SPINDLE CELL TUMOURS

Dr. Will. Merchant

Spindle cell

- Muscle
  - Leiomyoma
- Neural
  - Neurofibroma
  - Schwannoma
- Fibrous
  - Fibroma
  - Dermatofibroma
- Fat
  - Spindle cell lipoma
- Epithelial
  - Myoepithelioma
- Other

- LMS
- MPNST
- Fibrosarcoma's, DFSP
- Spindle cell liposarcoma
- Sarcomatoid Ca.
- Synovial sarcoma
- Melanoma

Case 1

- 40 M rapidly growing lump arm

What features to look for in spindle cell tumours for malignancy

Features suggestive of malignancy

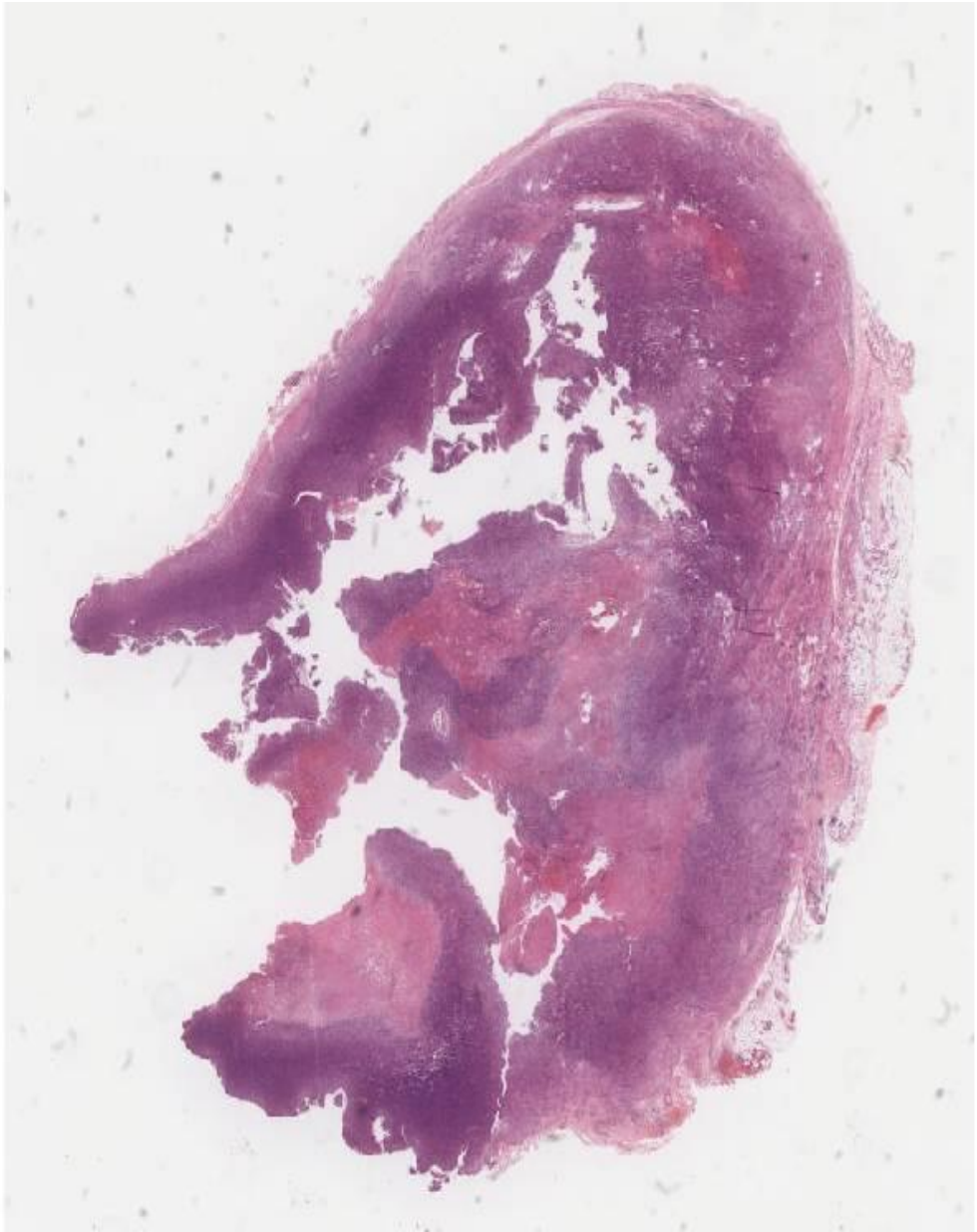
- Necrosis
- Nuclear atypia
- Mitoses,[?number]. Atypical forms

- BUT- frequent exceptions
- Accurate diagnostic tumour type most important. ‘If you don’t know what it is, how can you predict how it will behave.’

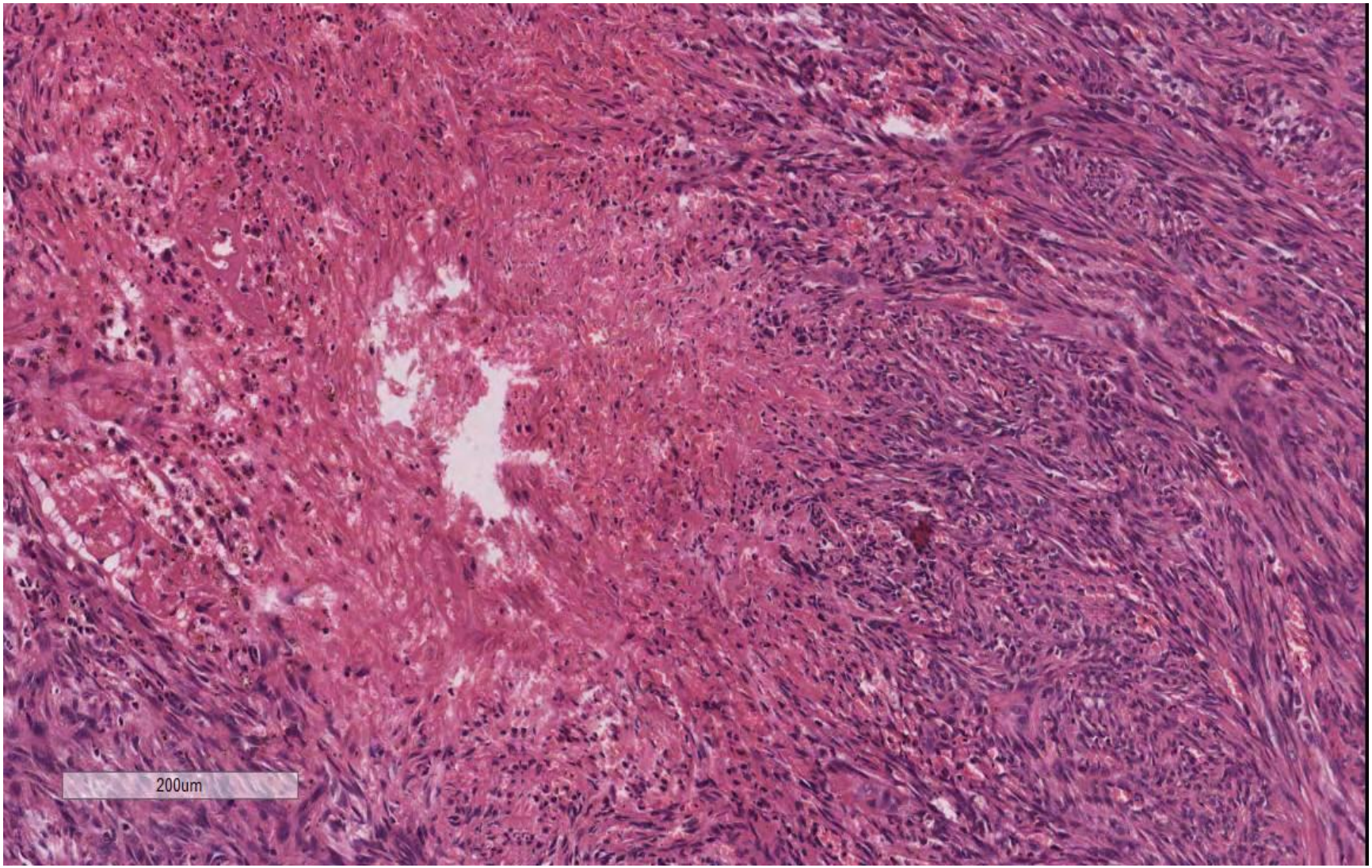
Cellular Dermatofibroma

- Top tips
  - Variable cellularity
  - Variable cell type
  - Cells wrap around prominent collagen at margin
  - More pink cytoplasm than DFSP
  - Immuno; SMA weak positive. CD34 neg (Beware halo phenomenon]
    - DFSP SMA Neg, CD 34 POS

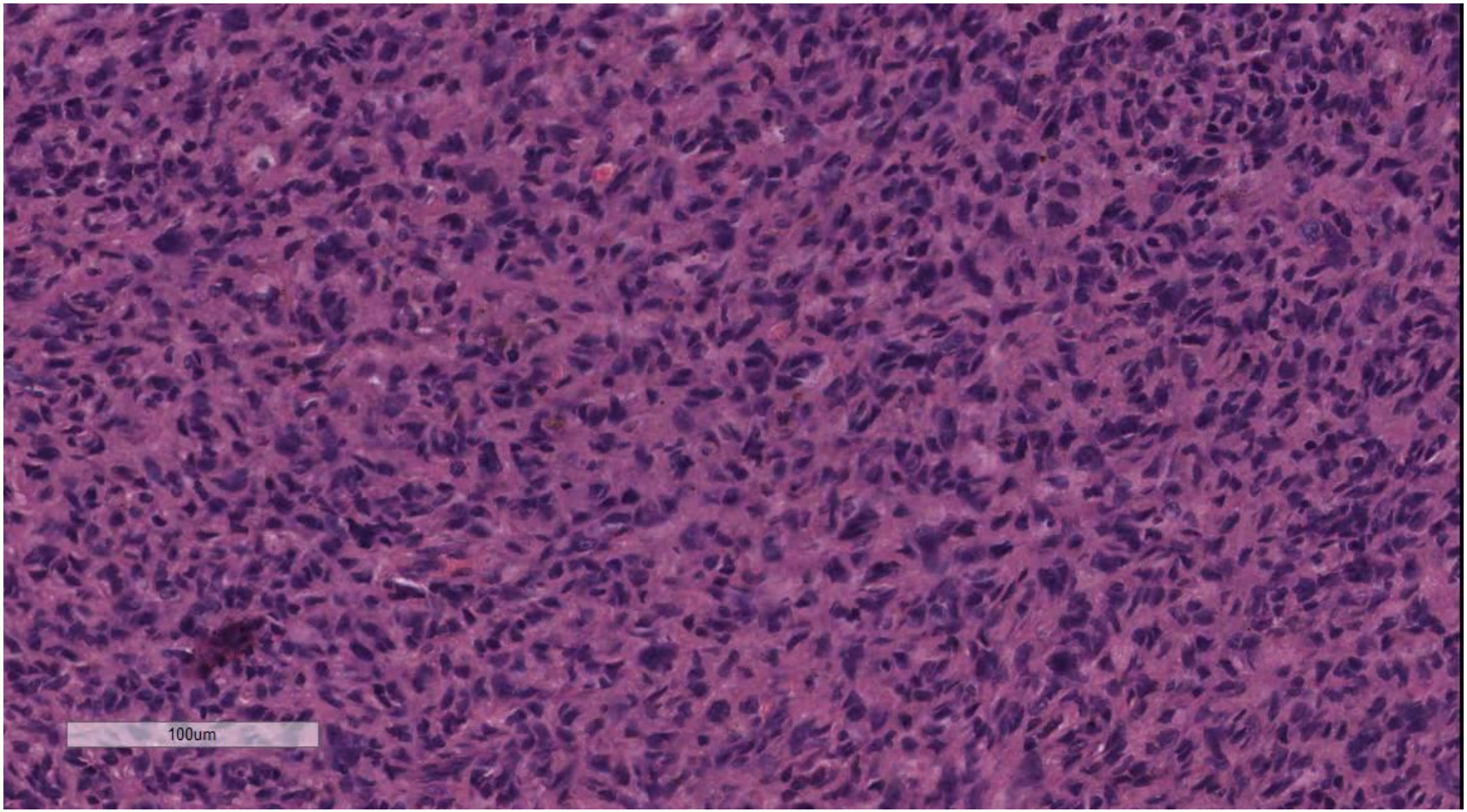
Fibrous lesions

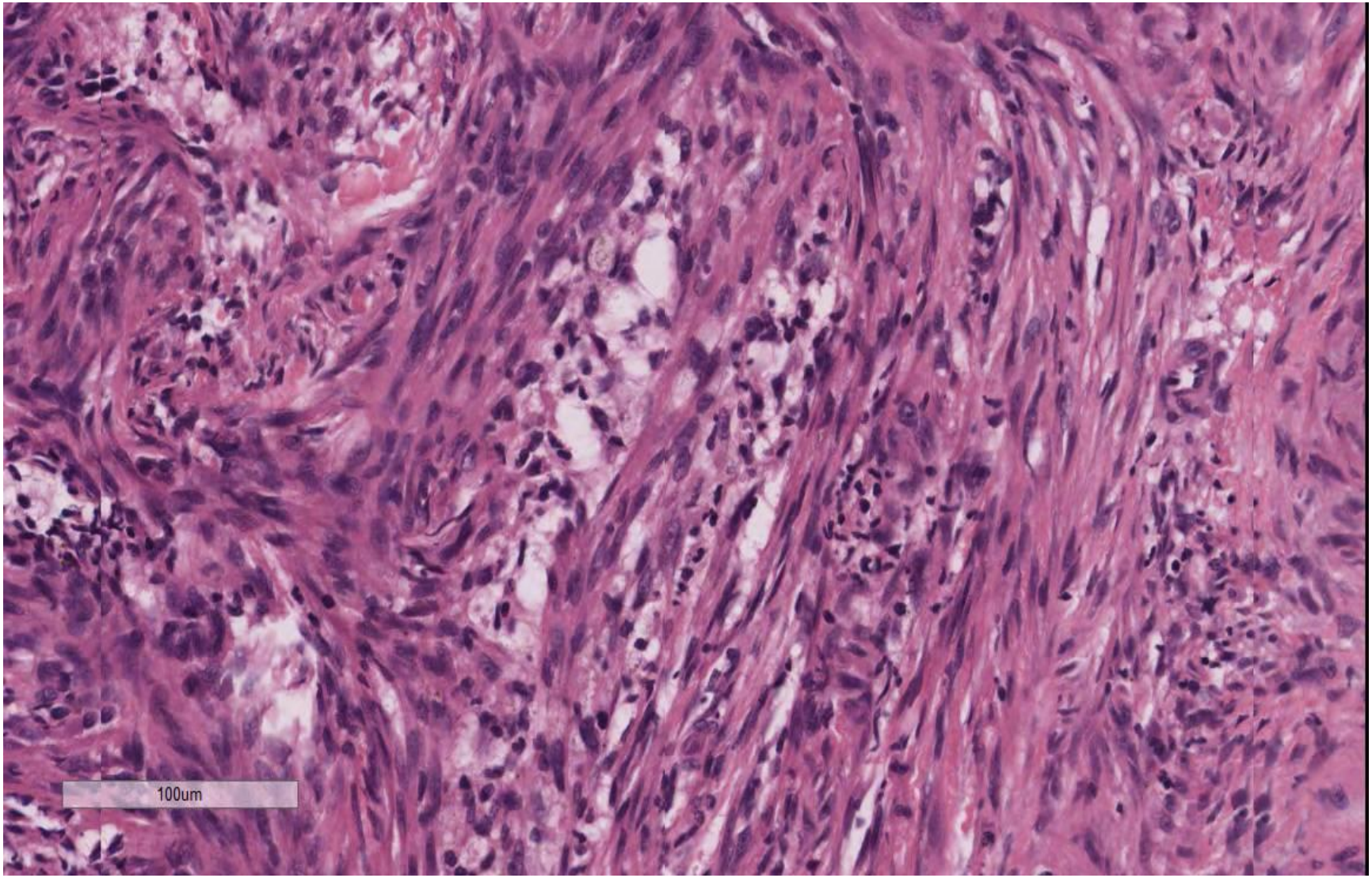


Dermatofibroma’s



Dermatofibroma’s




100um

Dermatofibroma Immunohistochemistry

- Not always very helpful.
- Variably Positive for- SMA, Factor X111a.
- Some cells positive for CD68, S100,
- Negative for CD34 [very rare cases positive], often halo phenomenon.
- Negative for, Caldesmon, Cytokeratin.
- But exceptions.

J. Cut. Path:12, 747-752

Desmin and CD34 positivity in cellular fibrous histiocytoma: an immunohistochemical analysis of 100 cases

Elgida R. Volpicelli and
Christopher D. M. Fletcher

Background: Cellular benign fibrous histiocytoma (CBFH) represents a morphologic variant of cutaneous fibrous histiocytoma (FH). Because

Cellular Dermatofibromas

- 100 cases
- 32% positive with desmin. Patchy [1 diffuse]
- 6% CD34 positive , patchy [diffuse]

Dermatofibroma’s

- Reactive or Neoplastic ????

