cells in 11 of 48 cases tested stained positively for alpha-smooth muscle actin, and a focal expression of this marker was noted in 20 cases. In addition, a focal expression of CD34 was seen in 10 of 45 cases tested. Follow-up information was available in 38 cases (range from 3 to 156 months, median 34 months), and despite marginal or incomplete excision in 17 cases, none of the cases recurred. Dermatomyofibroma represents a benign fibroblastic/myofibroblastic dermal neoplasm.

Key Words: dermatomyofibroma, mesenchymal neoplasms, plaque-like dermal fibromatosis, skin

(*Am J Dermatopathol* 2009;31:44–49)

INTRODUCTION

The spectrum of fibroblastic/myofibroblastic cutaneous tumors comprises a heterogeneous group of benign, atypical, and malignant neoplasms mainly composed of spindle-shaped tumor cells. Non-neoplastic myofibroblasts resemble fibroblasts; feature immunohistochemically heterogeneous phenotypes with regard to their content of intermediate filaments, muscle actin, and myosin; and are defined ultrastructurally by specialized organelles such as stress fibers and cell to stroma attachment sites (so-called fibronexus). Myofibroblasts are therefore regarded as a functional stage of fibroblasts seen in many physiological and pathological conditions.[1] In addition, with the advent of immunohistochemical markers, an increasing number of benign and more rarely malignant mesenchymal neoplasms showing a myofibroblastic line of differentiation have been reported in the past years. Dermatomyofibroma, first described as a plaque-like dermal fibromatosis,[2] represents a rare but distinct benign dermal proliferation of fibroblasts and myofibroblasts of the skin.[3] We report a series of 56 cases of dermatomyofibroma, discuss histologic and immunohistochemical features, and widen the clinicopathologic spectrum of this entity also in regard to other spindle cell lesions of the dermis and subcutis.

MATERIALS AND METHODS

The tissue in all cases was fixed in 4% buffered formalin, routinely processed, and embedded in paraffin; 4- μm-thick sections were stained with hematoxylin and eosin, and elastic stains were performed in 43 cases. In addition, representative sections in 48 cases were stained immunohistochemically by the labeled streptavidin–biotin technique using commercially available antibodies; antigen retrieval was used for all antibodies. Stainings for alpha-smooth muscle actin (clone: 1A4, dilution: 1:300, source: DAKO, Glostrup, Denmark), muscle actin (HHF35, 1:200; DAKO), h-caldesmon (h-CD, 1:200; DAKO), CD34 (Qbend10, 1:50; DAKO), desmin (D33, 1:200; DAKO), epithelial membrane antigen (Mc5, 1:400; Biogenex, San Ramon, CA), factor XIIIa (AC-1A1, 1:1000; LABVISION, Suffolk, UK), and S-100 protein (polyclonal, 1:4000; DAKO) were available in a varying number of cases. Appropriate positive and negative controls were used in all cases. Clinical information and follow-up were retrieved from the laboratory request forms and contributing clinicians. Cases 51, 52, and 53 have been reported in detail elsewhere.[4]

RESULTS

The clinical findings are summarized in Table 1. Briefly, the analyzed neoplasms arose in 40 female and 8 male patients (gender was unknown in 8 cases), and patients' age ranged

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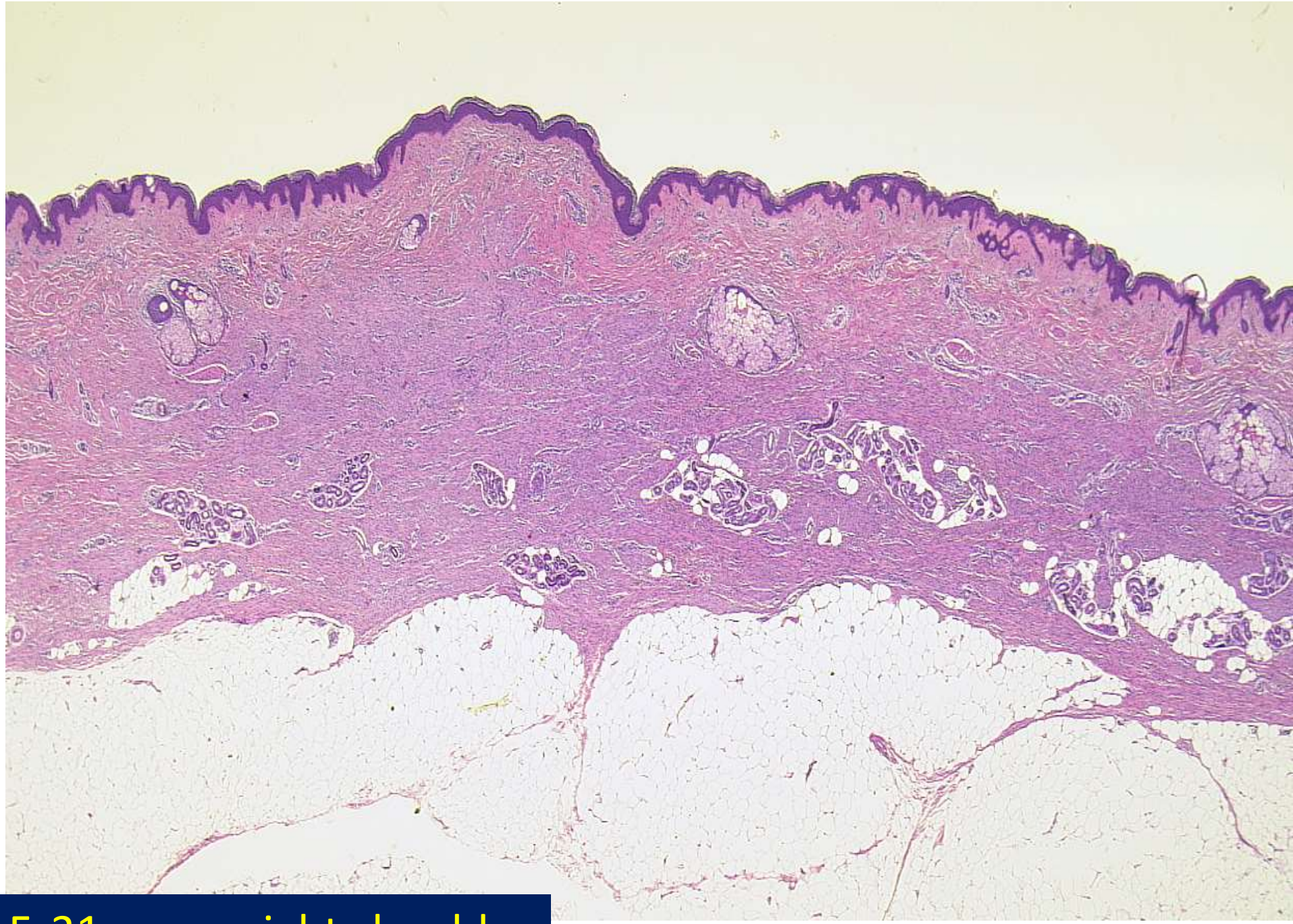
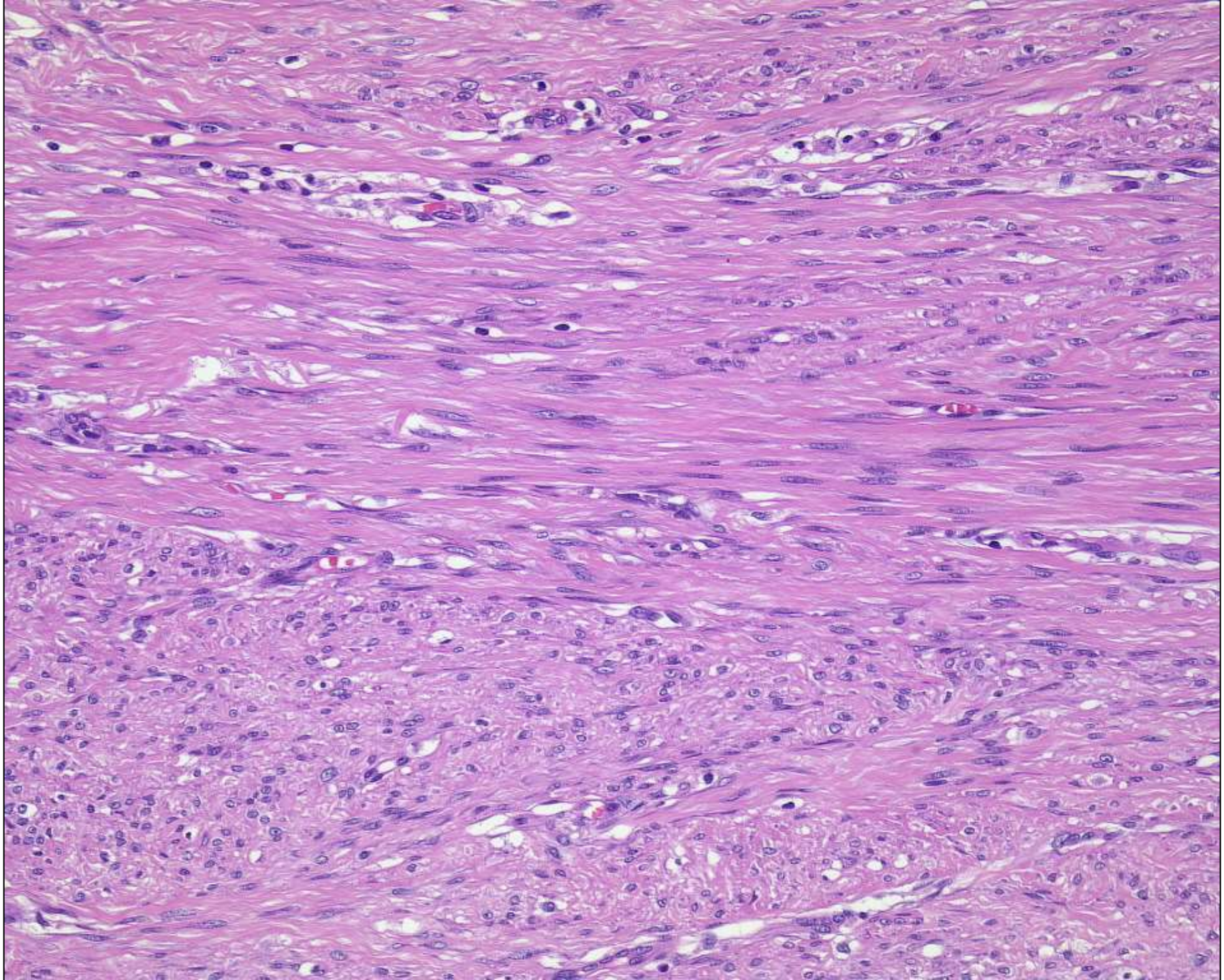
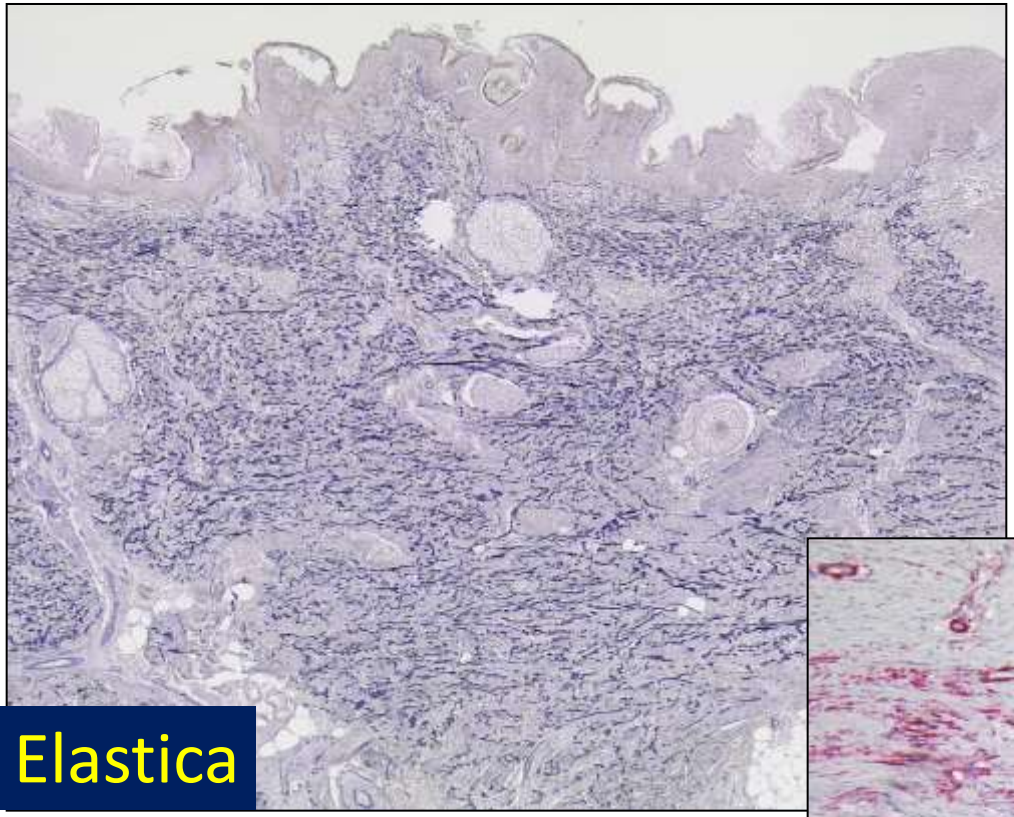
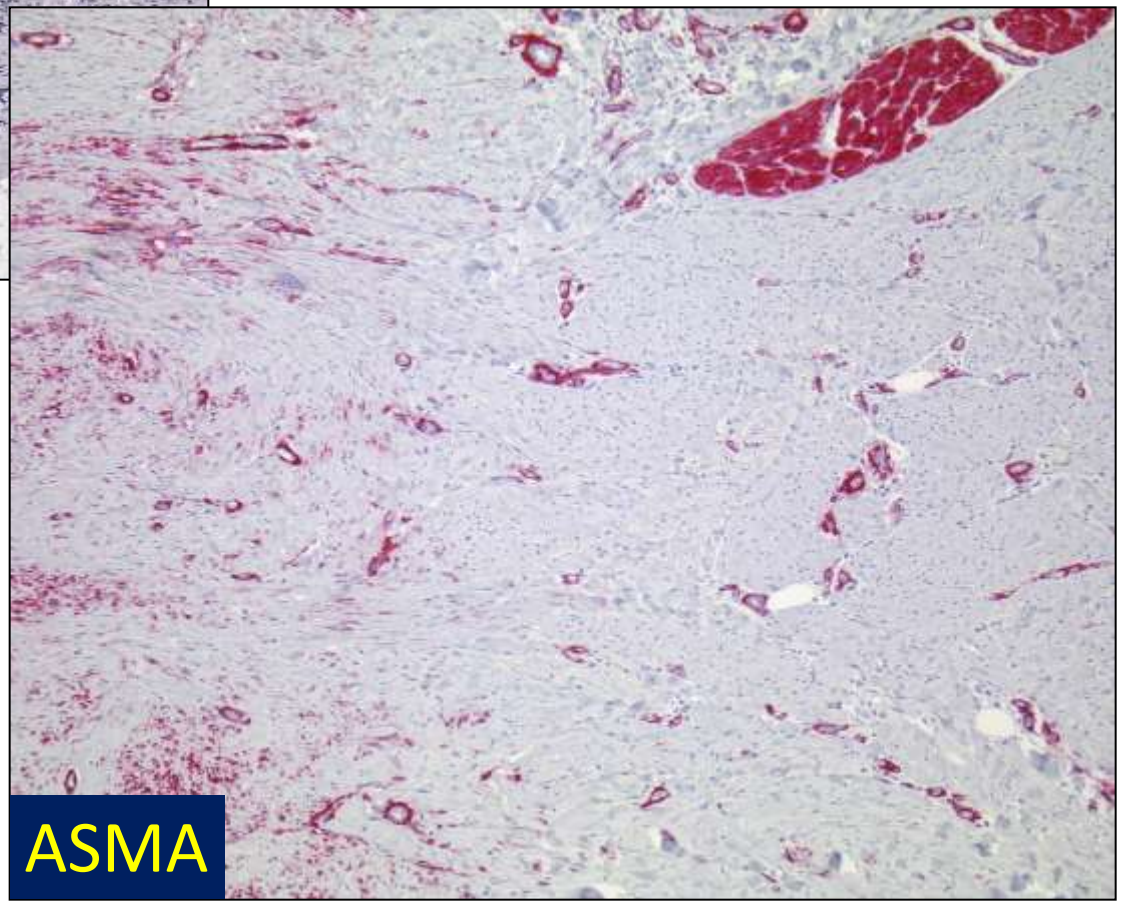


F, 31 years, right shoulder




Elastica


ASMA

Plaque-like CD34 positive dermal Fibroma („Medallion-like Dermal Dendrocyte Hamartoma“)

Plaque-like CD34-positive Dermal Fibroma (''Medallion-like Dermal Dendrocyte Hamartoma'')

Clinicopathologic, Immunohistochemical, and Molecular Analysis of 5 Cases Emphasizing its Distinction From Superficial, Plaque-like Dermatofibrosarcoma Protuberans

Heinz Kutzner, MD, Thomas Mentzel, MD,* Gabriele Palmedo, PhD,* Markus Hantschke, MD, Arno Rütten, MD,* Bruno E. Paredes, MD,* Leo Schärer, MD,* Carlos Serra Guillen, MD,† and Luis Requena, MD‡*

Abstract: Medallion-like dermal dendrocyte hamartoma (DH) and superficial (plaque-like) dermatofibrosarcoma protuberans (DFSP) are CD34-positive dermal neoplasms with overlapping clinicopathologic features. We analyzed the clinical, histomorphologic, and molecular criteria of 5 DH and 7 DFSP to delineate diagnostically relevant differences between incipient dermal DFSP and its benign look-alike, DH. We expand the clinical and histologic spectrum of DH. As medallion-like dermal DH is neither of dermal dendrocyte lineage nor a genuine hamartoma, we propose instead the descriptive term of plaque-like CD34-positive dermal fibroma (PDF). Both PDF/DH and DFSP presented as slightly pigmented and indurated plaques on neck, trunk, and extremities. Histologically, DFSP was characterized either by horizontally oriented spindle cell fascicles or by diffusely arranged fibroblasts within a slightly myxoid stroma in the upper two-thirds of the dermis, whereas PDF/DH presented with a cellular band-like fibroblastic proliferation mostly in the papillary and adjacent upper reticular dermis. Only one congenital PDF/DH in a 9-year-old boy extended into the septa of the subcutaneous fat. Formalin-fixed paraffin-embedded archival tissue was used for detection of the *COL1A1-PDGFB* gene rearrangement by multiplex reverse transcription-polymerase chain reaction (RT-PCR) and by dual color fusion fluorescence in-situ hybridization (FISH). Archival blocs older than 4 years did not yield amplifiable RNA because of RNA degradation, whereas FISH analysis was feasible in all investigated cases. FISH analysis revealed *COL1A1-PDGFB* gene rearrangement in all DFSP cases (n = 7), whereas RT-PCR could detect the *COL1A1-PDGFB* fusion transcript only in 1 DFSP. Two cases were negative. In 4 archival cases with st between 4.5 and 12 years, RNA had been degraded m these cases unsuitable for RT-PCR. In PDF/DH, both RT- and FISH analysis did not reveal any evidence of *COL PDGFB* gene rearrangement. We show that PDF/DH superficial (plaque-like) DFSP, subtle clinicopathologic c ences notwithstanding, are morphologic look-alikes that c kept apart by molecular studies of the *COL1A1-PDGFB* fusion. For the detection of the *COL1A1-PDGFB* gene rearr ment in diagnostically difficult cases, RT-PCR and FISH lysis are reliable and helpful diagnostic tools. In ar formalin-fixed paraffin-embedded tissue, however, FISH ysis is more robust and exhibits a higher clinical sensitivity RT-PCR.

Key Words: medallion-like dermal dendrocyte hamart plaque-like CD34+ dermal fibroma, superficial (plaque dermatofibrosarcoma protuberans, CD34, *COL1A1-PL* fusion gene

(*Am J Surg Pathol* 2010;34:190–201)

The spectrum of CD34-positive (CD34+) tumo the skin comprises a heterogeneous family of senchymal neoplasms with multiple lines of differe tion, ranging from the fibroblastic to the hematop lineage.[4,5] Among these, most diagnostic difficulties encountered within the group of dermal fibrocytic sp cell proliferations, some of which are poorly de and present with a wide clinical and histomorpho spectrum.[8,11,13,25,31,37]

Medallion-like dermal dendrocyte hamart (DH) is a recently described presumably hamartom neoplasm[34] showing morphologic overlap with conge atrophic dermatofibrosarcoma protuberans (DFSP).

We report a series of 5 cases of DH and 7 cas superficial (plaque-like) DFSP, expand the clinicop logic spectrum of these neoplasms, and discuss mole methods for differential diagnosis. We will show multiplex reverse transcription-polymerase chain rea

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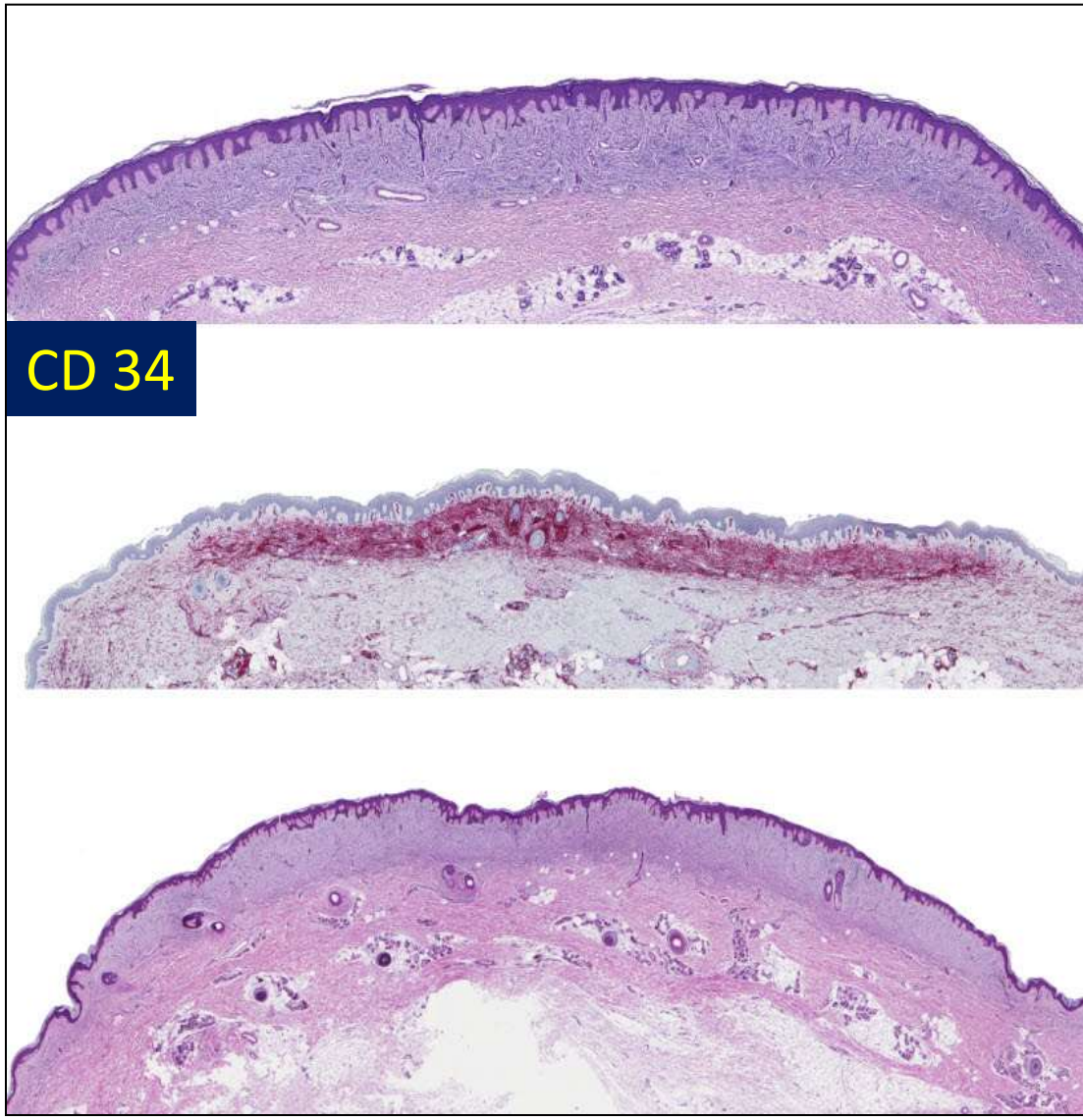
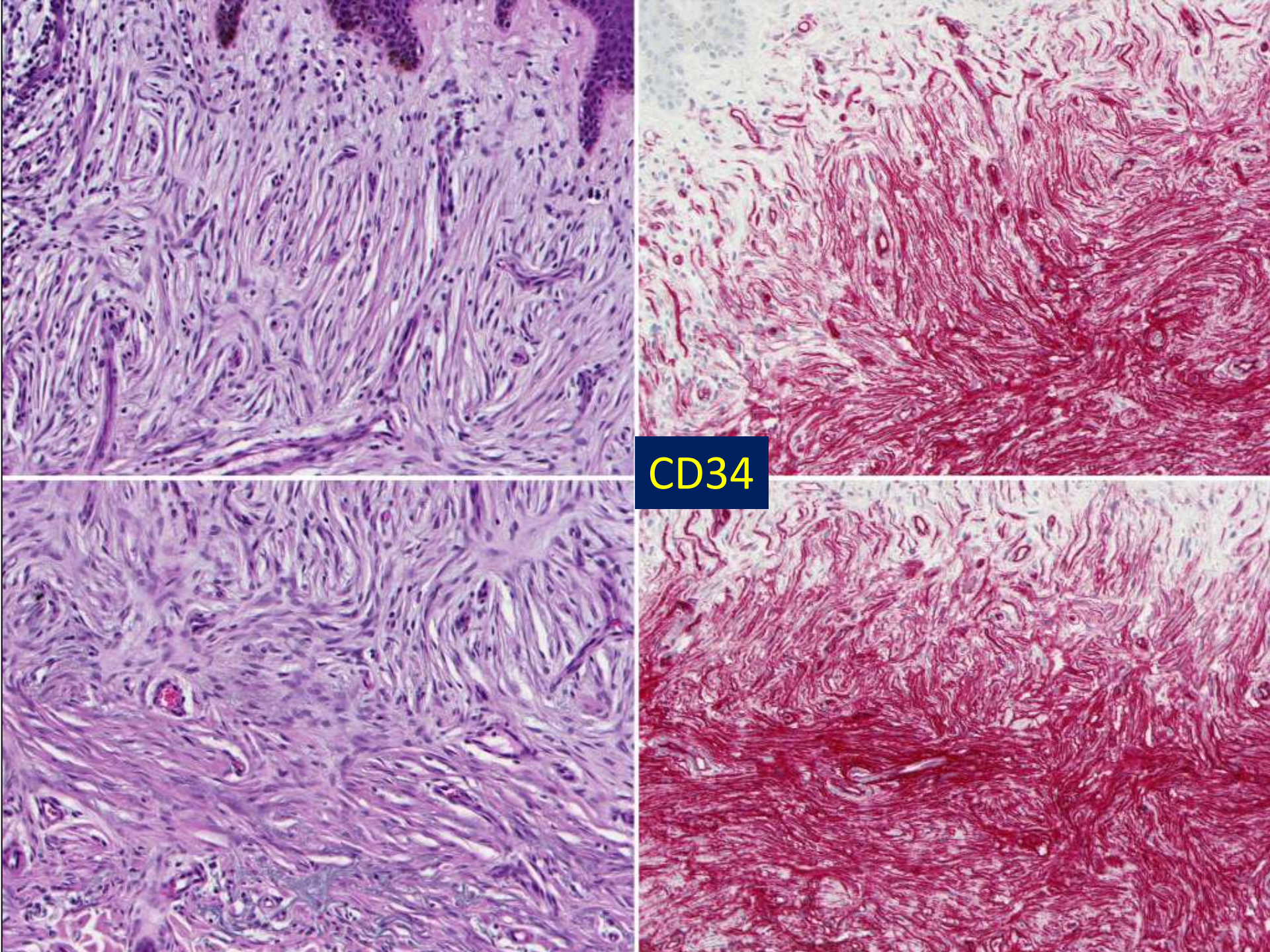
Plaque-like CD34-positive dermal Fibroma

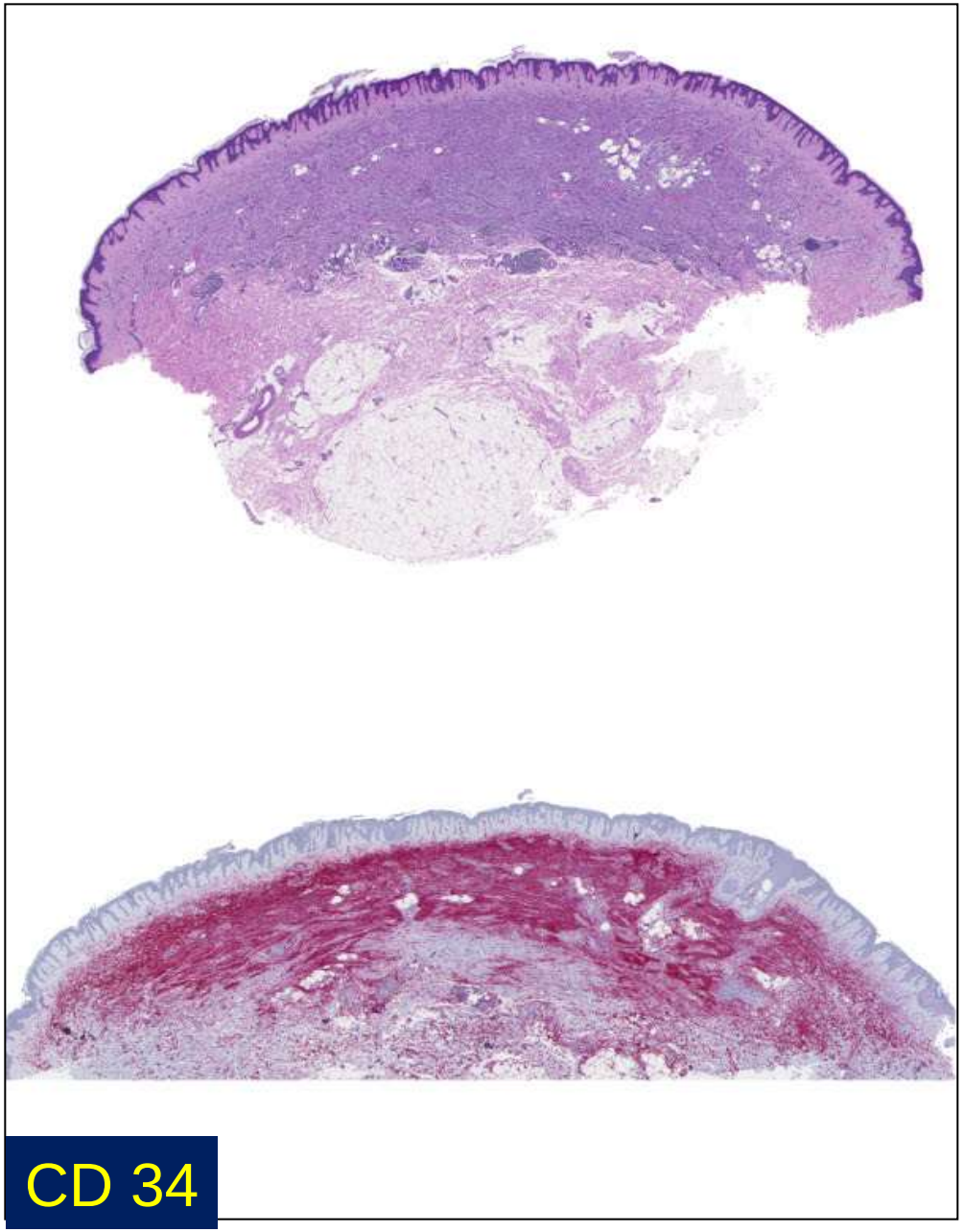
- children, adults
- bandlike fibroblastic proliferation
- upper half of the dermis
- no involvement of stratum papillare
- adnexal structures are spared
- many vessels
- biphasic growth

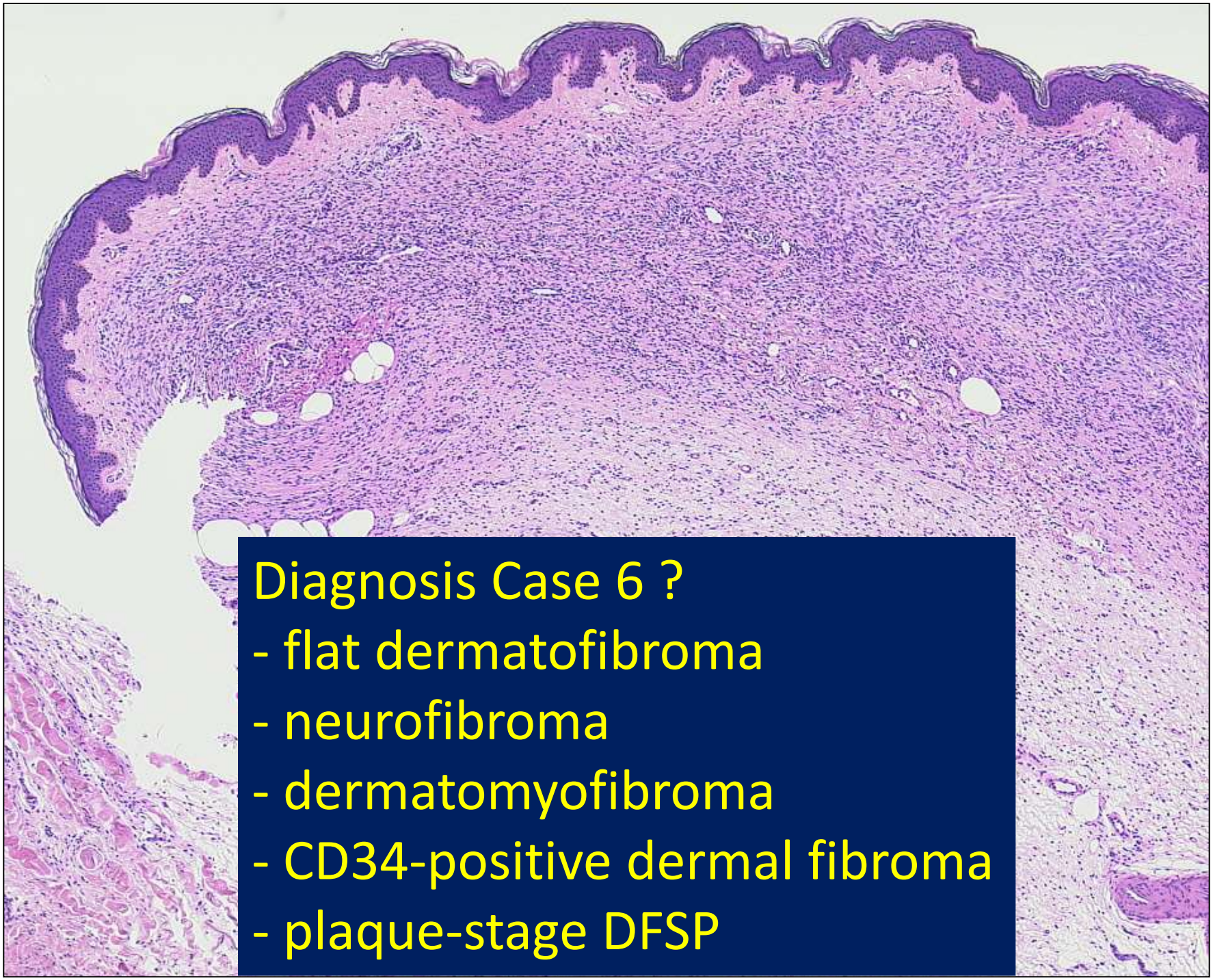


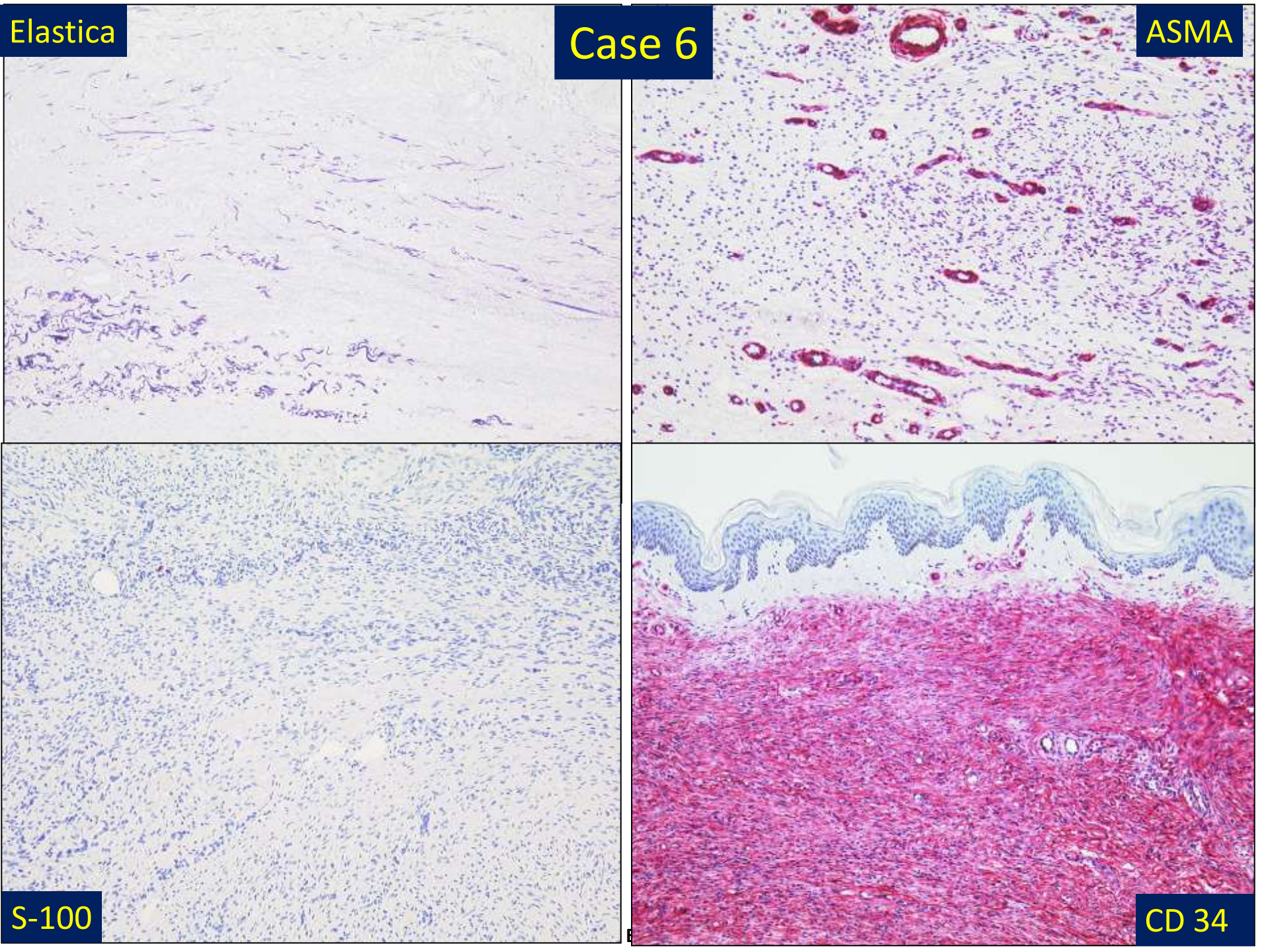

CD34

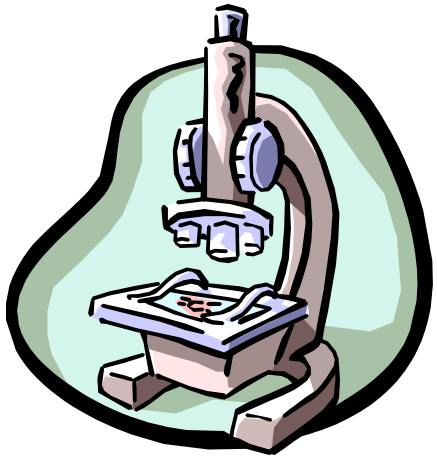
plaque-like DFSP

- horizontal growth
- also in deeper parts of the dermis
- myxoid stroma
- adnexal structures are not spared
- *COL1A1 / PDGFB* fusion