The International Journal of Biochemistry & Cell Biology 53 (2014) 475–481

Contents lists available at ScienceDirect

The International Journal of Biochemistry & Cell Biology

journal homepage: www.elsevier.com/locate/biocel

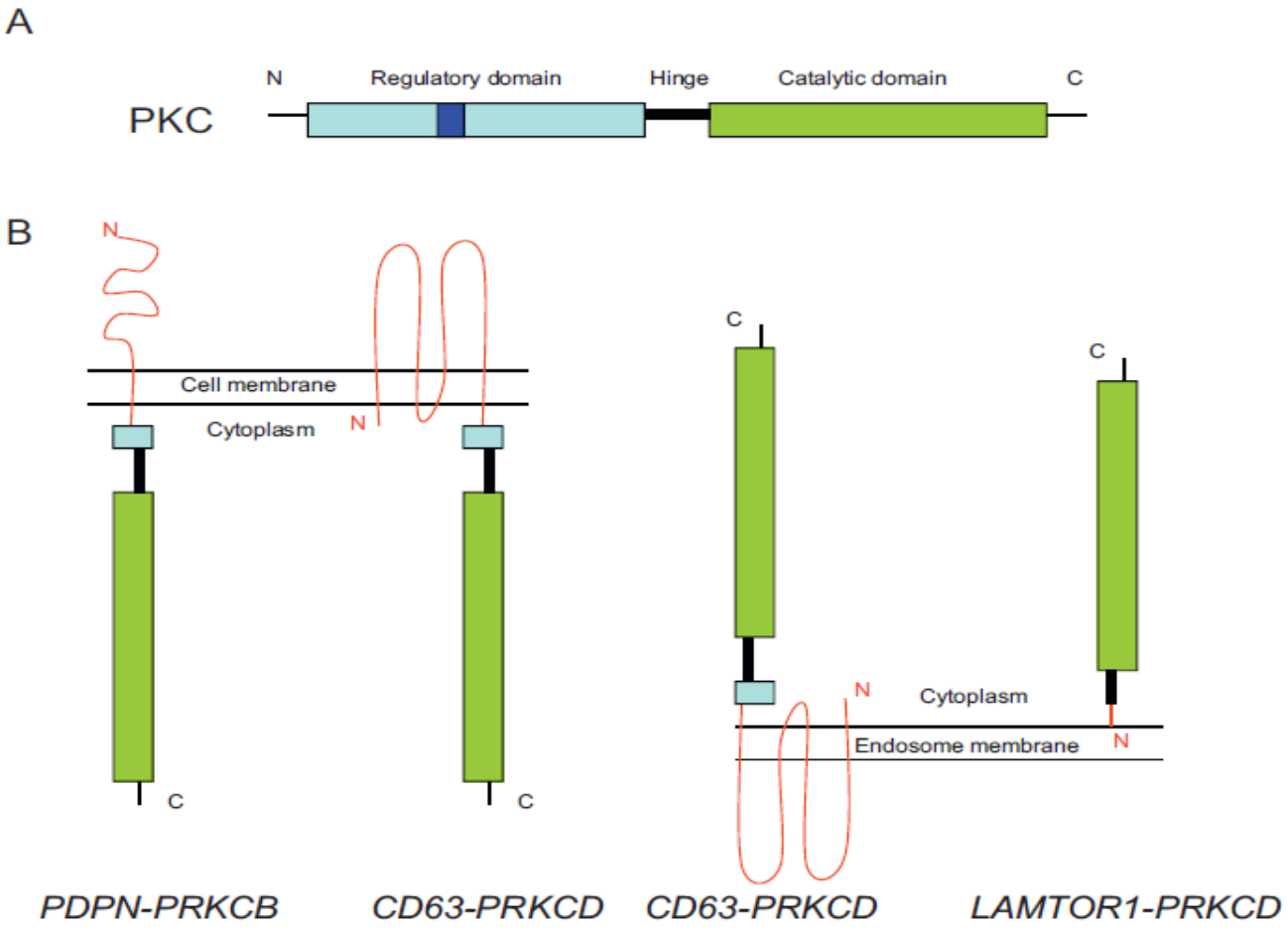
Fusions involving protein kinase C and membrane-associated proteins in benign fibrous histiocytoma☆

Anna Płaszczyca[a], Jenny Nilsson[a], Linda Magnusson[a], Otte Brosjö[b], Olle Larsson[c], Fredrik Vult von Steyern[d], Henryk A. Domanski[e], Henrik Lilljebjörn[a], Thoas Fioretos[a], Johnbosco Tayebwa[a], Nils Mandahl[a], Karolin H. Nord[a], Fredrik Mertens[a,*]

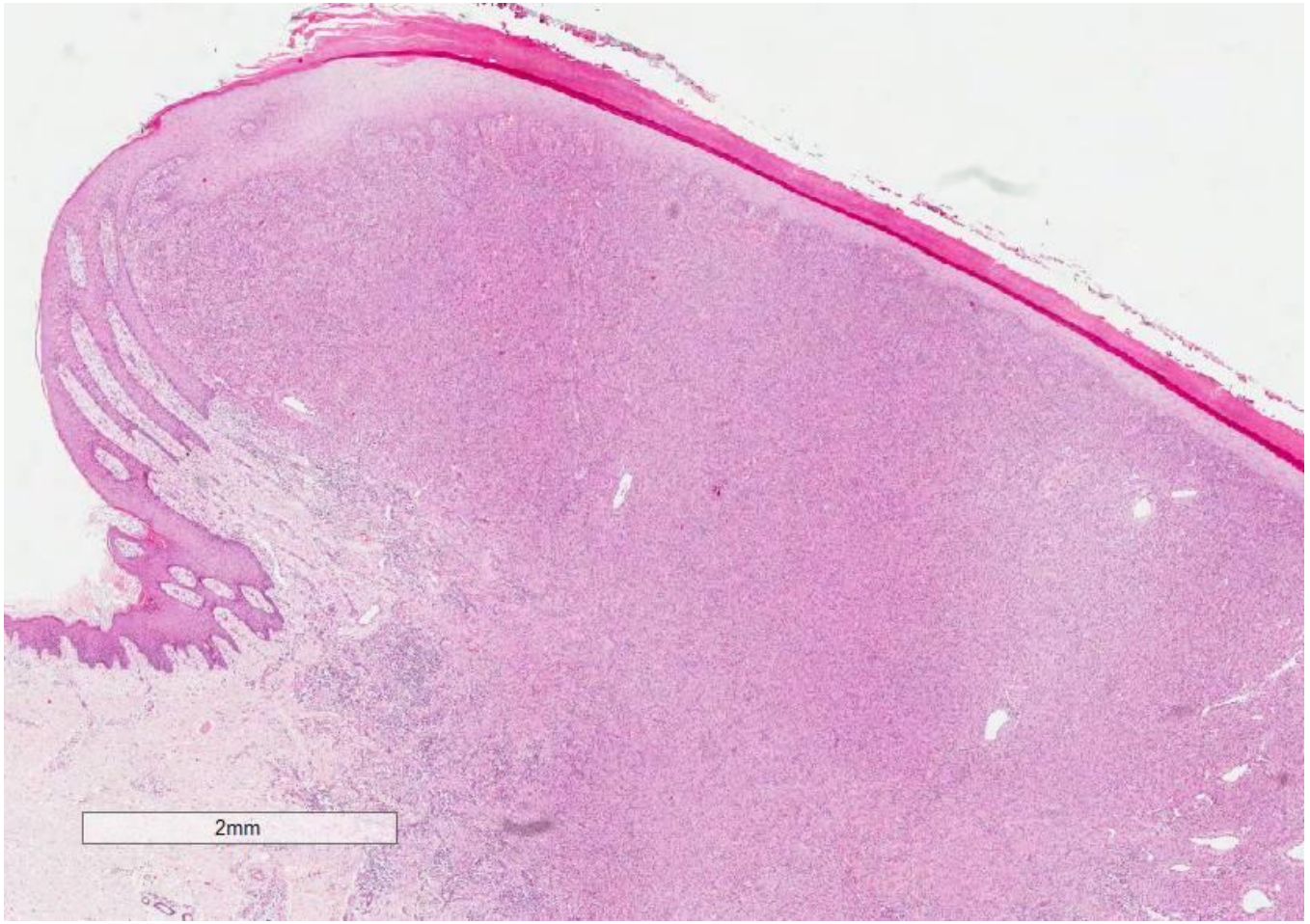
Dermatofibromas - genetics

- Fusion of 2 genes, one being a PKC
- PDPN- PRKCB
- CD63- PRKCB
- Lamtor1- PRKCD

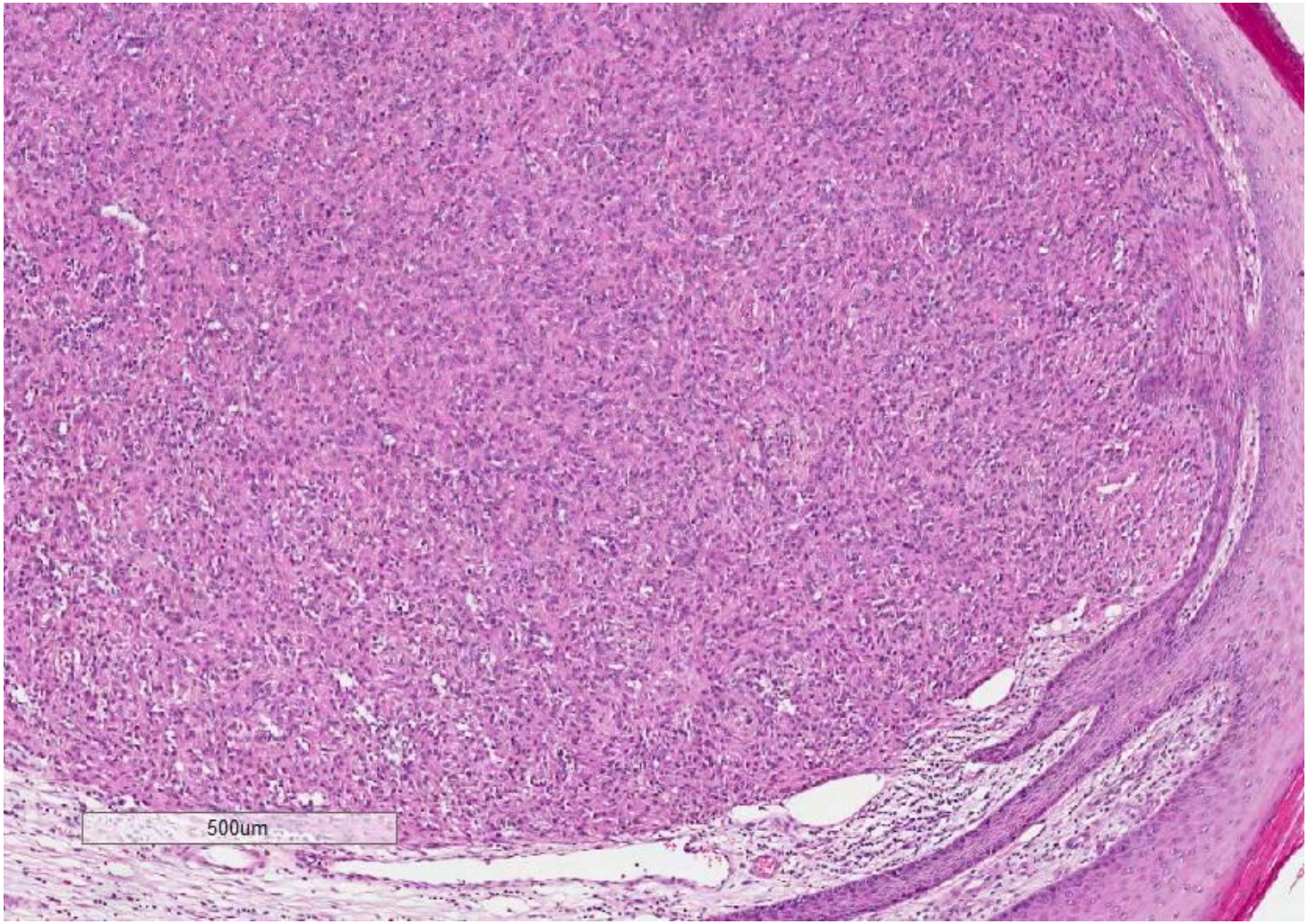
Int.Journal Biochem & cell Biology 53 (2014) 475 - 481

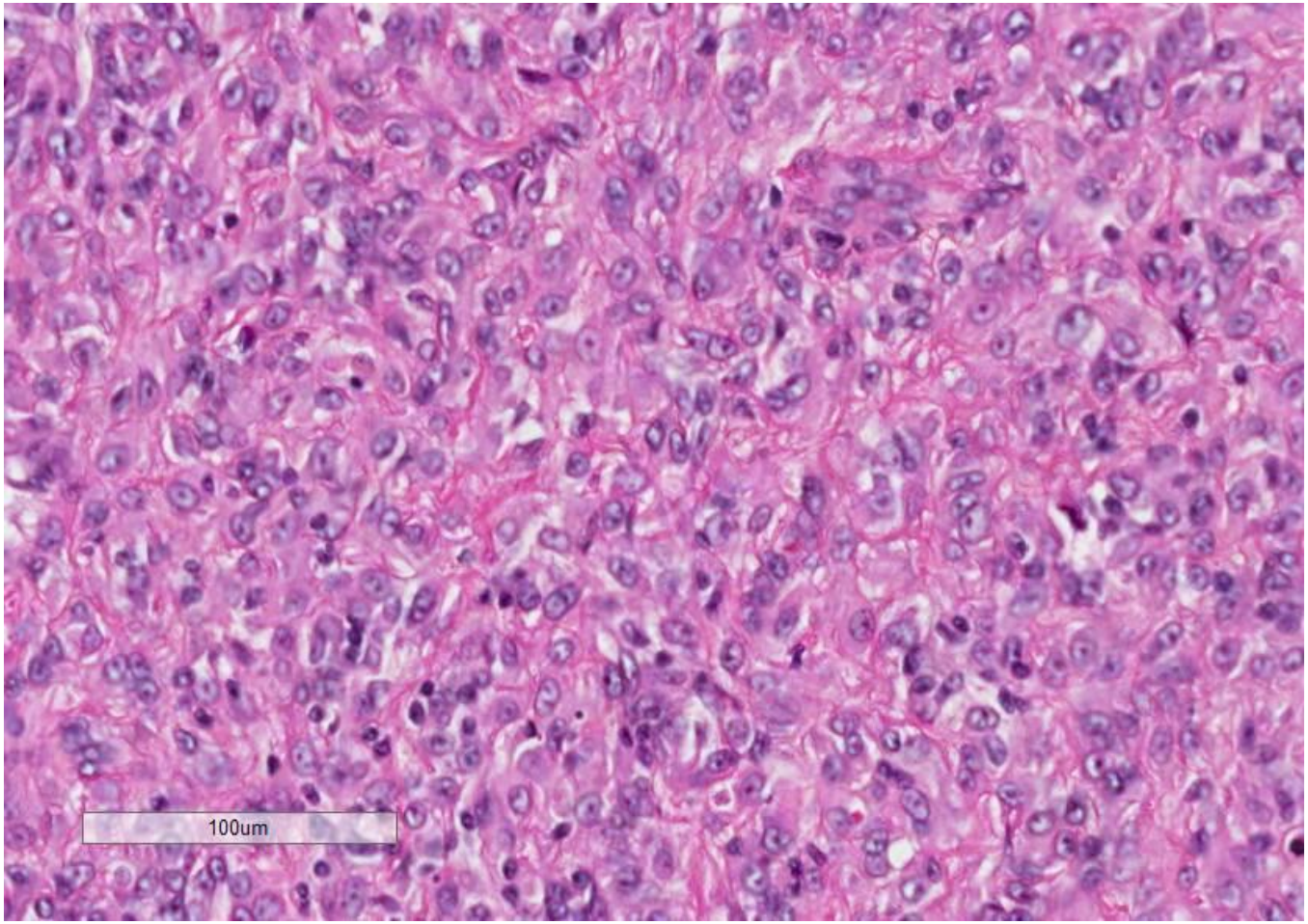


Special types Dermatofibroma



Epithelioid cell Fibrous Histiocytoma

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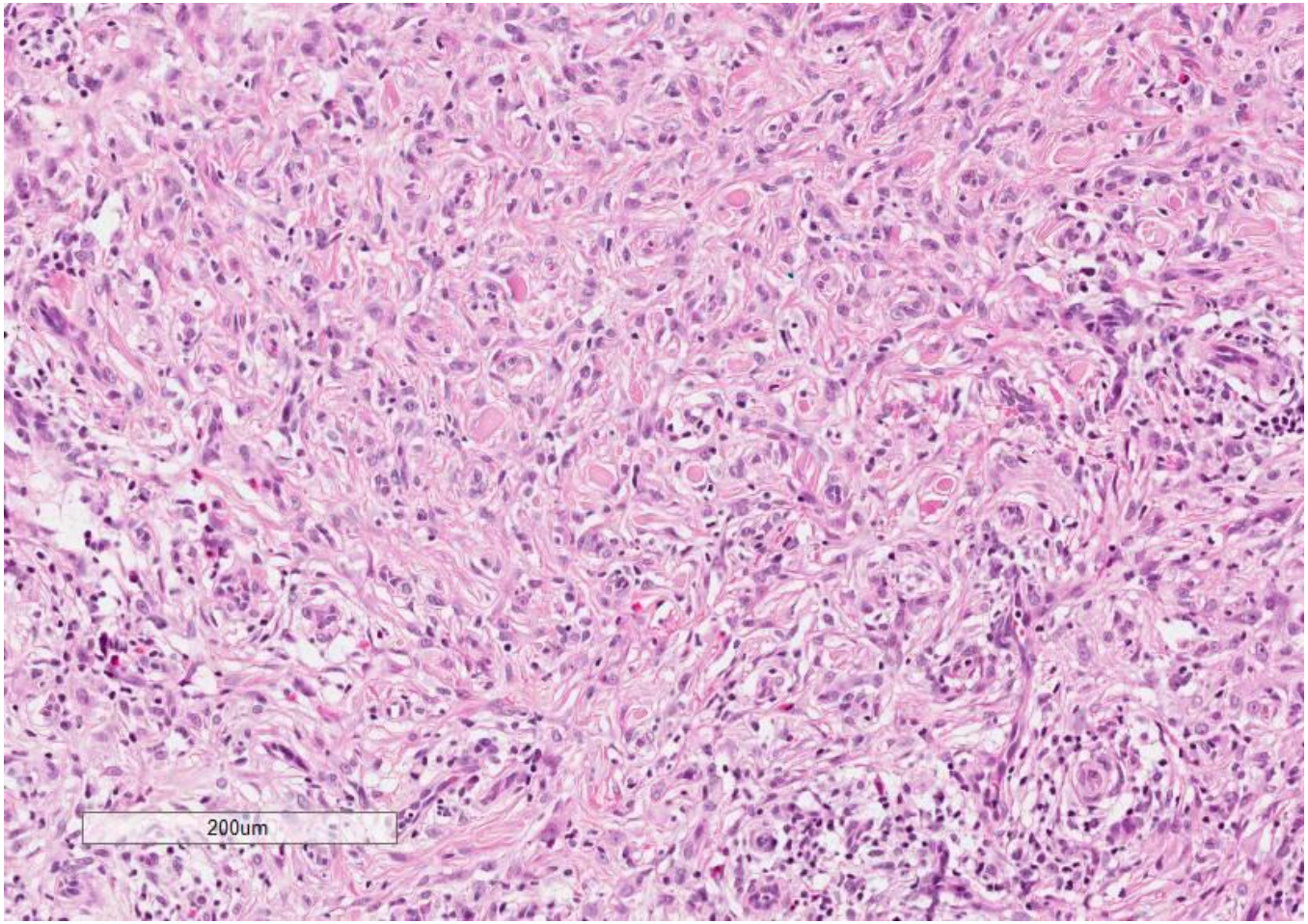
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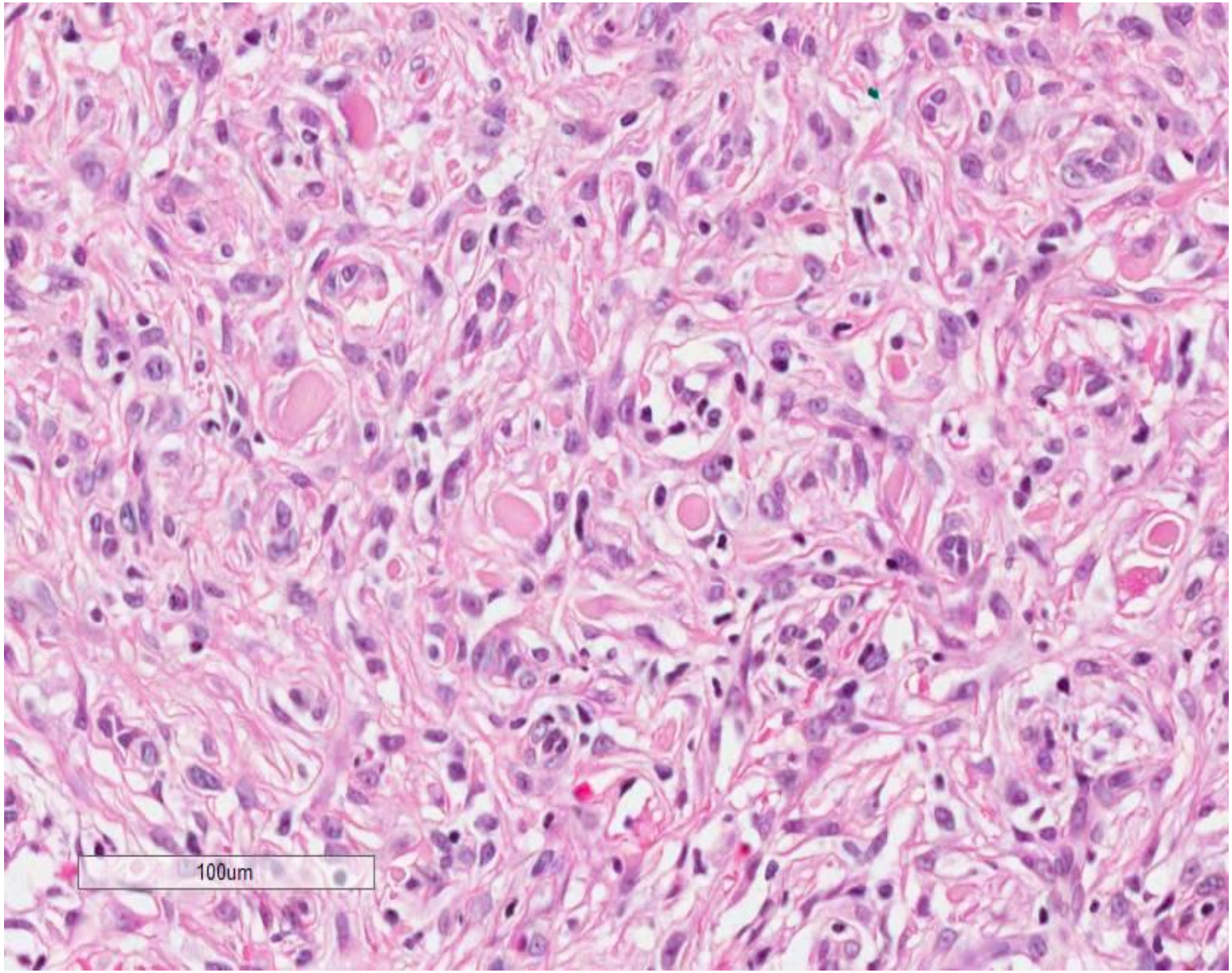
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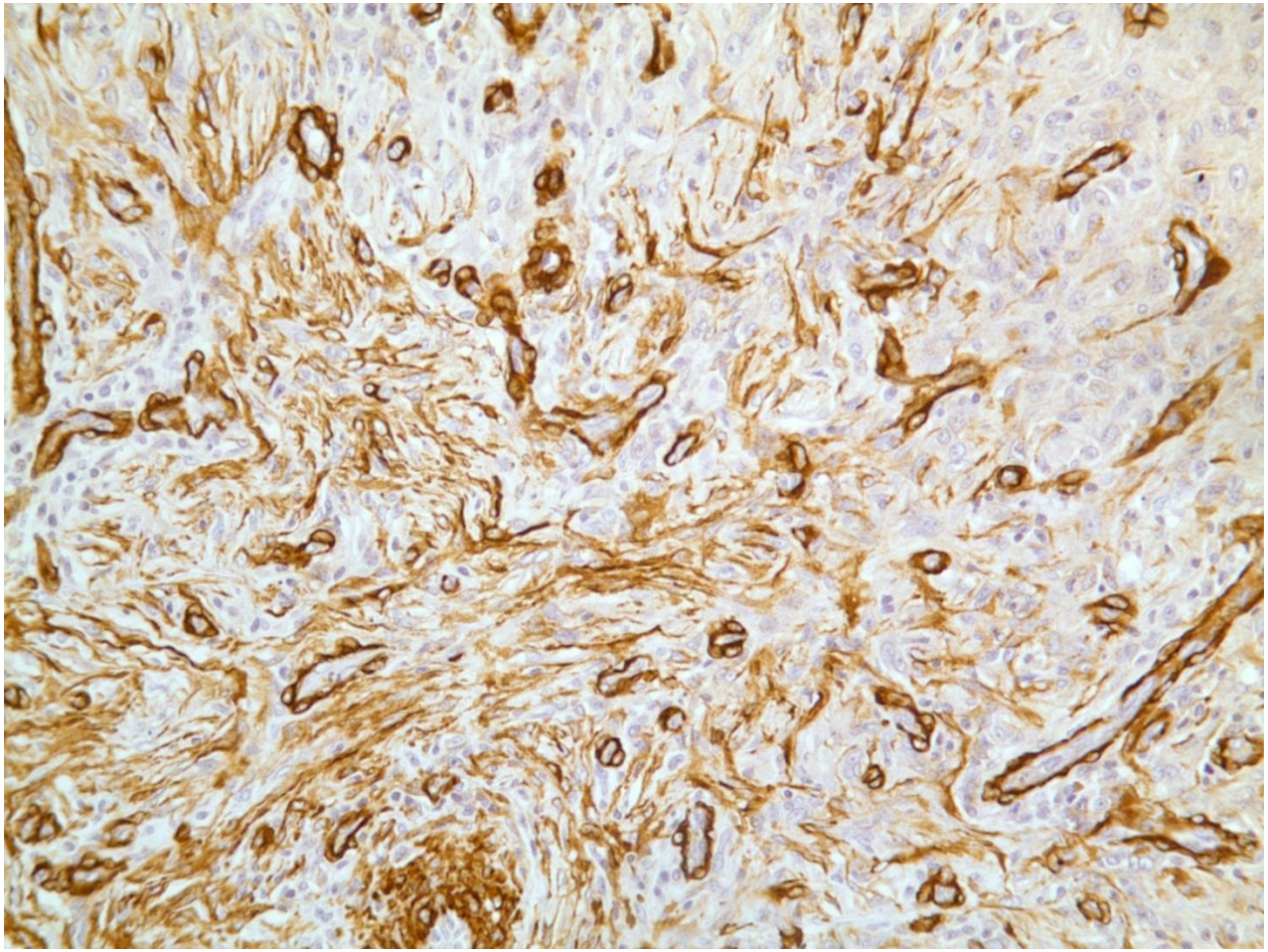
SMA



Epithelioid Dermatofibroma

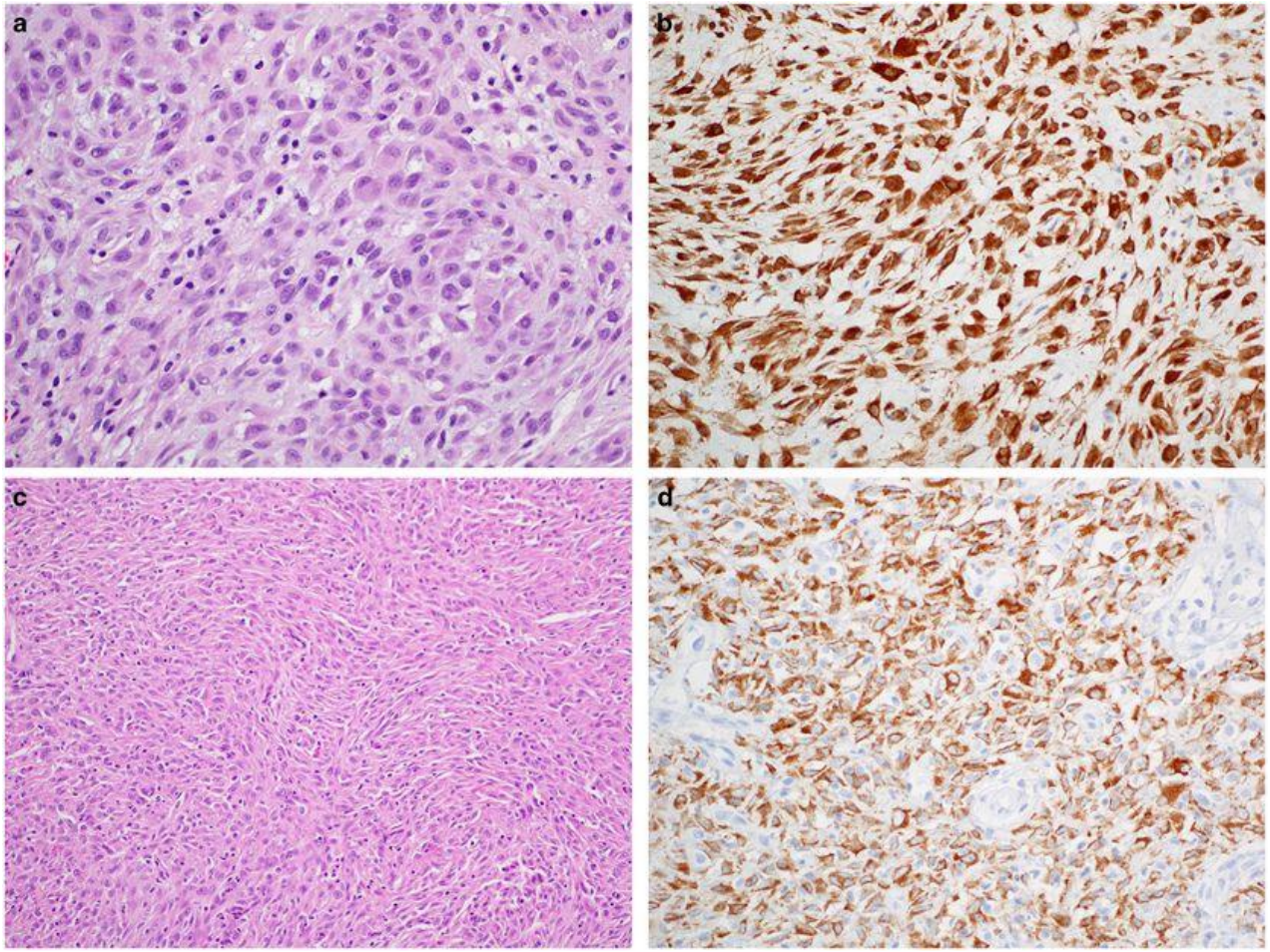
- Similar clinical setting as ordinary D.F., i.e. Young adults, peripheral sites.
- Often polypoid, with collaret, well circumscribed.
- SMA often positive, EMA positive in 50%.

Fibrous Histiocytoma Genetic Insights.

- Jedrych J et al. Epithelioid cell histiocytoma of the skin with clonal ALK gene rearrangement resulting in VCL–ALK and SQSTM1–ALK gene fusions
- Br. J. Dermatol.2015:172 1427-1429

L A Doyle, A Mariño-Enriquez, C DM Fletcher & J L Hornick

Modern Pathology volume 28, pages 904–912 (2015)



Storiform pattern

- Interwoven or rush mat pattern of tumour cells.
- Cell arranged in short fascicles which the interweave with each other.
- Commonly seen in spindle tumours of many types.

Case 2

- 75M s/c lump on leg

Case 2

- Lobulated
- Biphasic appearance; myxoid and pleomorphic spindle cell
- Curvilinear vessels
- Nuclear atypia

Myxofibrosarcoma

- Elderly, fairly common sarcoma
- Peripheral site
- S/C
- Non-specific immuno [Vimentin, focal SMA, focal CD34] or genetics
- Diagnosed on H+E

Case 3

- 20M, rapidly growing lump arm

Case 3

- Micro; Circumscribed unencapsulated tumour. Spindle cells with bland nuclei in a myxoid stroma. Appearance of myofibroblasts. Can become hyalinised.
- Red cell extravasation and patchy lymphocytic infiltrate.
- Immuno; SMA, HHF35 positive
- C.K., CD34 Negative

Nodular fasciitis

- Rule of 3's
- Third decade, present <3months and 3cm or less in size
- Immuno; myofibroblastic, SMA only
- **Nodular fasciitis: a novel model of transient neoplasia induced by MYH9-USP6 gene fusion.**
- **FISH probe now available**

Virchows Arch (2013) 463:97–98
DOI 10.1007/s00428-013-1418-0

LETTER TO THE EDITOR

Detection of *USP6* gene rearrangement in nodular fasciitis: an important diagnostic tool

M. Fernanda Amary · Hongtao Ye · Fitim Berisha · Roberto Tirabosco · Nadege Presneau · Adrienne M. Flanagan

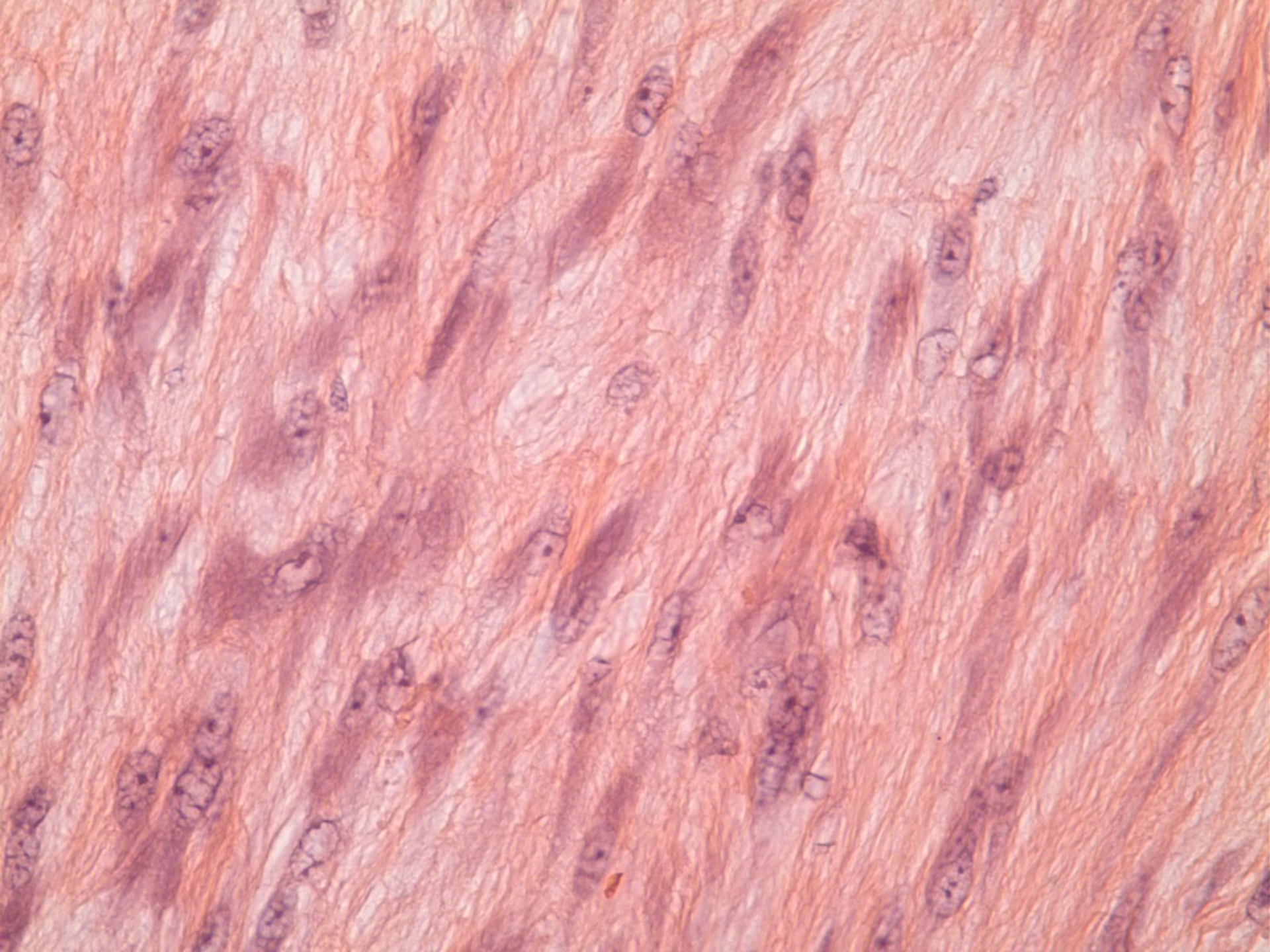
Received: 31 March 2013 / Revised: 17 April 2013 / Accepted: 19 April 2013 / Published online: 9 June 2013