Diagnosis Case 6 ?
- flat dermatofibroma
- neurofibroma
- dermatomyofibroma
- CD34-positive dermal fibroma
- plaque-stage DFSP

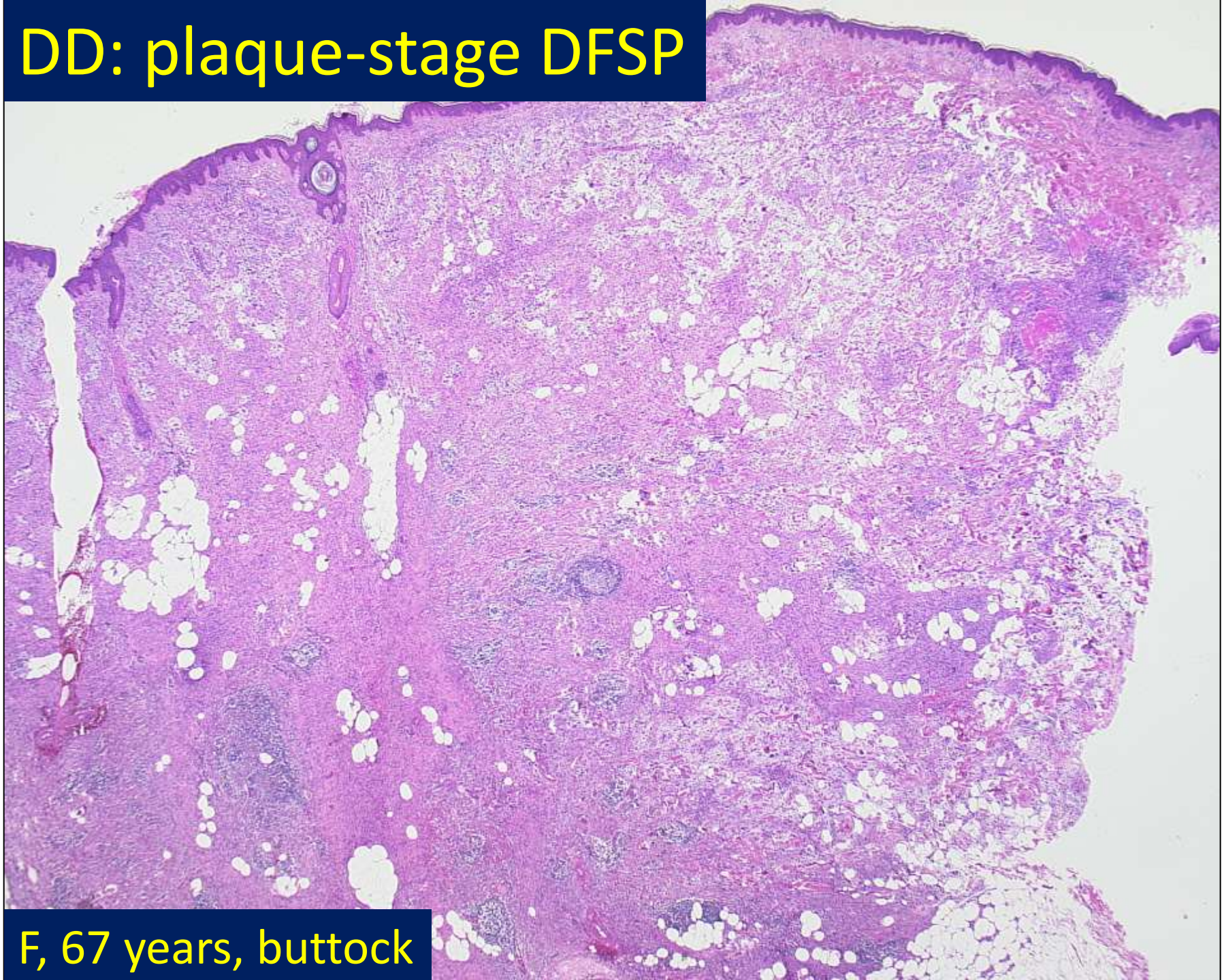

Elastica
Case 6
ASMA
S-100
CD 34



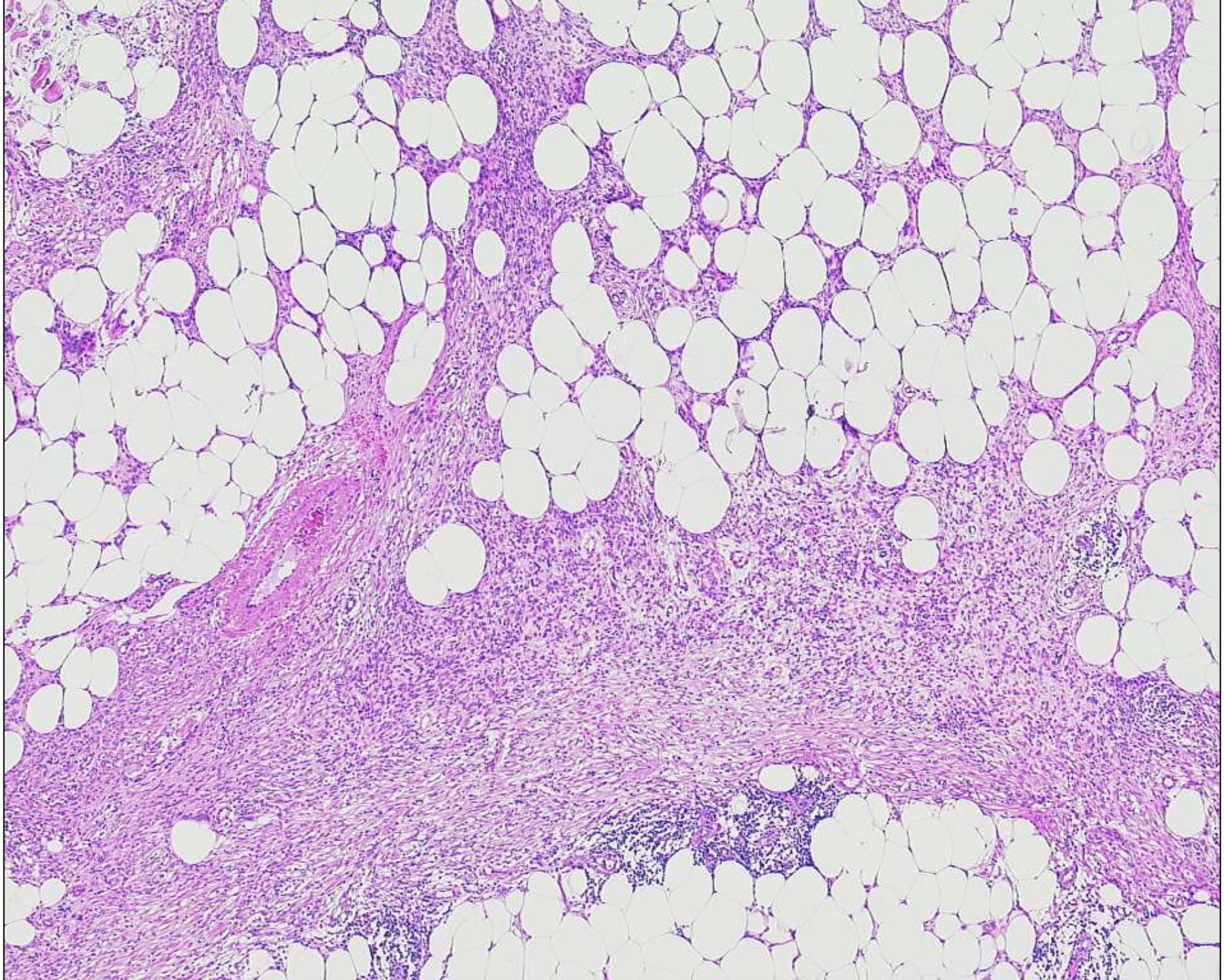
Diagnosis Case 6

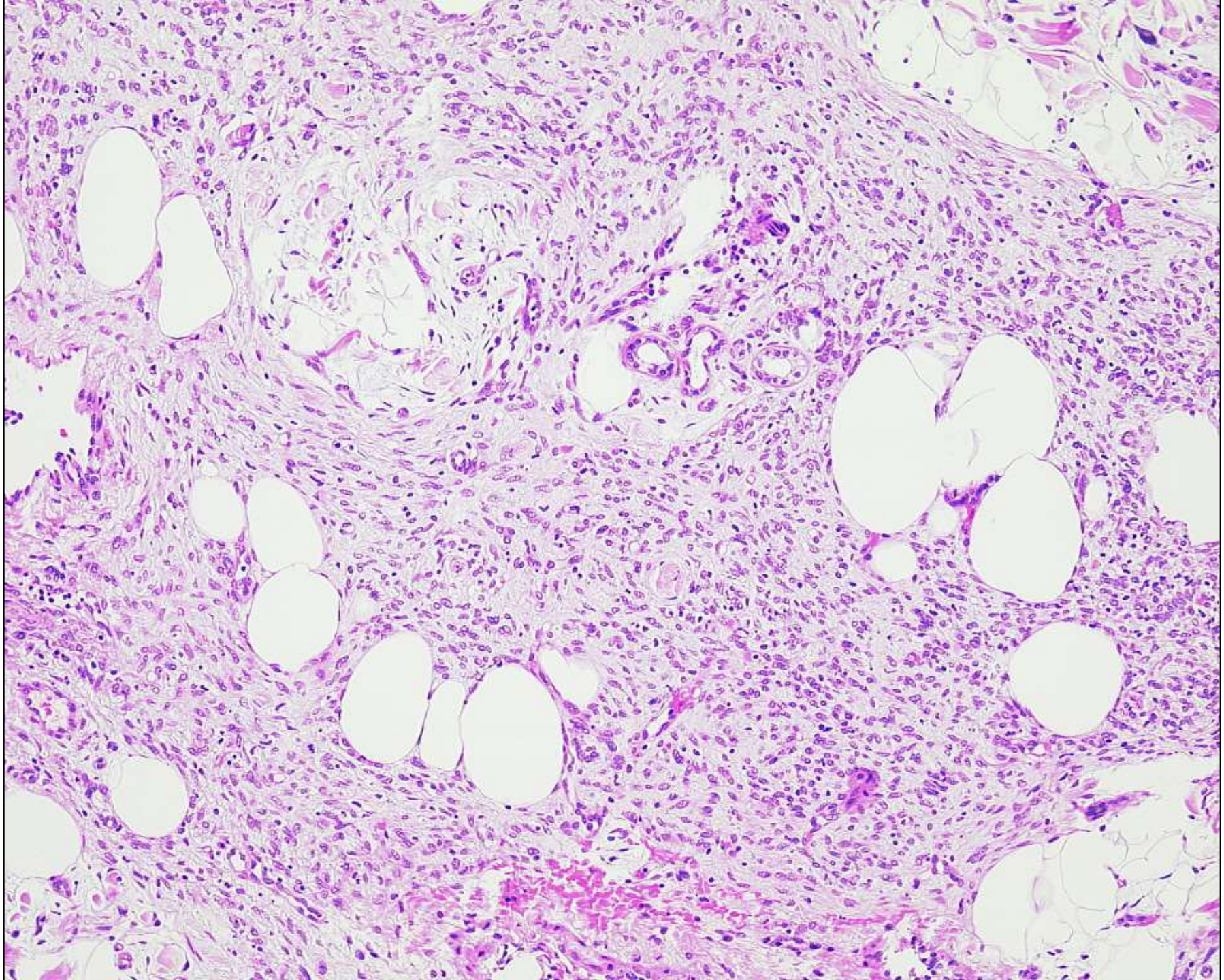
plaque-stage DFSP

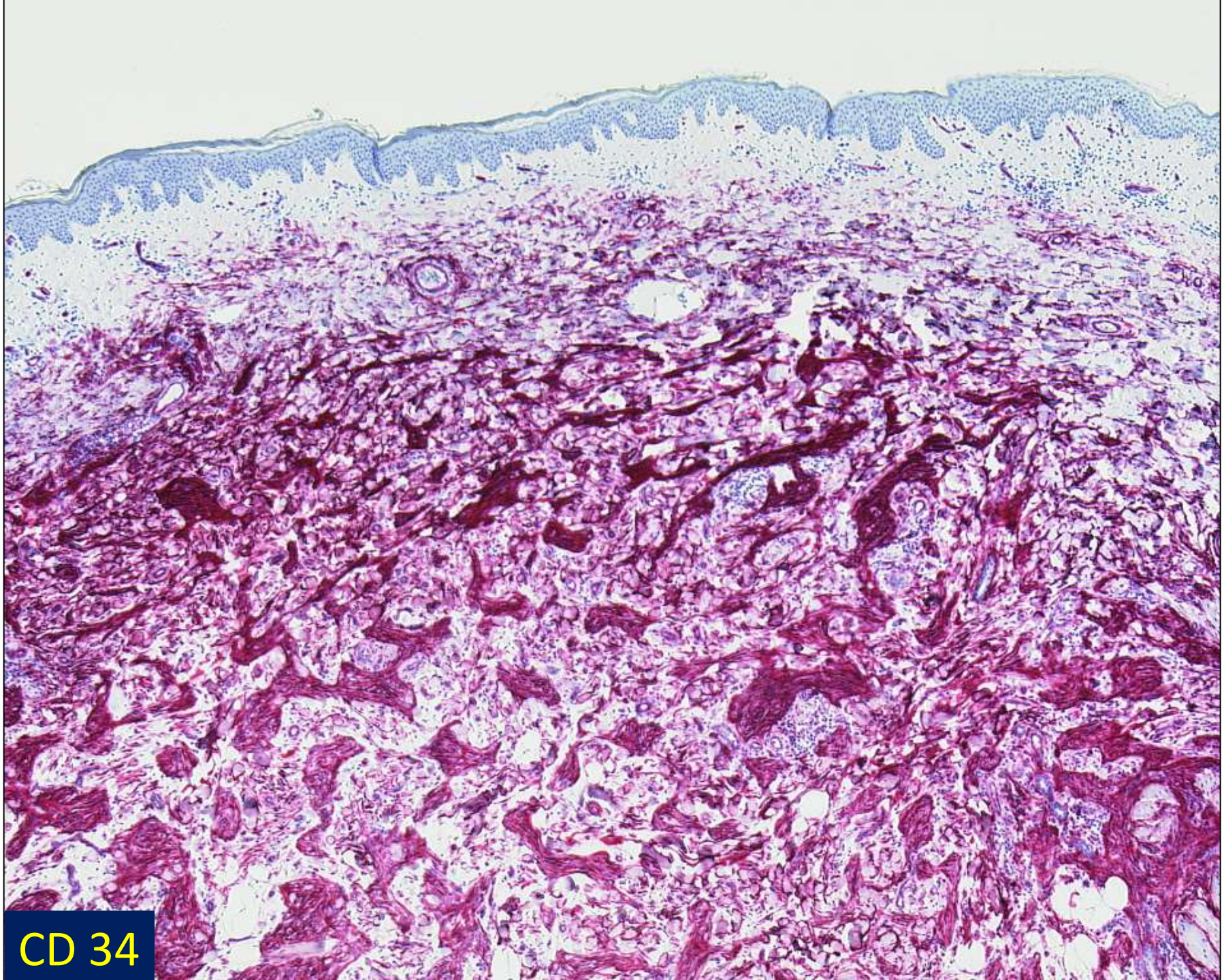
DD: plaque-stage DFSP

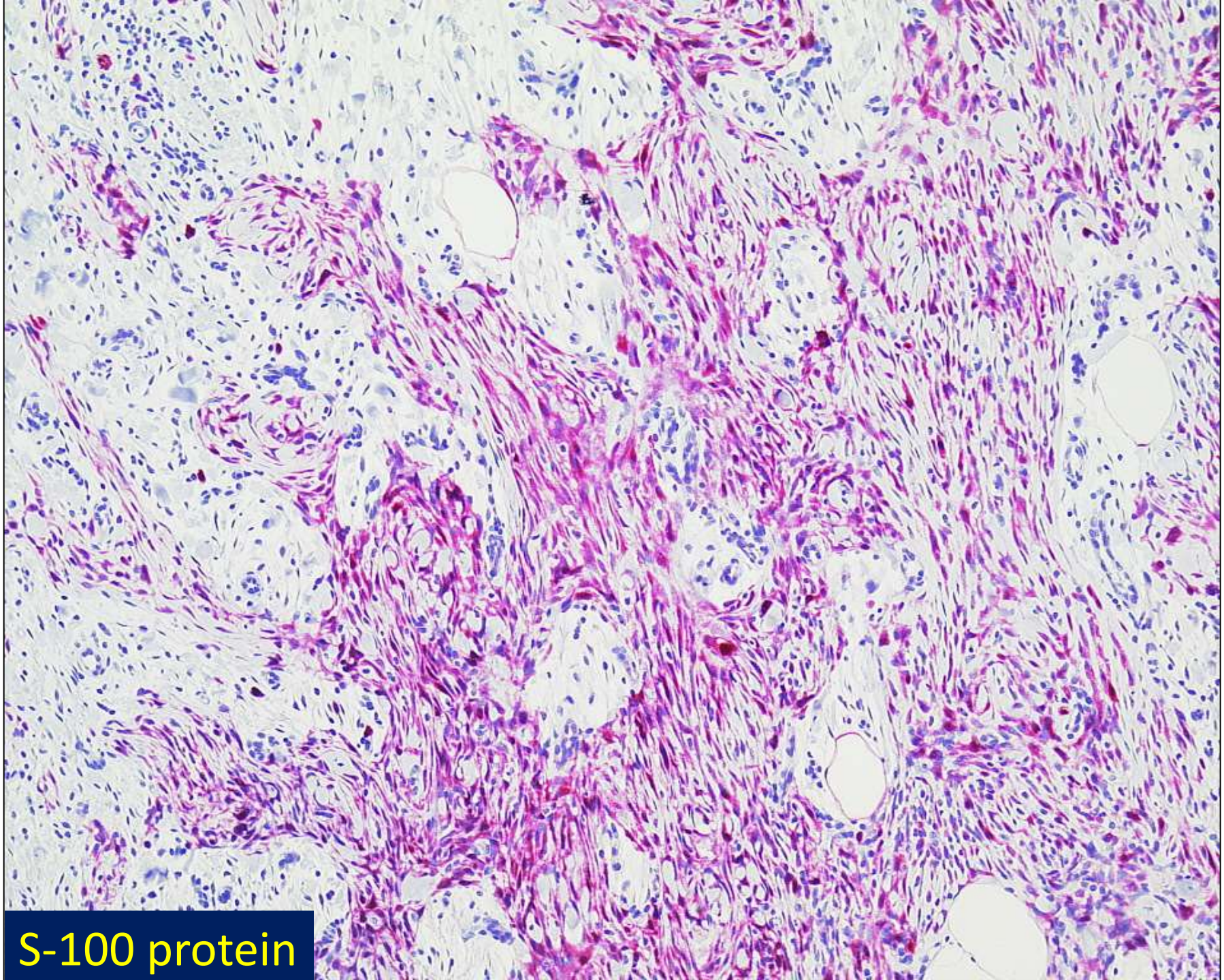


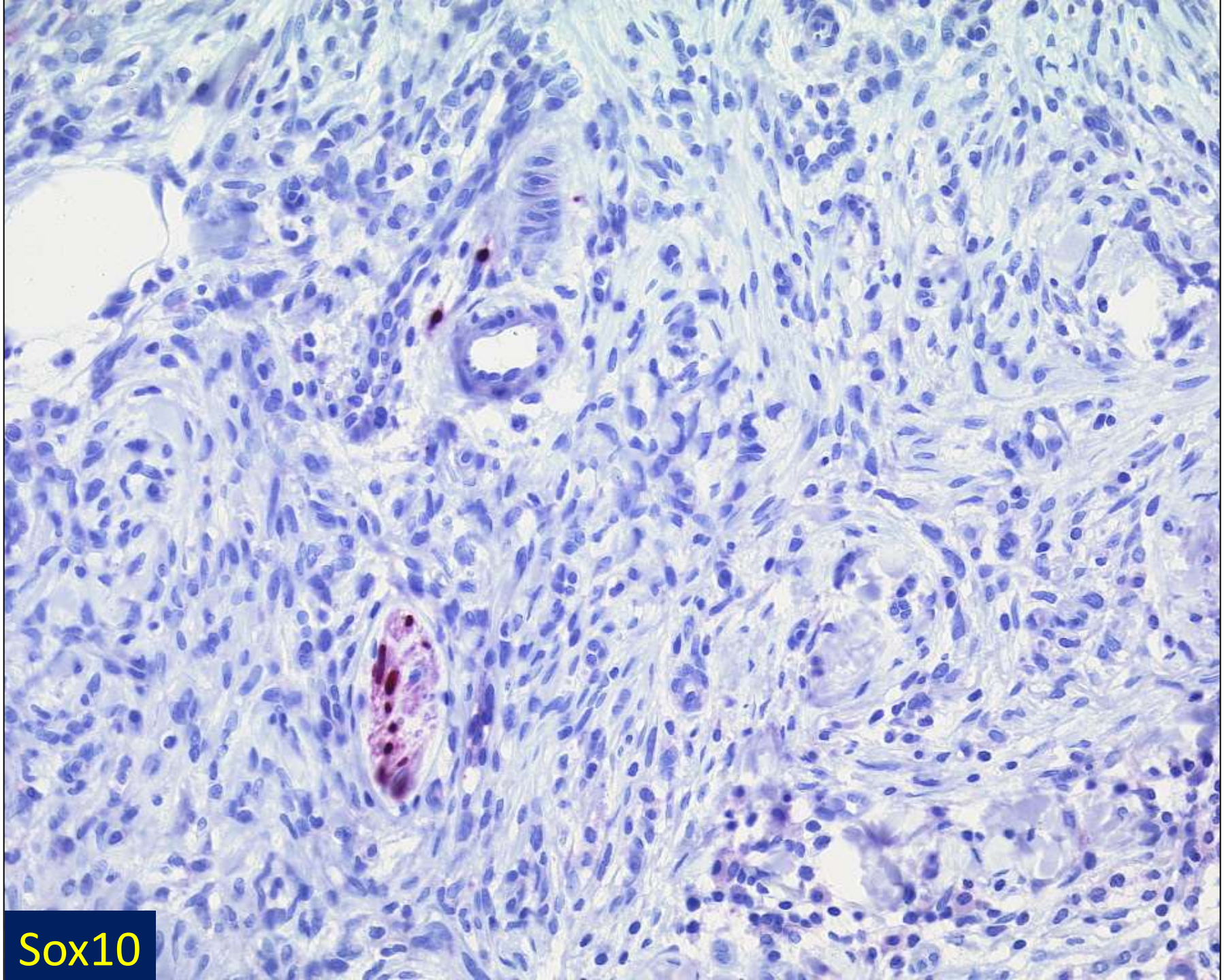
F, 67 years, buttock

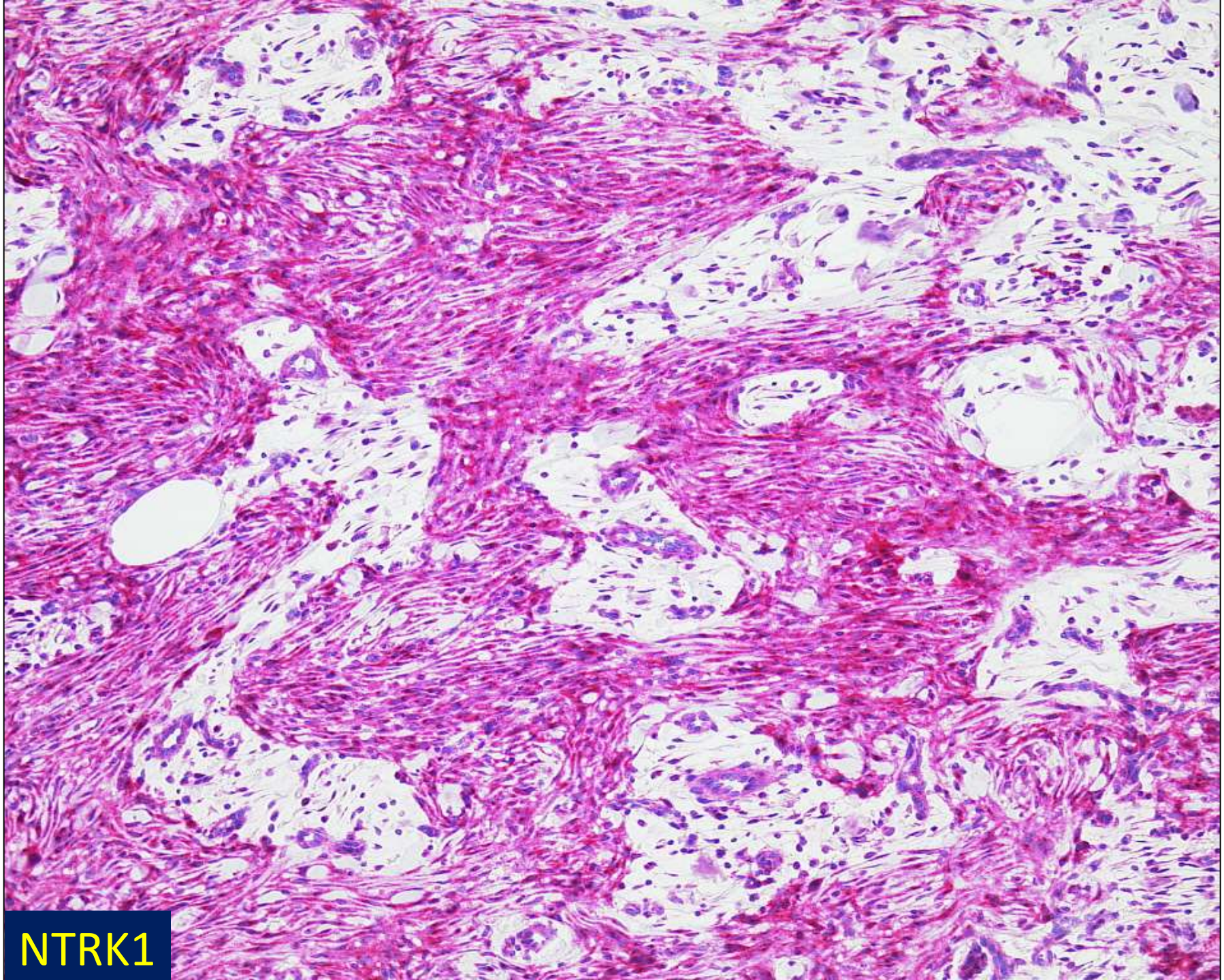





CD 34


S-100 protein


Sox10


NTRK1

Recurrent NTRK1 gene fusions define a novel subset of locally aggressive lipofibromatosis-like neural tumors

(NP Agaram et al. Am J Surg Pathol 2016; 40: 1407)

8 F, 6 M, 4-38 years, local recurrence in 5/12 cases

upper (6), lower extremity (5), head (2), flank (1)

1.3 – 5.4 cm, subcutaneous lesions

infiltrative spindle cell neoplasms

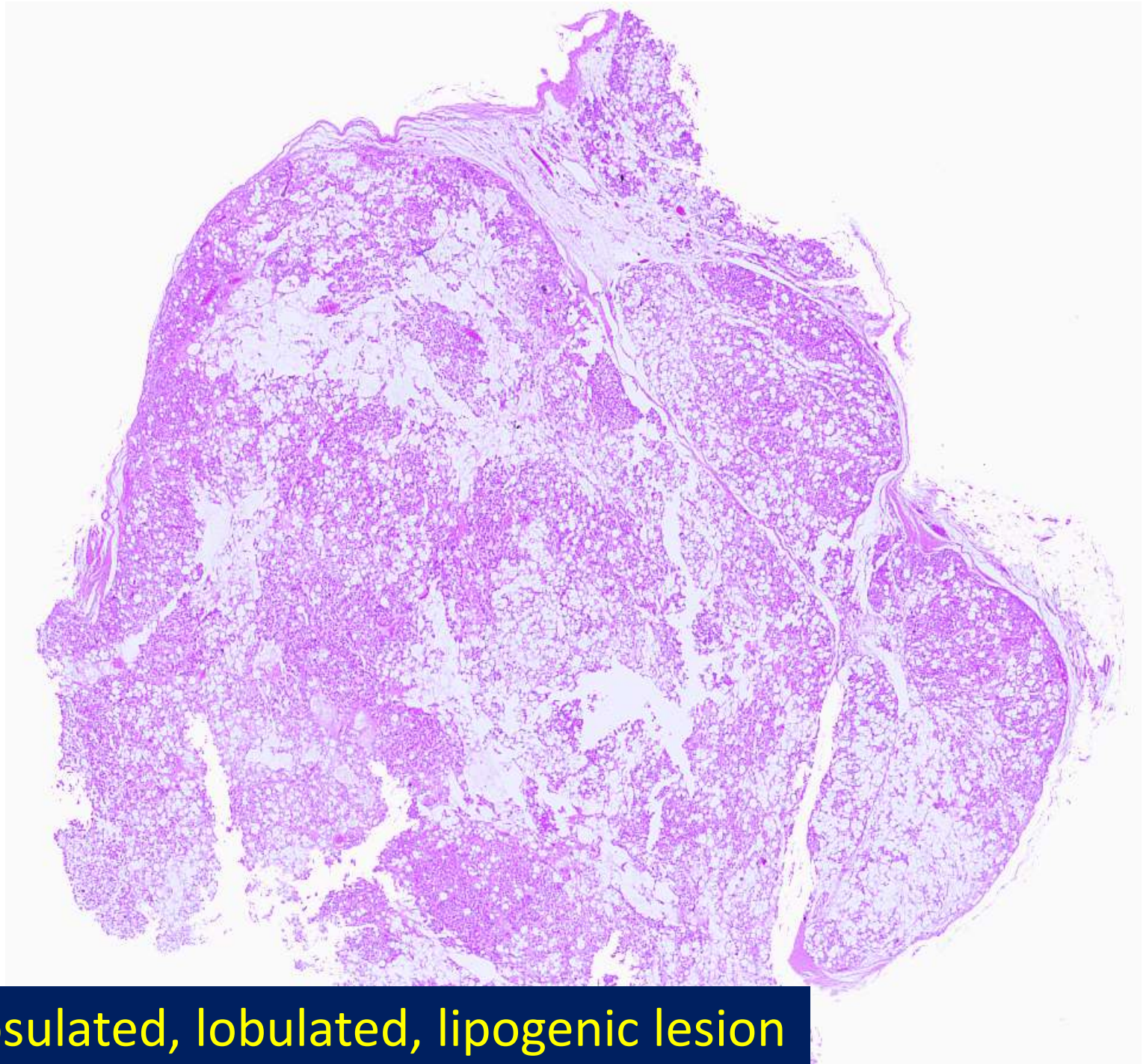
mild nuclear atypia, no / few mitoses

S-100 +, CD34 + (10/11), ASMA + (3/8), desmin -, Sox-10 -, HMB-45 -, Melan-A -, STAT6 -, H3K27me3 +

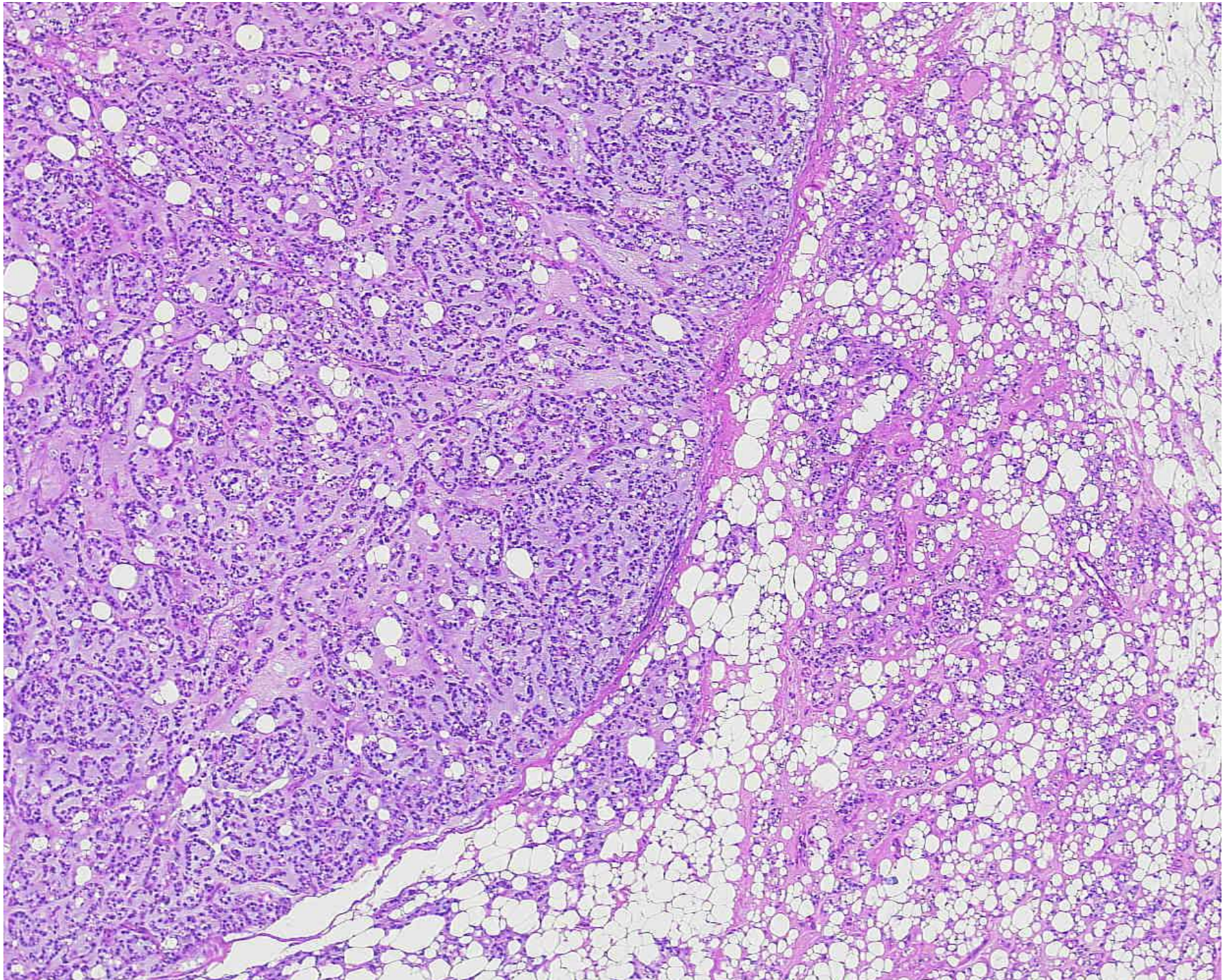
NTRK1 gene rearrangements with NTRK1 staining

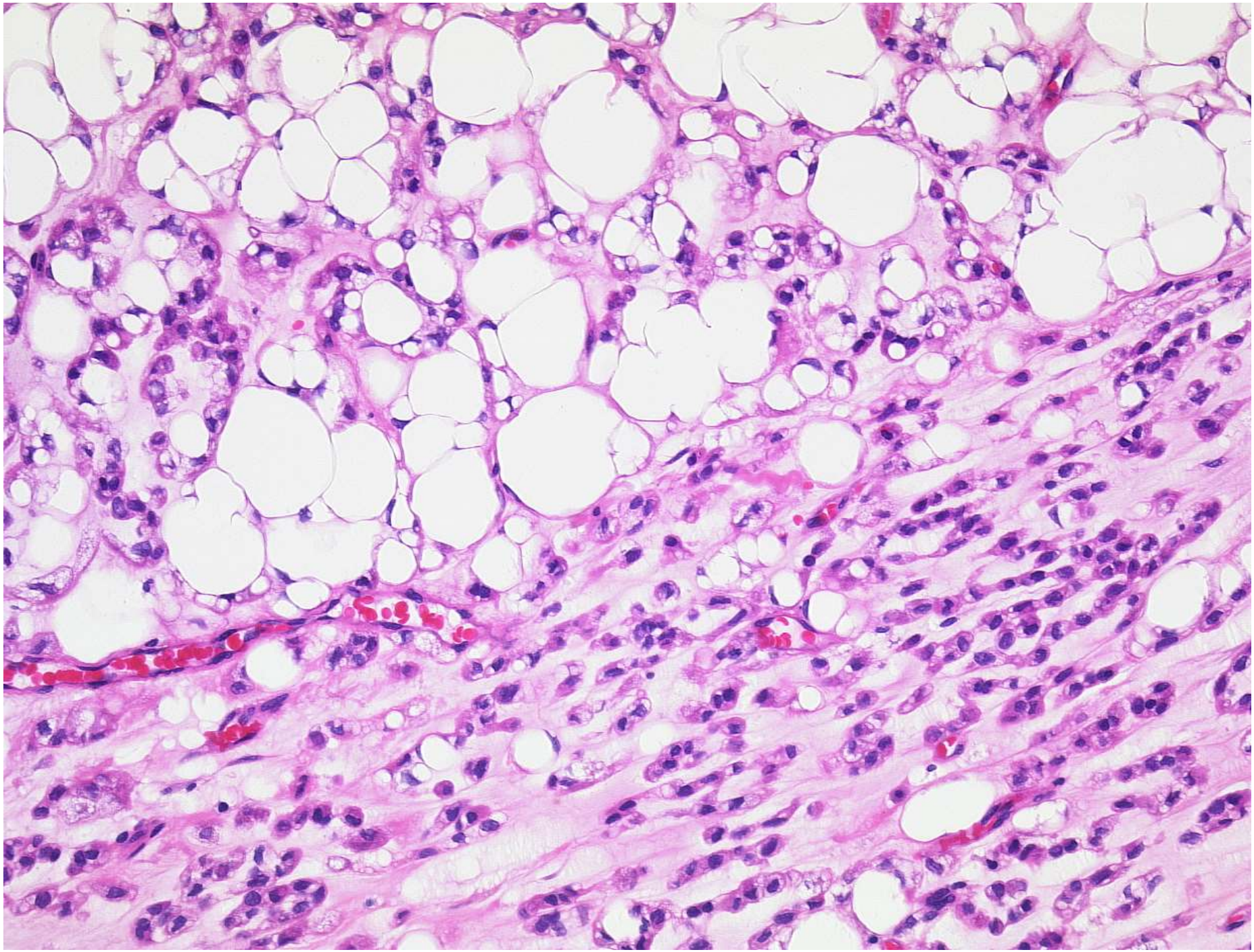
Case 7: Clinical Findings

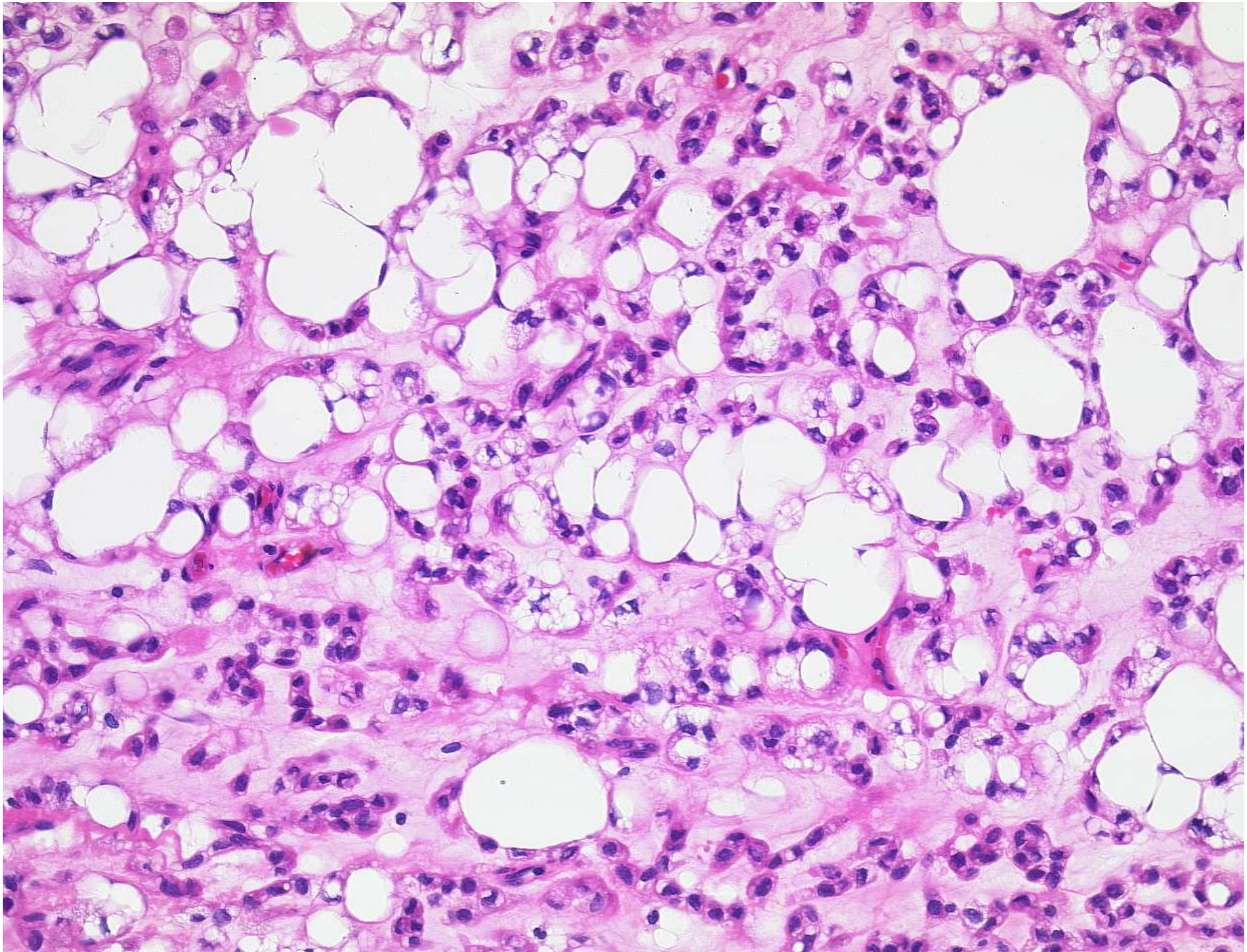
- F, 75 years
- left thigh, subcutis
- well-circumscribed nodular lesion
- 4.5 cm measuring neoplasm
- complete excision
- NSR at 2 years

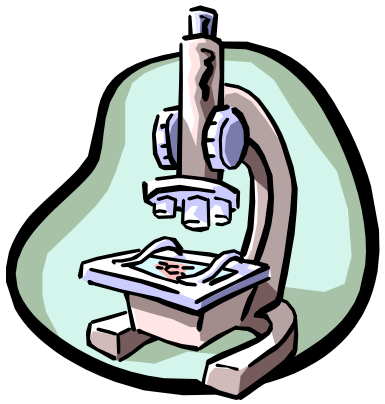


encapsulated, lobulated, lipogenic lesion









Diagnosis Case 7

chondroid Lipoma

chondroid Lipoma*

- adult patients, F > M
- slowly growing neoplasms
- subcutis / deep soft tissue
- encapsulated, lobular growth
- adipocytes, lipoblasts, eosinophilic cells
- myxochondroid stroma
  (hyaluronidase resistent)
- benign clinical course

* Meis JM, Enzinger F AJSP 1993; 17: 1103

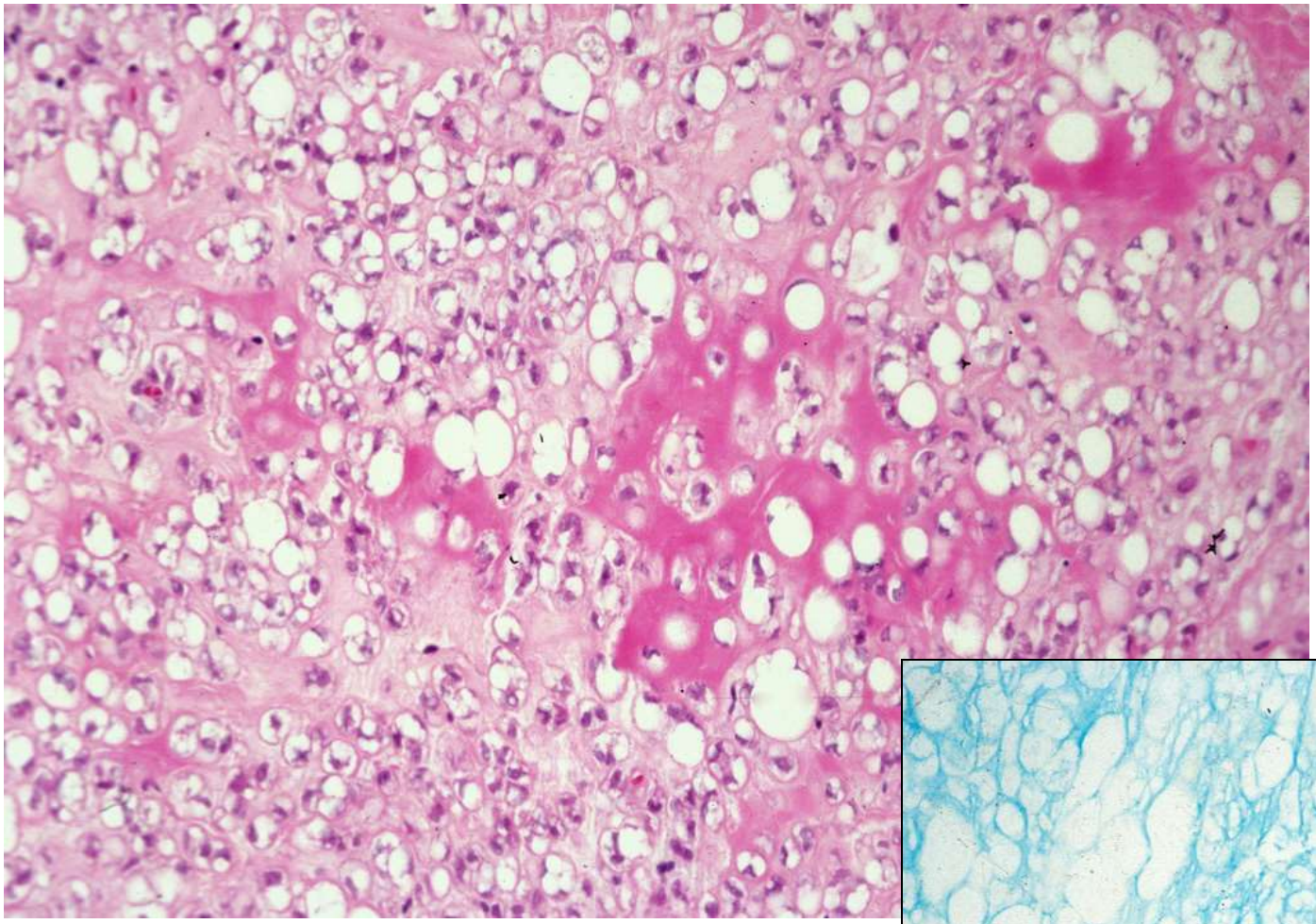
chondroid Lipoma

- vimentin +, S-100 +/-
- CD68 +/-, laminin +/-, collagen type IV +/-
- cytokeratin focal + in some cases
- EMA -, ASMA -, GFAP -
- t(11;16)(q13;p13) (*MGC3032-MKL2* fusion)

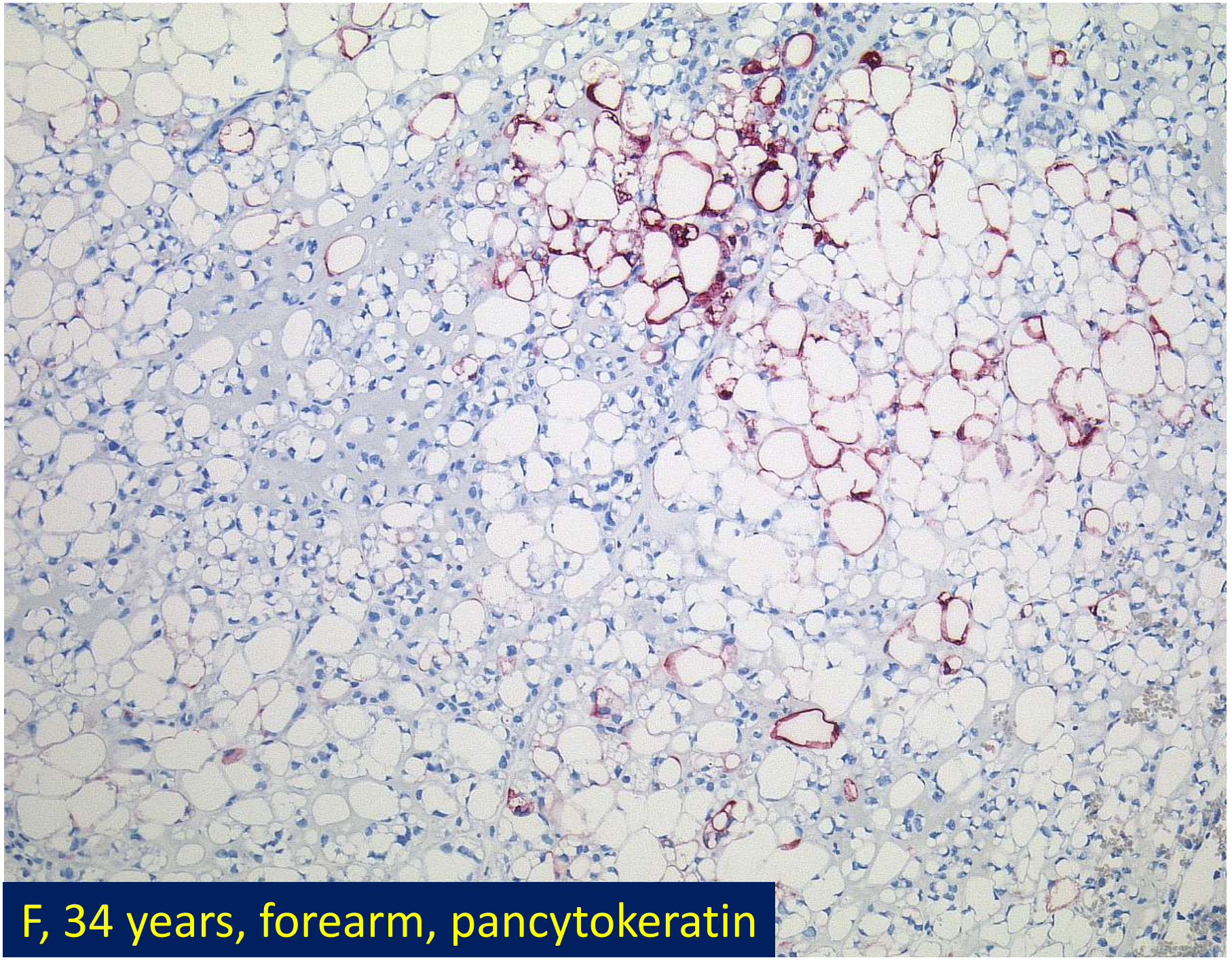
  MKL2: myocardin-related transcription factor

  MGC3032: hypothetical protein
- **ELMI:** scalloped, clefted nuclei, lipid droplets

  rough ER, mitochondria, knob-like protrusions




AB Hyaluronidase


F, 34 years, forearm, pancytokeratin

C11orf95-MKL2 is a consistent finding in chondroid lipoma: a study of 8 cases

U.Flucke et al. Histopathology 2013; 62: 925

- 4 F, 4 M, 21-81 years
- forearm (3), lower leg (2), back (1), thigh (1), scalp (1)
- 1 out of 6 cases recurred
- classical histopathology
- 7/8 cases showed *C11orf95-MKL2*

Lipoblasts in benign lipogenic neoplasms ?

Yes, no problem !

- Lipoblastoma / Lipoblastomatosis
- spindle cell / pleomorphic Lipoma
- chondroid Lipoma

Differential Diagnosis: chondroid Lipoma

extraskeletal myxoid Chondrosarcoma

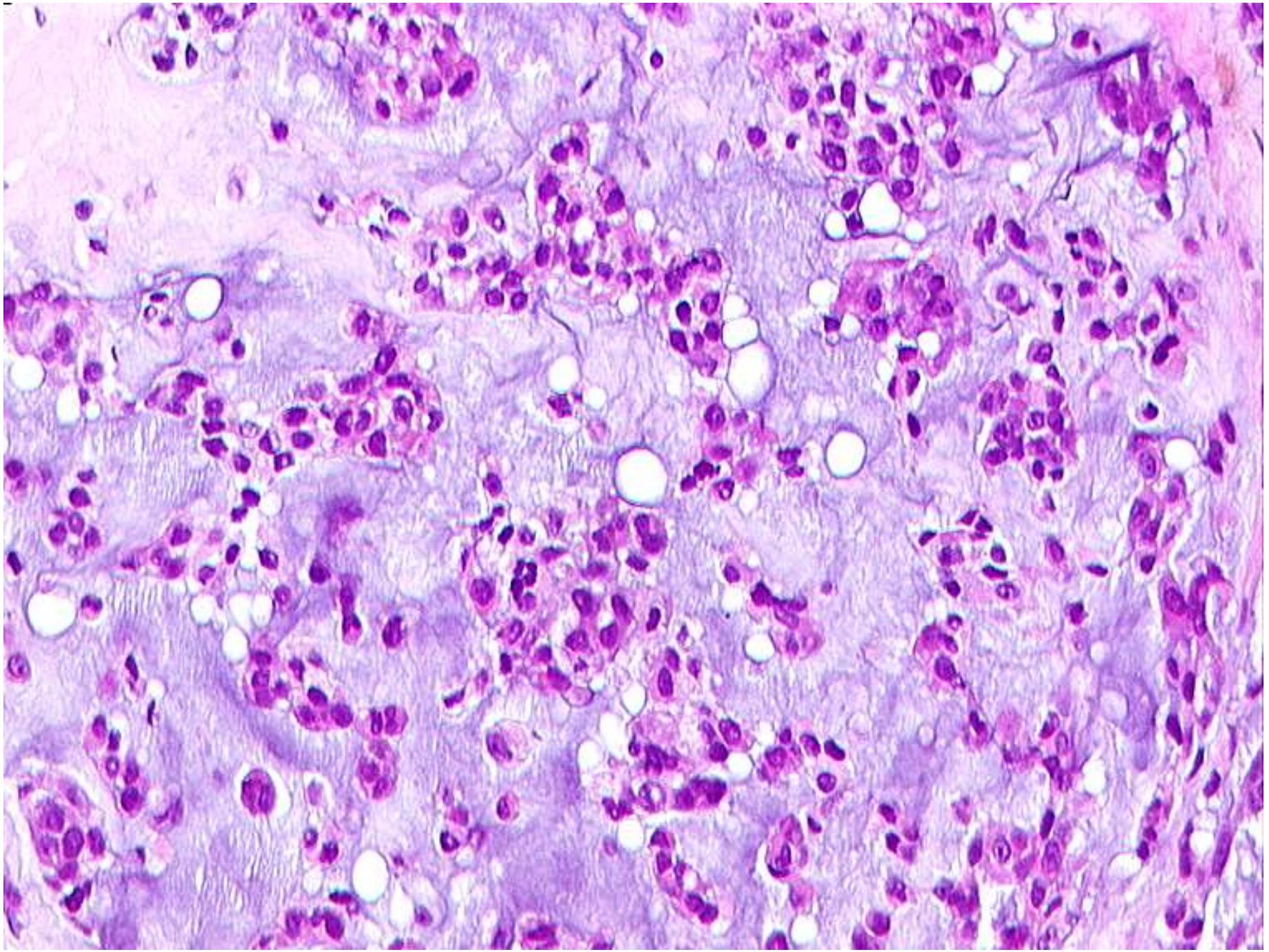
no lipogenic component

small, uniform,
round/spindled cells

no cytoplasmic
vacuolation

rather avascular
myxoid stroma

t(9;22)(q22;q12) >
t(9;17)(q22;q12)



Differential Diagnosis: chondroid Lipoma

atypical lipomatous Tumour

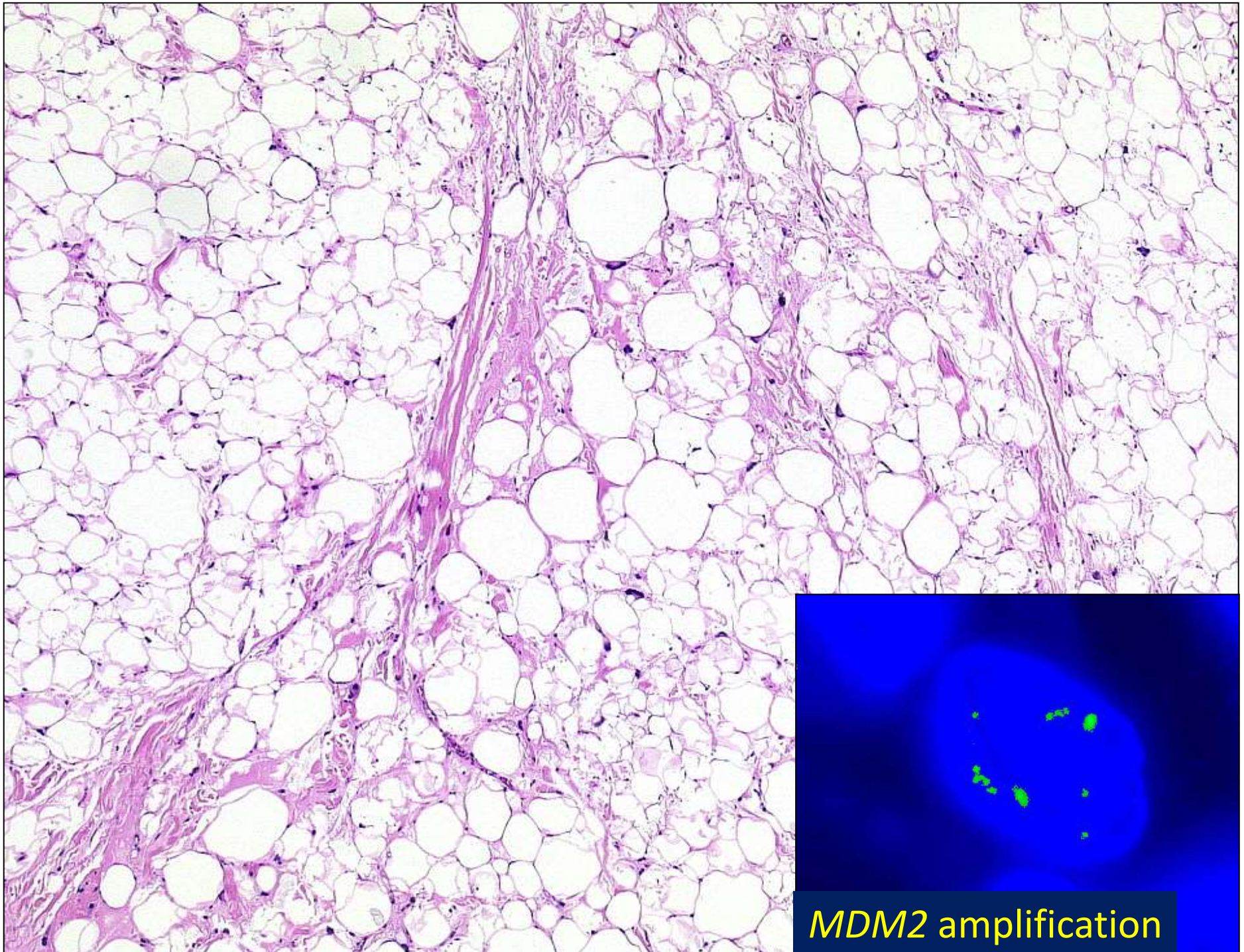
no lobular growth

no / few lipoblasts

enlarged, hyperchromatic nuclei

septa with atypical cells

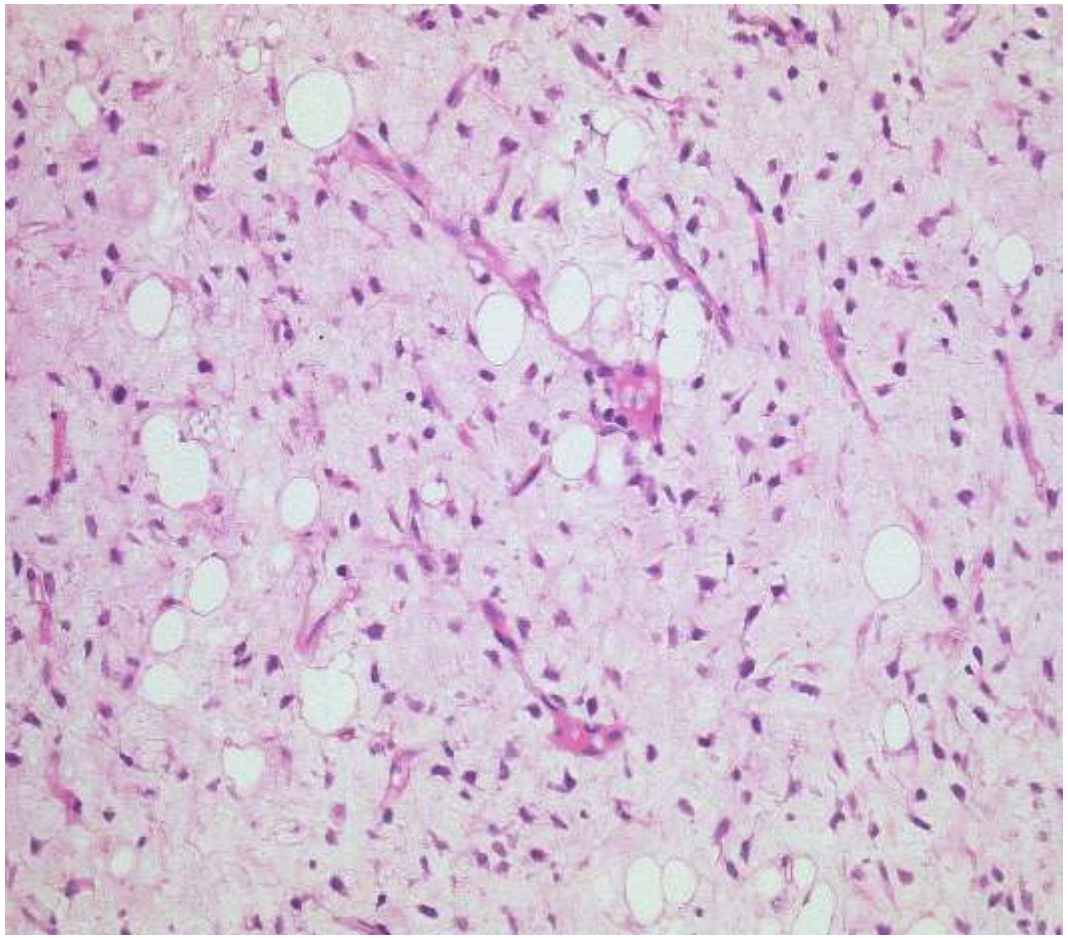
MDM2 / *CDK4* amplification


MDM2 amplification

Differential Diagnosis: chondroid Lipoma

myxoid Liposarcoma

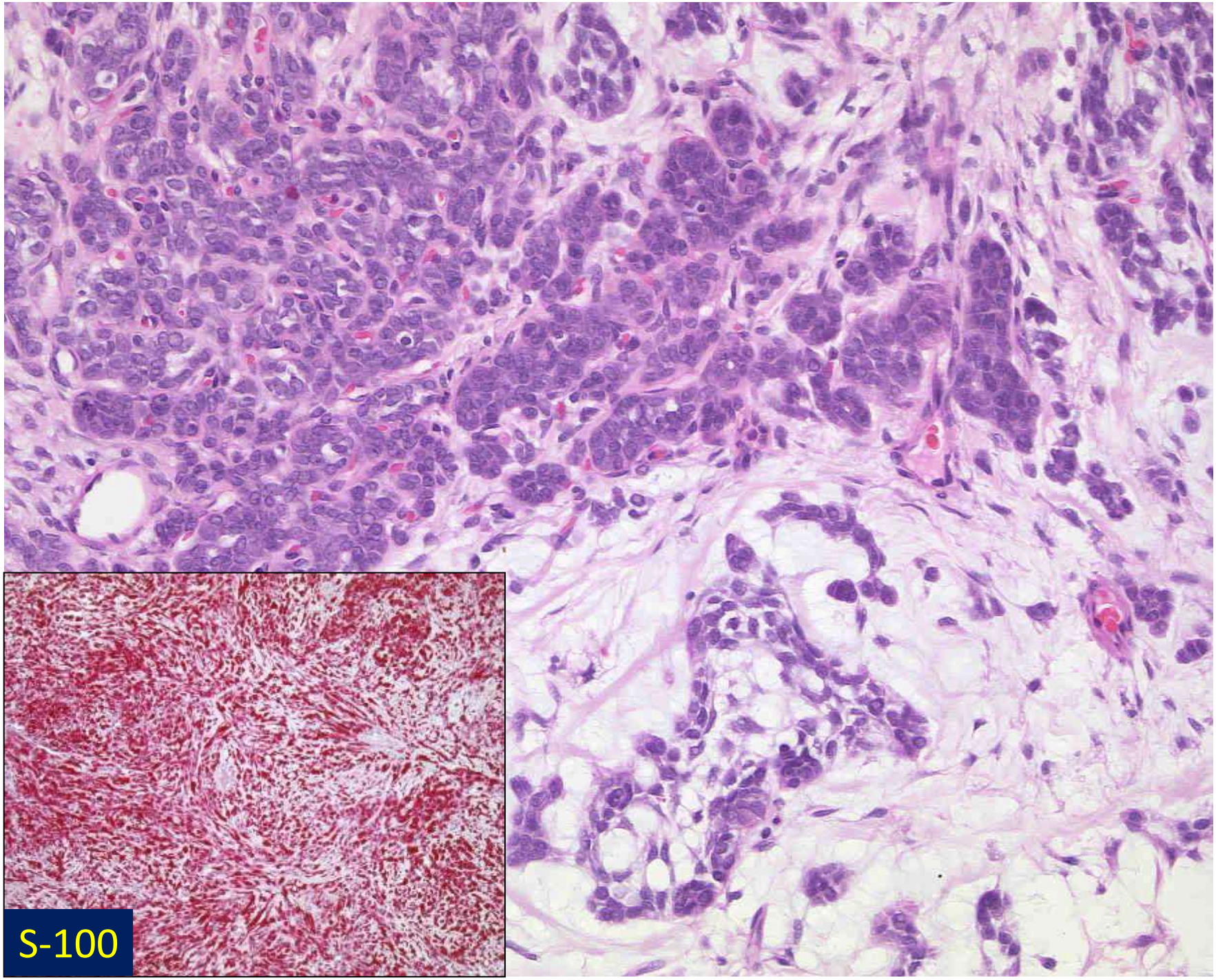
small immature cells
branching vessels
myxoid stroma
  (hyaluronidase
  sensitive)
PRAME +
t(12;16)(q13;p11)
  DDIT3-FUS fusion
t(12;22)(q13;q12)
  DDIT3-EWSR1 fusion



Differential Diagnosis: chondroid Lipoma

Myoepithelioma

focal epithelial
structures
no lipogenic cells
no multivacuolation
S-100 +/-,
CK +/-, EMA +/-
GFAP +/-, ASMA +/-
calponin +/-