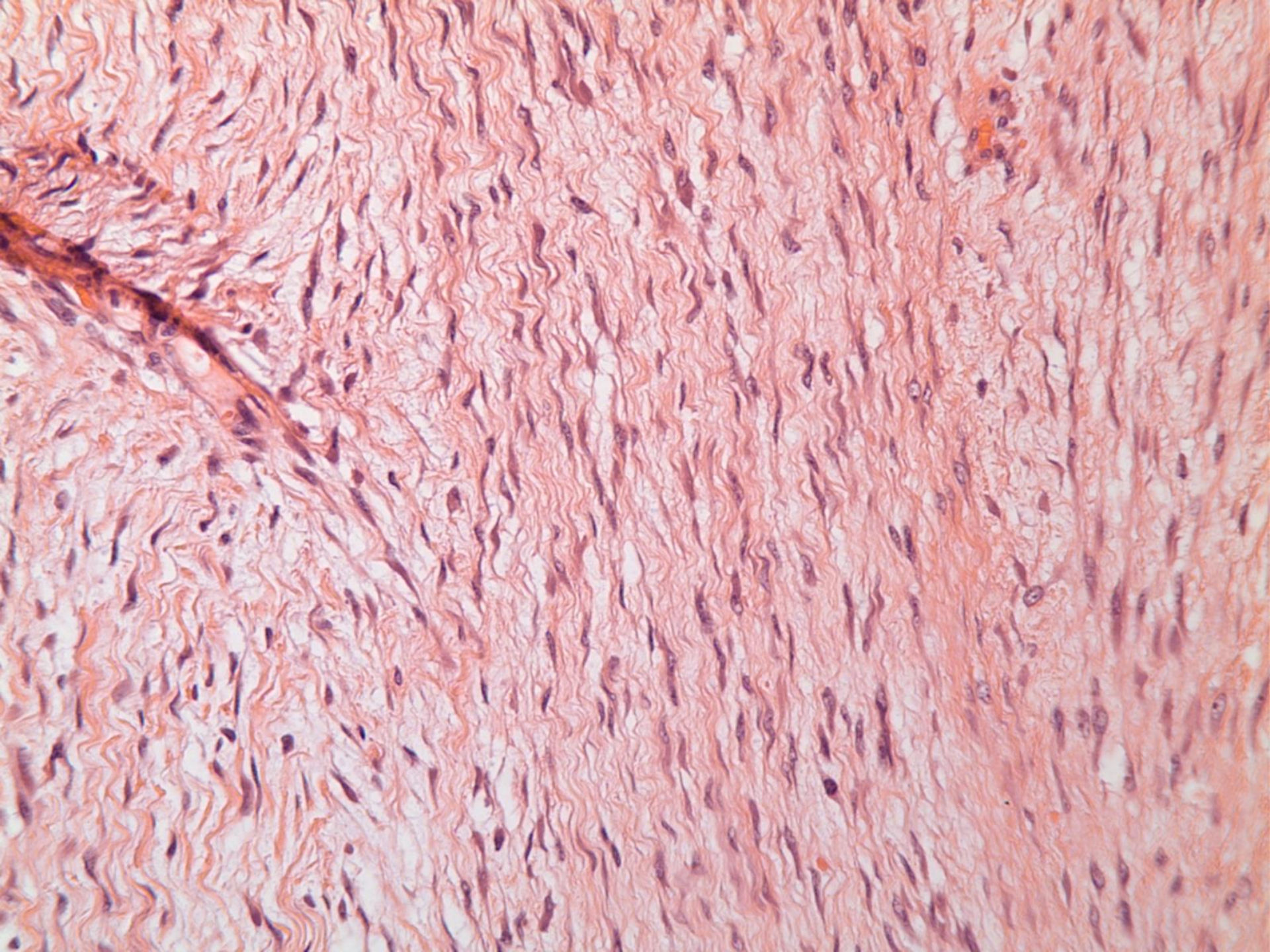
Fibrous

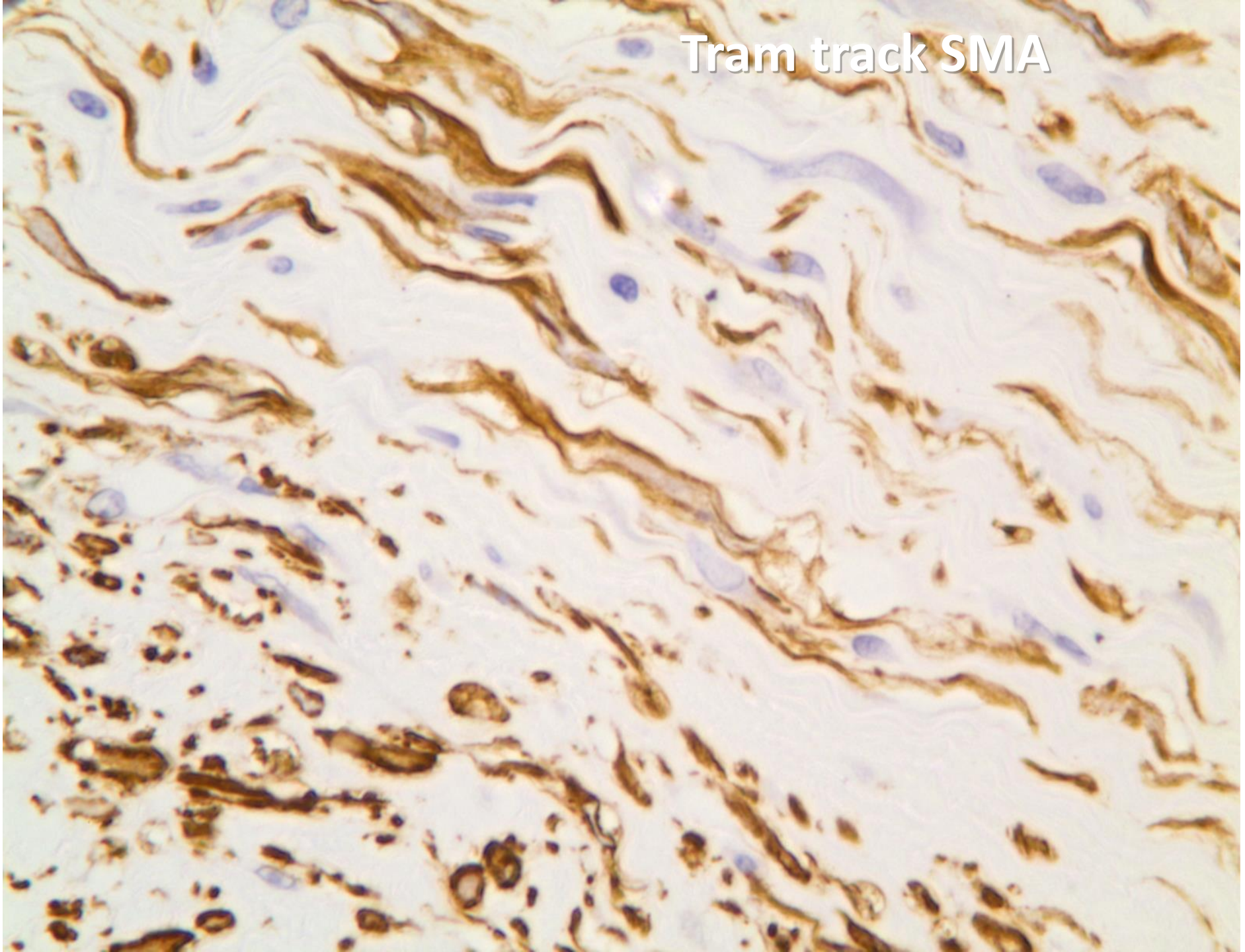
- **Myofibroblast**; Plump spindle cell with pale to purple/basophilic cytoplasm. Elongated nucleus, oval, often eccentric. Not as pink as smooth muscle. Less well defined cytoplasm
- **Fibroblasts**; small cells, often greatly elongated nucleus;wavy.Nucleus, hyperchromatic. Cytoplasm, small amount of poorly defined pale cytoplasm.
- Matrix; Collagen.

Immuno- fibrous

- SMA- tram-track [wispy].
- Desmin – usually neg. Can be positive, esp. at visceral sites.
- H-caldesmon negative.






Tram track SMA

Differential diagnosis

- Fibromatosis, much more organised into long fascicles. Infiltrative growth pattern.
- Malignancy, but Nodular Fasciitis lacks nuclear atypia, necrosis, abnormal mitoses [Can have normal mitoses ++]

Case 4

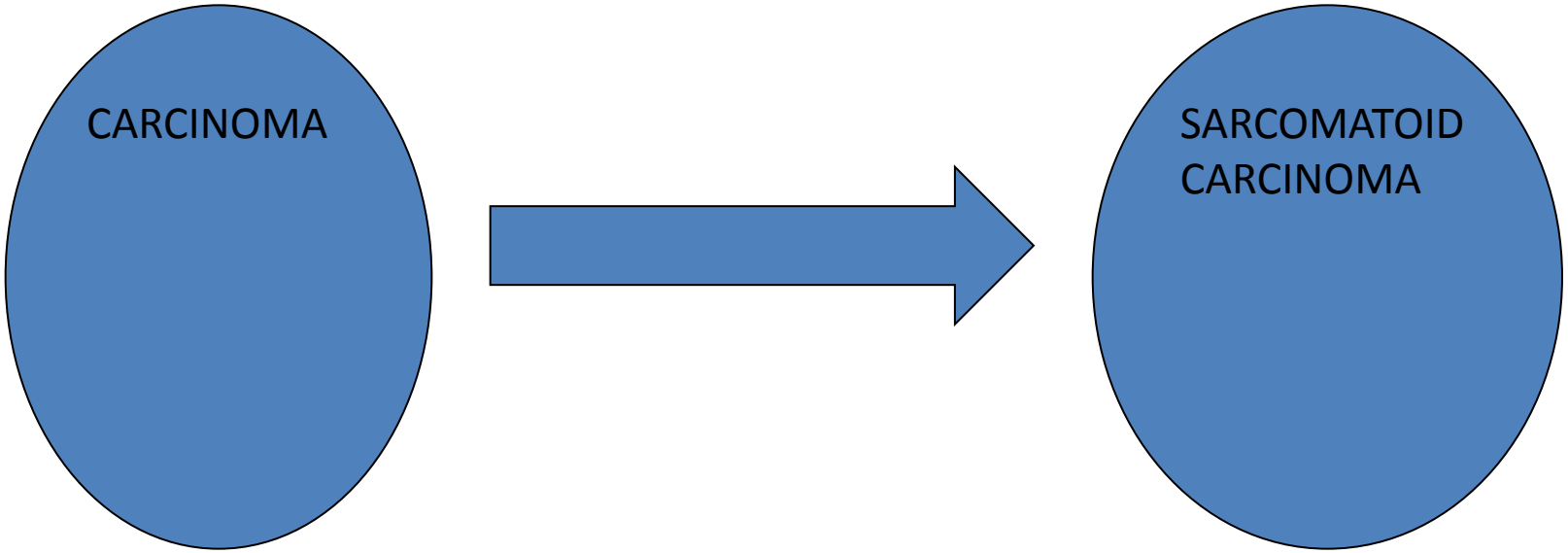
- 70F suspicious mass on x-ray left breast

Case 4
Differential diagnosis

- Fibromatosis
- Phyllodes
- Metaplastic/spindle cell carcinoma

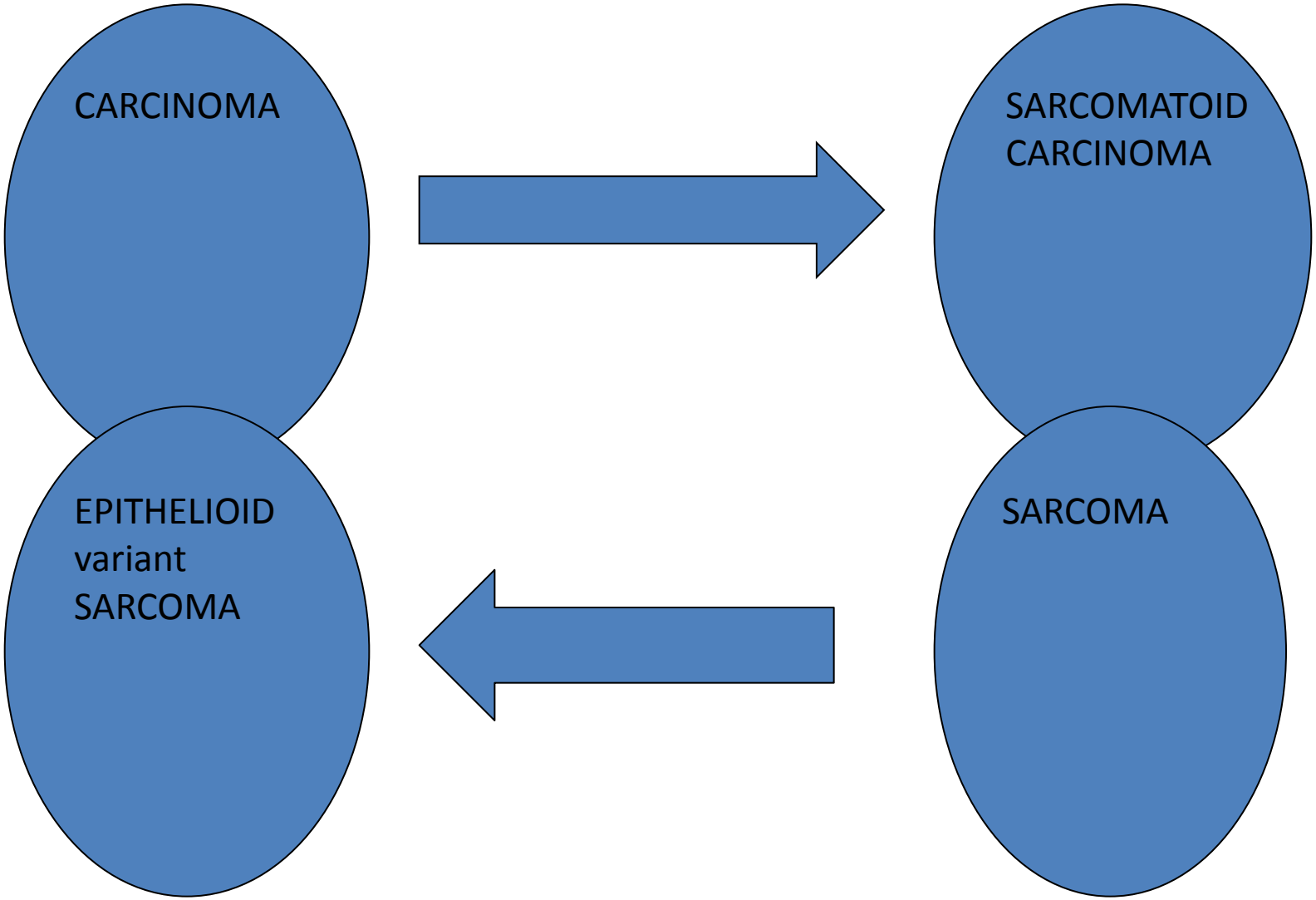
Metaplastic carcinoma

- Cytokeratins; Do LOTS ! ;
  - MNF116, AE1/AE3, [CK5/6, CK14, CK7,34bE12]
- P63, very useful
- S100; occasionally focally positive
- SMA can be positive
- CD34; Neg
- Beta-Catenin, can be focally positive.