S-100

Differential Diagnosis: chondroid Lipoma

Hibernoma

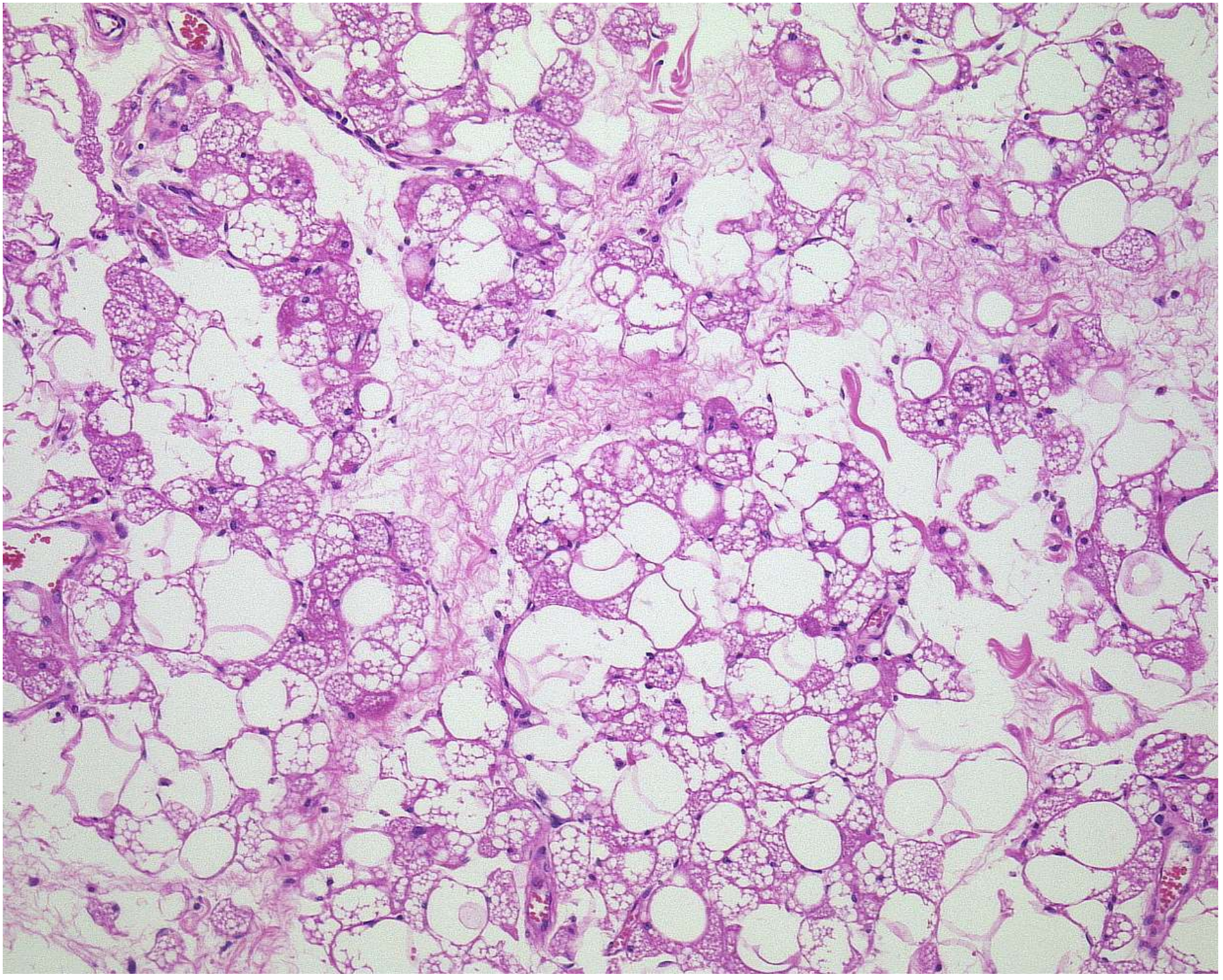
brown cut surfaces

more cytoplasm

small nuclei

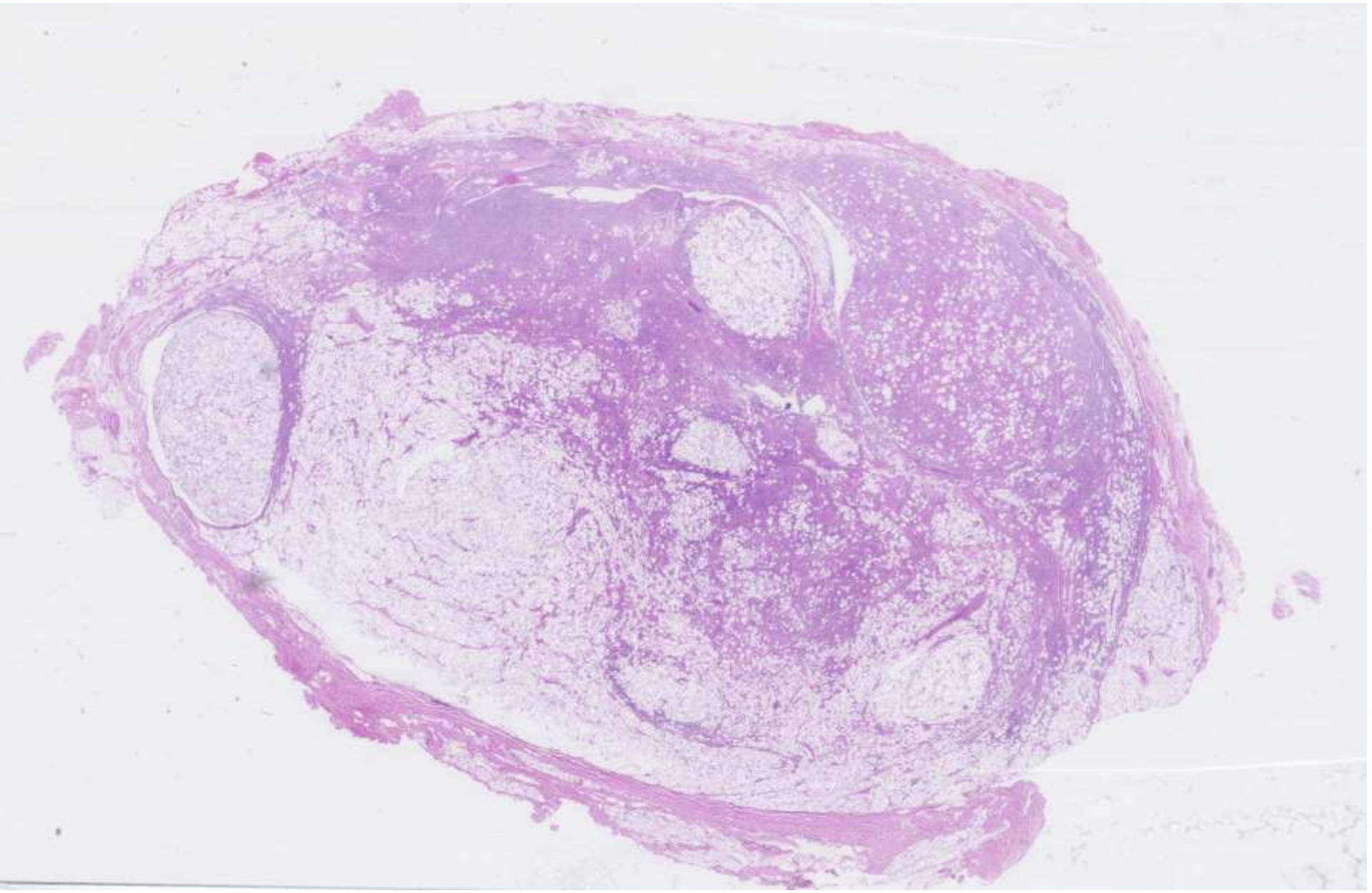
no myxochondroid stroma

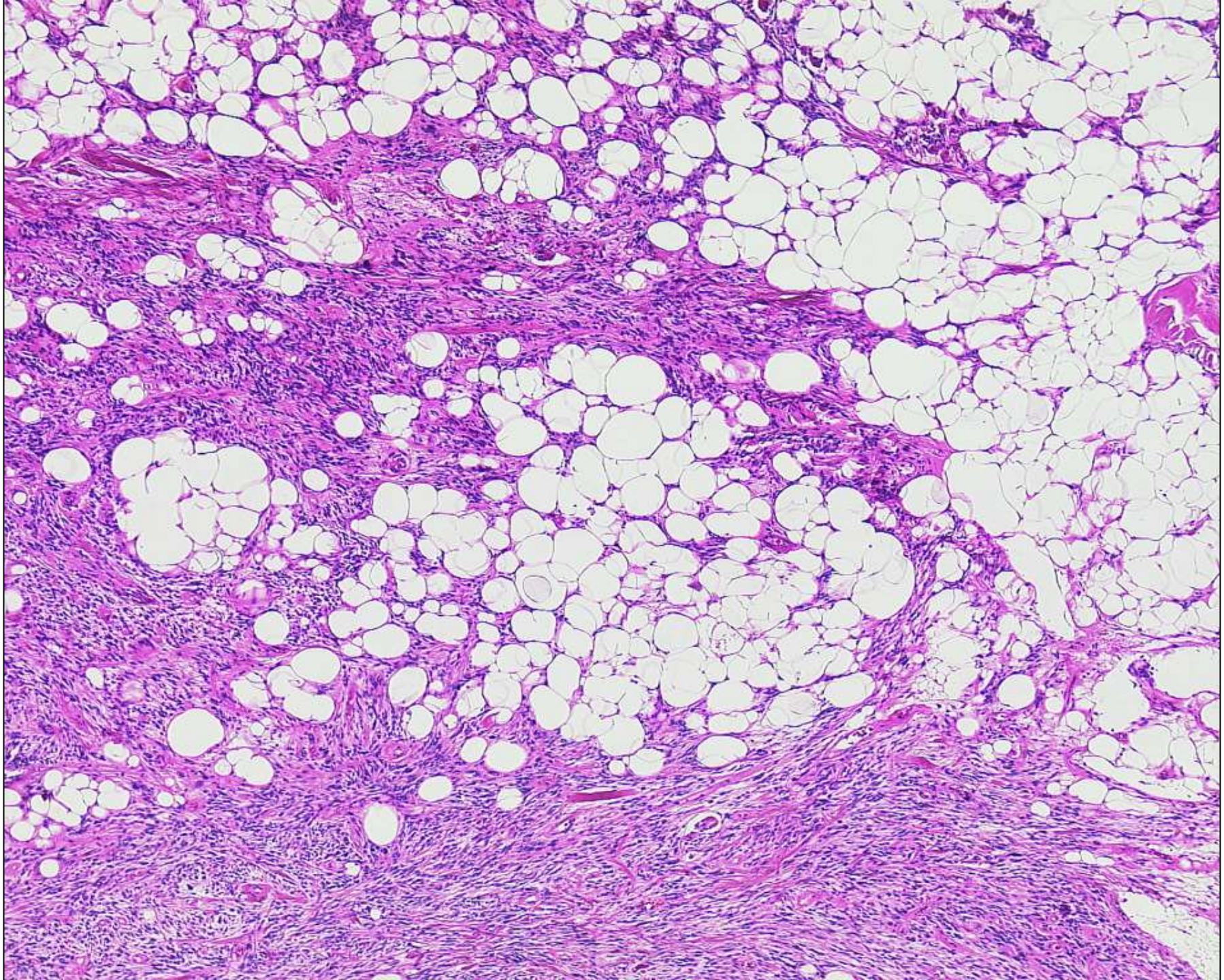
many mitochondria

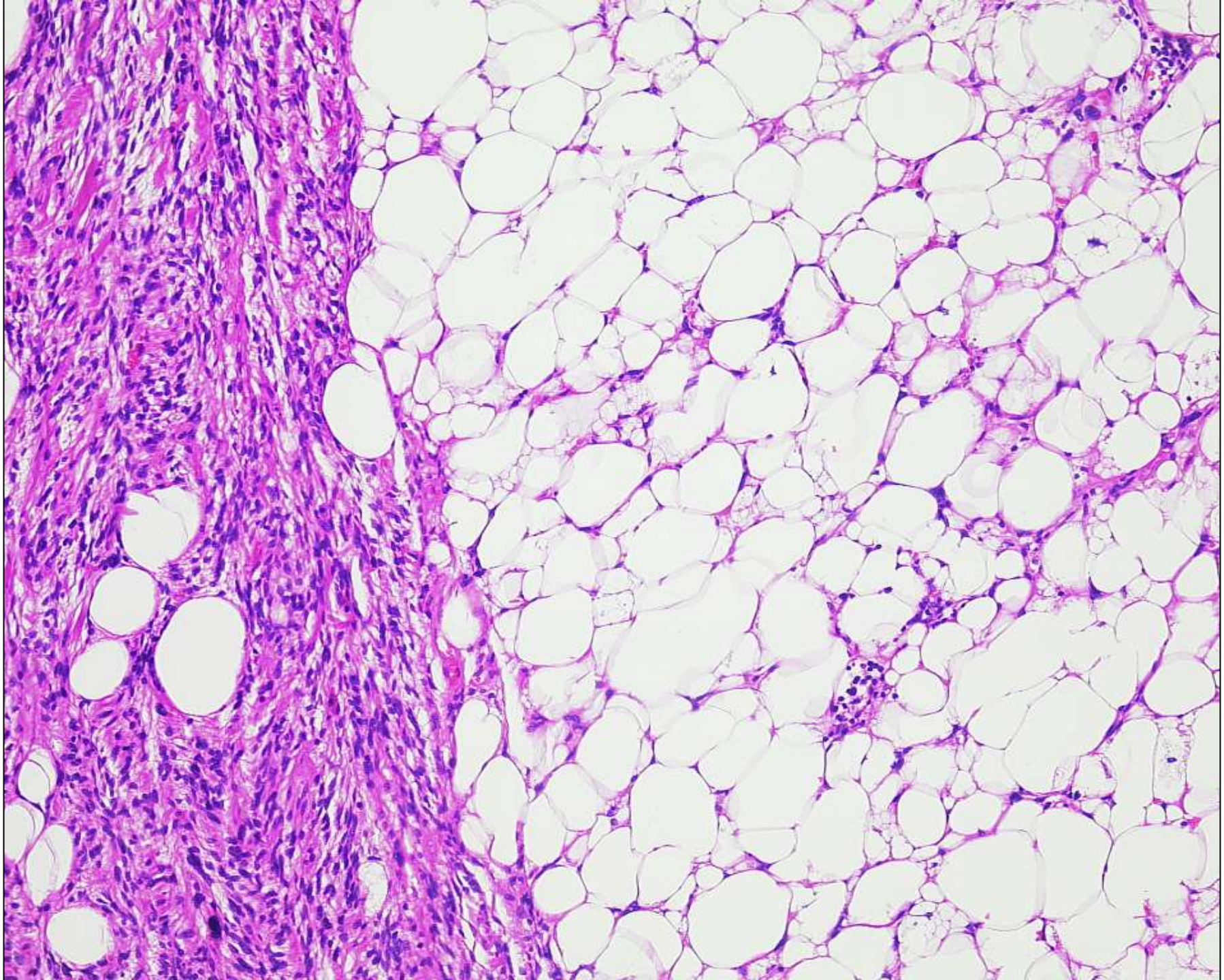


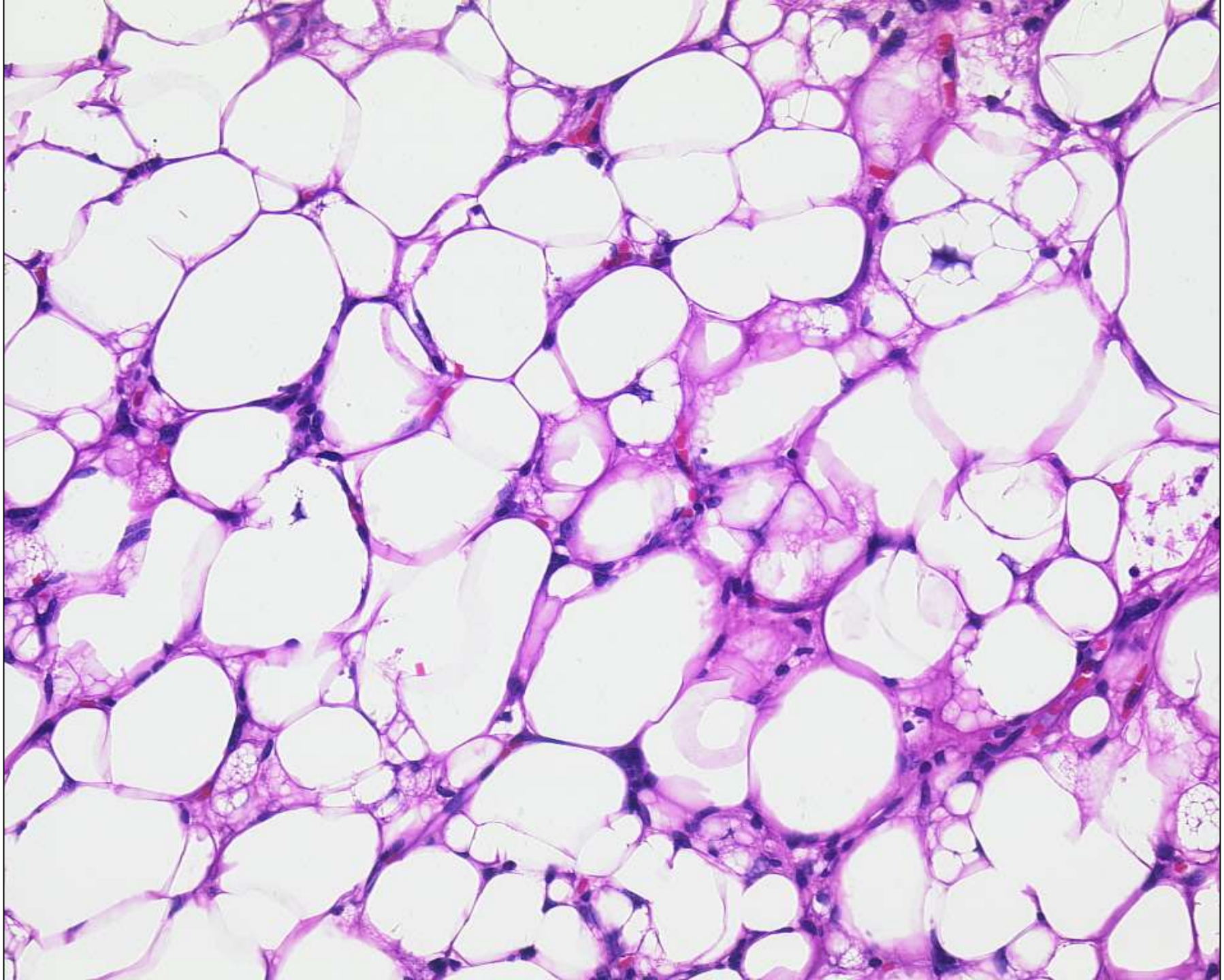
Case 8: Clinical Findings

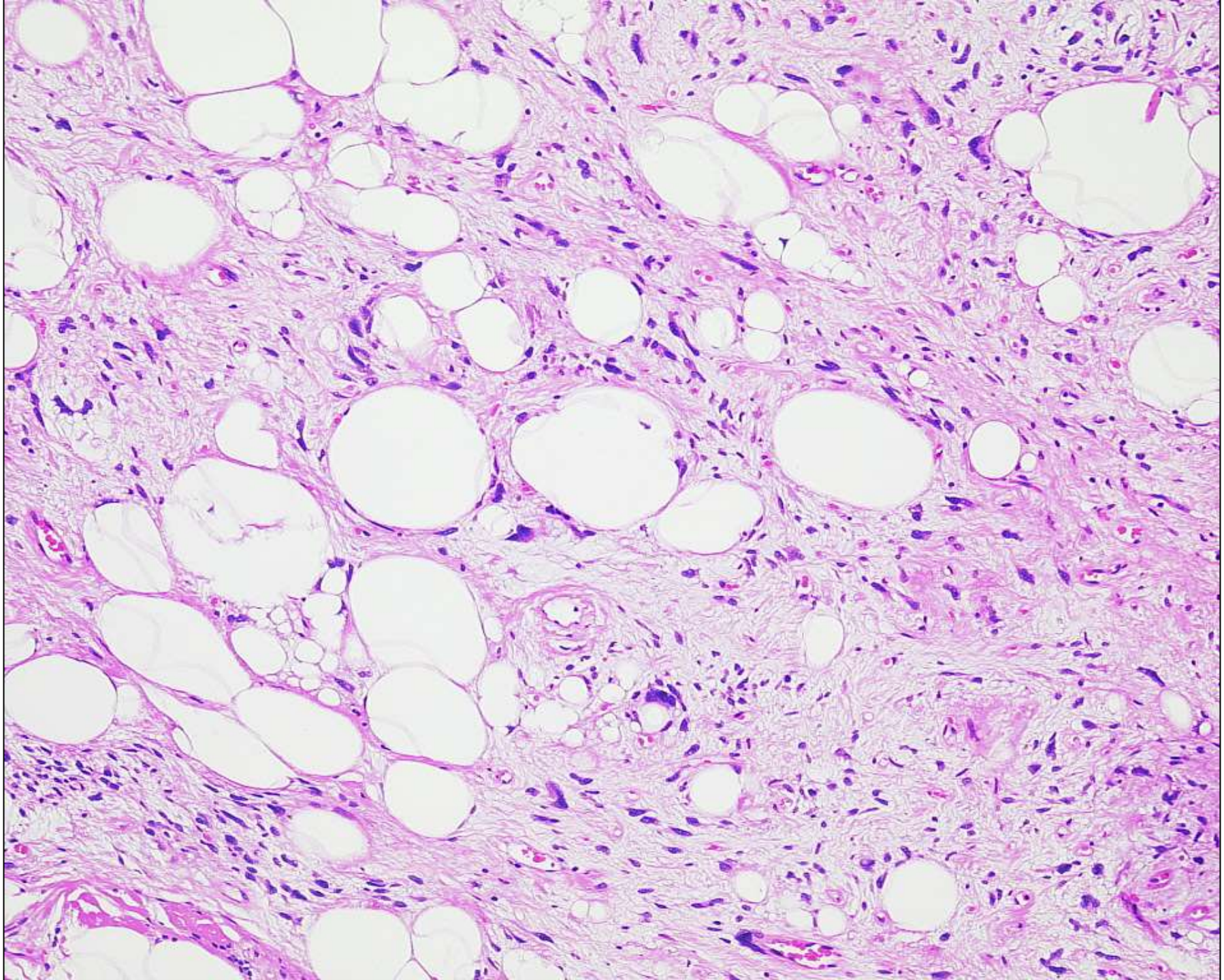
- M, 73 years, left shoulder
- slowly growing indurated lesion
- slightly painful
- subcutis, 3 x 3 cm
- complete excision

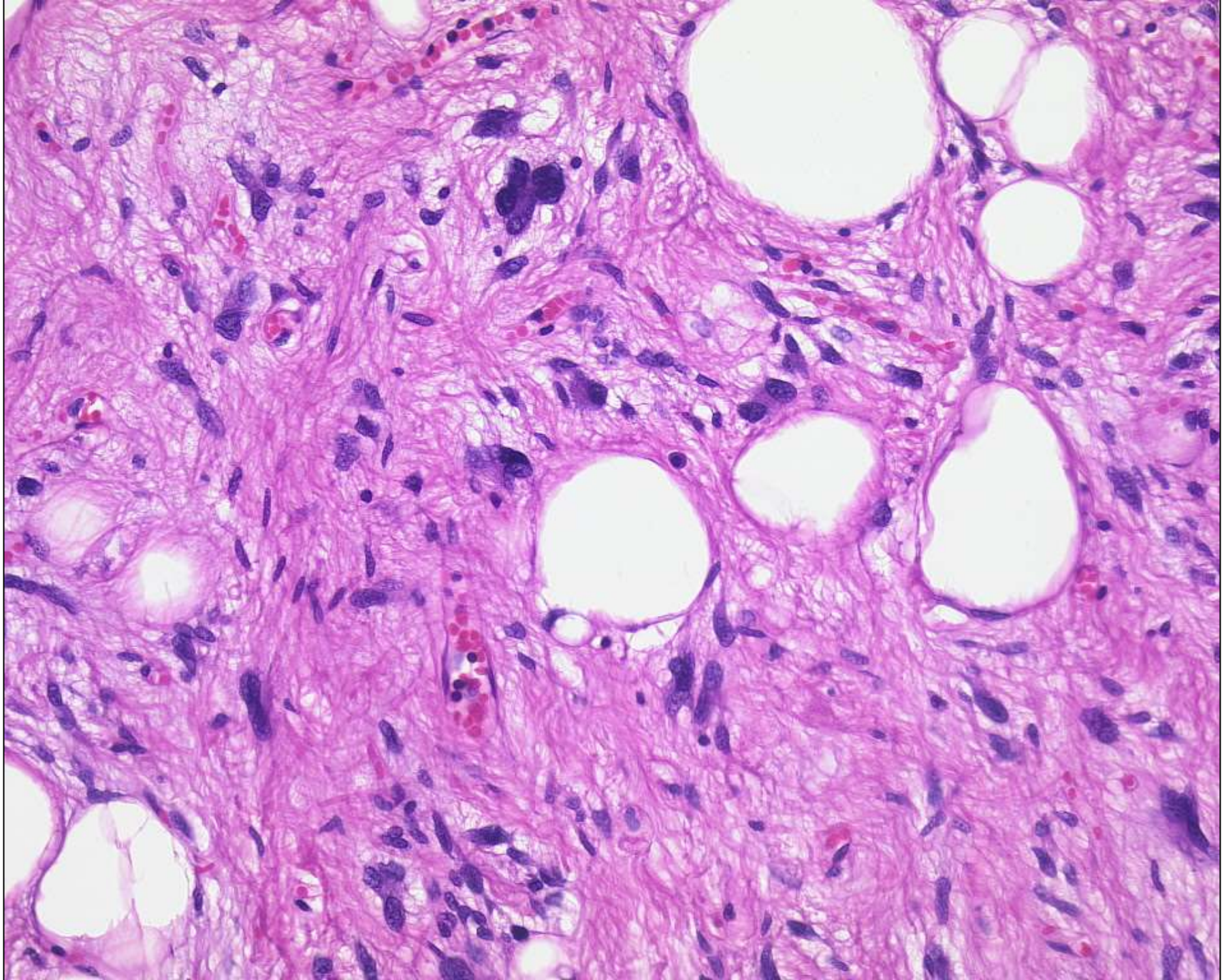


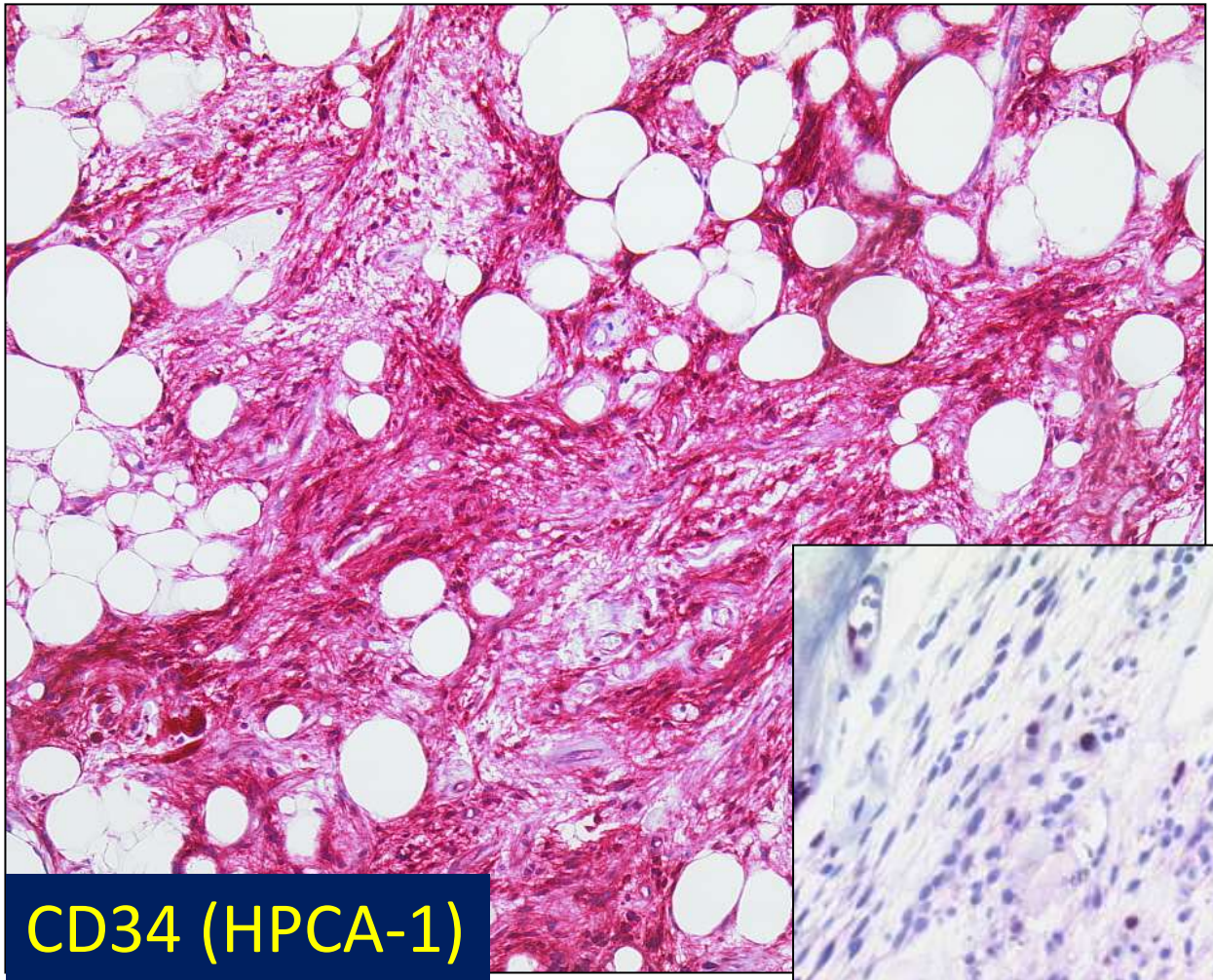


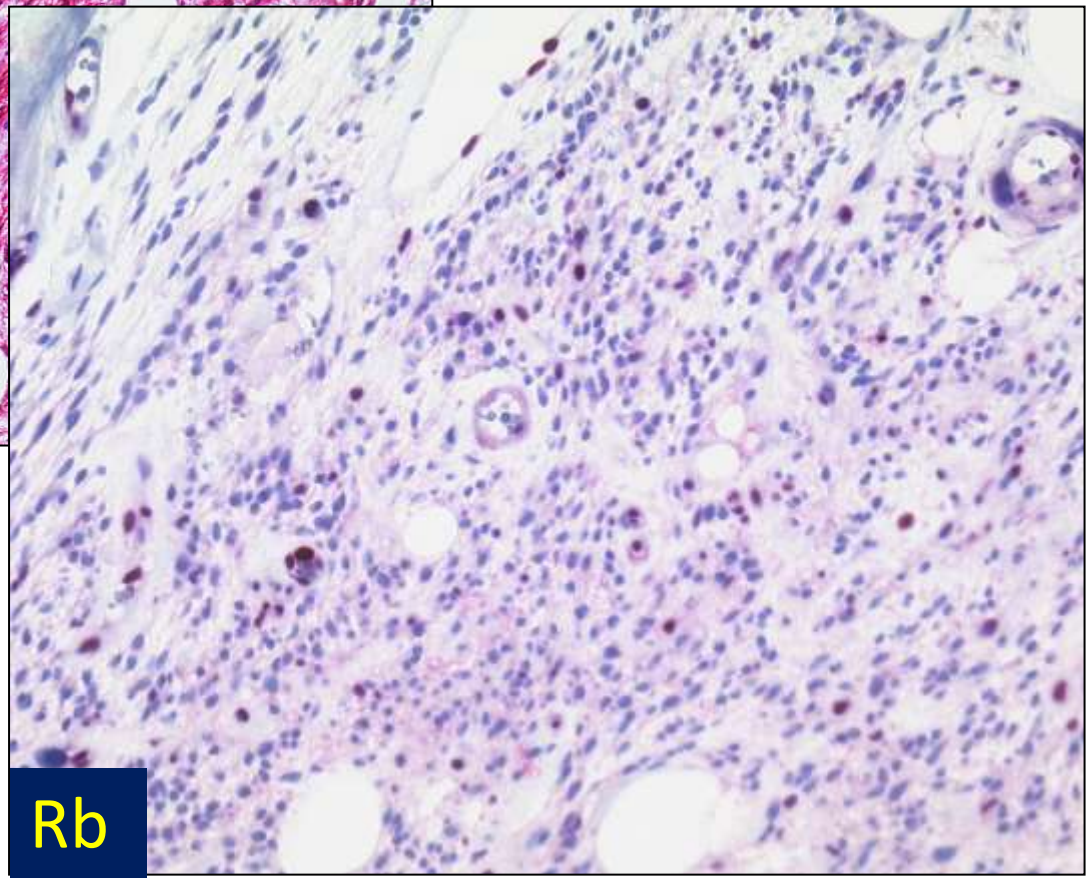


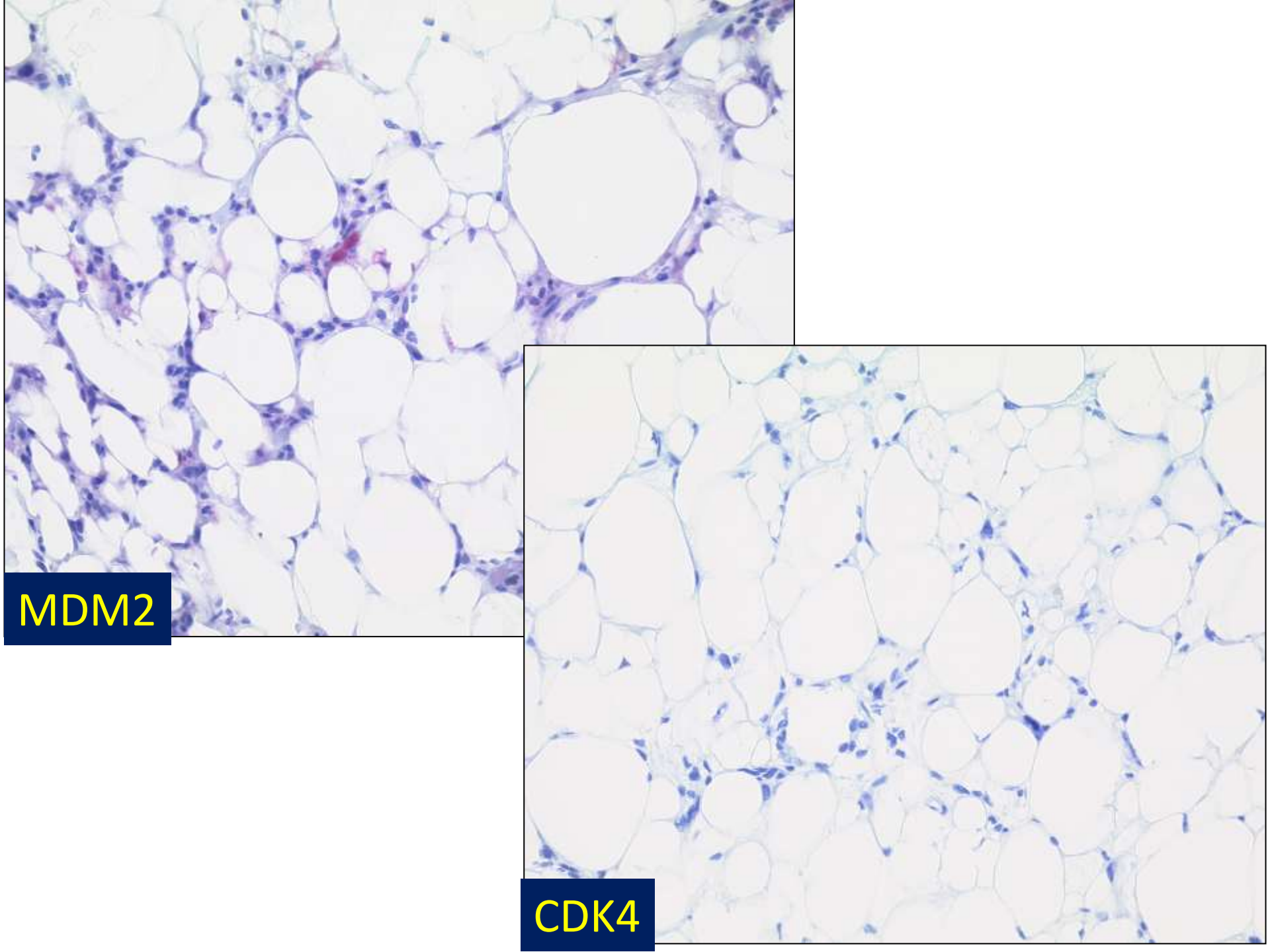


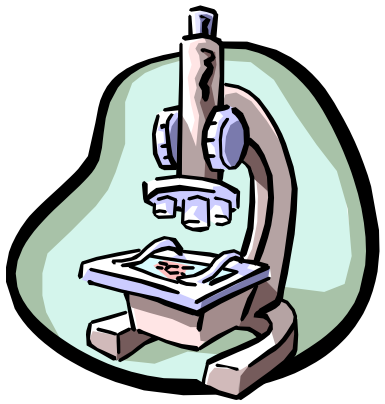





CD34 (HPCA-1)


Rb


MDM2
CDK4



Diagnosis Case 8

atypical spindle cell lipomatous Tumour

The American Journal of Surgical Pathology 18(9): 913-921, 1994

Spindle Cell Liposarcoma, A Hitherto Unrecognized Variant of Liposarcoma

Analysis of Six Cases

Angelo P. Dei Tos, M.D., Thomas Mentzel, M.D., Paul T. Newman, M.R.C.Path., and Christopher D.M. Fletcher, M.D., M.R.C.Path.

A series of six cases of a previously unrecognized variant of liposarcoma characterized by a prominent spindle cell component is reported herein. Clinically, all of the tumors arose in adults and developed around the shoulder girdle or upper limbs; all but one arose in subcutaneous tissue. Three patients developed multiple local recurrences over a period of 4–20 years. Recurrences in one case were purely lipoma-like. Following dedifferentiation into recurrence, one patient developed distant metastases and eventually died, 46 months after the primary excision. Grossly, these lesions are characterized by multinodularity, and microscopically they show a relatively bland spindle cell proliferation arranged in fascicles and whorls and set in a variably myxoid stroma. The spindle cell areas are accompanied by an adipocytic component, which exhibits the morphologic features required for inclusion in the well-differentiated liposarcoma–atypical lipoma group, including definite lipoblasts. Main differential diagnoses include benign lesions such as spindle cell lipoma and diffuse neurofibroma, as well as dermatofibrosarcoma protuberans and other malignancies such as sclerosing liposarcoma, low-grade myxofibrosarcoma, low-grade malignant peripheral nerve sheath tumor, and low-grade fibromyxoid sarcoma. In view of their distinctive histologic appearance, and because aggressive clinical behavior was observed despite their superficial location, we propose that these lesions be regarded as spindle cell variants of well-differentiated liposarcoma.

Key Words: Subcutaneous tissue—Spindle cell—Atypical lipoma—Liposarcoma—Sarcoma.

Am J Surg Pathol 18(9): 913–921, 1994.

Classification of lipomatous tumors has been a source of controversy in recent years, particularly with regard to the well-differentiated liposarcoma–atypical lipoma group—i.e., tumors with definite features of well-differentiated liposarcoma arising in surgically amenable soft tissue or adipocytic tumors arising deep to fascia which lack lipoblasts but show atypical stromal cells and variations in adipocyte size (11).

Long-term follow-up studies have shown that location and depth of the primary lesion are key parameters in the prediction of clinical behavior. Differentiated adipocytic neoplasms located in subcutaneous tissue generally do not recur, while those in deep soft tissue of the extremities may recur locally; however, formerly they had been said not to dedifferentiate and thus were believed not to give rise to distant metastases or disease-related deaths (3,7,9). For these reasons, it was suggested that the term *well-differentiated liposarcoma* be dropped and that such lesions in the limbs be called *atypical lipoma*. However, it has been demonstrated (17) that deep-seated differentiated fatty tumors of the extremities are capable of undergoing dedifferentiation and therefore of acquiring life-threatening potential. Weiss and Rao (17) thus preferred retention of the term *well-differentiated liposarcoma* for those lesions arising in the deep soft tissue of an extremity, while the denomination *atypical lipoma* was regarded by those authors as acceptable for histologically identical lesions arising in the subcutaneous fat.

We herein present a series of six cases of a previously unrecognized variant of liposarcoma, characterized histologically by spindled morphology of most of the proliferating cells and clinically by prevalent occurrence in subcutaneous tissue. In view of its distinctive histologic appearance and the clinical behavior observed, we suggest that this is a *spindle cell variant of well-differentiated liposarcoma*.

From the Soft Tissue Tumour Unit (A.P.D.T., C.D.M.F.), Department of Histopathology, St. Thomas's Hospital (A.P.D.T., C.D.M.F.), London, U.K.; Department of Pathology (A.P.D.T.), Hospital of Conegliano Veneto, Conegliano Veneto, Italy; and Pathology Department (P.T.N.), Memorial Hospital, Darlington, U.K.

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6 cases, 2 F, 4 M
35-82 years, 2-25 cm
shoulder (3), arm (2), back (1)
subcutis (5), intramuscular
multiple recurrences (3)
dedifferentiation, MTS (1)
spindle cells with mild to moderate atypia + atypical lipogenic component
desmin focal + (5)
CD34 focal + (2)

Modern Pathology (2010) 23, 729–736

Well-differentiated spindle cell liposarcoma ('atypical spindle cell lipomatous tumor') does not belong to the spectrum of atypical lipomatous tumor but has a close relationship to spindle cell lipoma: clinicopathologic, immunohistochemical, and molecular analysis of six cases

Thomas Mentzel[1], Gabriele Palmedo[2] and Cornelius Kuhnen[2]

[1]Dermatopathologie, Friedrichshafen, Germany and [2]Institute of Pathology, Medical Center, Minden, Germany

Well-differentiated spindle cell liposarcoma represents a rare atypical/low-grade malignant lipogenic neoplasm that has been regarded as a variant of atypical lipomatous tumor. However, well-differentiated spindle cell liposarcoma tends to occur in subcutaneous tissue of the extremities, the trunk, and the head and neck region, contains slightly atypical spindled tumor cells often staining positively for CD34, and lacks an amplification of *MDM2* and/or *CDK4* in most of the cases analyzed. We studied a series of well-differentiated spindle cell liposarcomas arising in two female and four male patients (age of the patients ranged from 59 to 85 years). The neoplasms arose on the shoulder, the chest wall, the thigh, the lower leg, the back of the hand, and in paratesticular location. The size of the neoplasms ranged from 1.5 to 10 cm (mean: 6.0 cm). All neoplasms were completely excised. The neoplasms were confined to the subcutis in three cases, and in three cases, an infiltration of skeletal muscle was seen. Histologically, the variably cellular neoplasms were composed of atypical lipogenic cells showing variations in size and shape, and spindled tumor cells with slightly enlarged, often hyperchromatic nuclei. Multivacuolated lipoblasts were present in three neoplasms. Focal myxoid stromal changes were seen in three cases. Immunohistochemically, CD34 was at least focally positive in all cases, whereas scattered tumor cells only showed a nuclear expression of MDM2 in two neoplasms. FISH analysis revealed a deletion of the *Rb-1* gene in all six cases, whereas no *MDM2/CDK4* amplification was identified in all cases tested. Follow-up information was available in four cases (range from 4 to 24 months), and revealed a local recurrence in one case. Although well-differentiated spindle cell liposarcoma and atypical lipomatous tumor behave clinically similar, it can be speculated on the basis of clinicopathologic and molecular findings that well-differentiated spindle cell liposarcoma may constitute an independent entity rather than a morphologic variant of atypical lipomatous tumor, and may represent the atypical/low-grade counterpart of spindle cell lipoma.
Modern Pathology (2010) **23**, 729–736; doi:10.1038/modpathol.2010.66; published online 12 March 2010

Keywords: liposarcoma; atypical lipomatous tumor; spindle cell liposarcoma; spindle cell lipoma; immunohistochemistry; cytogenetics

Atypical and malignant lipogenic neoplasms represent the most common soft tissue sarcoma in adults, accounting for approximately 20% of all sarcomas. Liposarcoma is currently subclassified into five main subtypes, including atypical lipomatous tumor/well-differentiated liposarcoma, dedifferentiated liposarcoma, myxoid liposarcoma,

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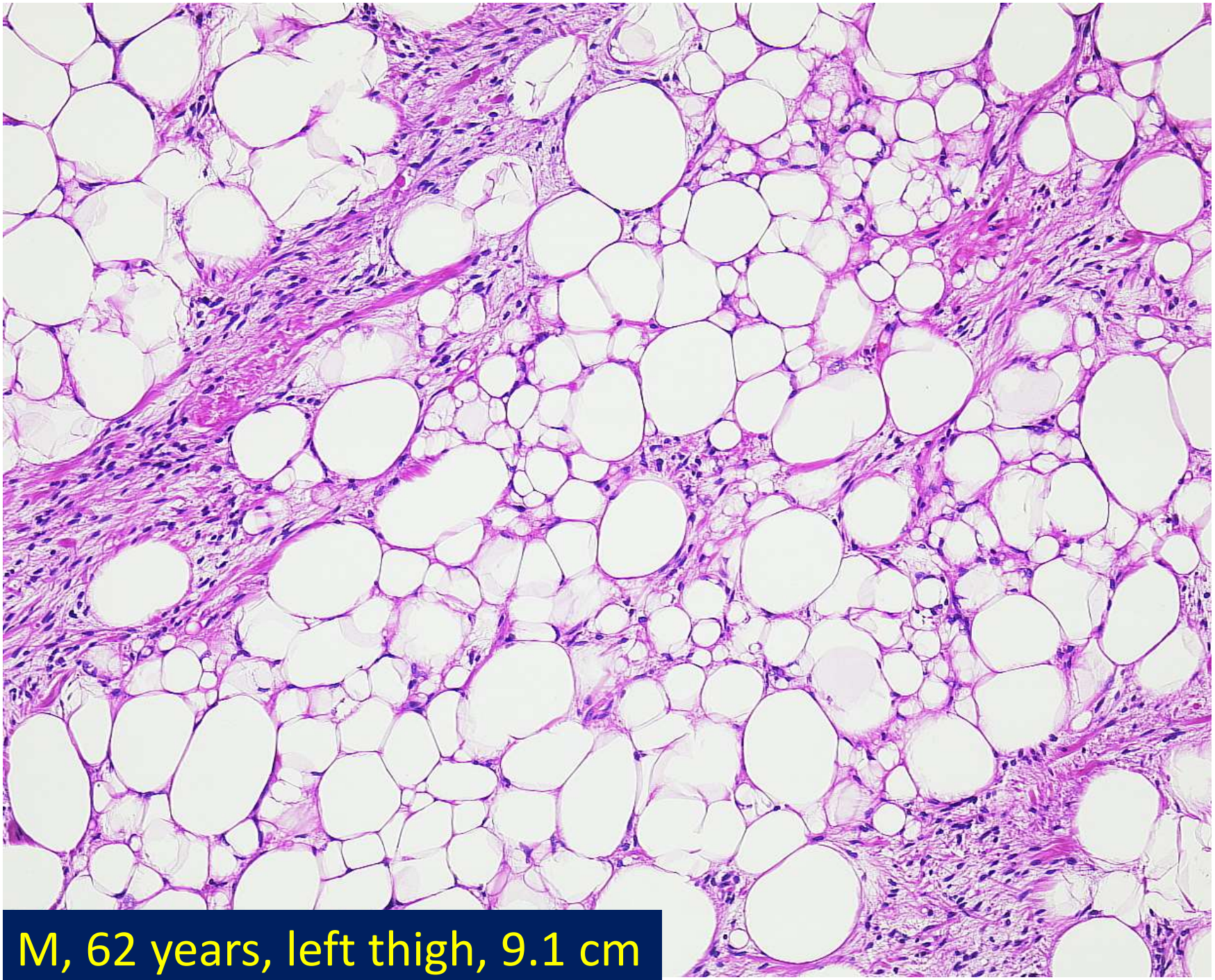
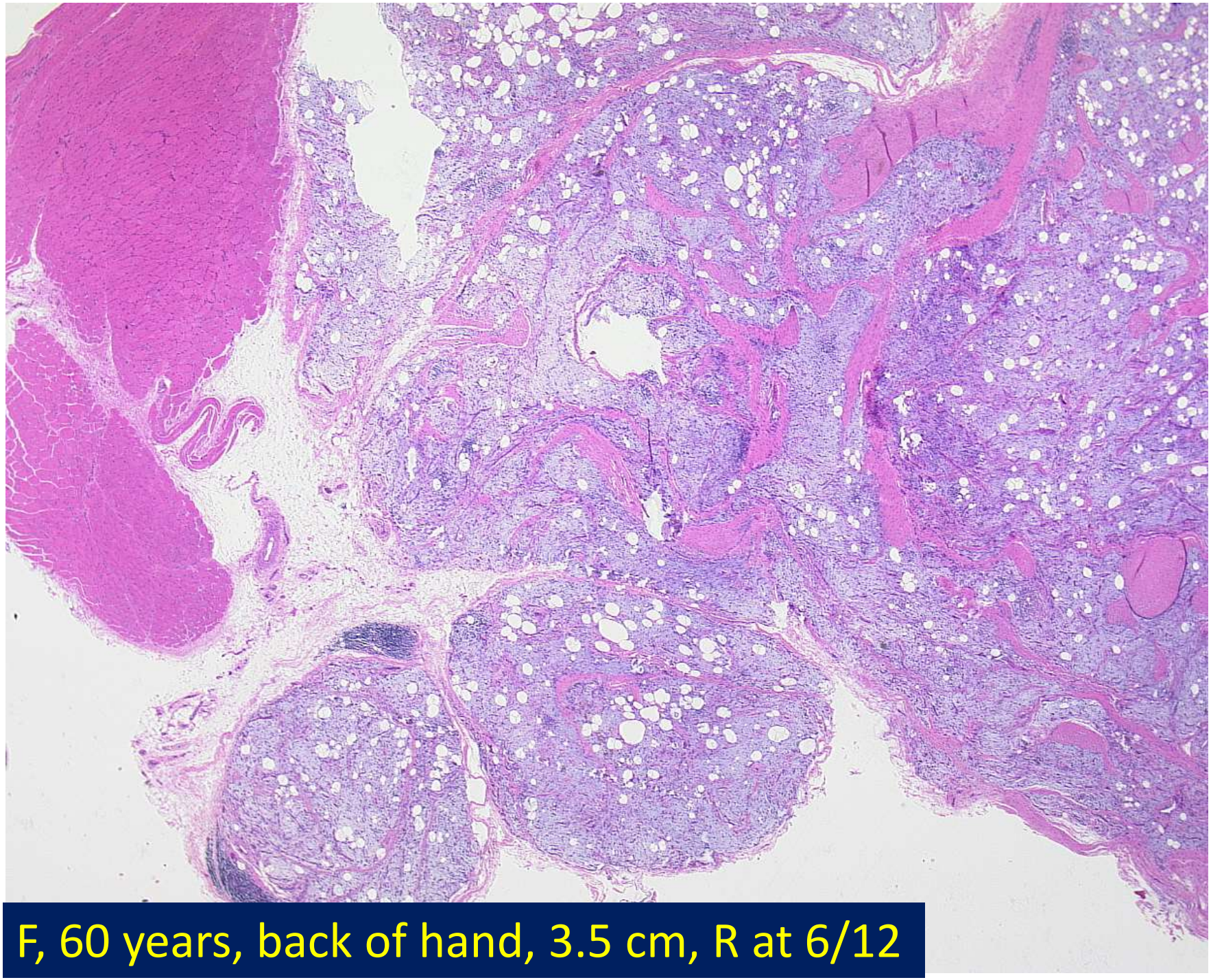
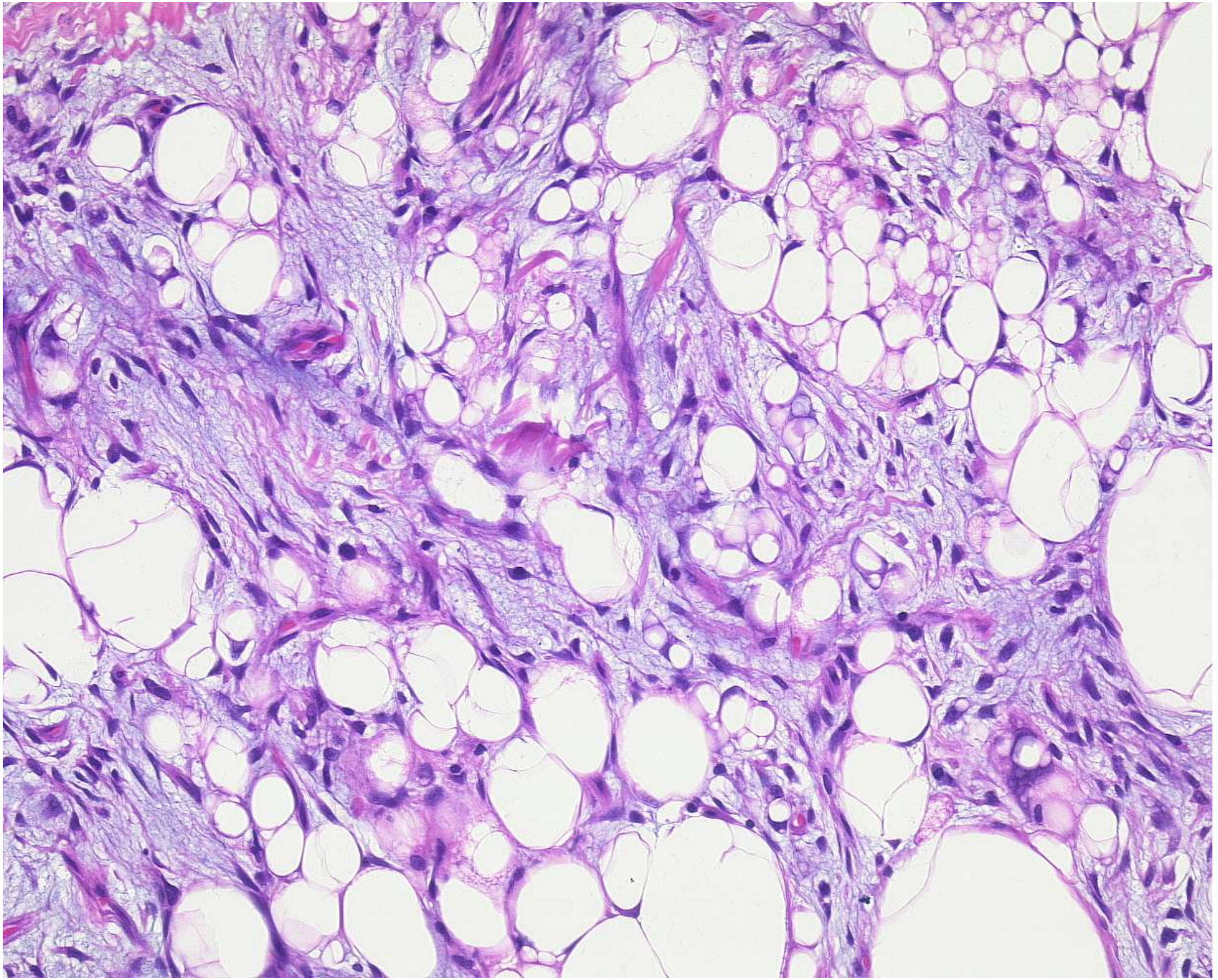
Received 22 October 2009; revised 28 January 2010; accepted 18 January 2010; published online 12 March 2010

2 F, 4 M, 59-85 years
shoulder, trunk, thigh, lower leg, hand, paratesticular
1 out of 4 cases recurred locally
1.5-10 cm, subcutis (3) deep soft tissue (3)
CD 34 focally +
Rb-1 deletion (6)
no *MDM2/CDK4* amplification


M, 62 years, left thigh, 9.1 cm



F, 60 years, back of hand, 3.5 cm, R at 6/12



ORIGINAL ARTICLE

Atypical Spindle Cell Lipomatous Tumor

Clinicopathologic Characterization of 232 Cases Demonstrating a Morphologic Spectrum

Brian Marifio-Enriquez, MD, PhD, Alessandra F. Nascimento, MD,* Azra H. Ligon, PhD,* Cherwei Liang, MD,† and Christopher D.M. Fletcher, MD, FRCPath**

t: The classification of atypical adipocytic neoplasms ndle cell features remains challenging. To better define epory of low-grade lipomatous neoplasms, we present he clinical, histologic, and immunohistochemical chara- es of a large series of 232 atypical spindle cell lipomatous

The lesions affected 140 males and 92 females, at an age of 56 years (range, 6–87 y), clinically presenting as ter- or enlarging mass with a median size of 5 cm. The ion distribution of the tumors was wide, predominating in ks and limb girdles (147 cases, 63%), mainly in the lunda - (17% and 11%, respectively), with equal distribution subcutaneous and deeper locations. Microscopic ex- on revealed a spectrum of histologic appearances. All nsisted of a poorly marginated proliferation of mildly spindle cells set in a fibrous or myxoid stroma, with a prominent admixed adipocytic component showing n to adipocyte size and scattered bizarre stromal, fre- with univacuolated or multivacuolated lipoblasts. Tu- linarity and the relative proportion of the different ents were very variable. Tumor margins were often ill with invasion into surrounding tissues. Two tumors morphologic features reminiscent of dedifferentiation. unohistochemistry, the neoplastic spindle cells expressed 54%), S100 protein (40%) and, less frequently, desmin Expression of Rb was lost in 57% of cases examined. and CDK4 were never coexpressed and FISH for amplification was consistently negative, highlighting biological differences from atypical lipomatous tumor/ ntiated liposarcoma. The morphologic differential di- of atypical spindle cell lipomatous tumor is broad, and

including spindle cell lipoma, diffuse neurofibroma, nonmyxoid type myofibroblastoma, dermatofibrosarcoma protuberans, fat-forming solitary fibrous tumor, and morphologically low grade malignant peripheral nerve sheath tumor. Most patients underwent surgical excision of the primary mass. With a median follow-up of 4 years (range, 1 mo to 20 y), 67% of patients (69/72) were alive with no evidence of recurrence or metastatic disease. Local recurrence of the tumor was observed in 12% of patients (9 out of 72, multiple in 3 of them) at intervals between 6 months and 17 years after resection of the primary tumor. None of the patients developed tumor metastasis or died of disease. Identification of the neoplastic adipocytic component admixed with spindle cells, and recognition of the range of histologic appearances are key for the diagnosis of atypical spindle cell lipomatous tumor. Whereas the risk of metastatic dissemination is minimal, there is a non-negligible risk for local recurrence (13%) which warrants surgical resection with clear margins whenever feasible.

Key Words: soft tissue, liposarcoma, atypical lipomatous tumor, spindle cell liposarcoma, dedifferentiated liposarcoma, atypical spindle cell lipomatous tumor

(*Am J Surg Pathol* 2007;31:1834–1844)

Atypical spindle cell lipomatous neoplasms were first described by Dei Tos et al[1] in 1994, in a series of 6 cases designated spindle cell liposarcoma. Microscopically, spindle cell liposarcoma shows distinctive morphology, with atypical spindle cells and a variably prominent adipocytic component. Locally aggressive growth and local recurrence were common, whereas dedifferentiation and metastasis occurred rarely.[1] At that time, spindle cell liposarcoma was considered a morphologic variant of well-differentiated liposarcoma, given its overlapping clinicopathologic characteristics and distinct morphology. Additional examples of spindle cell lipomatous tumor have been reported since, as isolated case reports or as part of small series of atypical lipomatous tumor/well-differentiated liposarcoma.[2–5]

Over the last 2 decades, the classification of atypical and malignant adipocytic tumors has evolved, thanks to a better biological understanding, with substantial con-

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92 F, 140 M, 6-87 years
median size 5 cm
limbs, limb girdles (63%)
head / neck (10%)
genital area (7%)
trunk (6%), back (6%)…
poorly marginated
atypical spindled cells +
atypical lipogenic cells
variable cellularity
local recurrence 12%
(3 x multiple)

subcutis > deep soft tissues >> visceral
admixture of atypical spindled + lipogenic cells
low cellularity (62%) > high cellularity (38%)
mild atypia (52%) > prominent atypia (28%)
uni- or multivacuolated lipoblasts (45%)
rare mitoses, no tumour necrosis
purely myxoid to collagenous stroma
CD 34 + (64%), S-100 + (40%), desmin + (22%),
Rb loss (57%), no tumour with MDM2 **and** CDK4 +
FISH analysis: no *MDM2/CDK4* amplification
loss of Rb-1 locus in 71%
monosomy 7 in 43%

DD atypical spindle cell lipomatous Tumour

spindle cell lipoma:	elderly male patients, neck, encapsulated, no atypia
ALT:	*MDM2 / CDK4* amplification no *Rb-1* deletion
DDLS:	deep soft tissue abrupt transition, more atypia *MDM2 / CDK4* amplification
spindle cell myxoid LS:	young patients, vasculature t(12;16), t(12;22)

(Alaggio R et al. AJSP 2009; 33: 645)

lipomatous SFT, diffuse neurofibroma, DFSP, mammary-type myofibroblastoma, MPNST

"Atypical" Pleomorphic Lipomatous Tumor

A Clinicopathologic, Immunohistochemical and Molecular Study of 21 Cases, Emphasizing its Relationship to Atypical Spindle Cell Lipomatous Tumor and Suggesting a Morphologic Spectrum (Atypical Spindle Cell/Pleomorphic Lipomatous Tumor)

David Creytens, MD, PhD,*† Thomas Mentzel, MD, PhD,‡ Liesbeth Ferdinande, MD, PhD,*† Evelyne Lecoutere, MD,* Joost van Gorp, MD, PhD,§ Lilit Atanesyan,‖ Karel de Groot,‖ Suvi Savola, PhD,‖ Nadine Van Roy,†¶ Jo Van Dorpe, MD, PhD,*† and Uta Flucke, MD, PhD#

Abstract: The classification of the until recently poorly explored group of atypical adipocytic neoplasms with spindle cell features, for which recently the term atypical spindle cell lipomatous tumor (ASLT) has been proposed, remains challenging. Recent studies have proposed ASLT as a unique entity with (in at least a significant subset of cases) a specific genetic background, namely deletions/losses of 13q14, including *RB1* and its flanking genes *RCBTB2*, *DLEU1*, and *ITMB2*. Similar genetic aberrations have been reported in pleomorphic liposarcomas (PLSs). This prompted us to investigate a series of 21 low-grade adipocytic neoplasms with a pleomorphic lipoma–like appearance, but with atypical morphologic features (including atypical spindle cells, pleomorphic [multinucleated] cells, pleomorphic lipoblasts and poor circumscription), for which we propose the term "atypical" pleomorphic lipomatous tumor (APLT). Five cases of PLS were also included in this study. We used multiplex ligation-dependent probe amplification to evaluate genetic changes of 13q14. In addition, array-based comparative genomic hybridization was performed on 4 APLTs and all PLSs. Multiplex ligation-dependent probe amplification showed consistent loss of *RB1* and its flanking gene *RCBTB2* in all cases of APLT. This genetic alteration was also present in all PLSs, suggesting genetic overlap, in addition to morphologic overlap, with APLTs. However, array-based comparative genomic hybridization demonstrated more complex genetic alterations with more losses and gains in PLSs compared with APLTs. APLTs arose in the subcutis (67%) more frequently than in the deep (subfascial) soft tissues (33%). With a median follow-up of 42 months, recurrences were documented in 2 of 12 APLTs for which a long follow-up was available. Herein, we also demonstrate that APLTs share obvious overlapping morphologic, immunohistochemical, genetic and clinical characteristics with the recently defined ASLLT, suggesting that they are related lesions that form a spectrum (atypical spindle cell/pleomorphic lipomatous tumor).

Key Words: "atypical" pleomorphic lipomatous tumor, atypical spindle cell lipomatous tumor, pleomorphic liposarcoma, *RB1*, MLPA

(*Am J Surg Pathol* 2017;00:000–000)

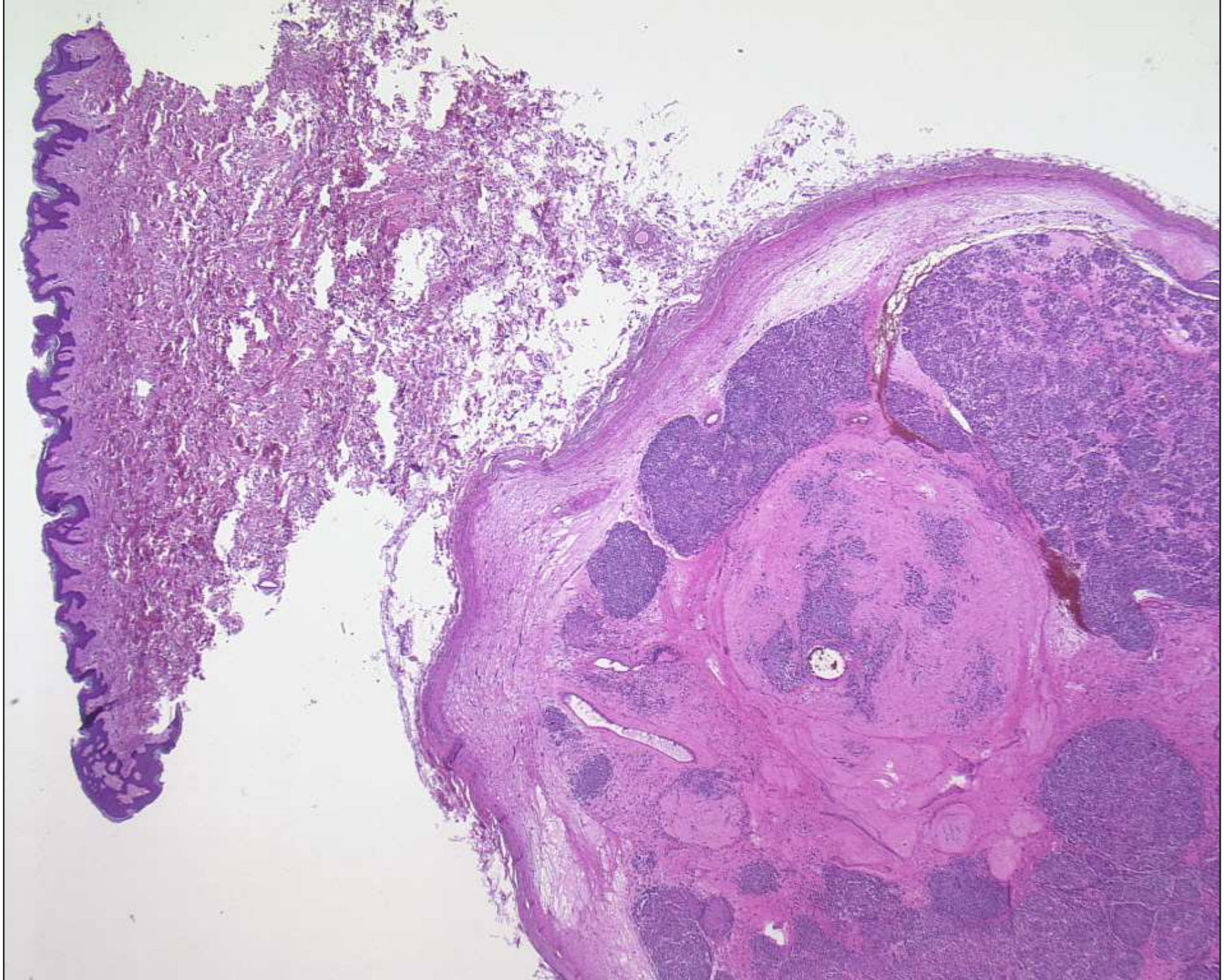
Liposarcomas are the most common sarcomas in adults. They are a heterogeneous family of tumors consisting of 4 major well-defined entities. In decreasing frequency, the 4 entities are atypical lipomatous tumor (ALT),

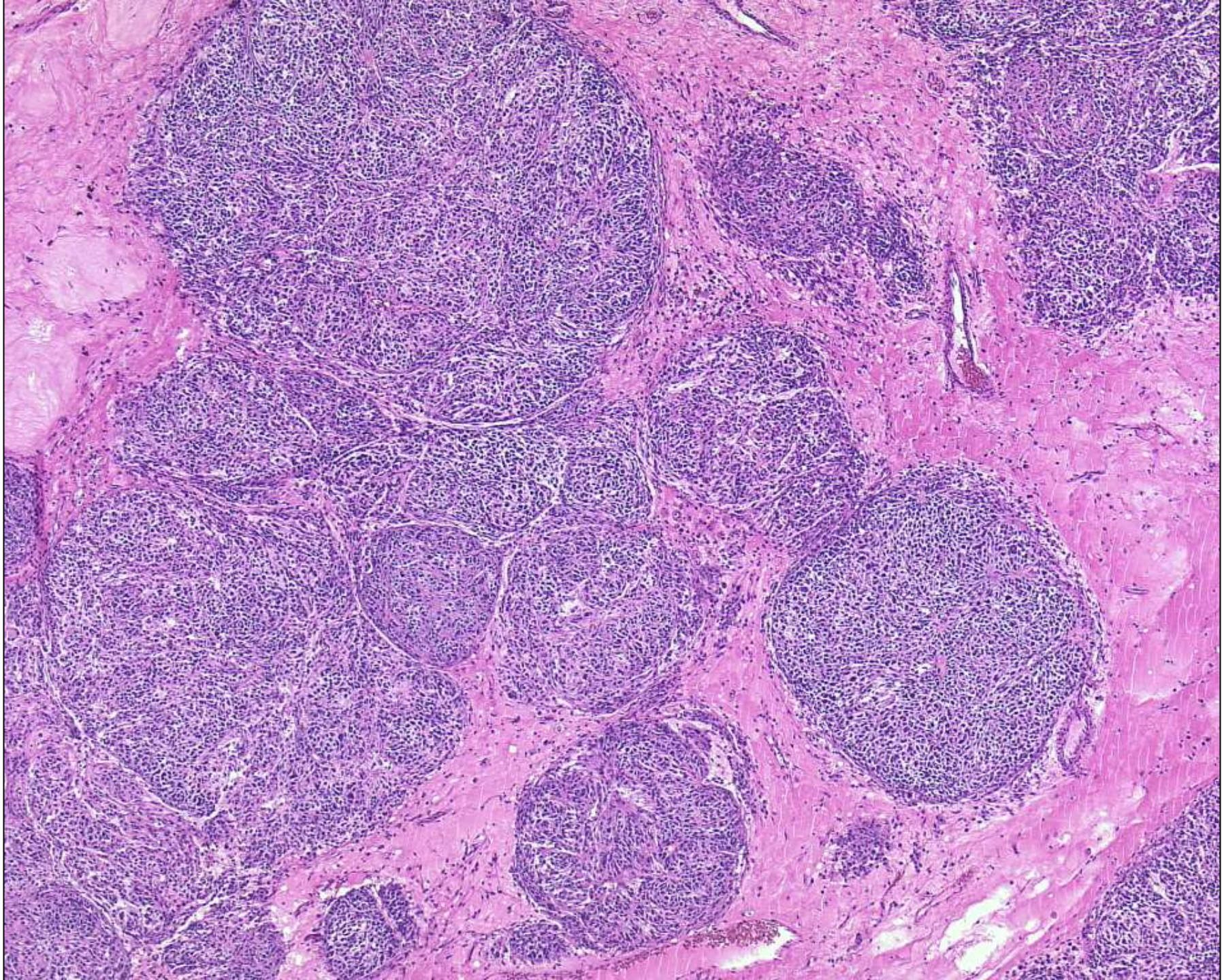
Conclusions Case 8

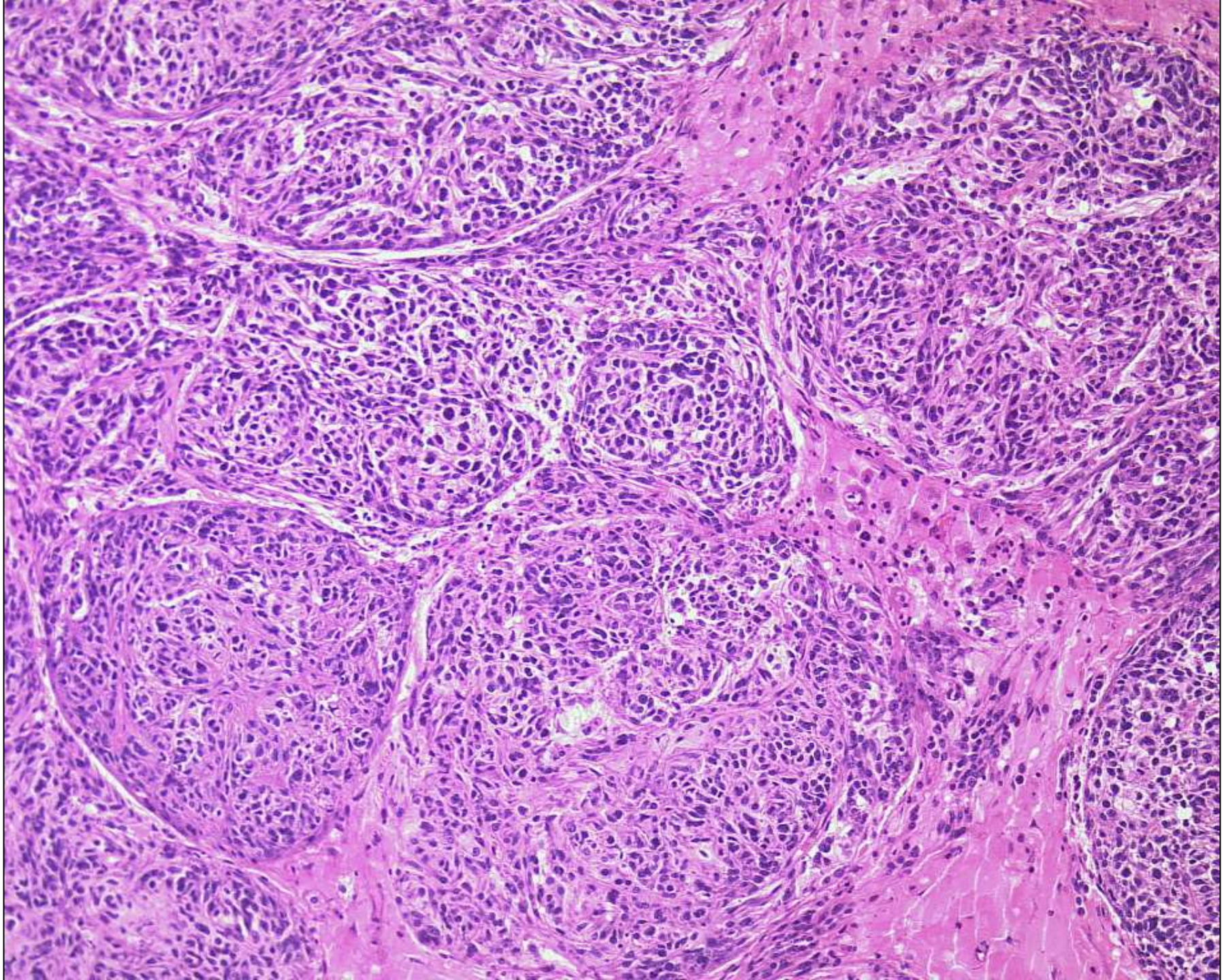
ASCLTs and APLT are…
distinct categories of adipocytic neoplasms
represent clinically low-grade neoplasms
require surgical excision with clear margins
low risk for local recurrence
very low risk for dedifferentiation
often adult males with predilection for the limbs
variable proportions of atypical spindled cells,
adipocytes, lipoblasts myxoid/coll. stroma
CD 34 +, Rb -, MDM2 -, CDK4 -

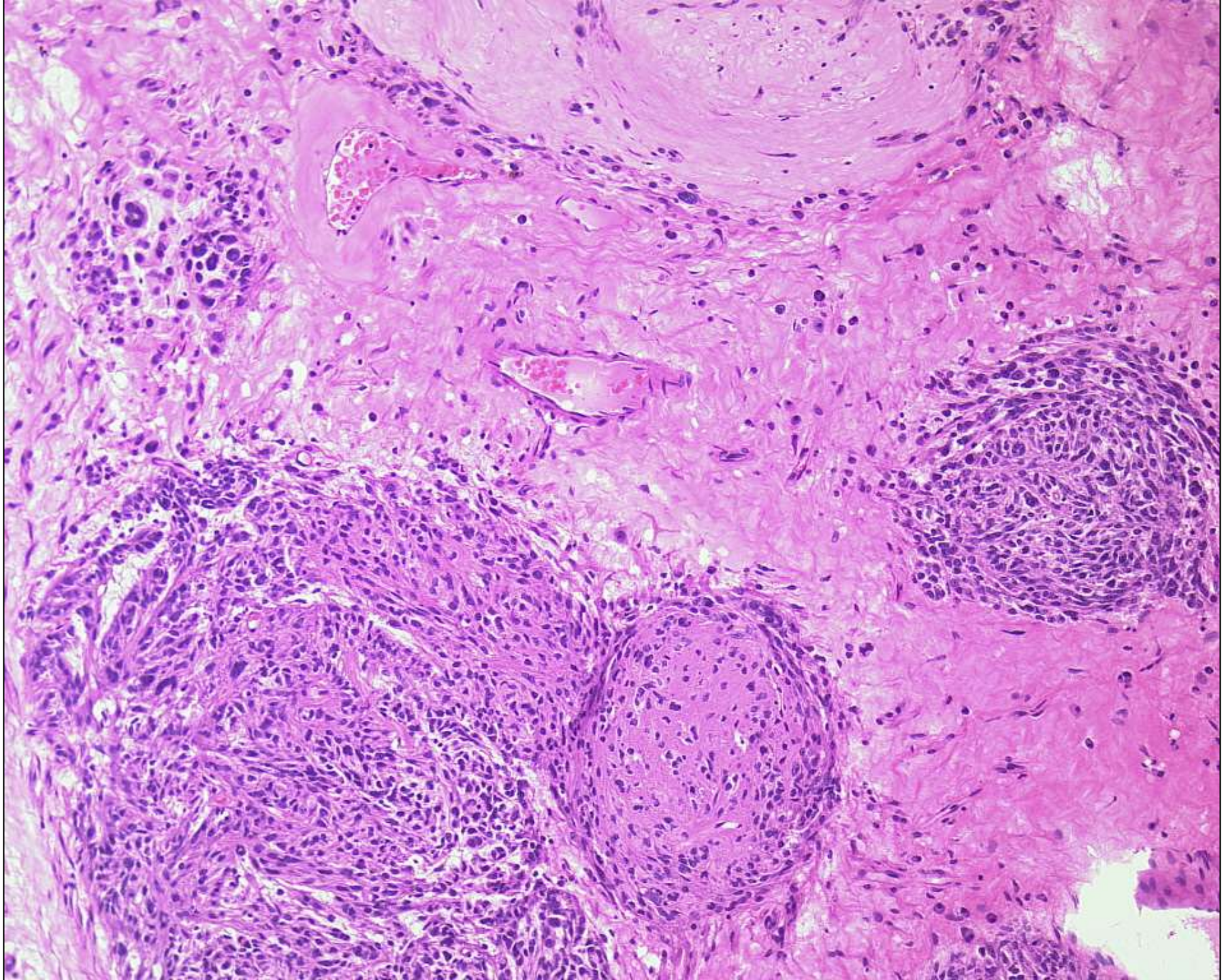
Case 9: Clinical Findings

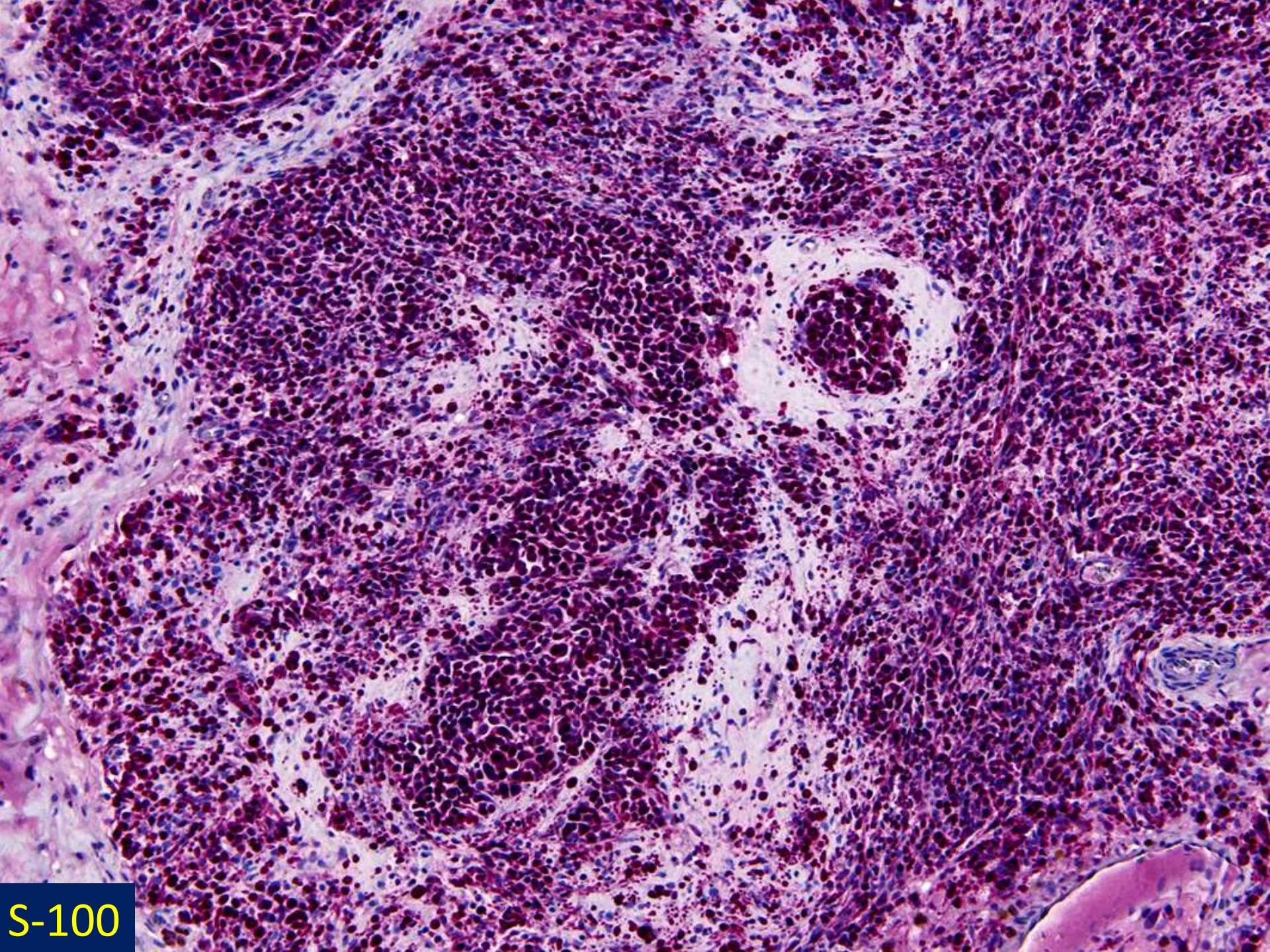
- F, 57 years
- left thigh
- 2 x 1.5 x 1 cm
- subcutaneous lesion







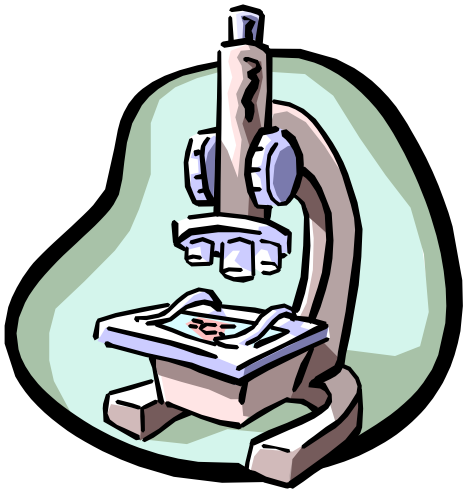



S-100

Pathological Findings

encapsulated epithelioid tumour
nested arrangement of tumour cells
uniform nuclei, small nucleoli
hyalinised connective tissue
vessels with hyalinised walls
S-100 +, Sox 10 +
Melan-A -, HMB45 -
Pancytokeratin -

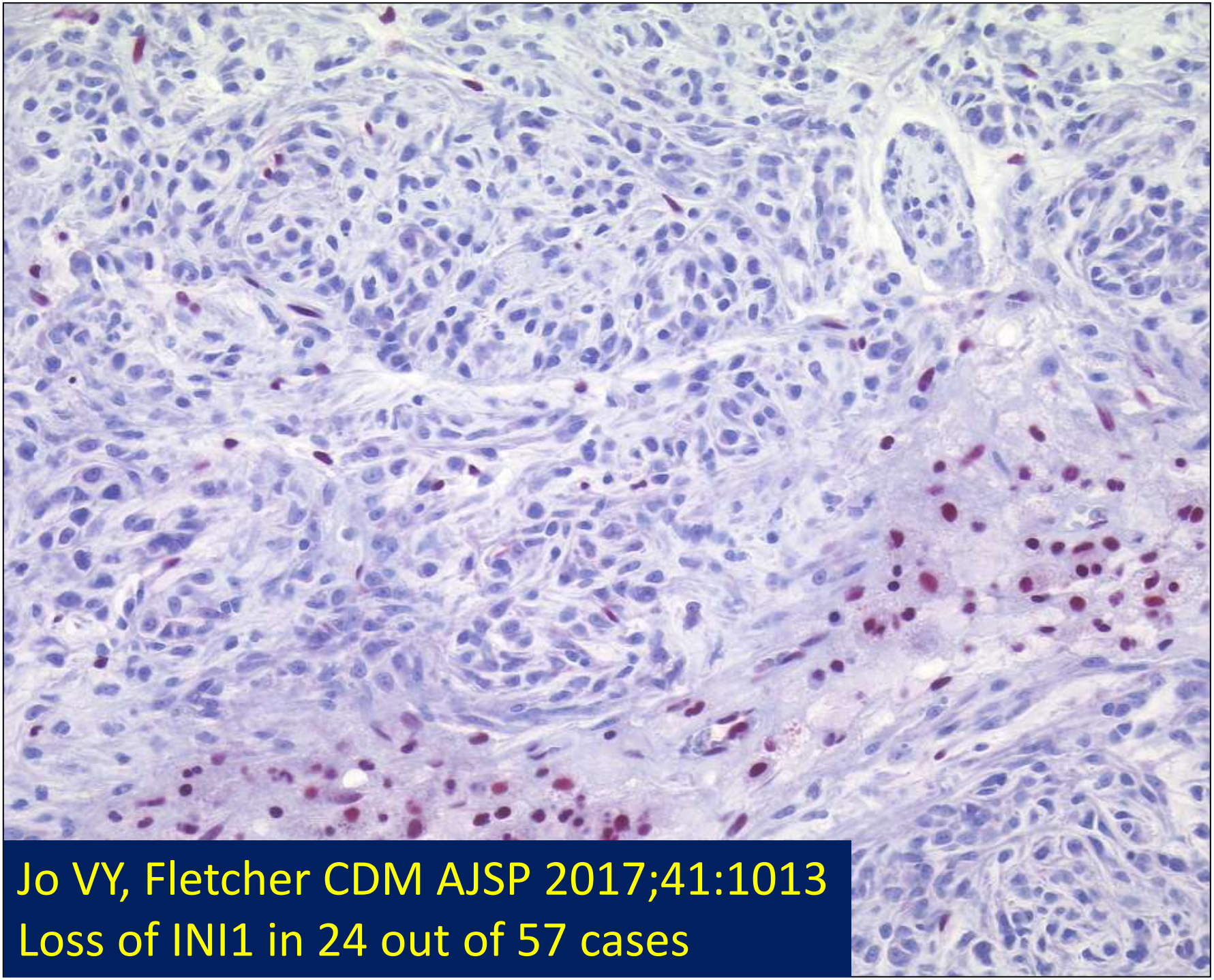
Diagnosis Case 9



epithelioid Schwannoma

epithelioid Schwannoma

rare, dermis, subcutis
F > M, middle aged adults
distal extremities, trunk, painless nodule
encapsulated, multinodular, nested growth
uniform epithelioid cells, scattered spindled cells
mild nuclear atypia may be present
may show myxoid stromal changes
S-100 +, Sox 10 +, GFAP +
loss of INI1 in 42% (AJSP 2017; 41: 1013)
may recur in a nondestructive fashion
very rarely malignant transformation
(AJSP 2017; 41: 1013)