CARCINOMA
SARCOMATOID
CARCINOMA

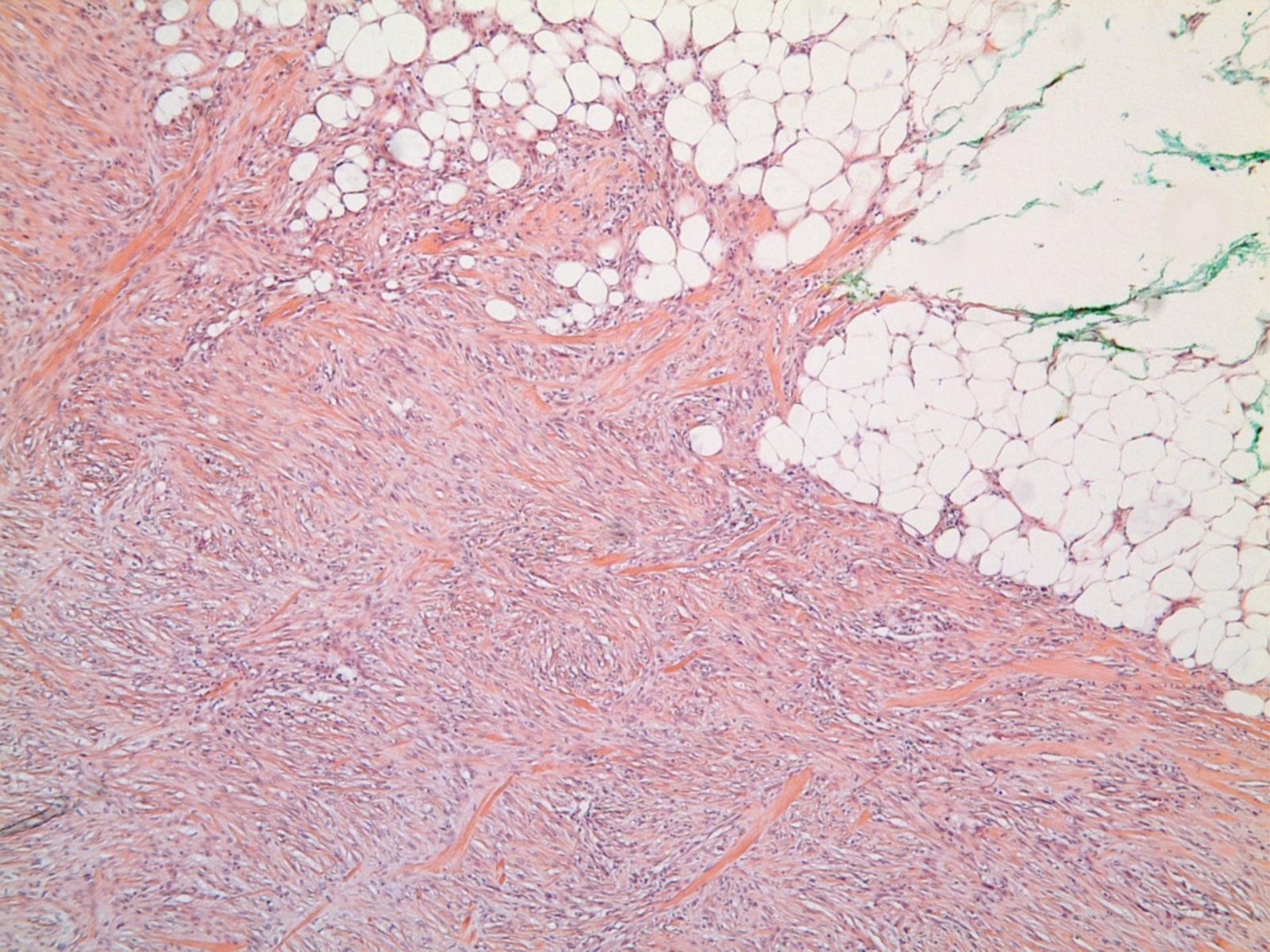
When epithelial tumours go spindly

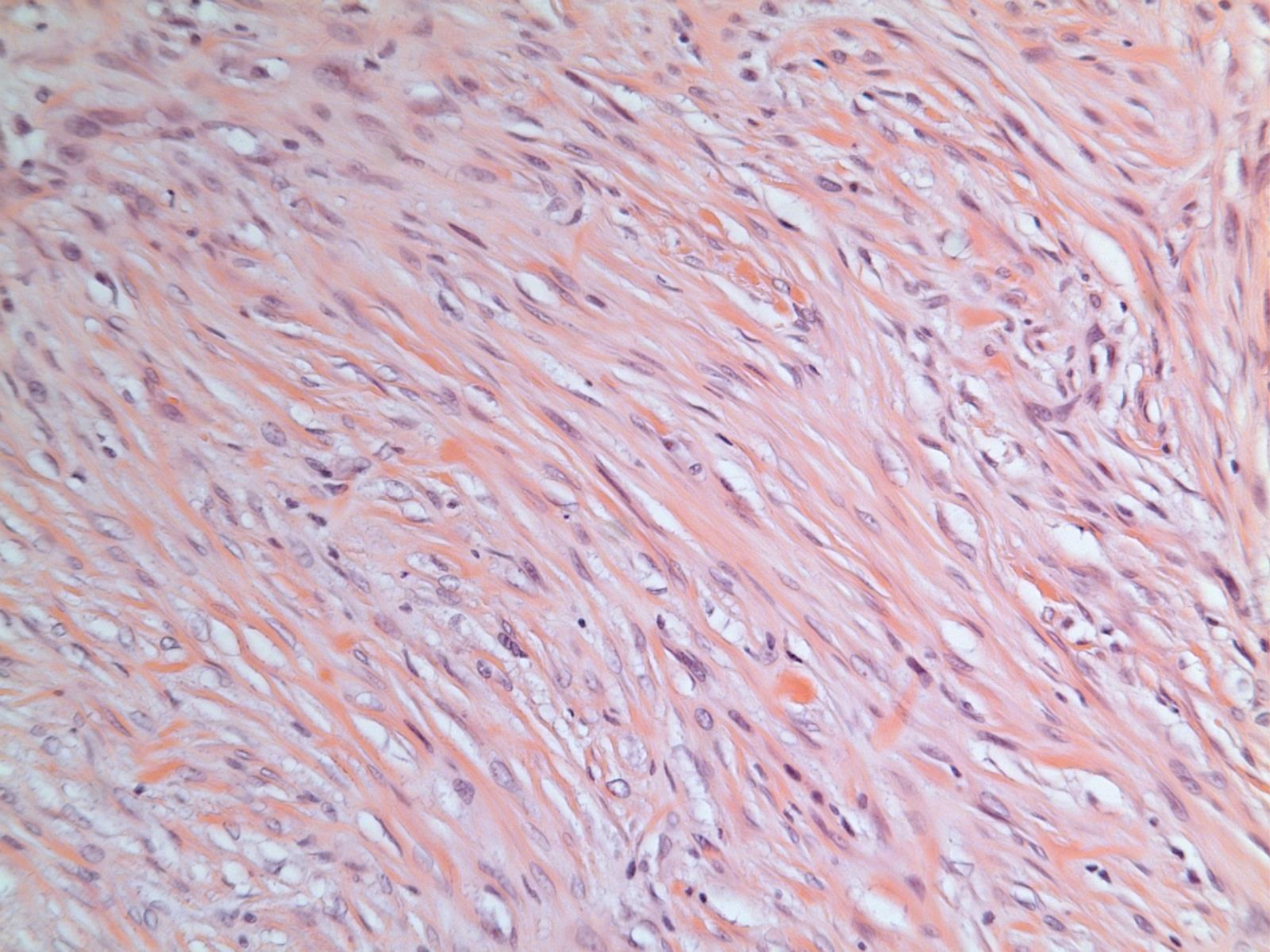
- Acquire SMA, +/- a stroma
- Retain immunological evidence of origin;
  - C.K positive, especially high molecular weight, may be more specific eg 34betaE12 [CK34]
  - P63 positive
- Lack more specific markers of mesenchymal differentiation; CD34, CD31, H-caldesmon.

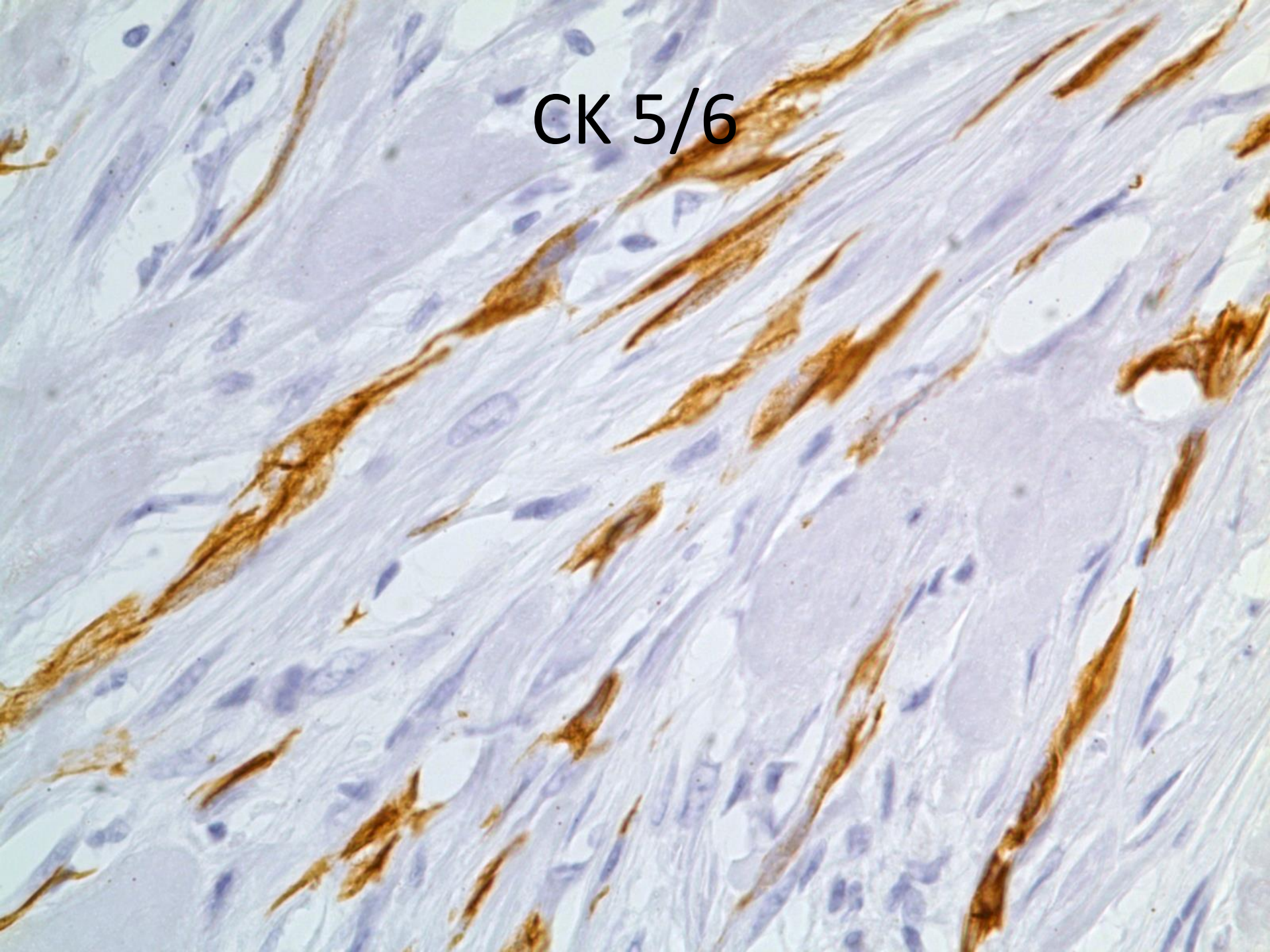

CARCINOMA
SARCOMATOID
CARCINOMA
EPITHELIOID
variant
SARCOMA
SARCOMA

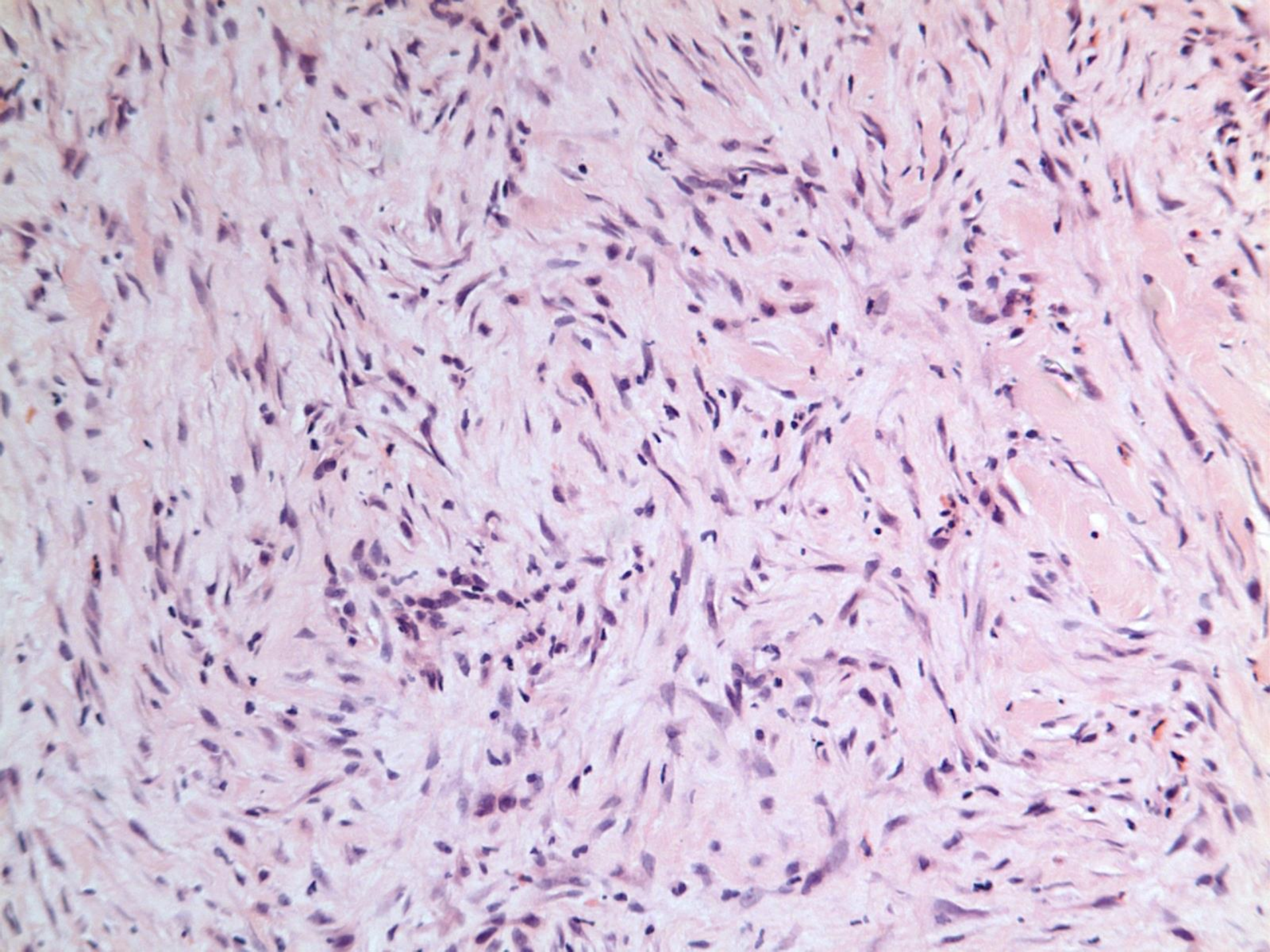
When mesenchymal cells go epithelioid

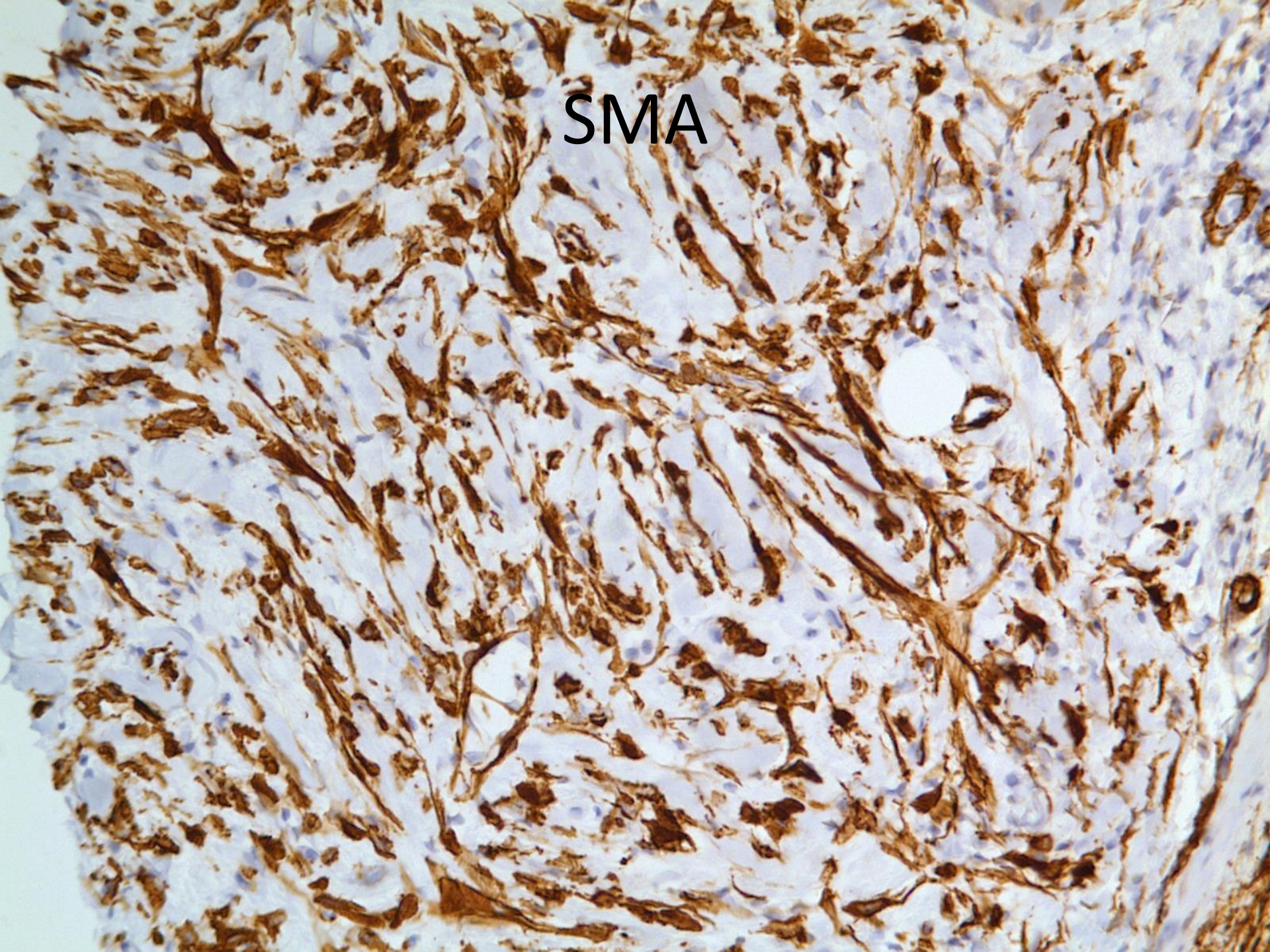
- Cells will acquire Cytokeratin. Usually focal, and rarely high molecular weight.
- Lack more specific marker of epithelial origin, p63, with few exceptions
- Retain more specific markers of origin; CD34, CD31, H-caldesmon.