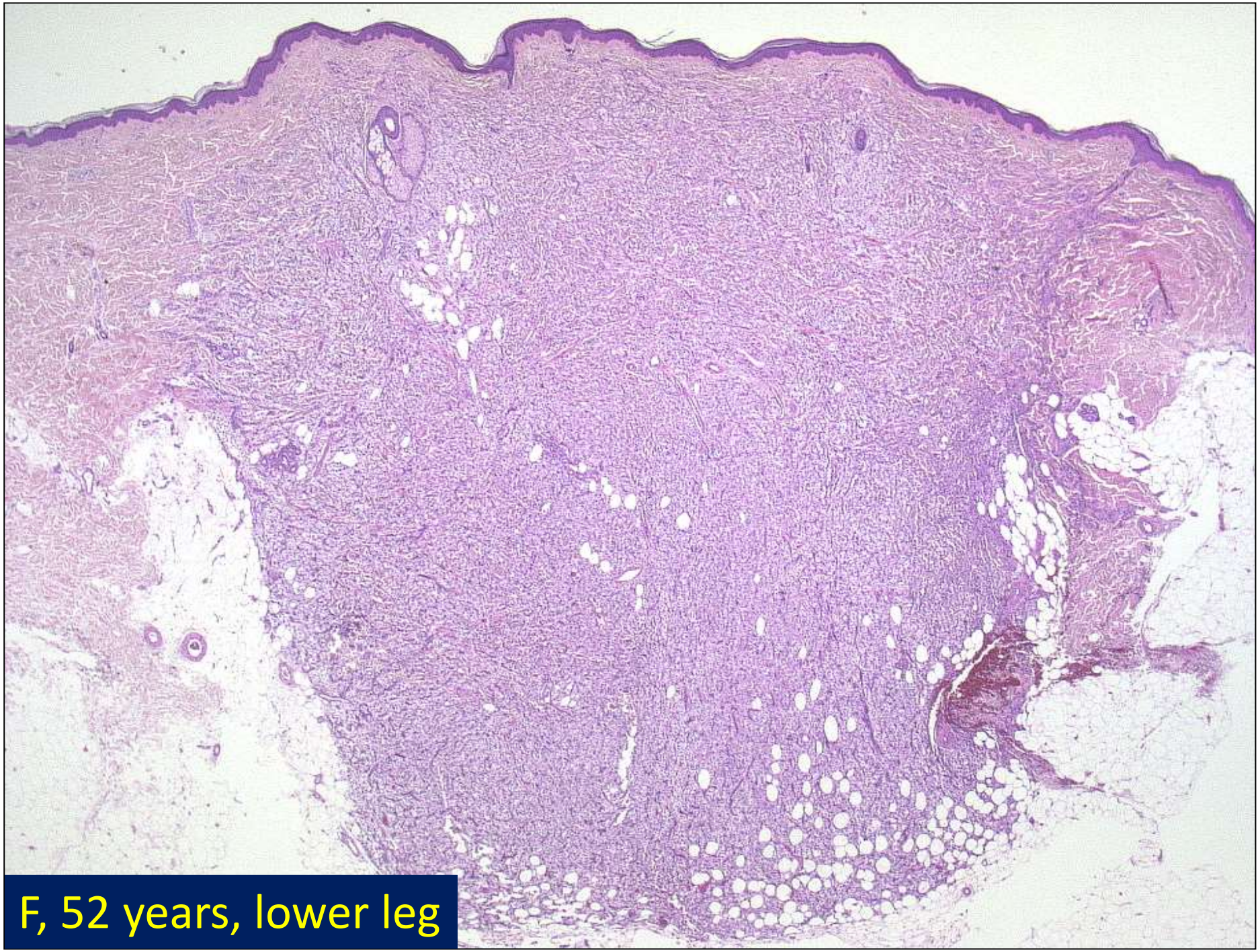

Jo VY, Fletcher CDM AJSP 2017;41:1013
Loss of INI1 in 24 out of 57 cases

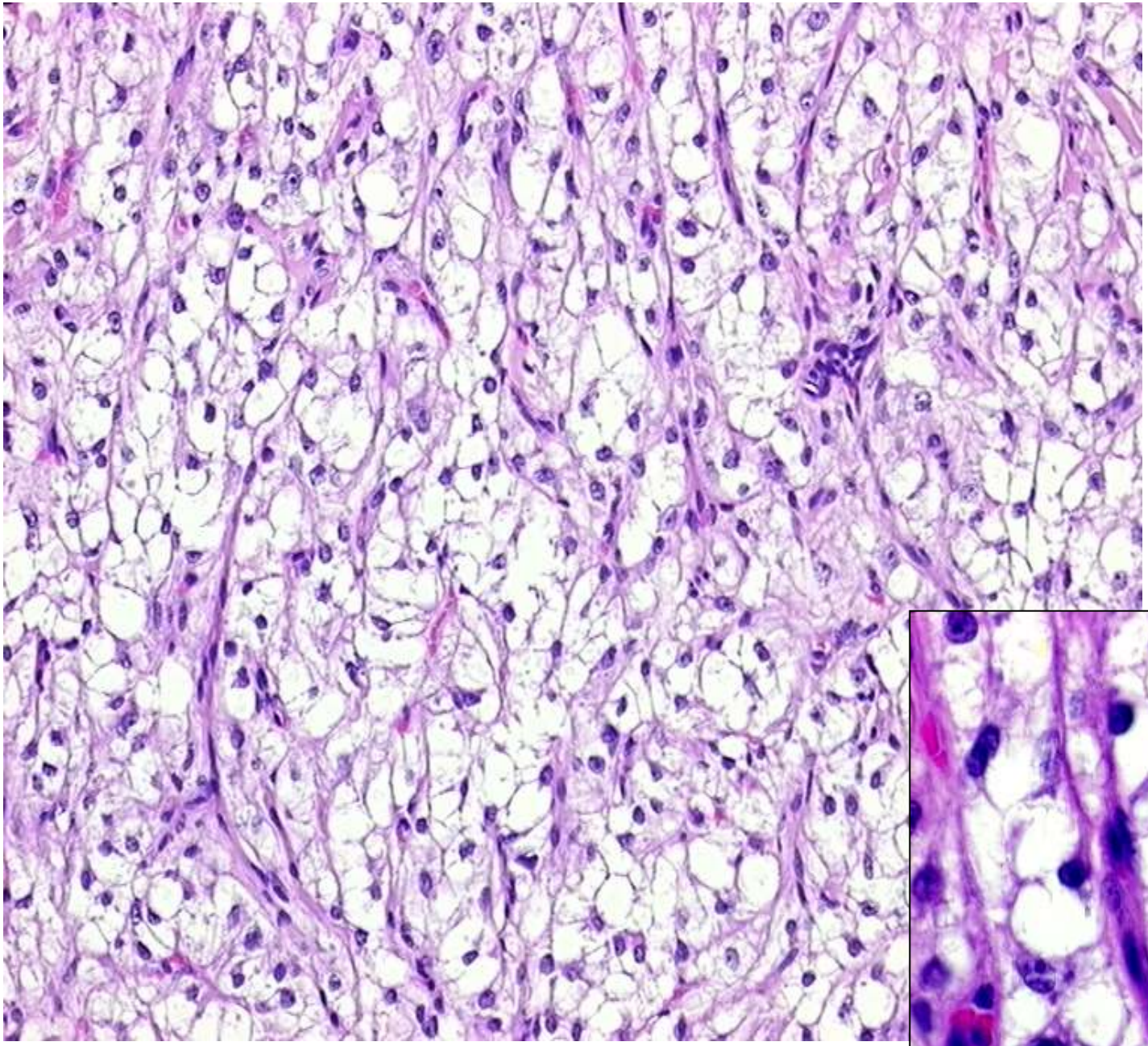
DD: epithelioid Schwannoma

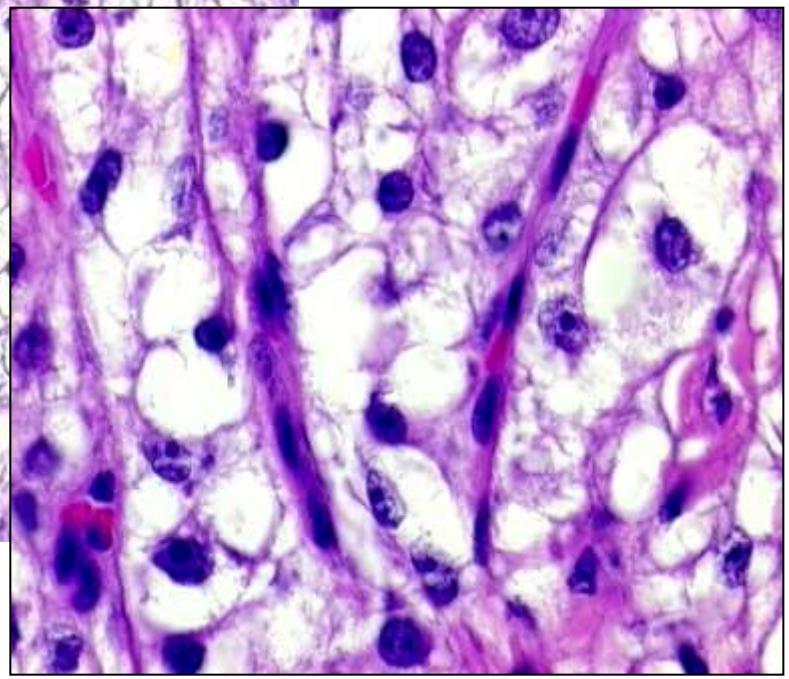
epithelioid MPNST: deep soft tissue, infiltrative
significant atypia, loss of INI1 in 50%

myoepithelioma: unencapsulated
more heterogenous
pancytokeratin +/-, EMA +/-

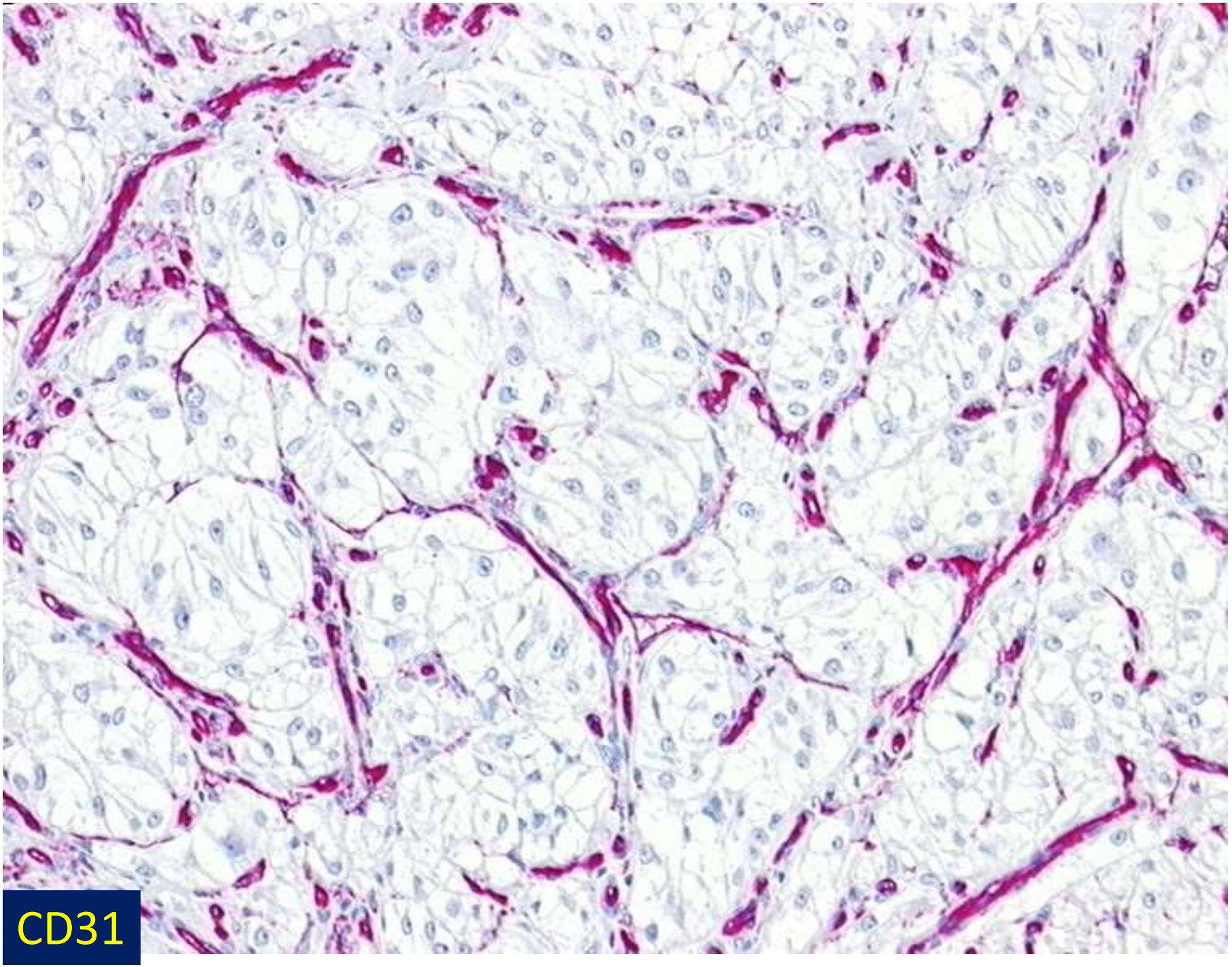
melanocytic neoplasms: unencapsulated
Melan-A +, HMB-45 +/-

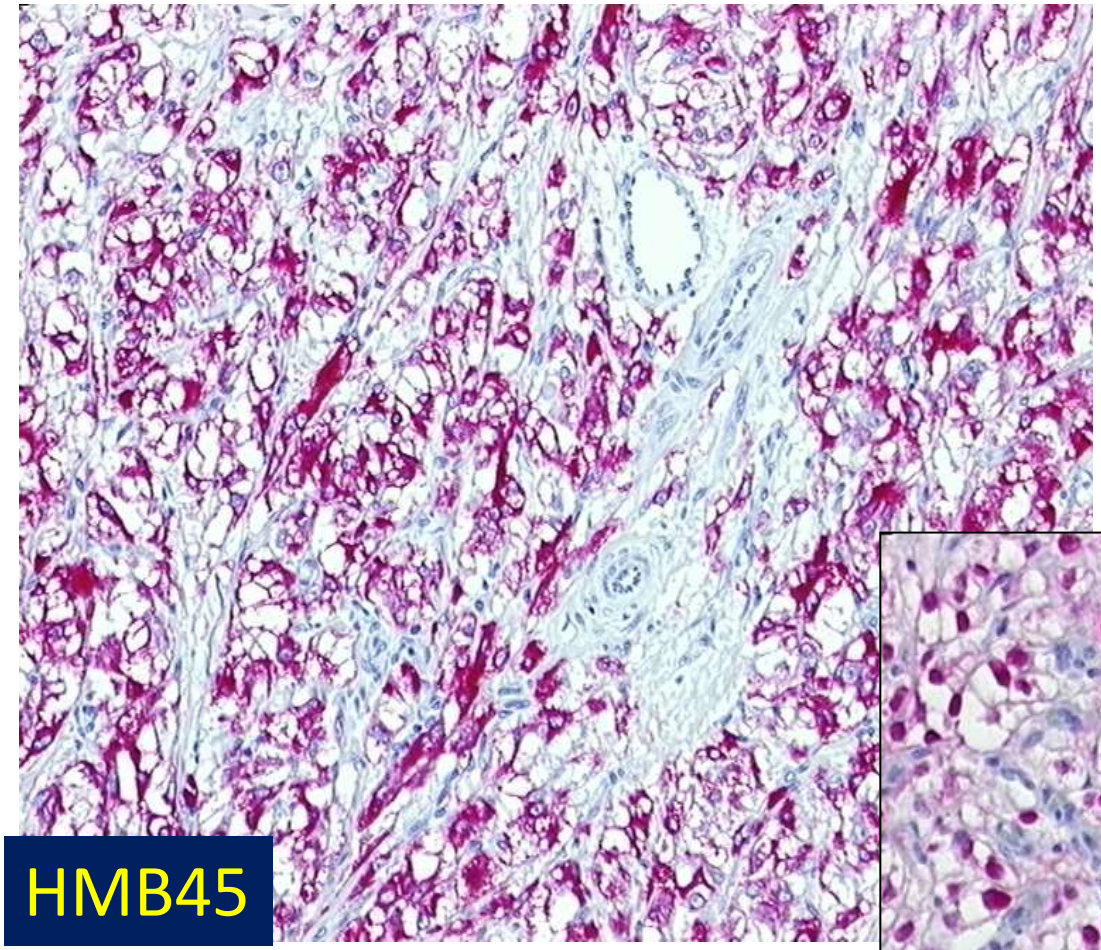

F, 52 years, lower leg

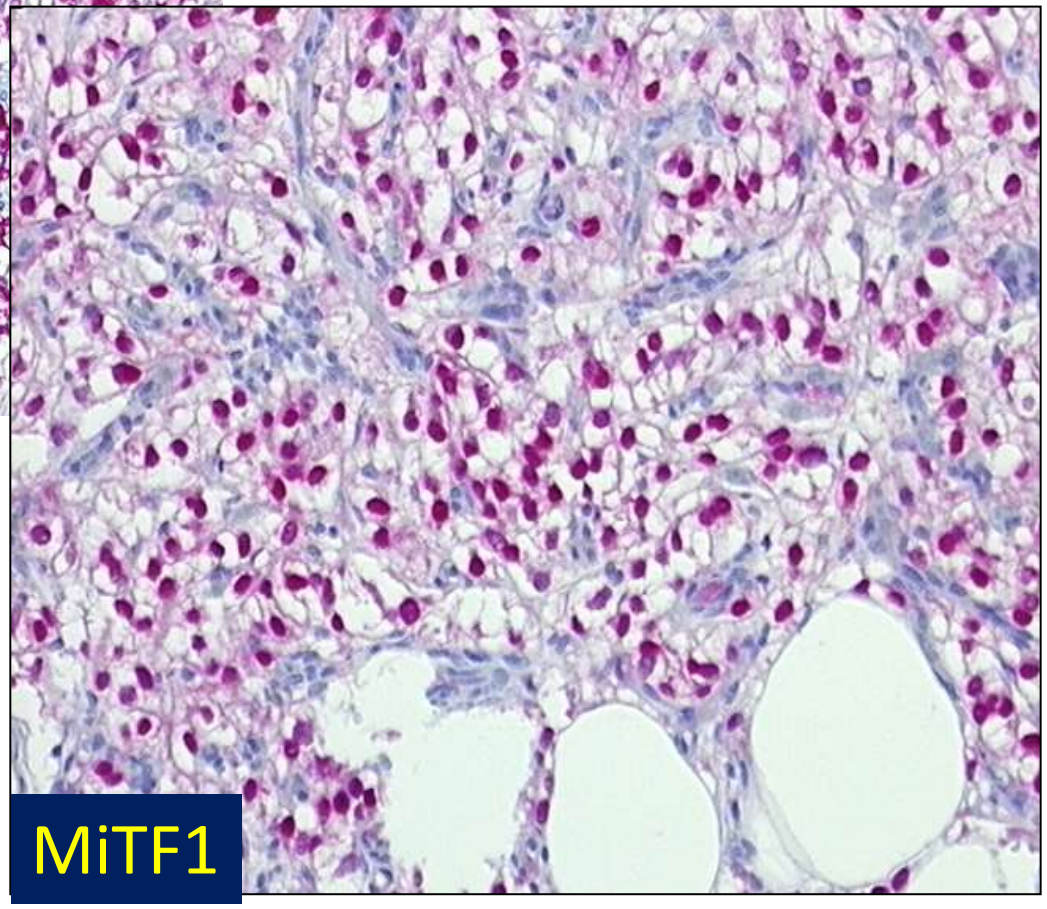


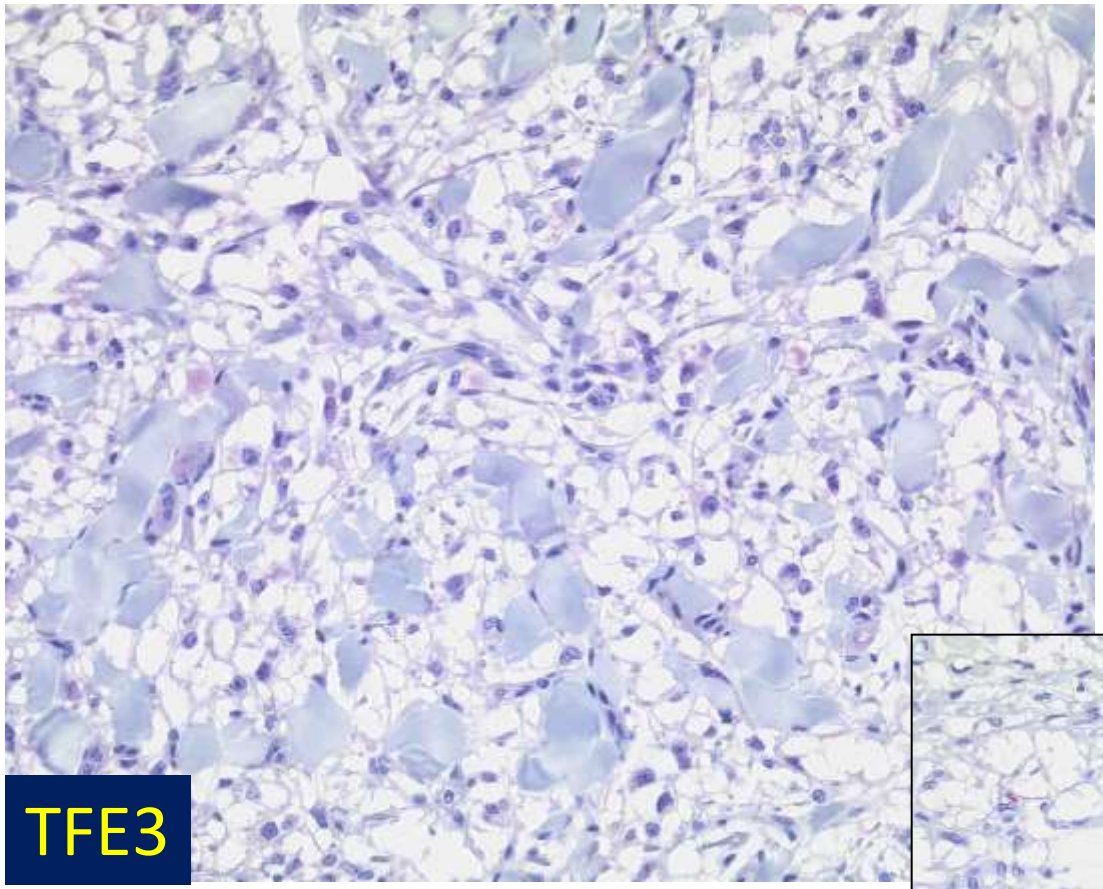


nested growth pattern

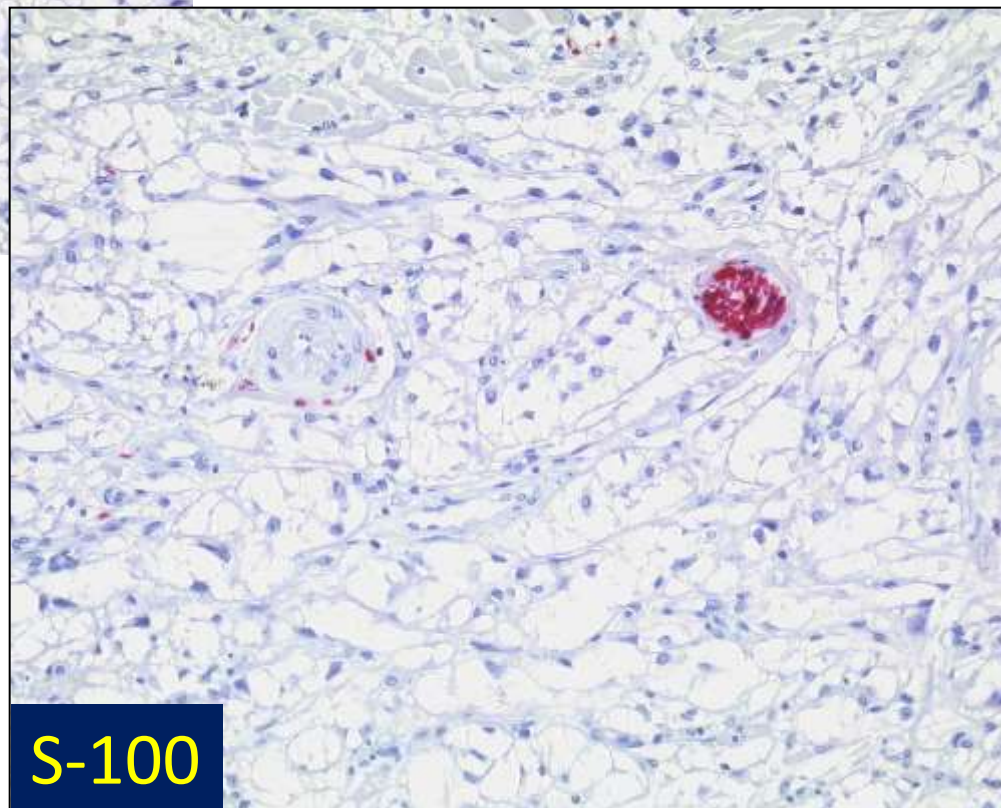

CD31


HMB45


MiTF1



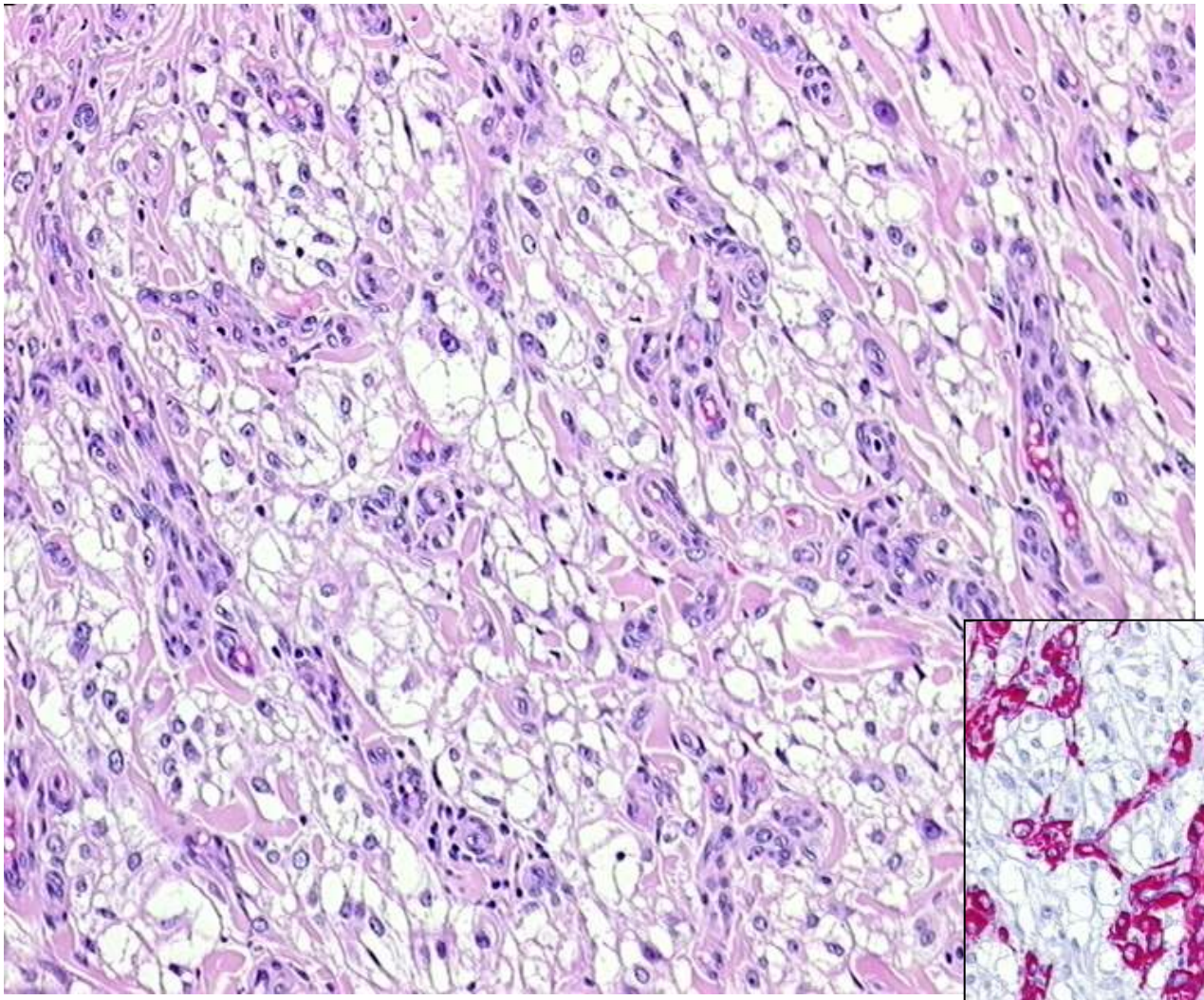
Diagnosis: cutaneous clear cell PEComa

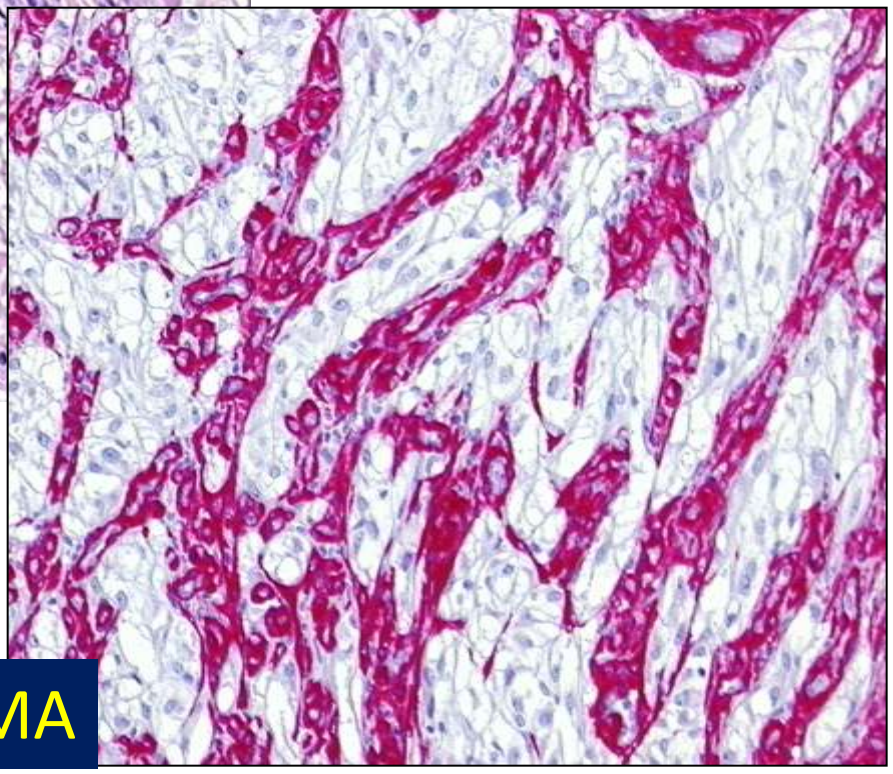


cutaneous PEComa*

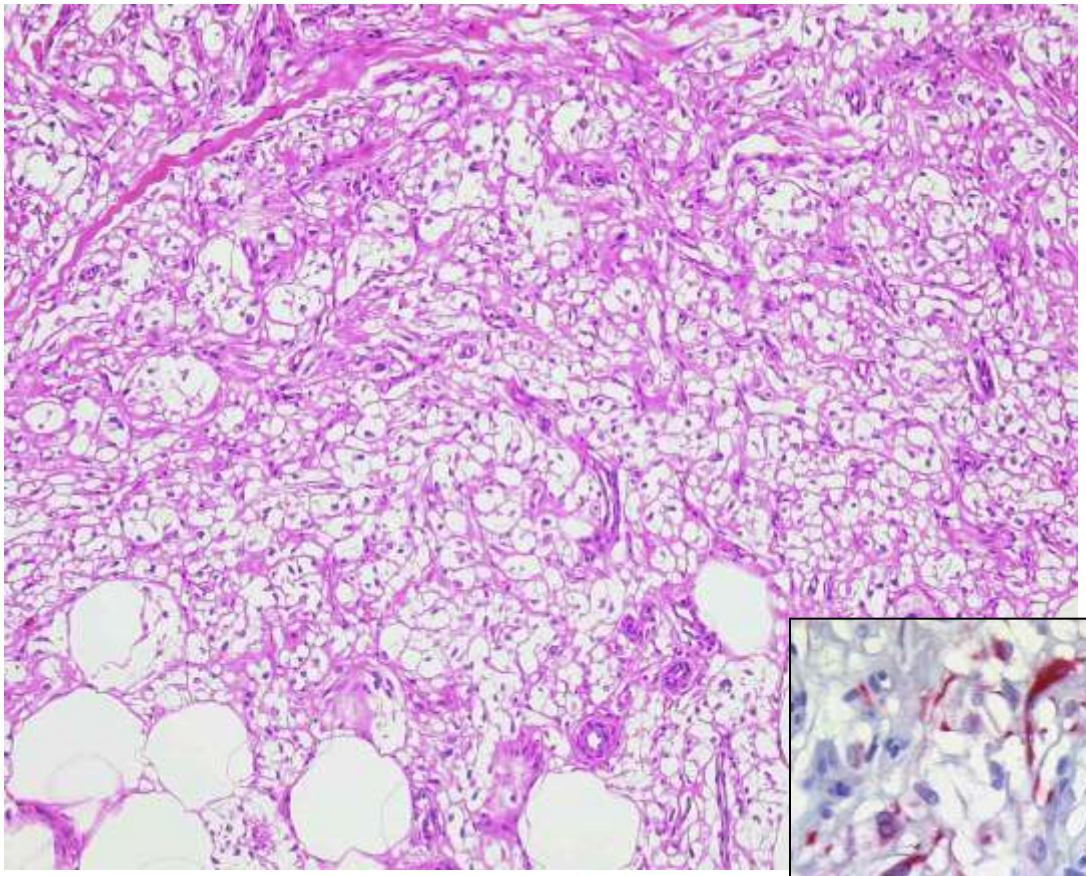
- 15 F, 2 M, 15-81 years, no tuberous sclerosis
- 15 x extremities (lower > upper), 2 x back
- dermal lesions, extension into subcutis
- network of thin-walled capillaries
- perivascular / trabecular growth
- clear > granular, eosinophilic tumour cells
- HMB45 +, MiTF1 +, NKIC3 +, S-100 -
- ASMA + (2), Desmin + (6), CK -, CD68 -/+
- biologically rather benign

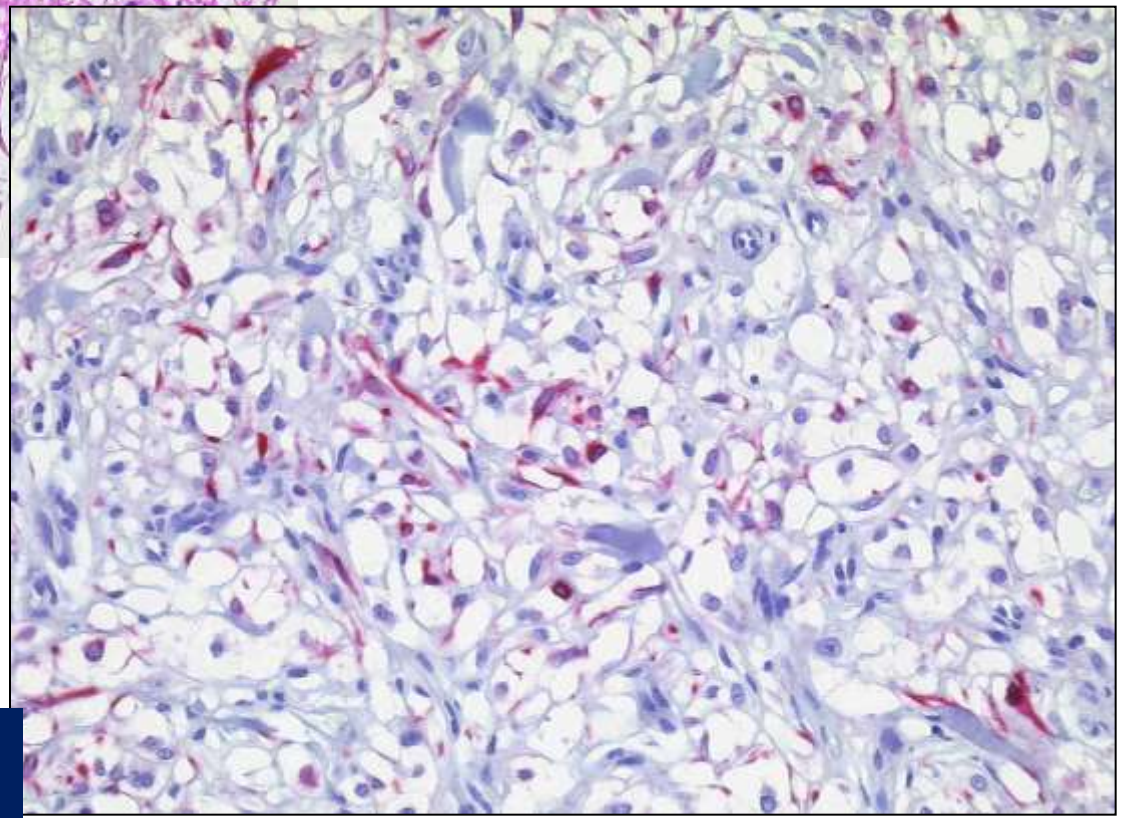
*** Mentzel T et al. Histopathology 2005; 46: 498**
Liegl B et al. AJSP 2008; 32: 608





ASMA

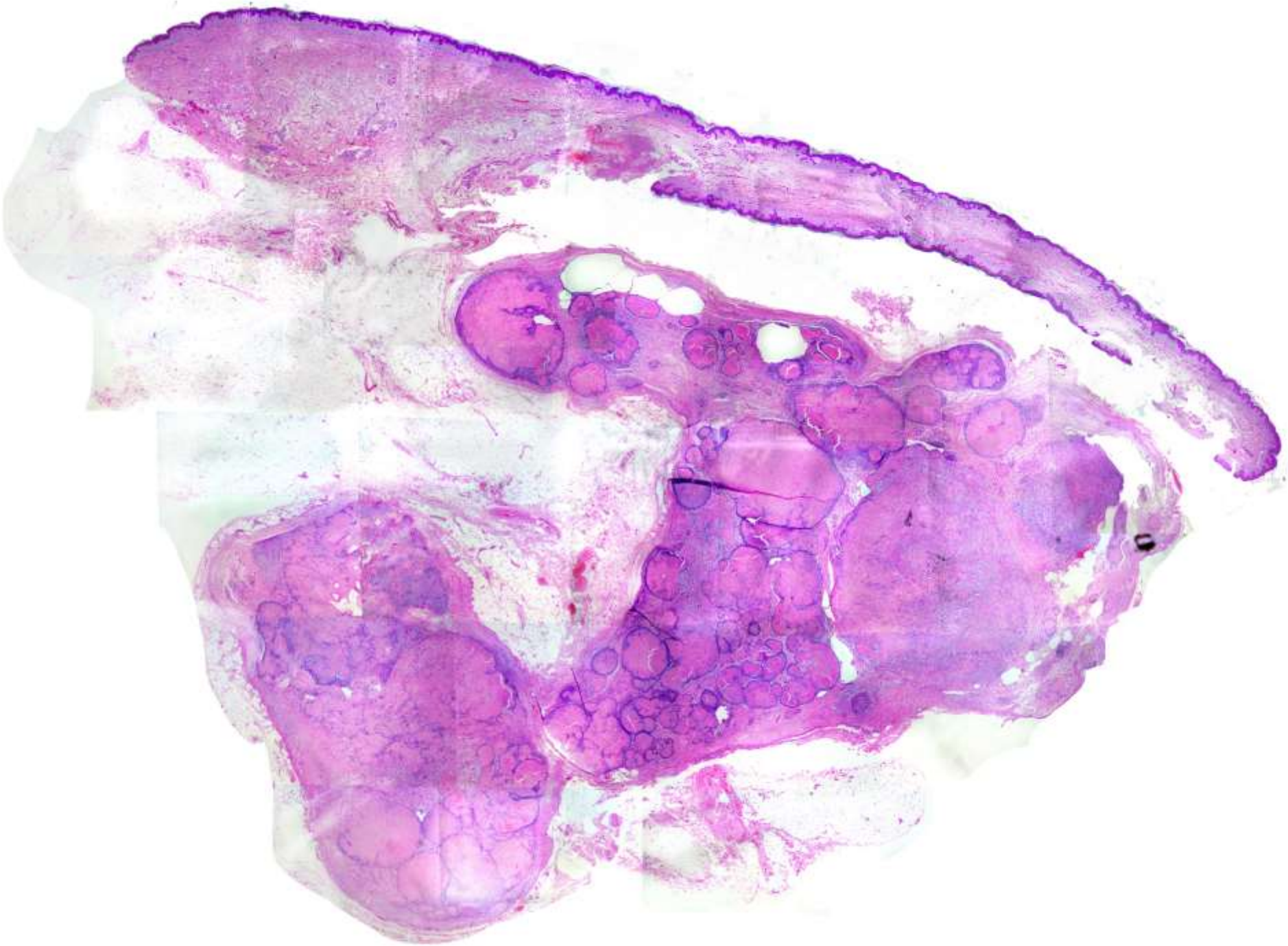


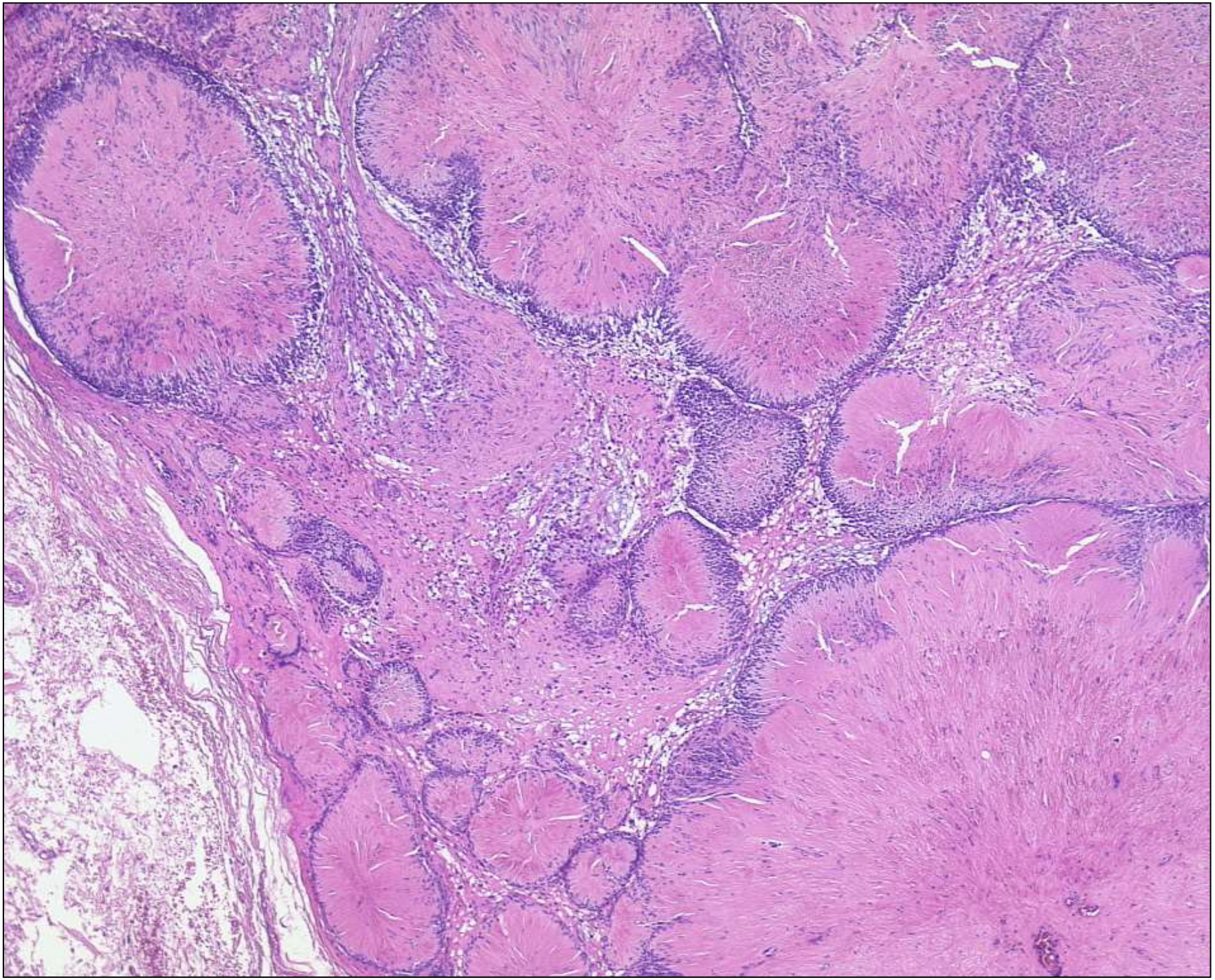


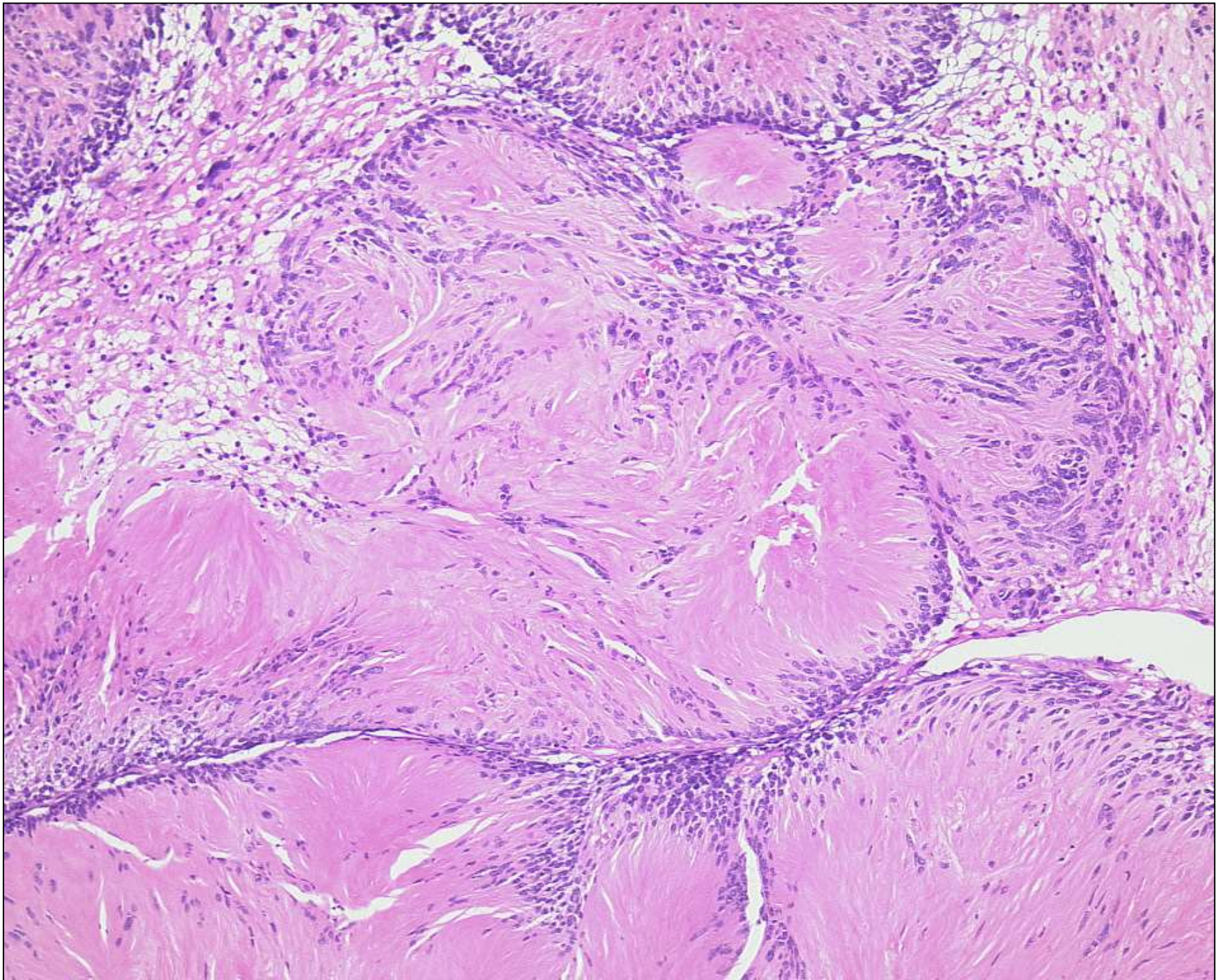
Desmin

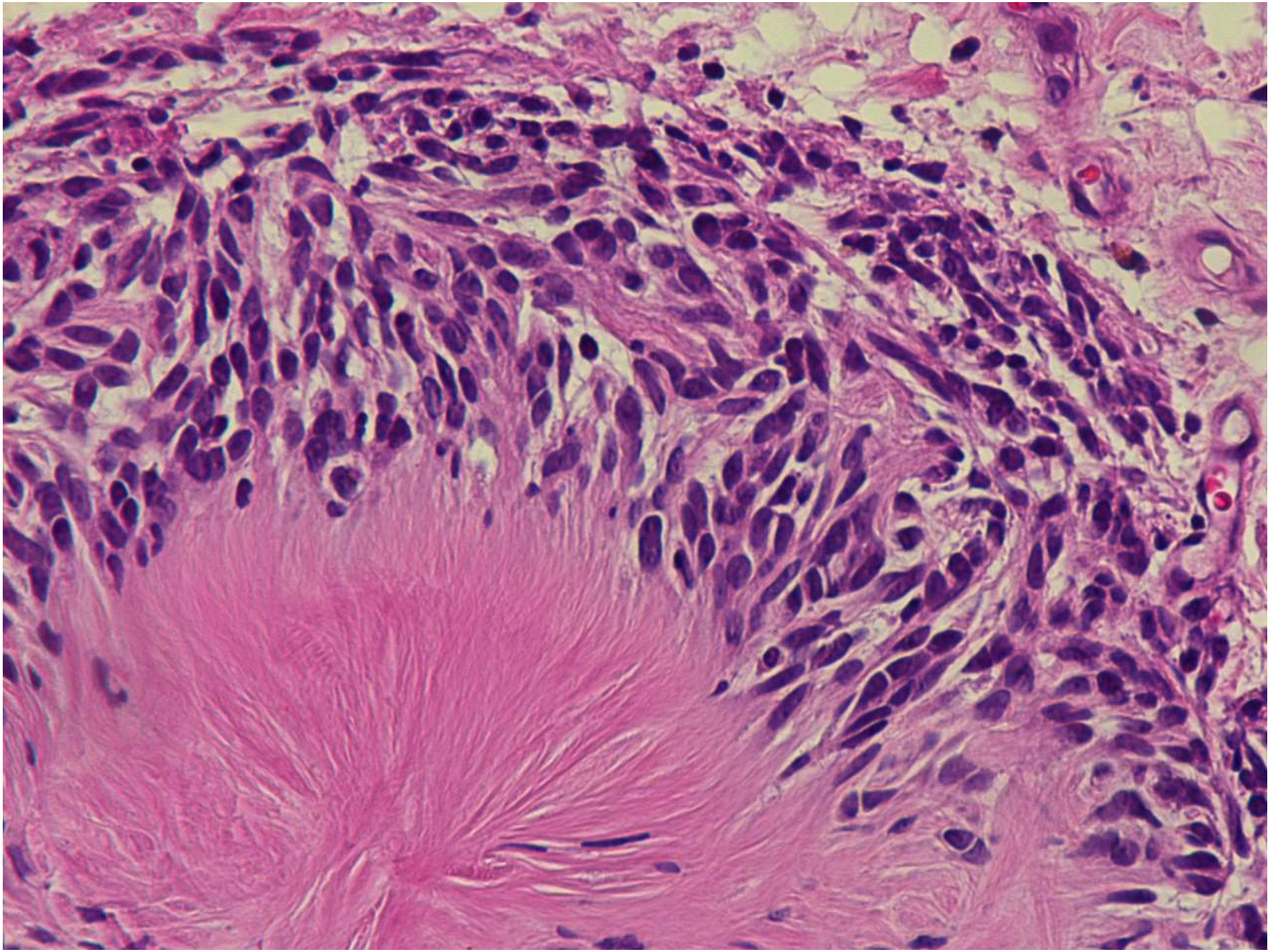
Case 10: Clinical Findings

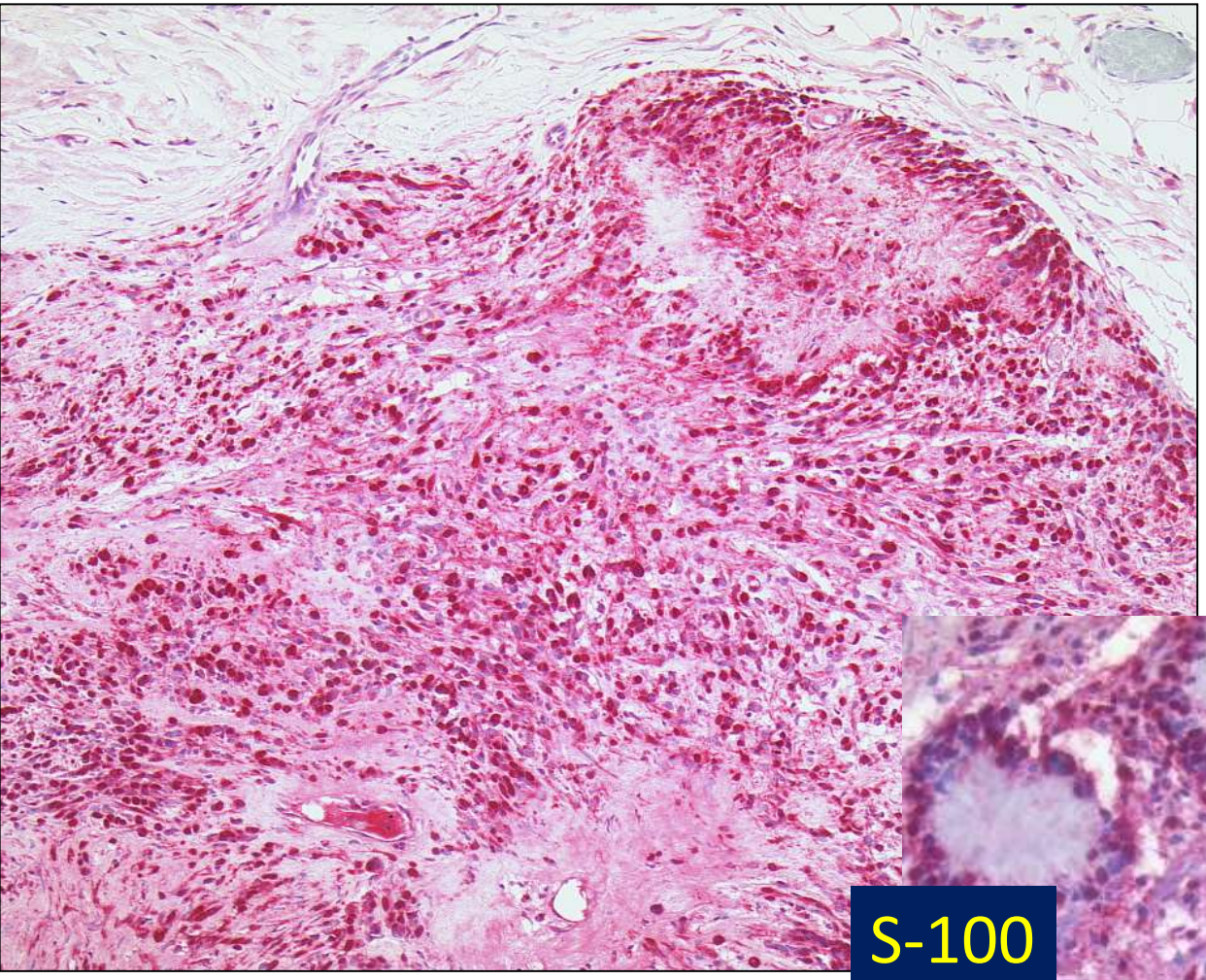
- F, 64 years
- abdominal wall

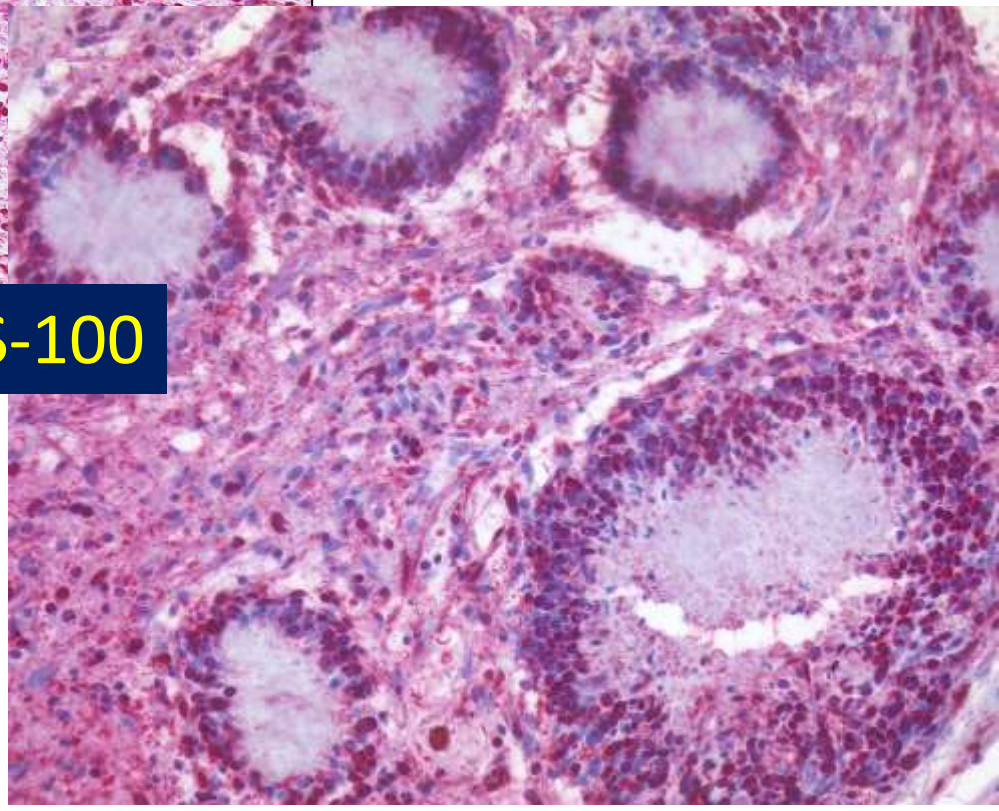






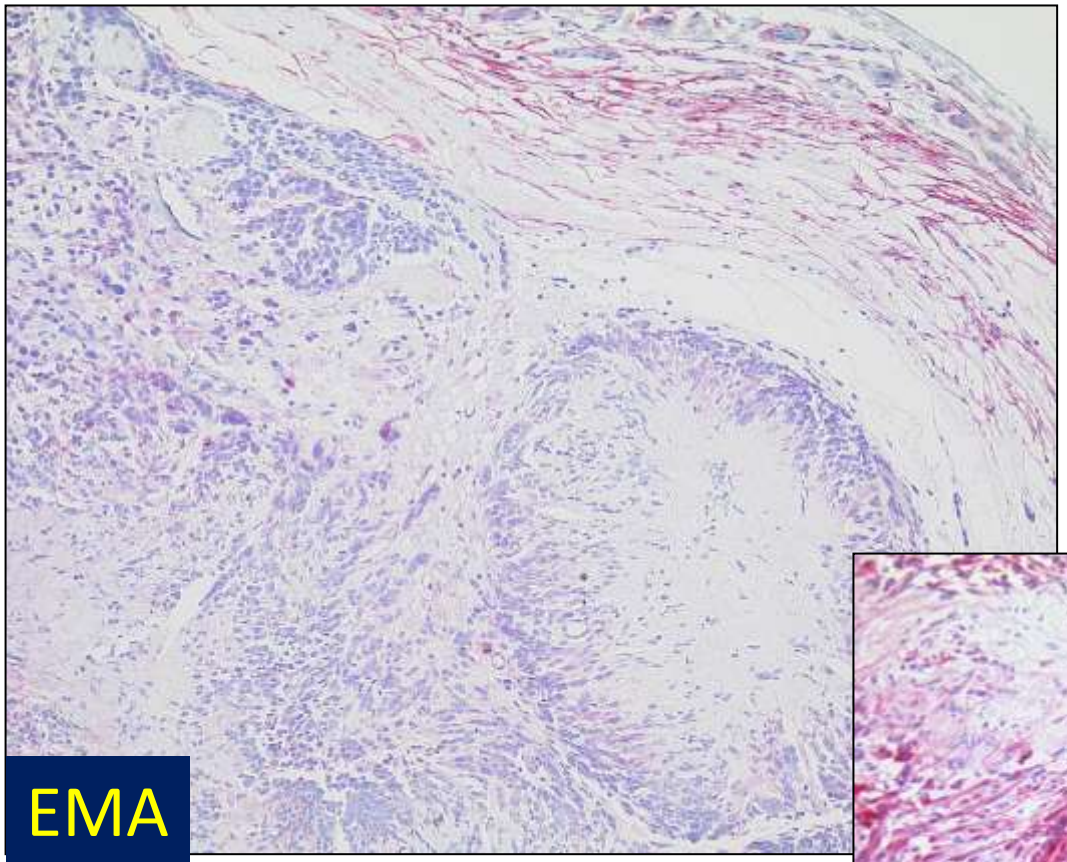


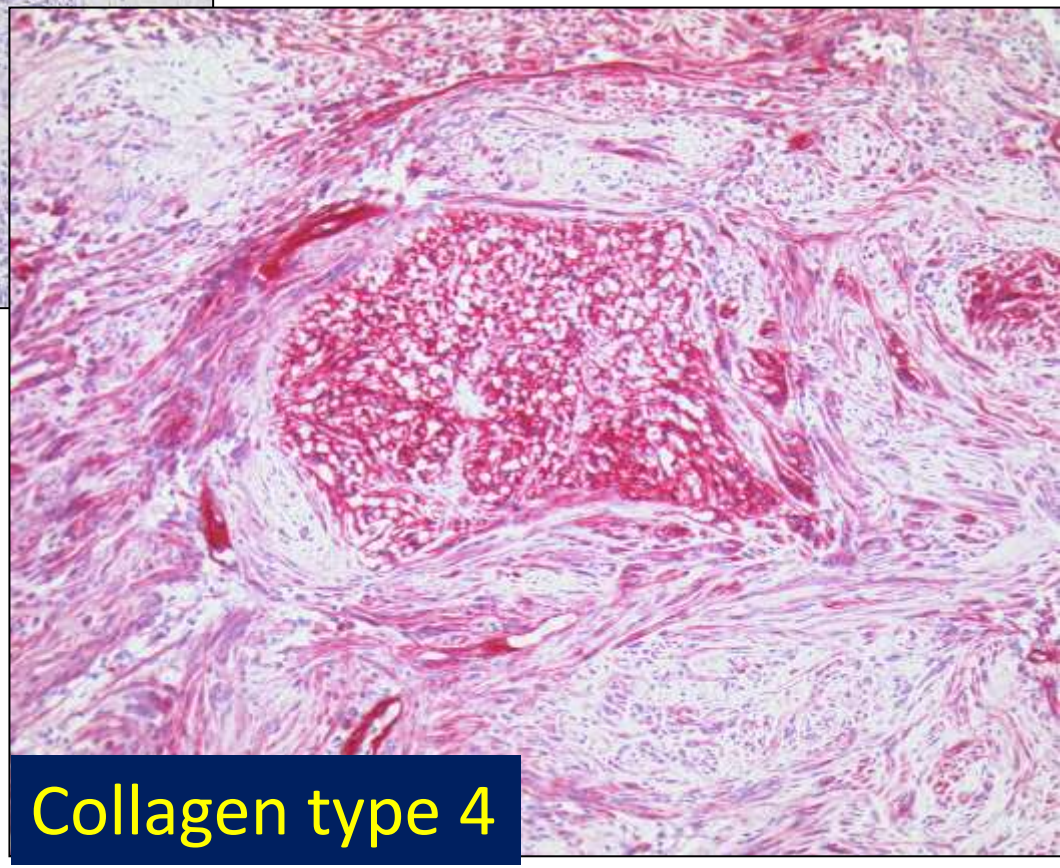




S-100

Diagnosis Case 10: Neuroblastoma-like Schwannoma





Neuroblastoma-like Schwannoma

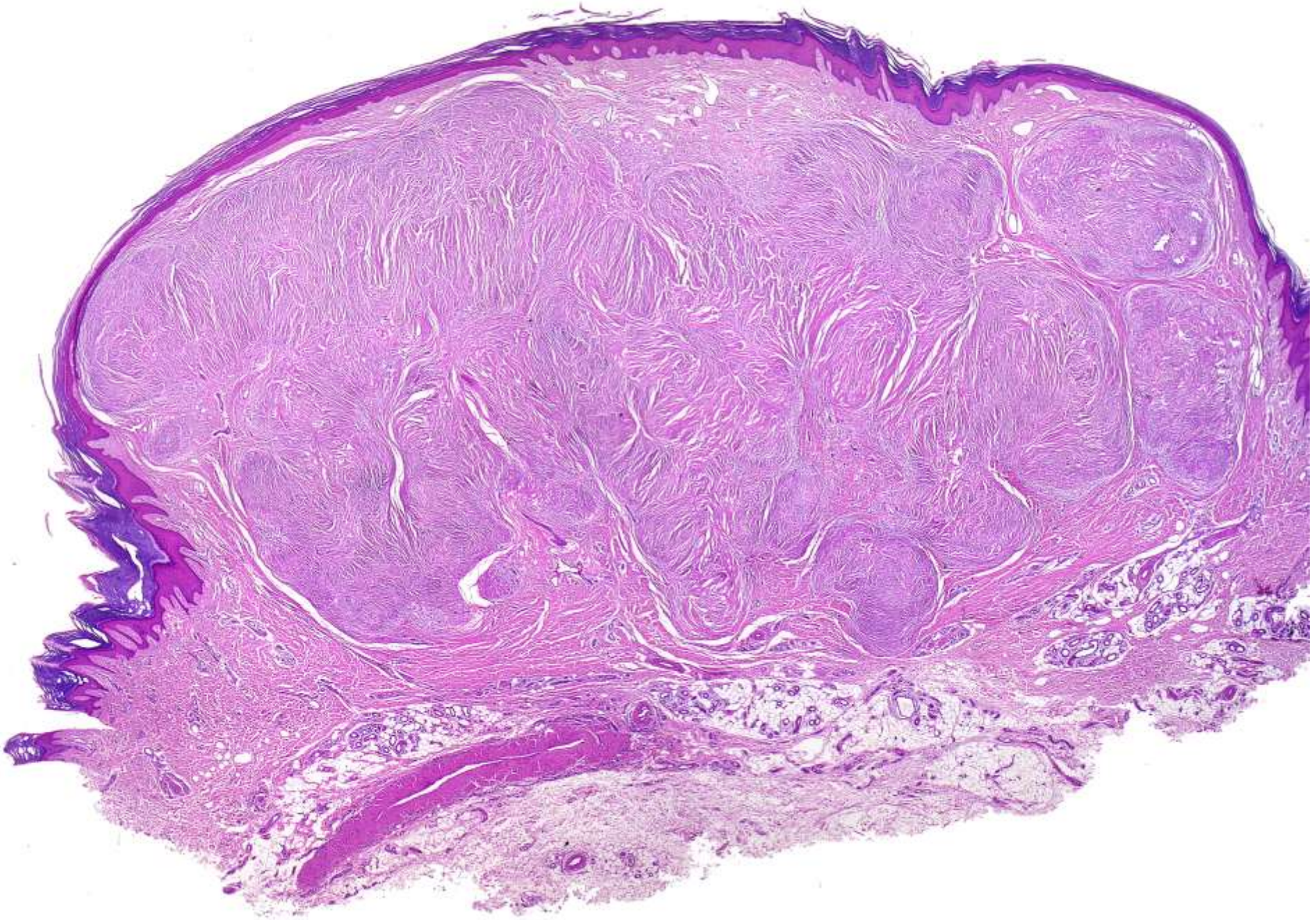
Neuroblastoma-like neurilemoma

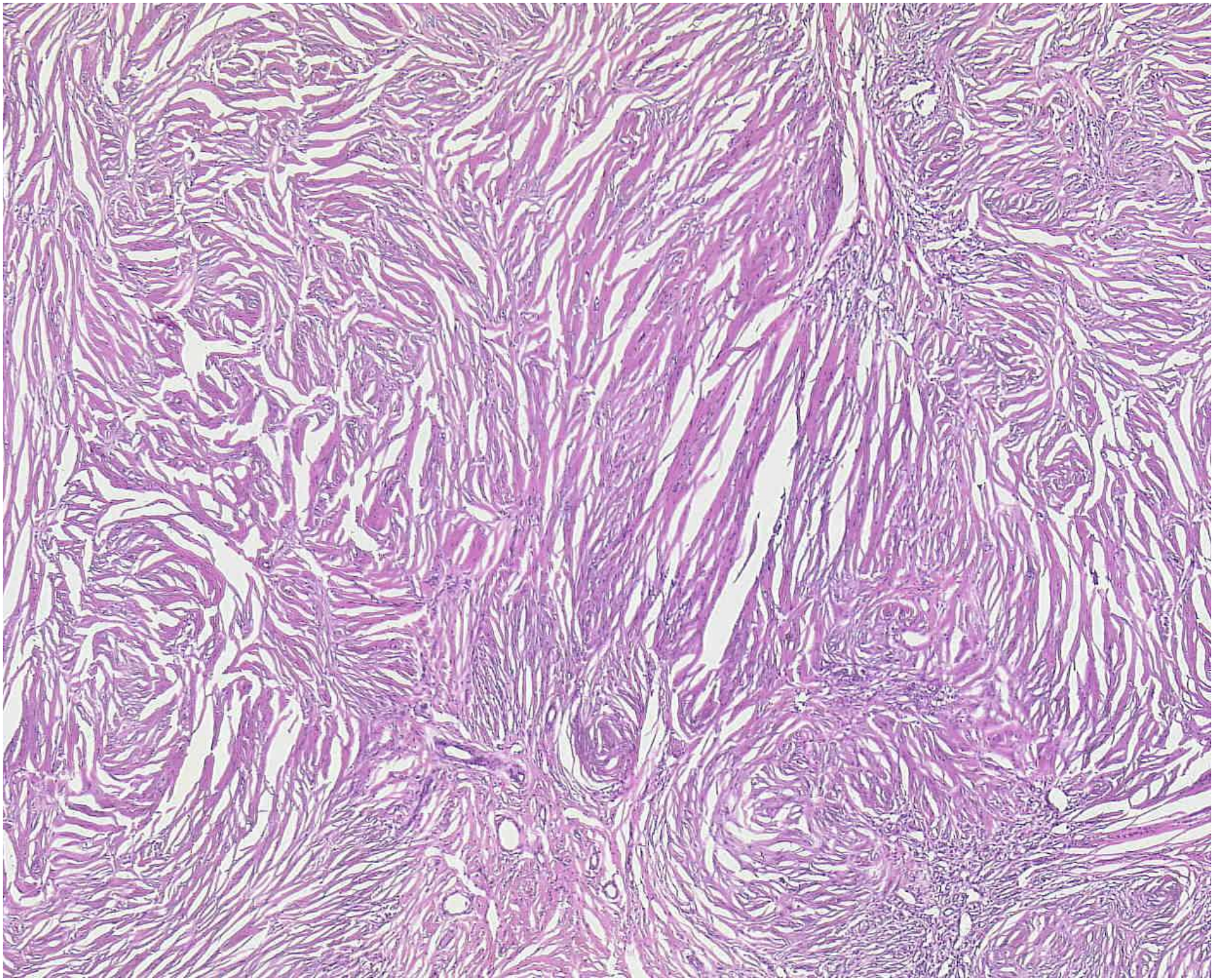
Goldblum JR et al. AJSP 1994; 18: 266

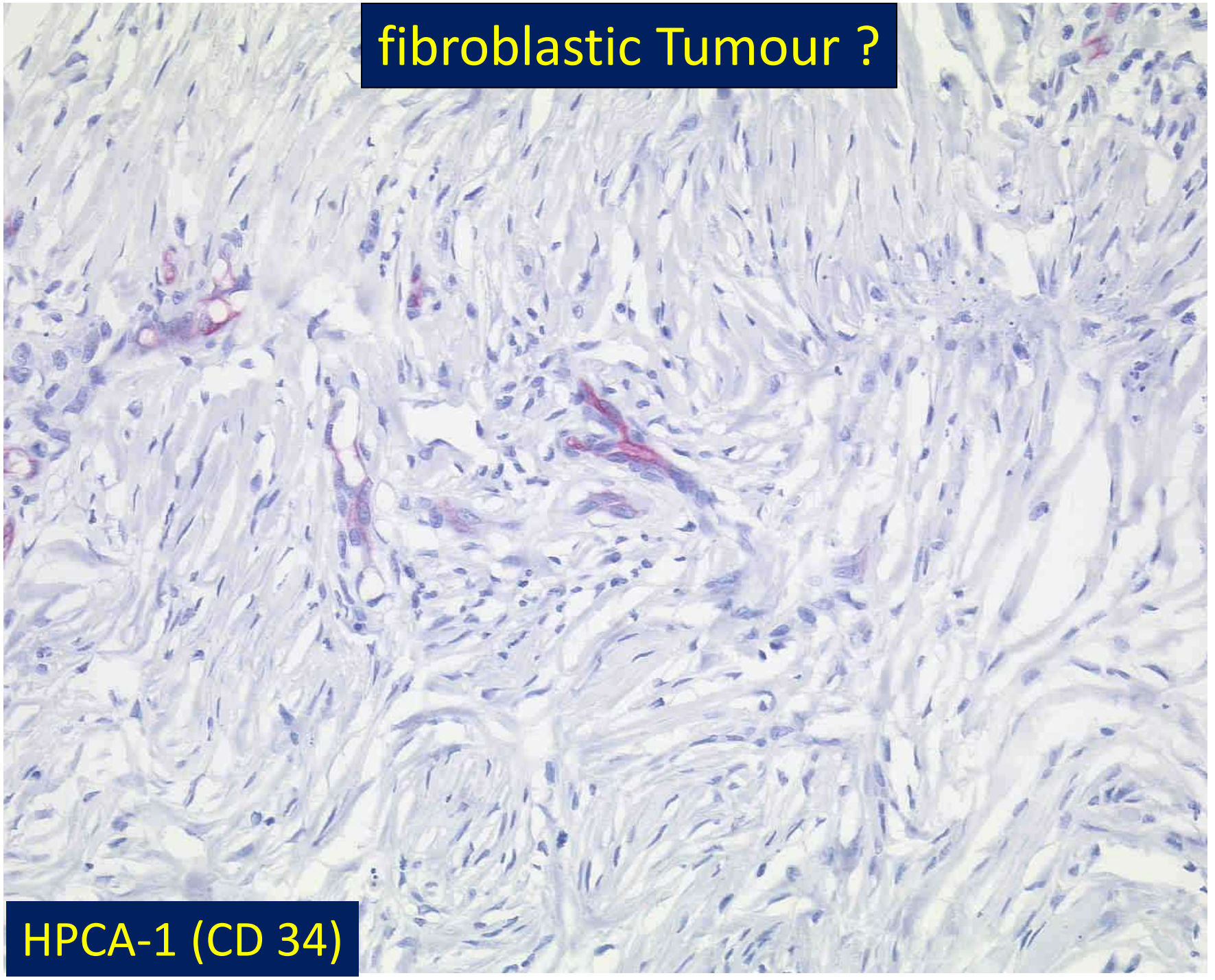
- solitary, sporadic
- neuroblastoma-like schwannomatosis very rare
- may contain areas of classical schwannoma
- DD: neuroblastoma, dendritic cell neurofibroma
  Spitz nevus with Homer-Wright rosettes
  low-grade fibromyxoid sarcoma with giant rosettes