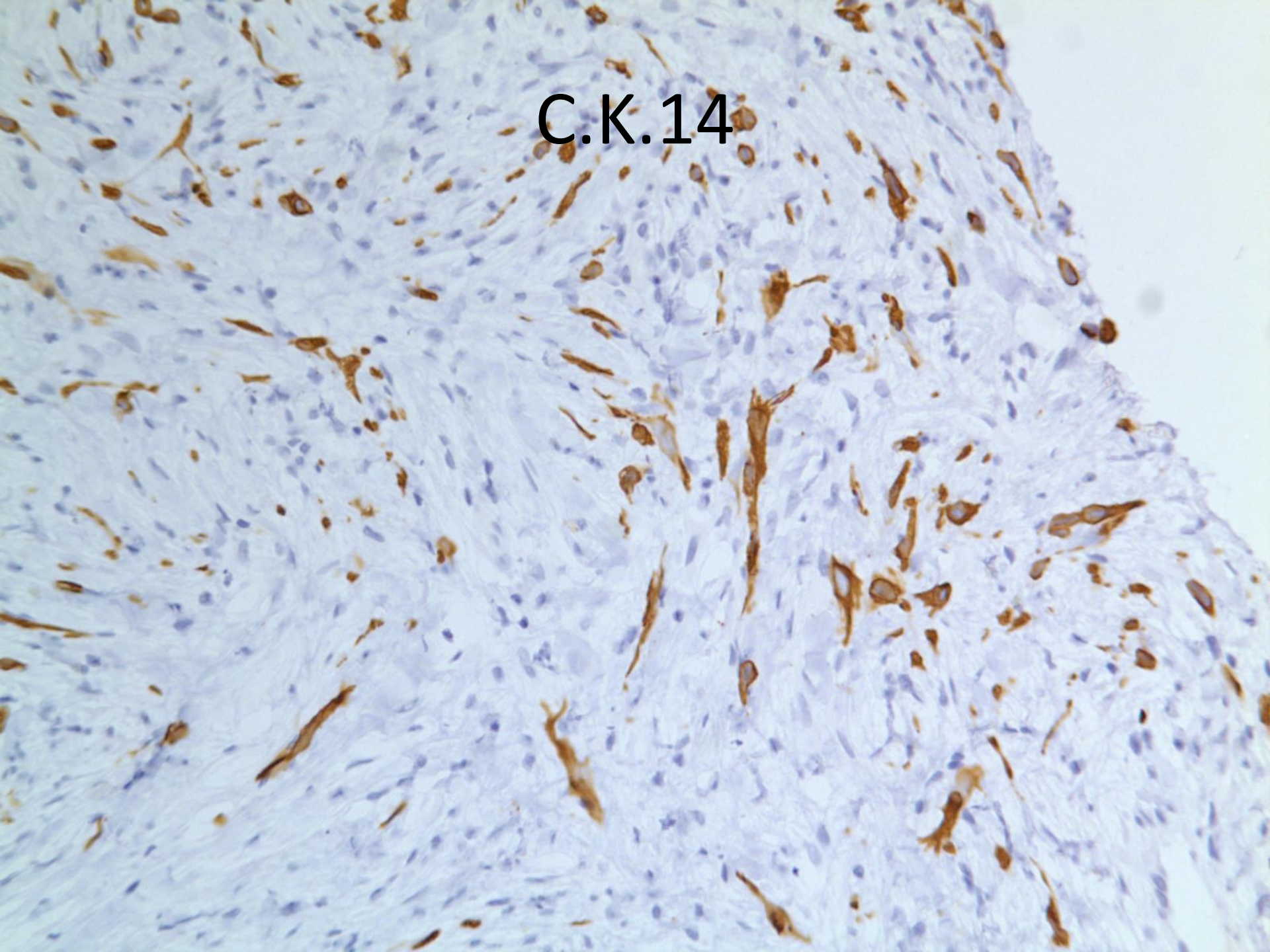


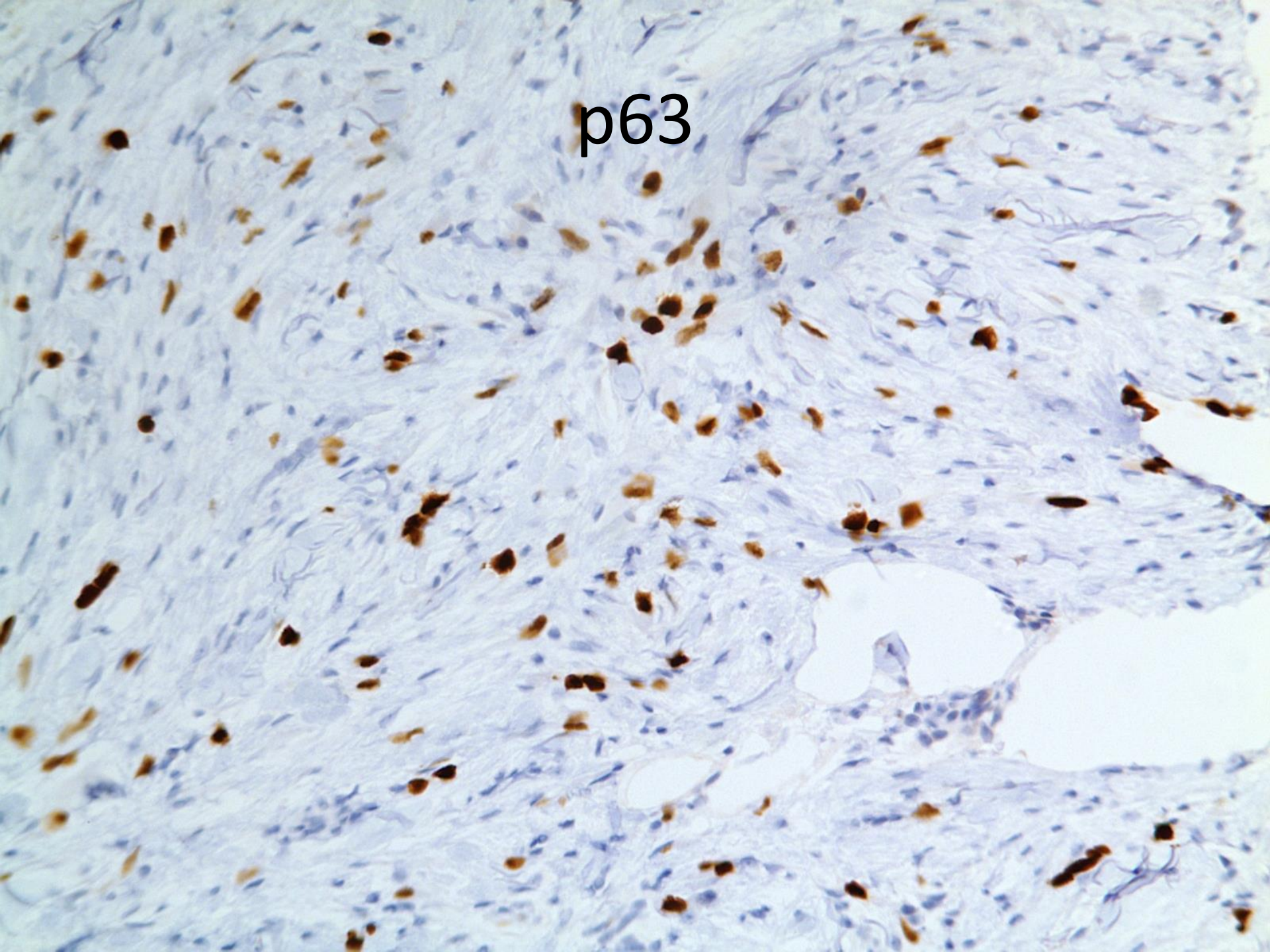



CK 5/6




SMA


C.K.14


p63

P63 in soft tissue tumours

- 650 soft tissue tumours Am.J.Clin.Path.2011:136; 762-6
- Negative; Angiosarcoma's, lipomatous neoplasms, DFSP, SFT,Schwannoma, neurofibroma, LMS.
- Positive mesenchymal tumours; Myoepithelioma/Ca of soft tissues, Neurothekeoma, perineurioma, giant cell tumour of tendon sheath & soft parts.
- Weak focal staining seen in rest eg AFX, RMS

CD34

- Very useful immuno.
- Should be in your panel.
- Has an eclectic range of positive lesions.

CD 34, consistently positive;

- Vascular Tumours, including Kaposi's
- GIST [80%]
- Solitary fibrous tumour [SFT]
- DFSP
- Breast specialist stromal tumours; PASH, F.A., Phyllodes, myofibroblastoma’s.
- Adipocytic tumours, benign and malignant
- Nerve sheath Tumours
- Other; Epithelioid sarcoma, LMS[25%]
- Hemopoietic tumours, AML, ALL.

CD 34 Negative

- Carcinomas of all types [expt Trichilemmomas, rare NUT tumours]
- Melanoma [very rare cases +]
- Fibromatosis
- Nodular Fasciitis

Immunohistochemical Panel

	Main Use	Other points
CK,s Lots	Spindle cell ca.	Occ. Sarcoma, when epithelioid
P63	Spindle cell ca.	Rare in soft tissue
CD 34	Mesenchymal; Phyllodes, DFSP	Very rare in Ca.
Beta-catenin	Fibromatosis, Phyllodes	Rare and weak in Ca
S100	Melanoma Met.	Rare in Ca
SMA	Reactive scars, Nod. Fasciitis	Relatively non-specific

Important points

- Mesenchymal tumours/sarcomas of Breast are rare and most cases where considered turn out to be spindle cell/metaplastic carcinomas or malignant phyllodes.
- Older age group, unlikely to be fibromatosis
- Use broad panel of immunohistochemistry with all those suggested.

Case 5

- Large plaque covering shoulder

Pilar Leiomyoma

- Can be multiple ;linear, grouped, zosteriform
- Can be painful

Smooth Muscle

- Spindle cells with abundant eosinophilic cytoplasm.
- Fascicular pattern, Fascicles at right angles
- Elongated, blunt ended nuclei [cigar shaped].
- Peri-nuclear vacuole – not common. More often GIST.

Case 6

70 Male, deep mass in thigh

What pattern is this?

Case 5

- Giant cell MFH pattern

Giant cell MFH pattern

- Sarcoma's – Leiomyosarcoma, giant cell tumour of soft tissue, osteosarcoma
- Carcinoma's- pancreas , breast

Clues for high grade sarcoma's

- Look for low grade areas at edge.
- Not lots of immuno.

Case 6

- Leiomyosarcoma

Case 7

- 45 Male, deep mass in thigh

Low grade Fibromyxoid sarcoma

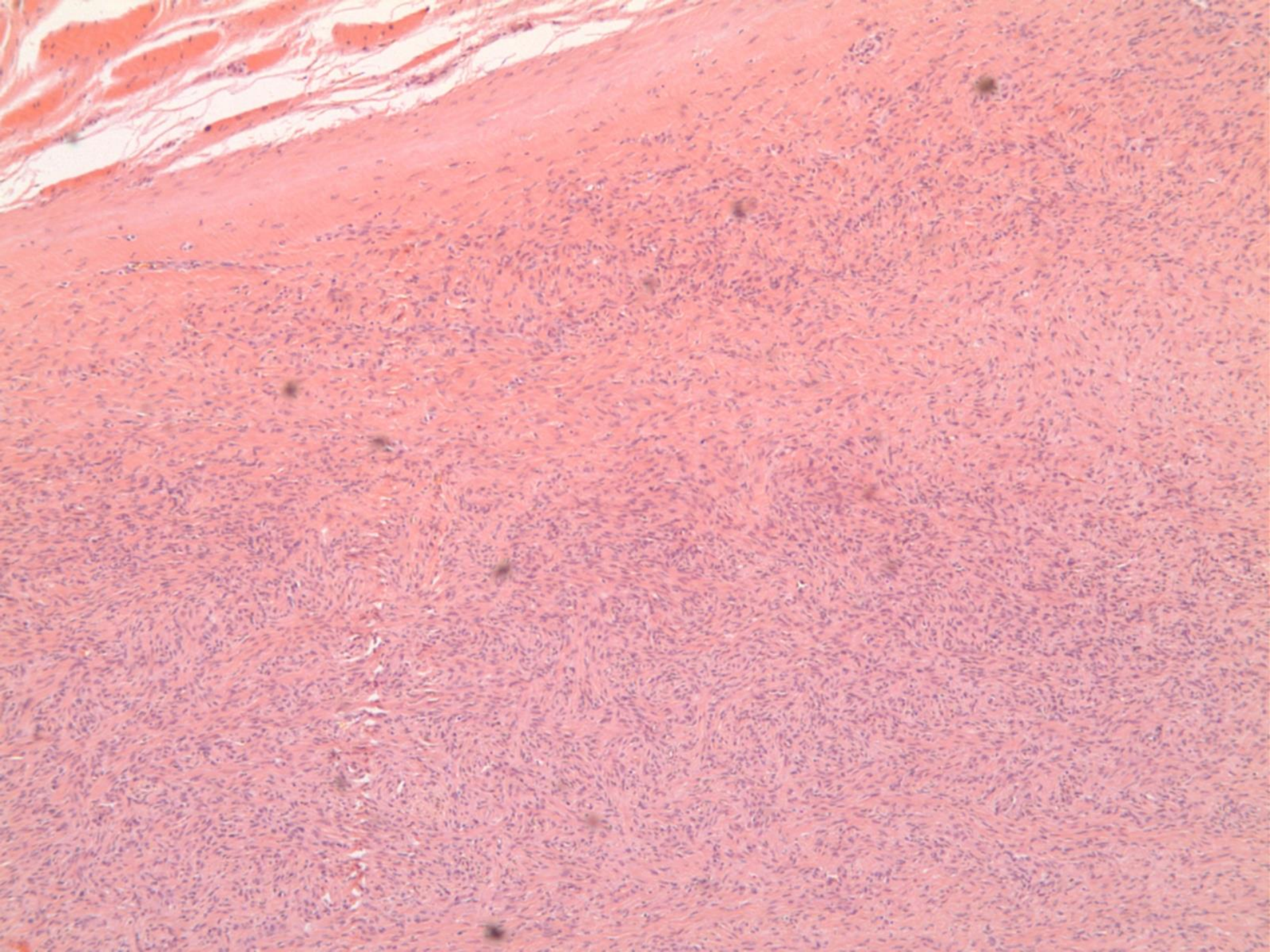
- Hyalinising spindle cell tumour with giant rosettes

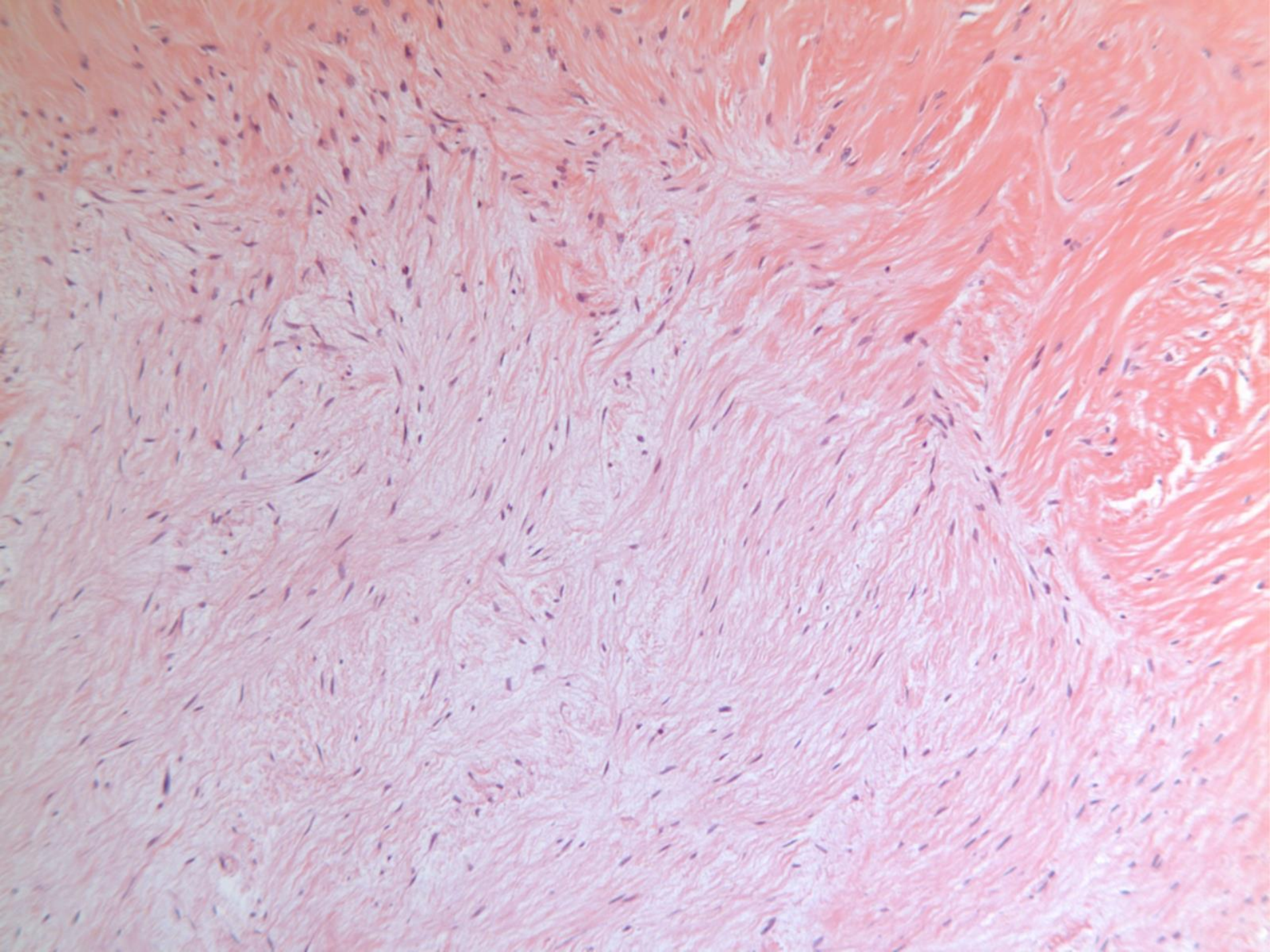
Low grade Fibromyxoid sarcoma

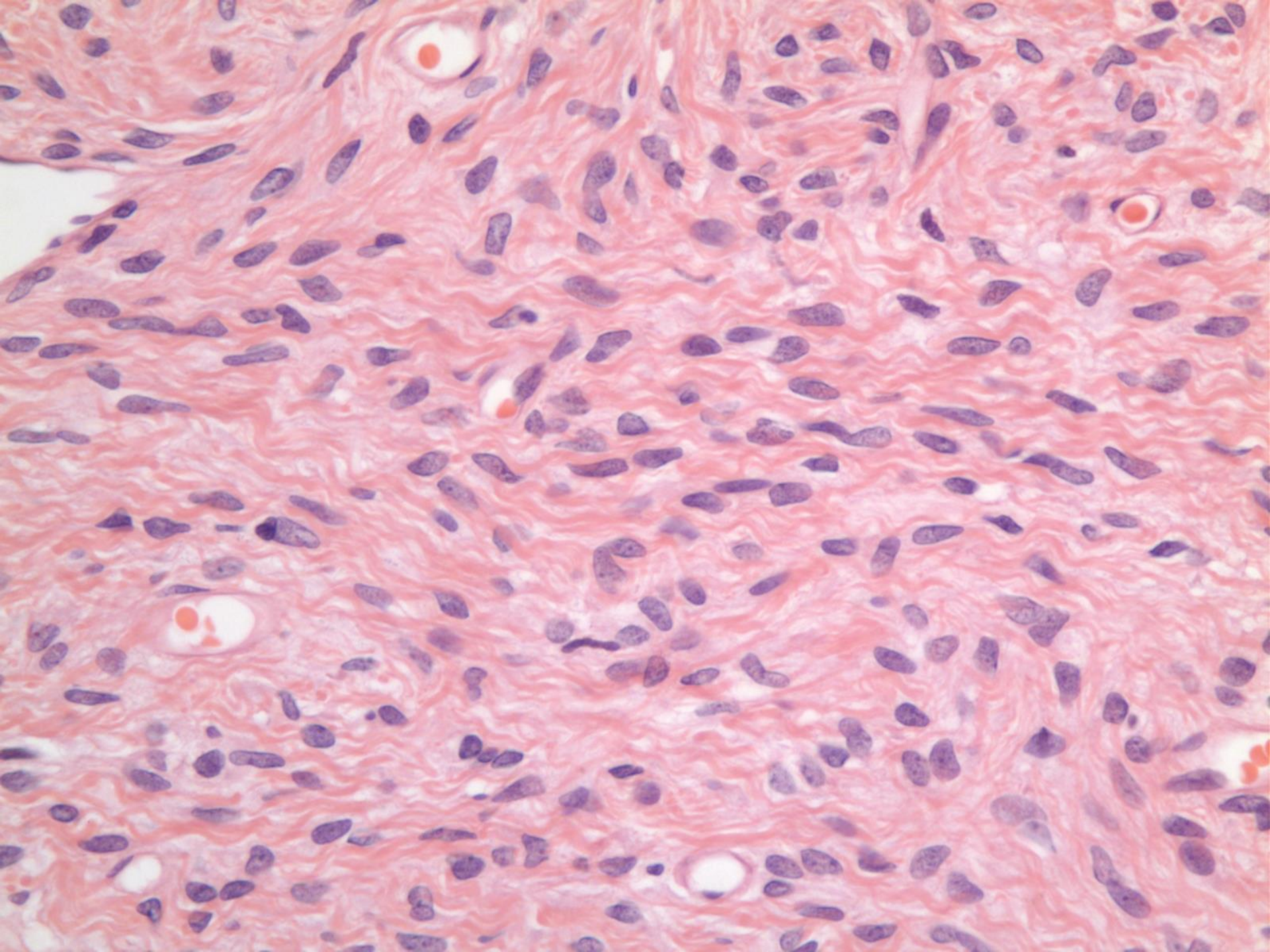
- Young Adults, wide range of sites.
- Often intra muscular but can present as subcutaneous tumour. Circumscribed lobulated tumour.
- Slow growing

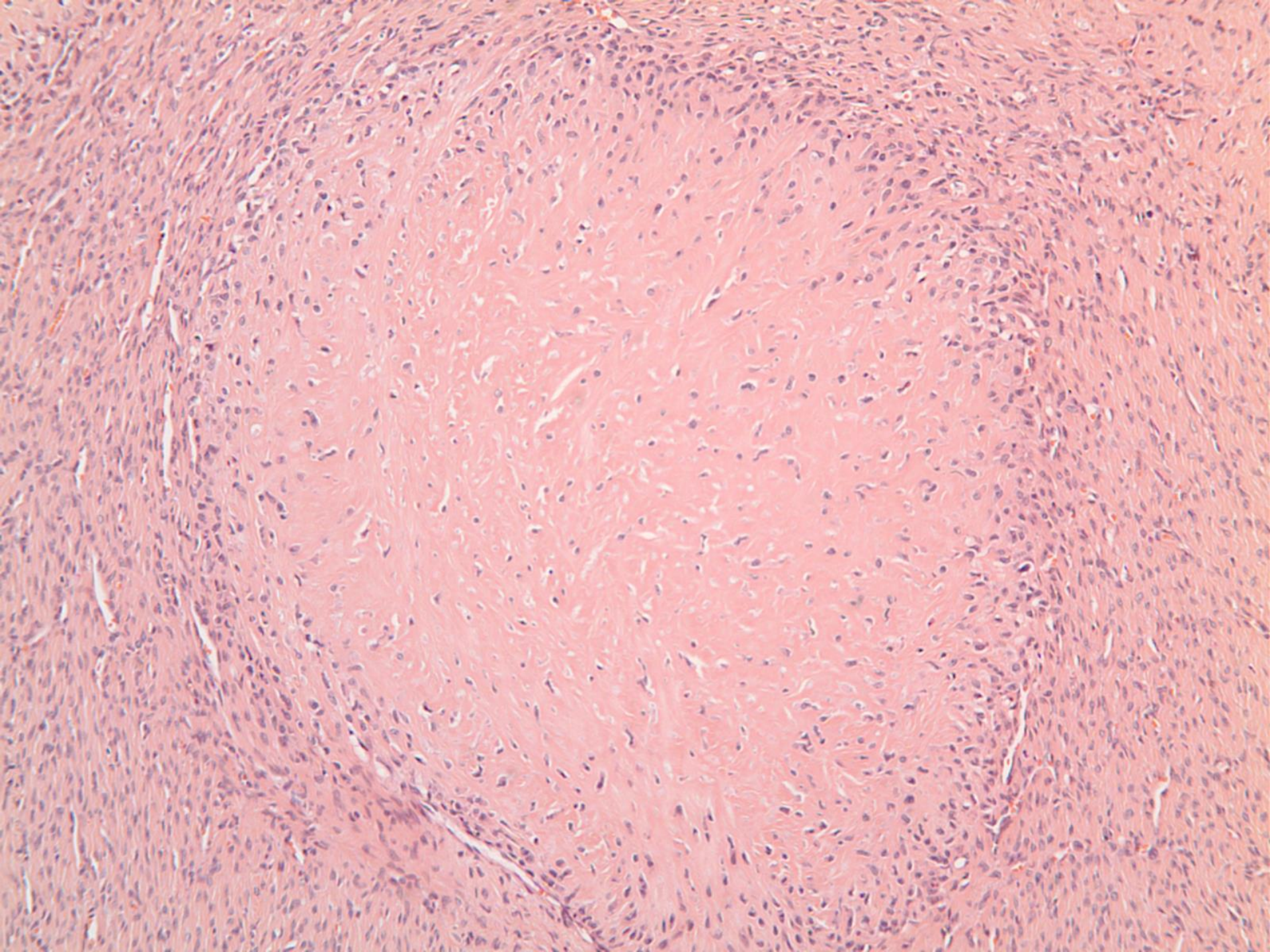
Low grade Fibromyxoid sarcoma

- Micro. Low to moderate cellularity. Very bland appearance
- Cells Spindled, with small hyperchromatic nuclei. Indistinct cytoplasm. Only mild nuclear atypia,
- Alternating myxoid and fibrous stroma.
- Can have branching thick walled capillaries in myxoid zone.
- May have foci higher grade, especially in recurrence.
- Occasionally Giant Rosettes





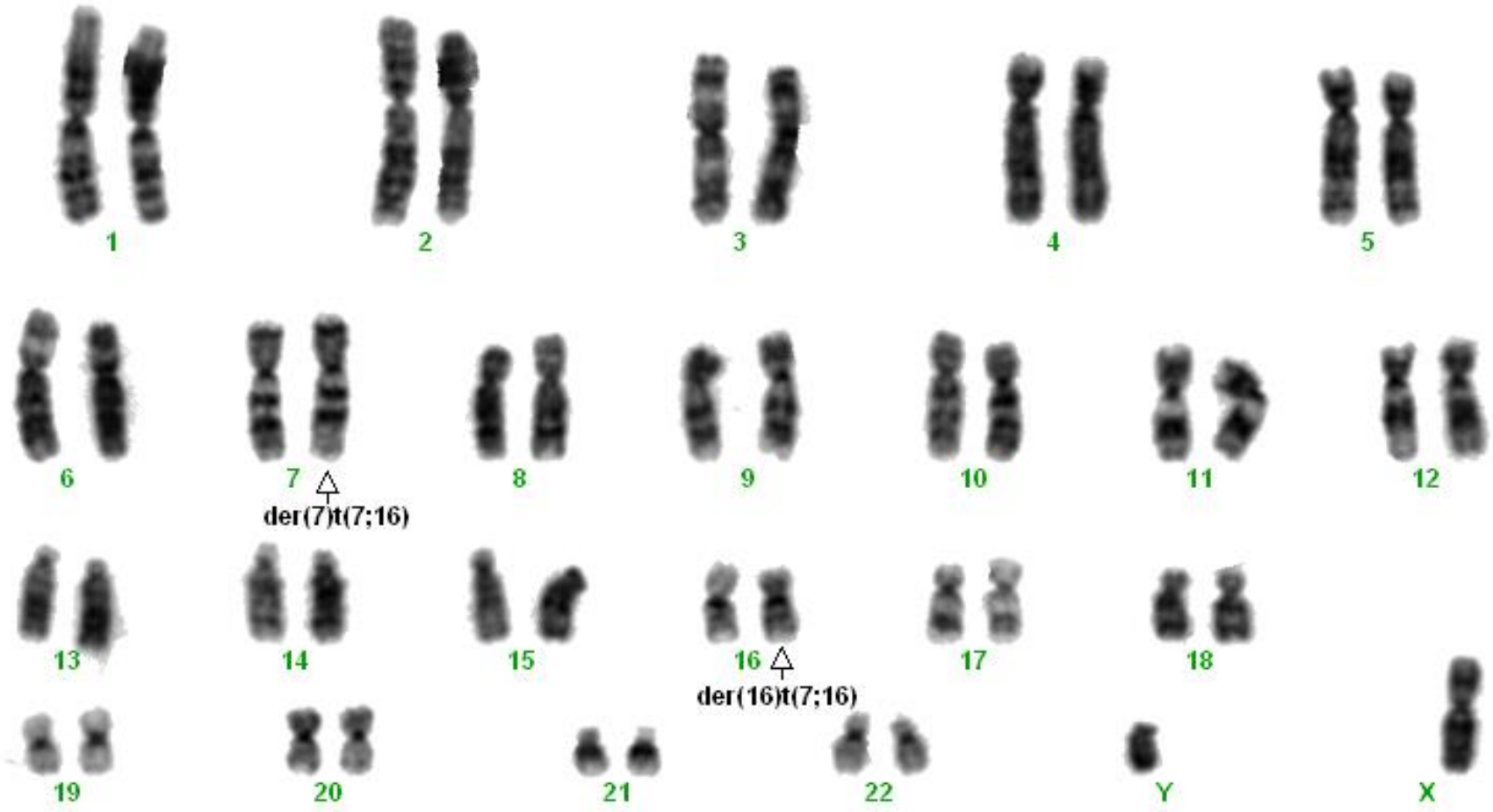




Low grade Fibromyxoid sarcoma

- Immuno. May stain for SMA. Rare cases focal Cytokeratin. Beta catenin and S100 negative.
- EMA- often positive [confuse with perineurioma]
- Recently, MUC 4 immuno shown to be useful.
- Genetics- Translocation Involving FUS gene Chromosome 7 and CREB3l2 on Chromosome 16 in many.
- Can use FISH, PCR better.

N H – t(7;16)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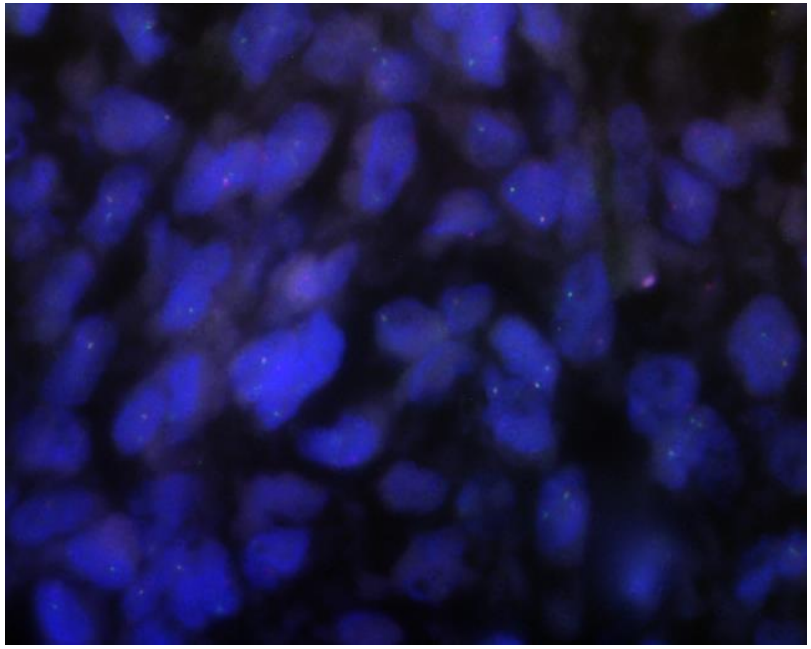
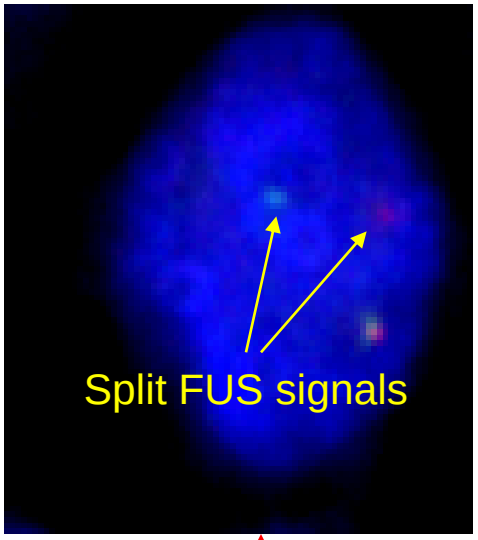
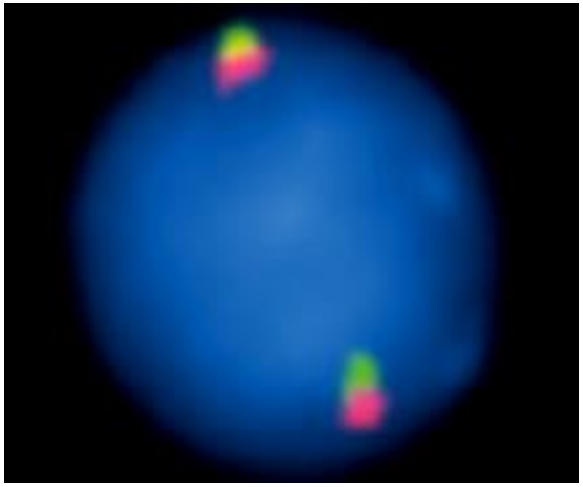
FISH with FUS break-apart probe



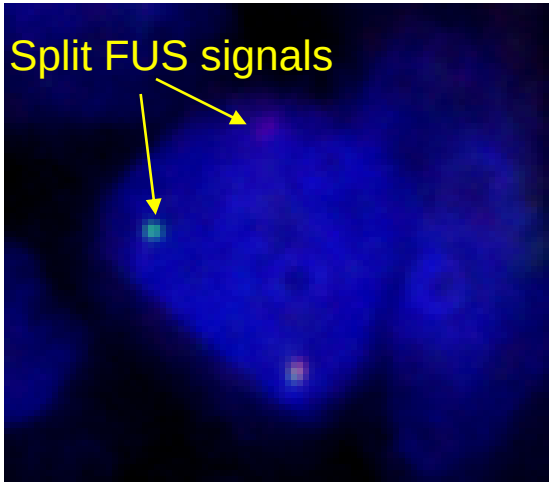
Multiple abnormal cells



FUS rearranged



FUS normal



Fibrosarcoma

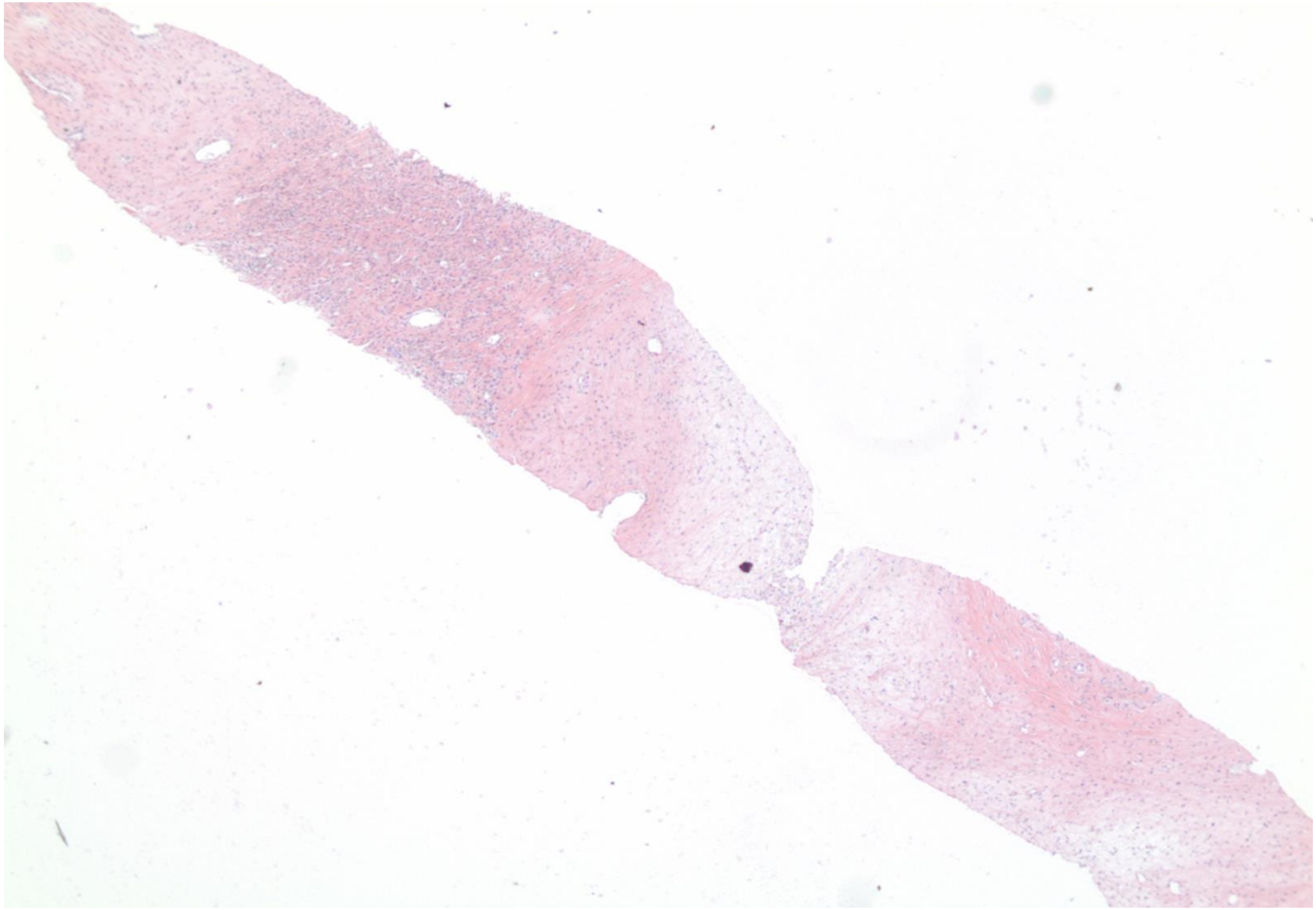
- Can you name any?