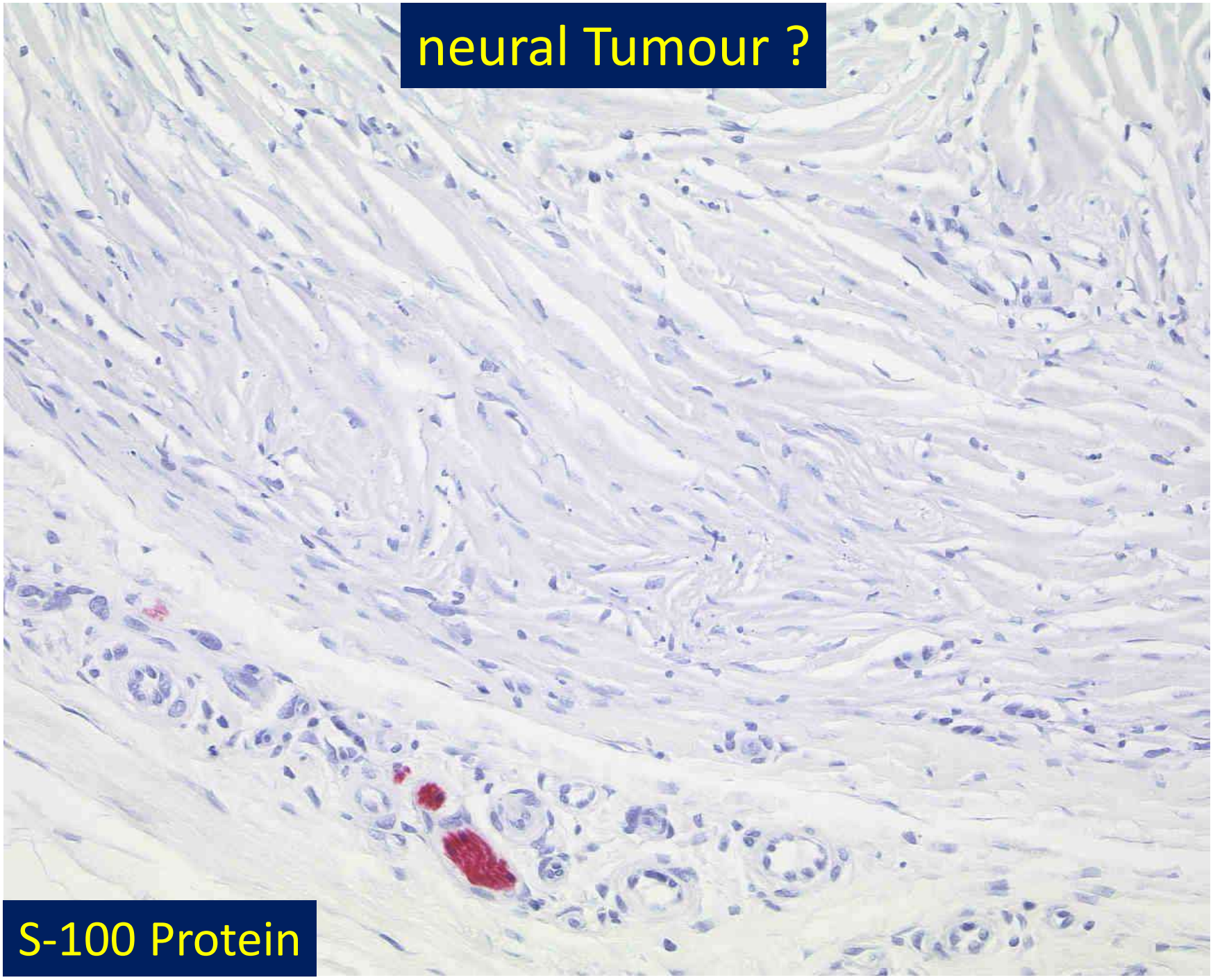
Case 11: Clinical Findings

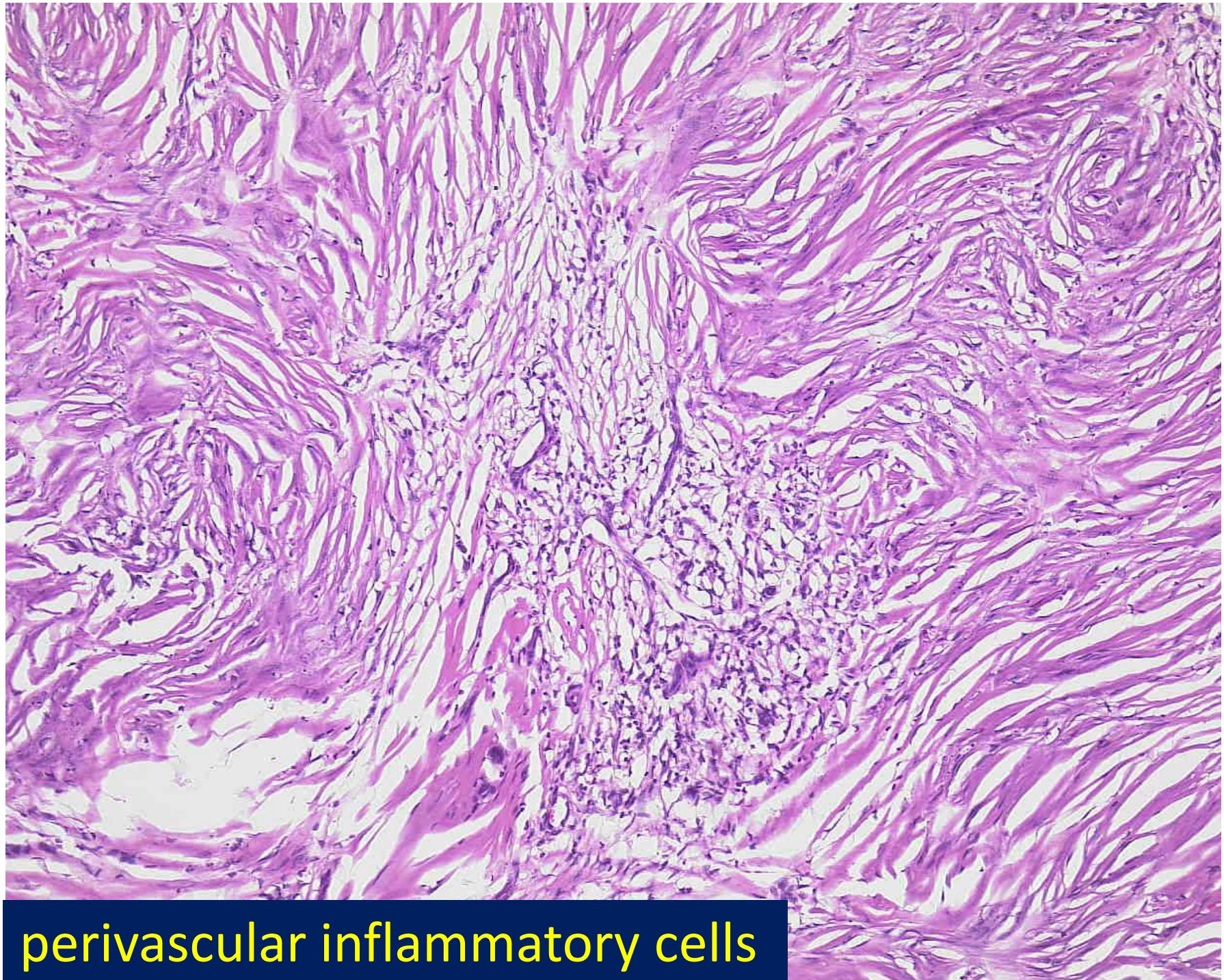
- F, 57 years
- multiple lesions on both feet
- fibromatosis was suspected

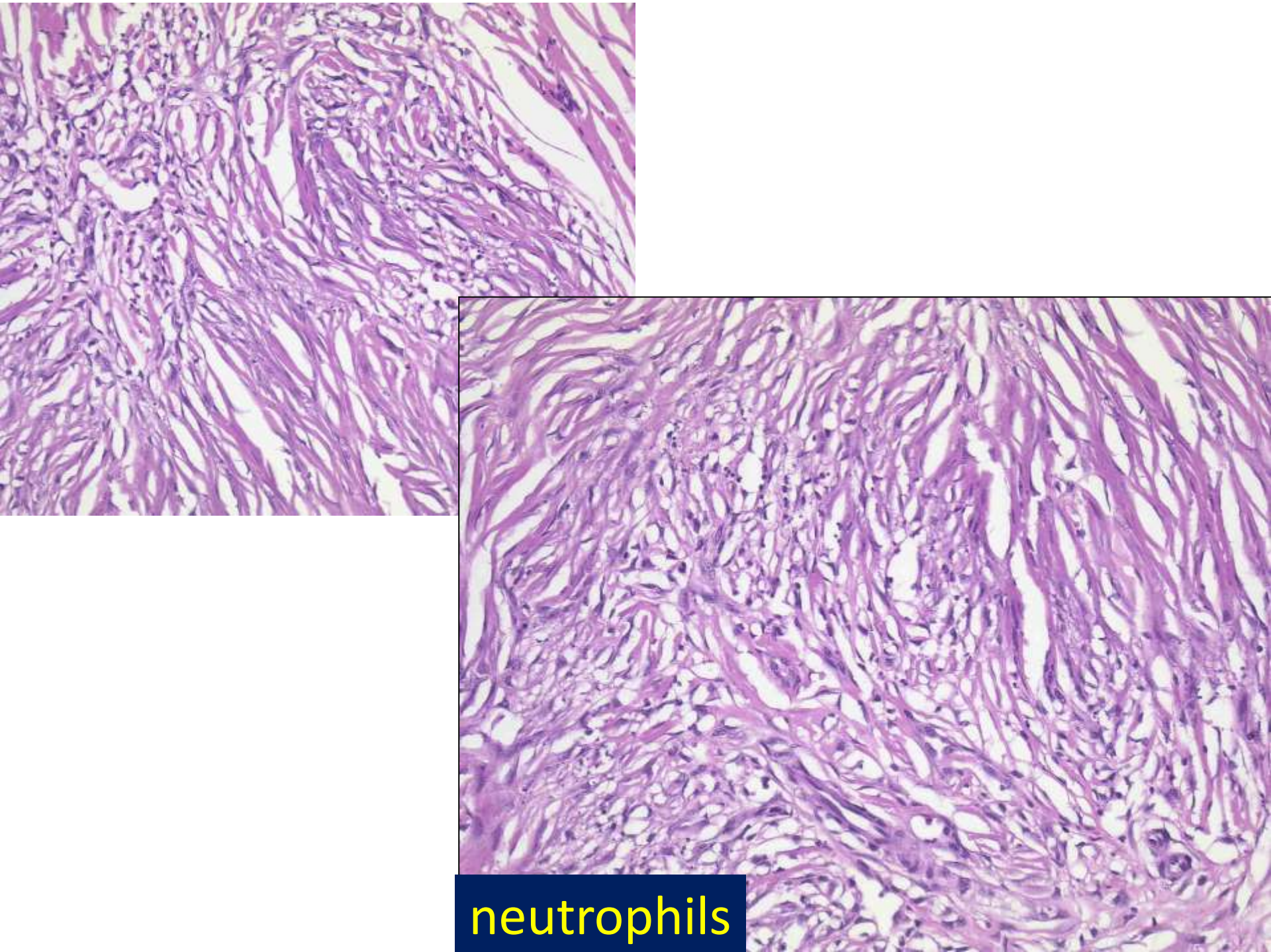


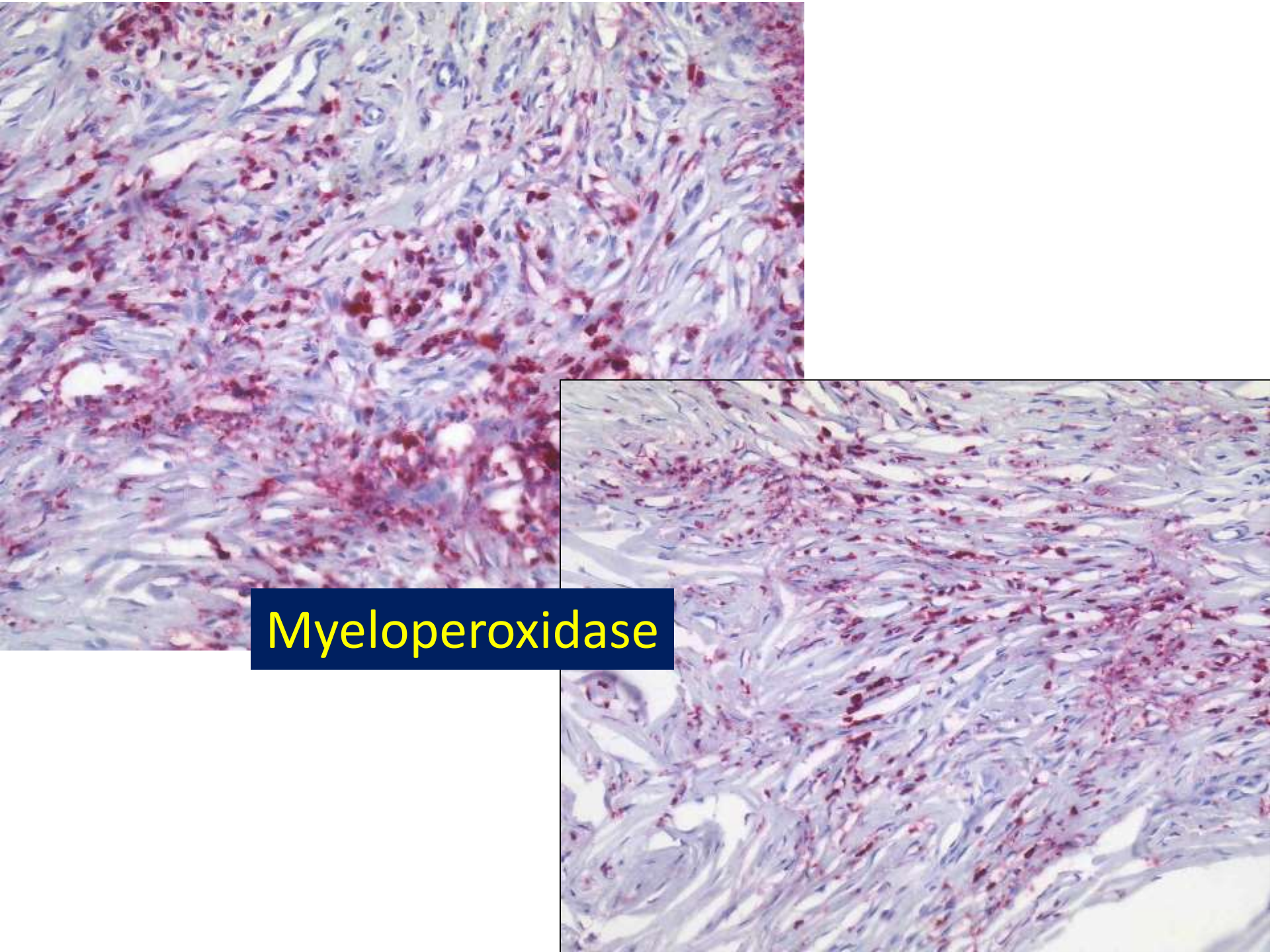



fibroblastic Tumour ?
HPCA-1 (CD 34)

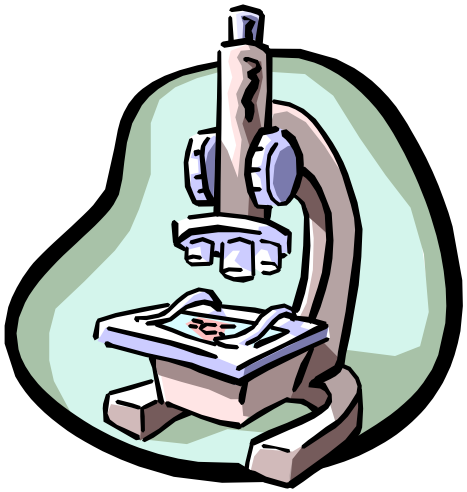

neural Tumour ?
S-100 Protein


perivascular inflammatory cells


neutrophils


Myeloperoxidase

Diagnosis Case 11



Erythema elevatum et diutinum (tumour stage)

Erythema elevatum et diutinum

- variant of chronic vasculitis
- long duration
- persistent papules, plaques and nodules
- multiple, symmetrical lesions,
  distal extremities
- associated systemic diseases
  (MDS, lymphoma, IgA gammopathy…)
- different stages of disease

Erythema elevatum et diutinum

early lesions:

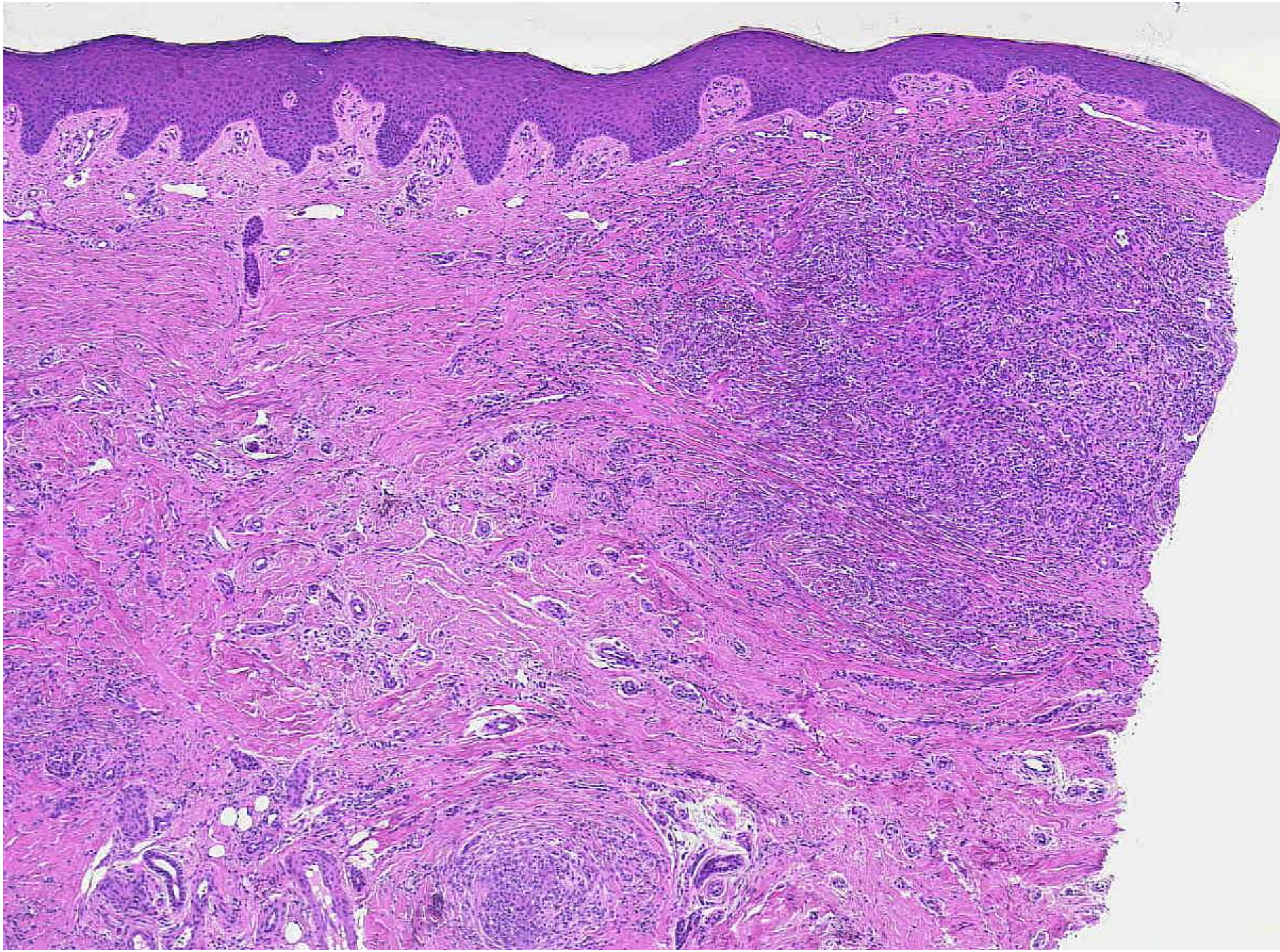
- perivascular infiltrate of neutrophils
- leukocytoclasis, fibrin deposition

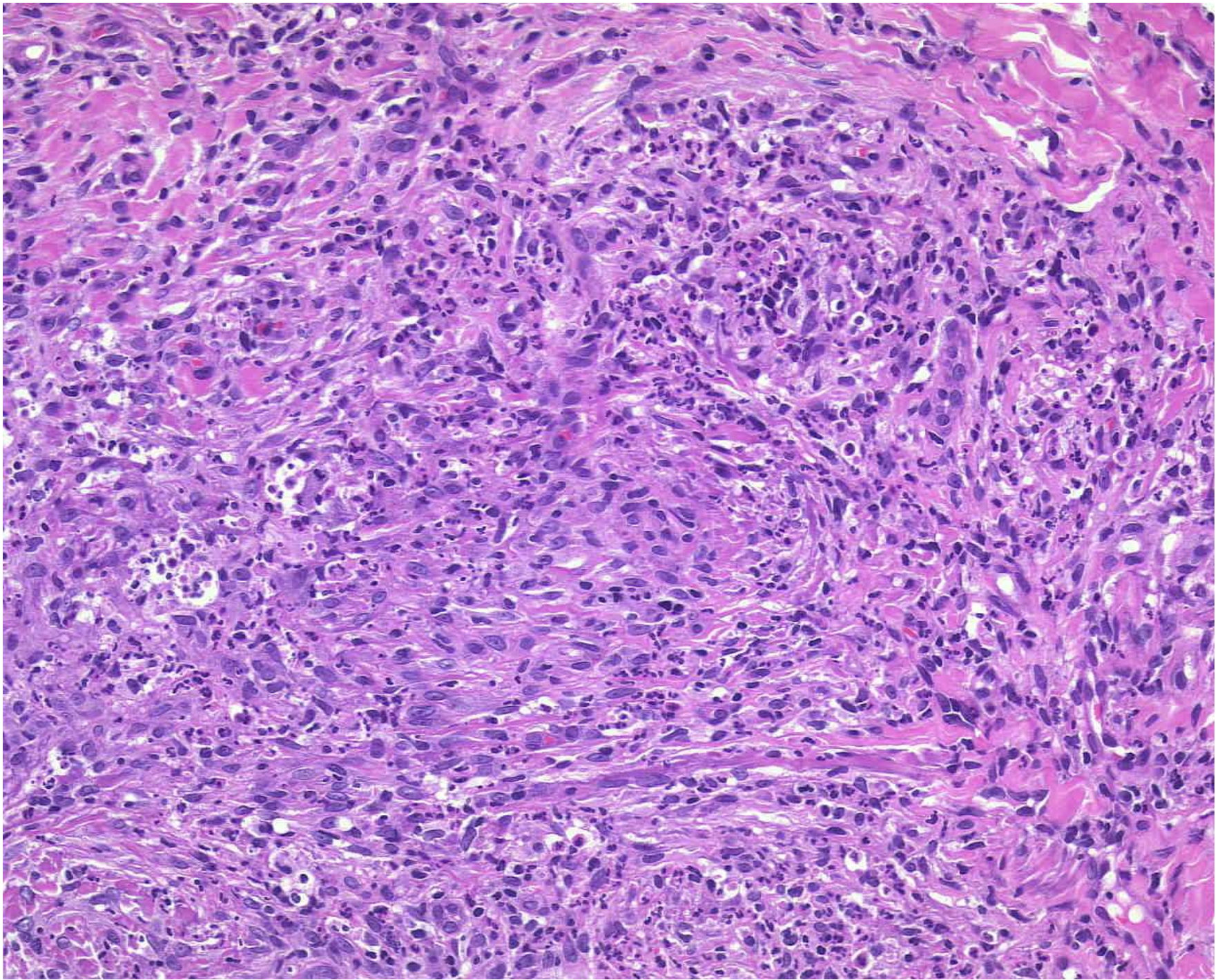
established lesions:

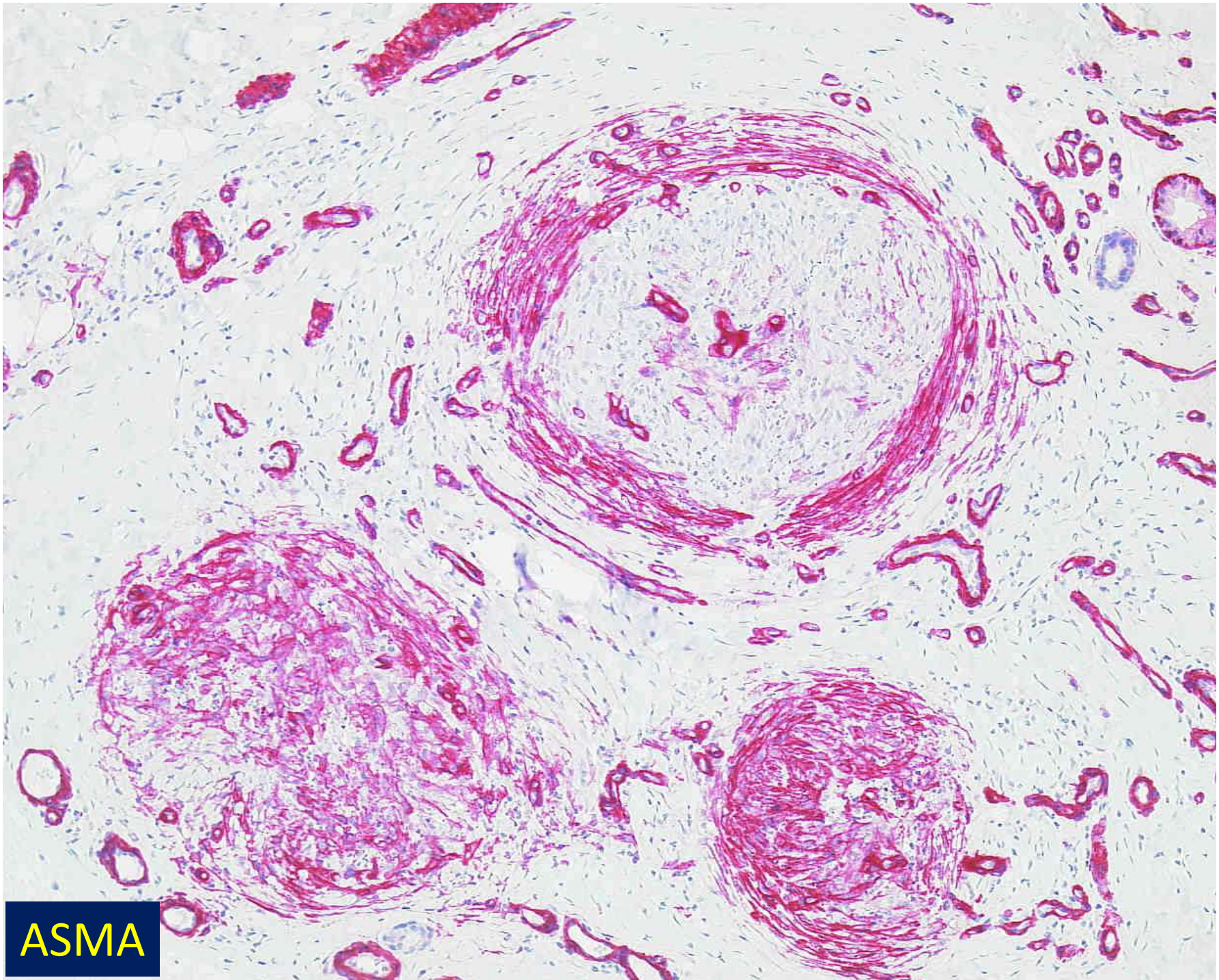
- neutrophilic infiltrate of the entire dermis
- sometimes spongiosis, blister, necrosis

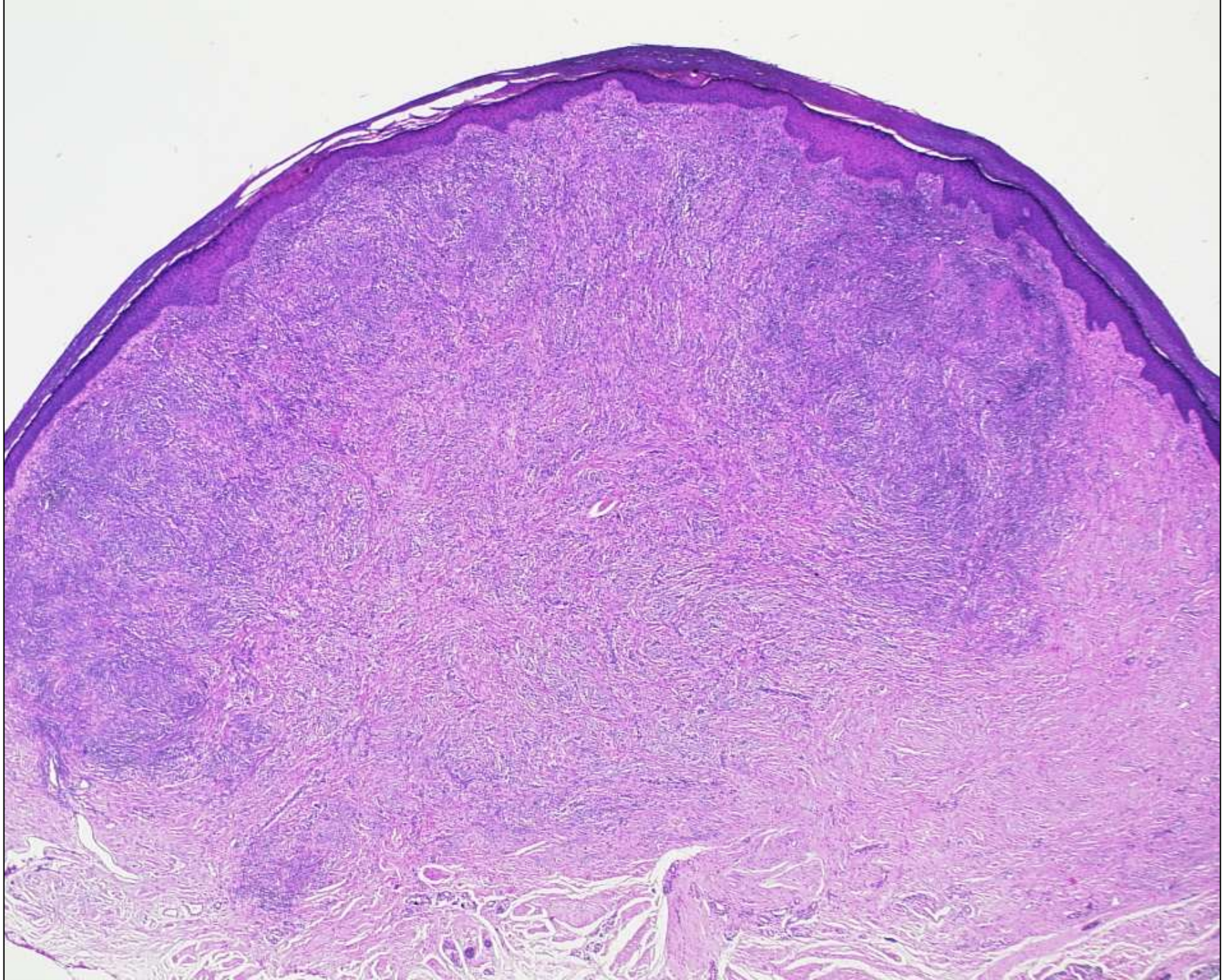
late lesions:

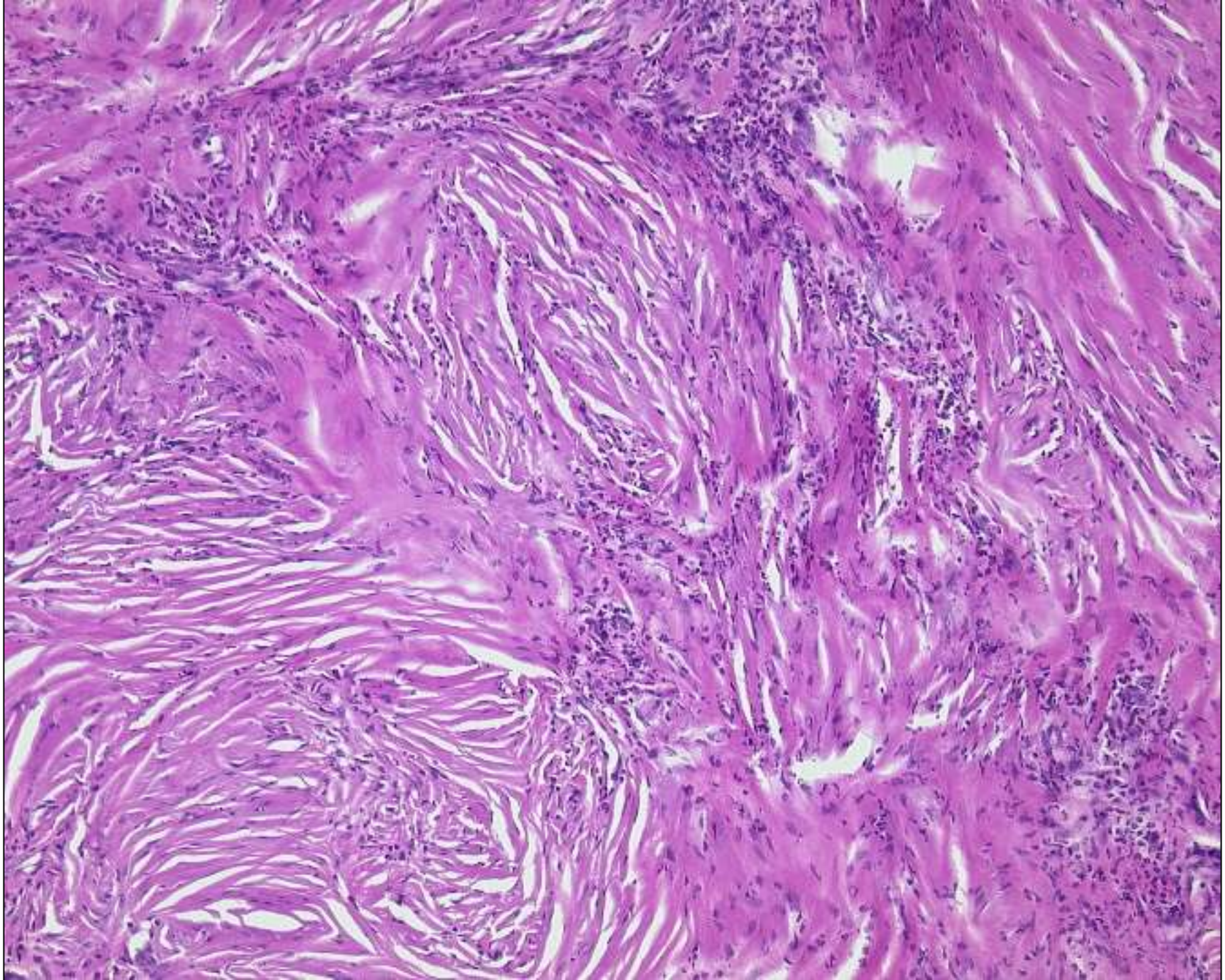
- variable fibrosis, capillary proliferation
- tumour-like fibroblastic proliferation
- scattered neutrophils

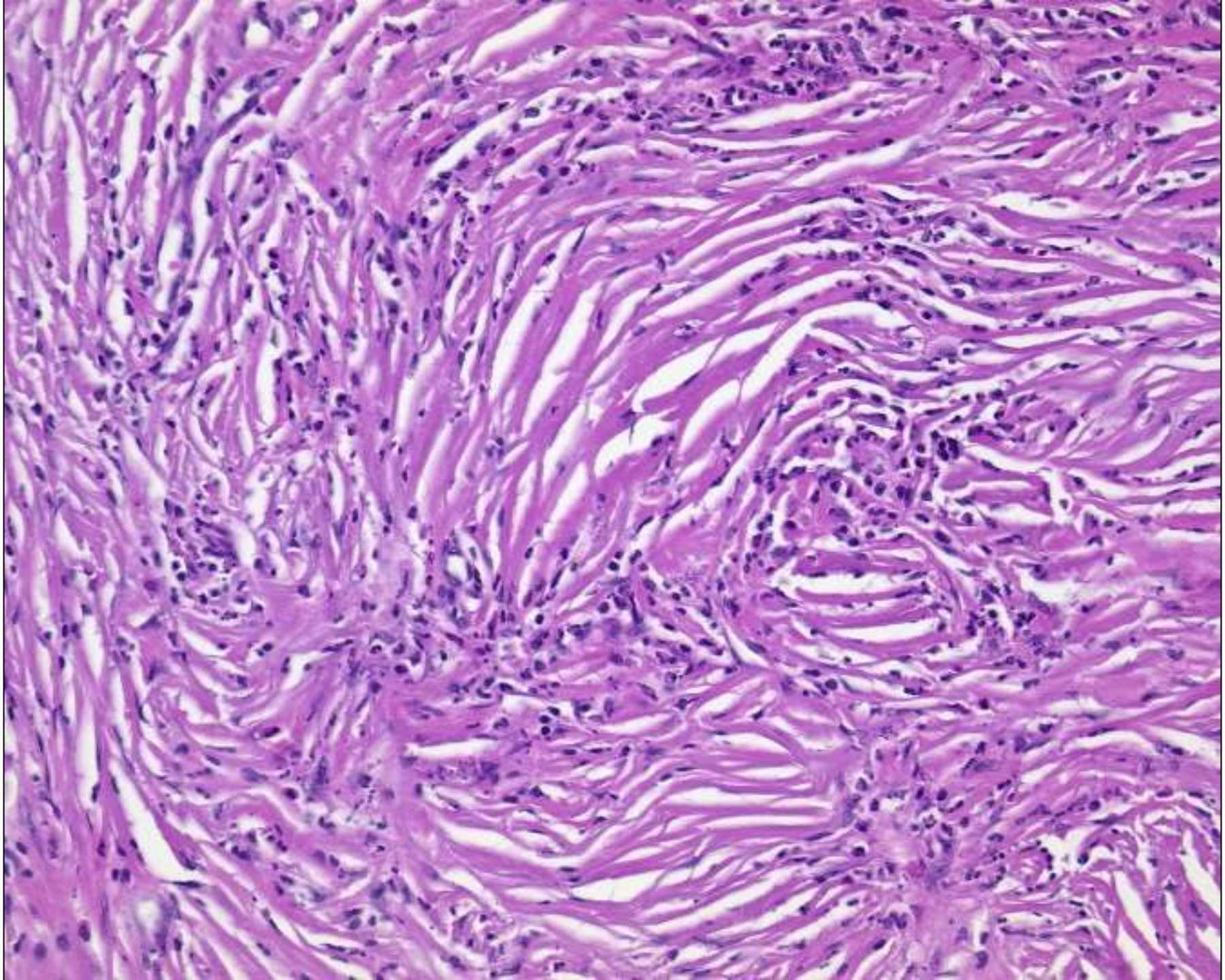





ASMA







Many thanks for your attention !