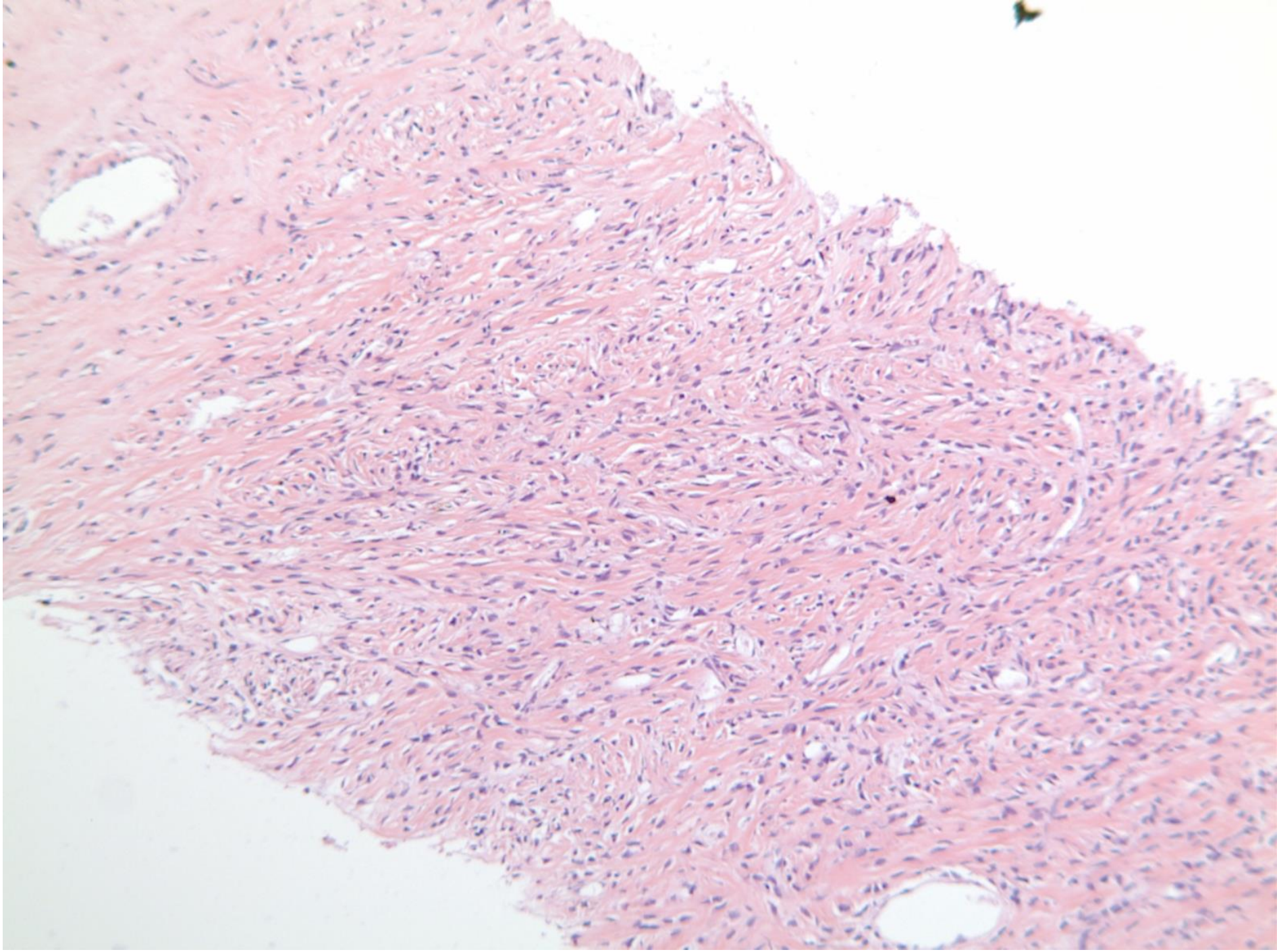
‘Fibro’ ‘sarcoma’ WHO Classification

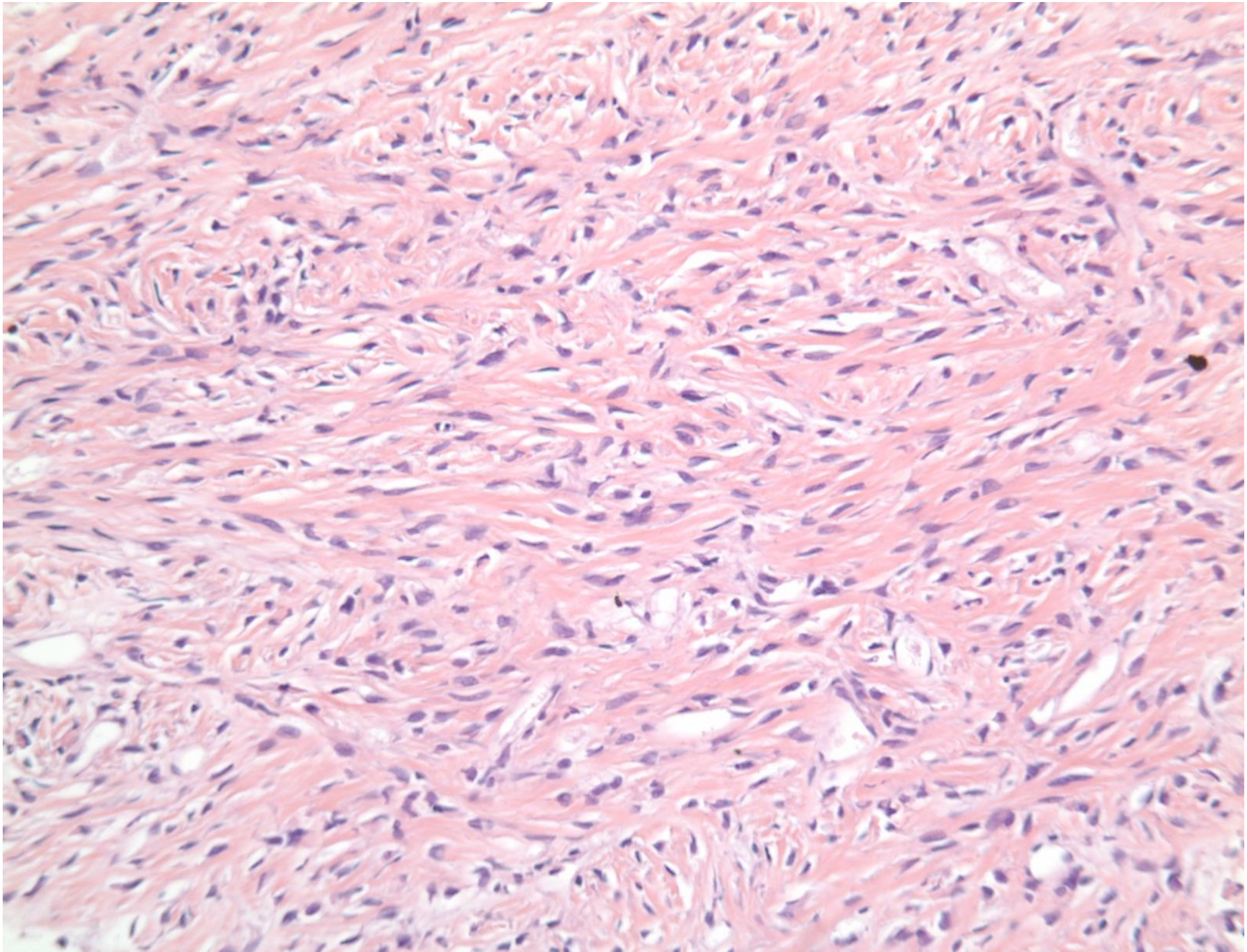
- Myxoinflammatory fibroblastic sarcoma
- Myxofibrosarcoma
- Low grade fibromyxoid sarcoma
- Sclerosing epithelioid fibrosarcoma
- DFSP
- Infantile fibrosarcoma
- Low grade myofibroblastic sarcoma
- Adult fibrosarcoma [?exists]

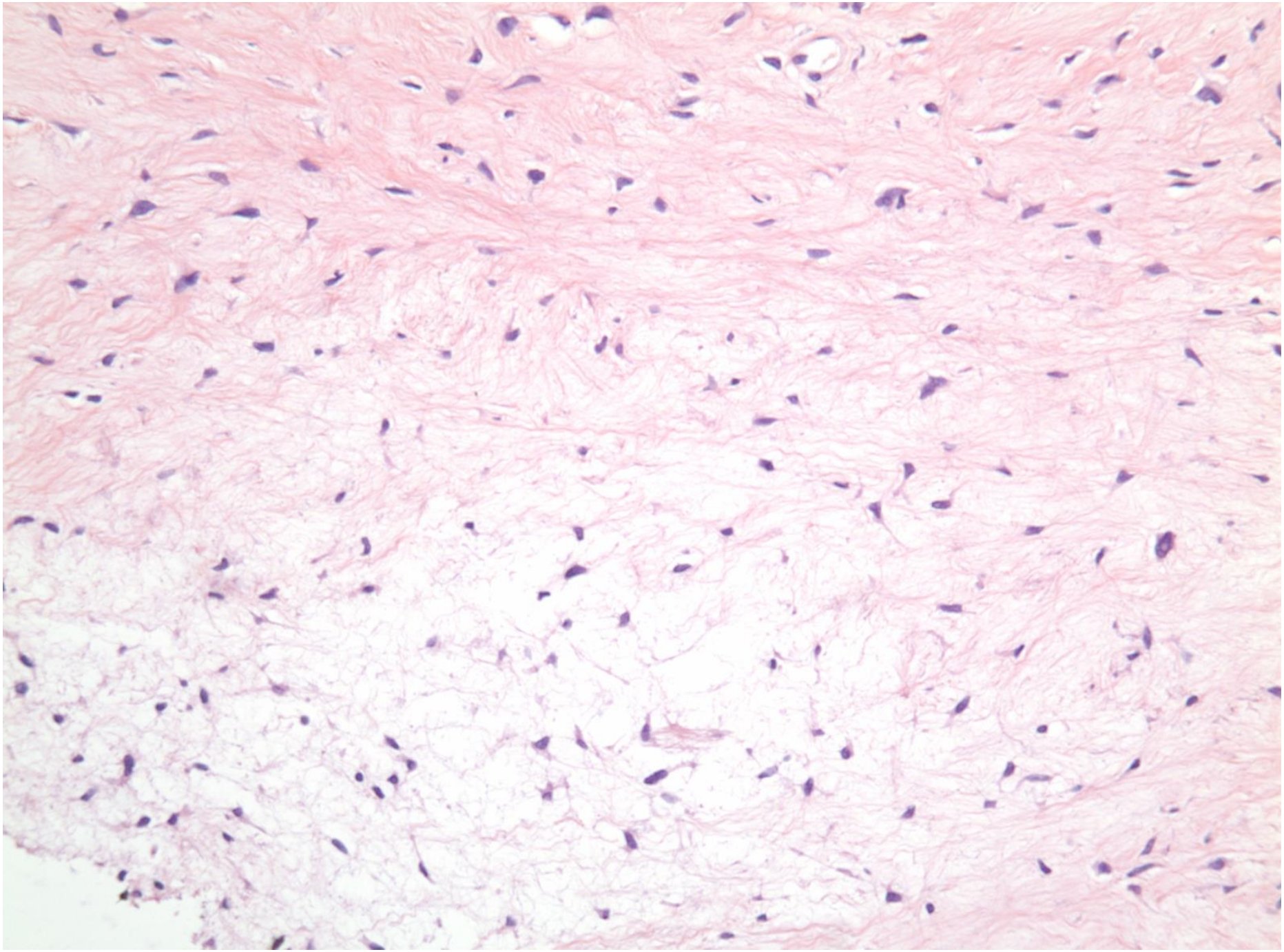
Low grade Fibromyxoid sarcoma

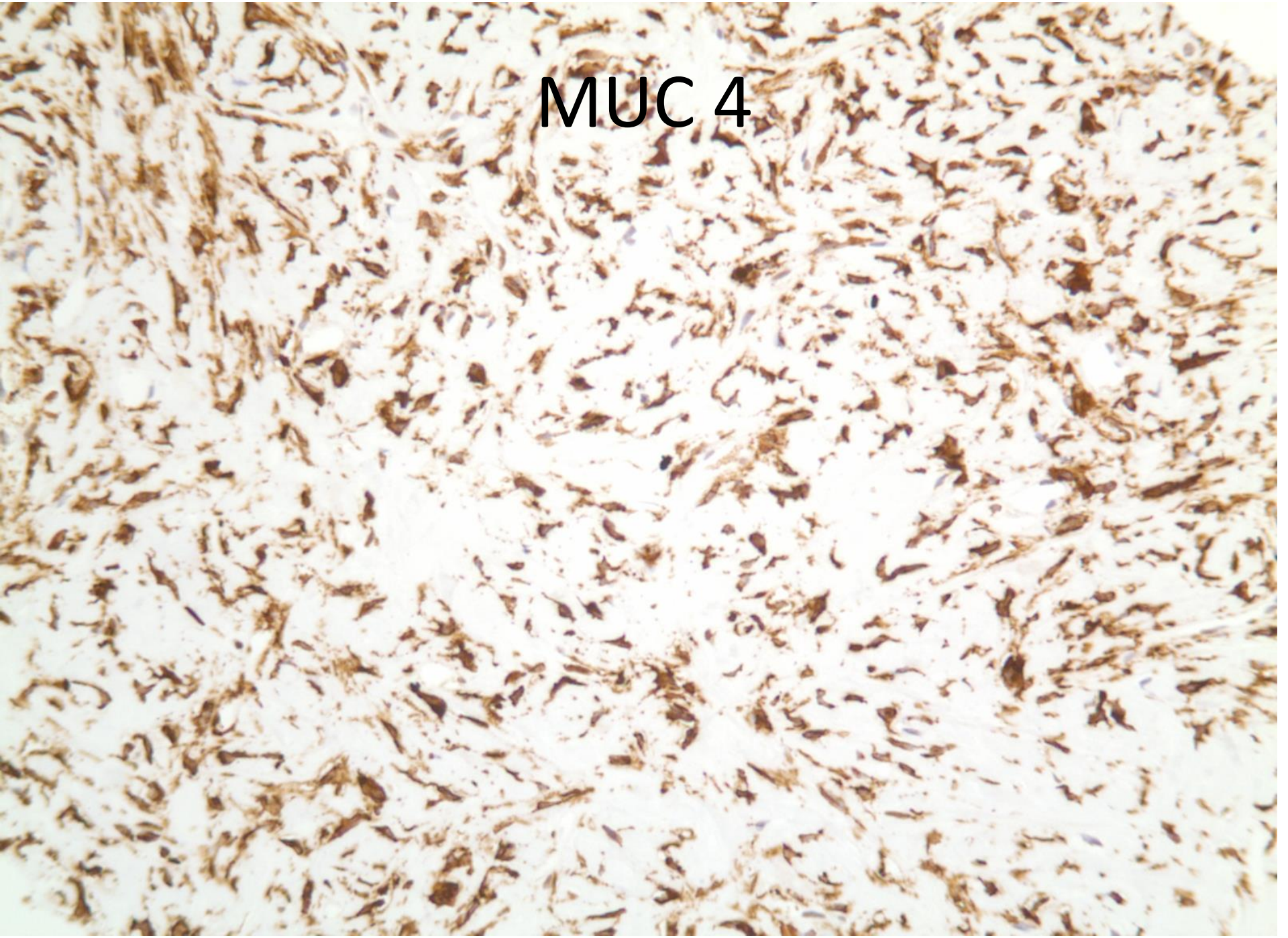
- Prognosis. New reports-
- At 5 years recurrence 10%, Mets 5%
- At > 10years, Recurrence- 64%, mets 45%, death 42%.










MUC 4

MUC 4

- Low grade Fibromyxoid sarcoma
- Sclerosing epithelioid sarcoma
- Glands of synovial sarcoma
- Focal in OFMT, epithelioid GIST

Case 8

- 70 Male with ulcerated nodule scalp

Case 8

- Main differential
- How make diagnosis.

High grade cutaneous tumours

- Carcinoma, including metastasis
- Melanoma
- Sarcoma
  - LMS
  - Angiosarcoma
- Lymphoma, anaplastic large cell
- AFX

Atypical Fibroxanthoma AFX
Clinical

- Elderly, sun damaged sites, esp. head & neck
- Raised cutaneous nodule

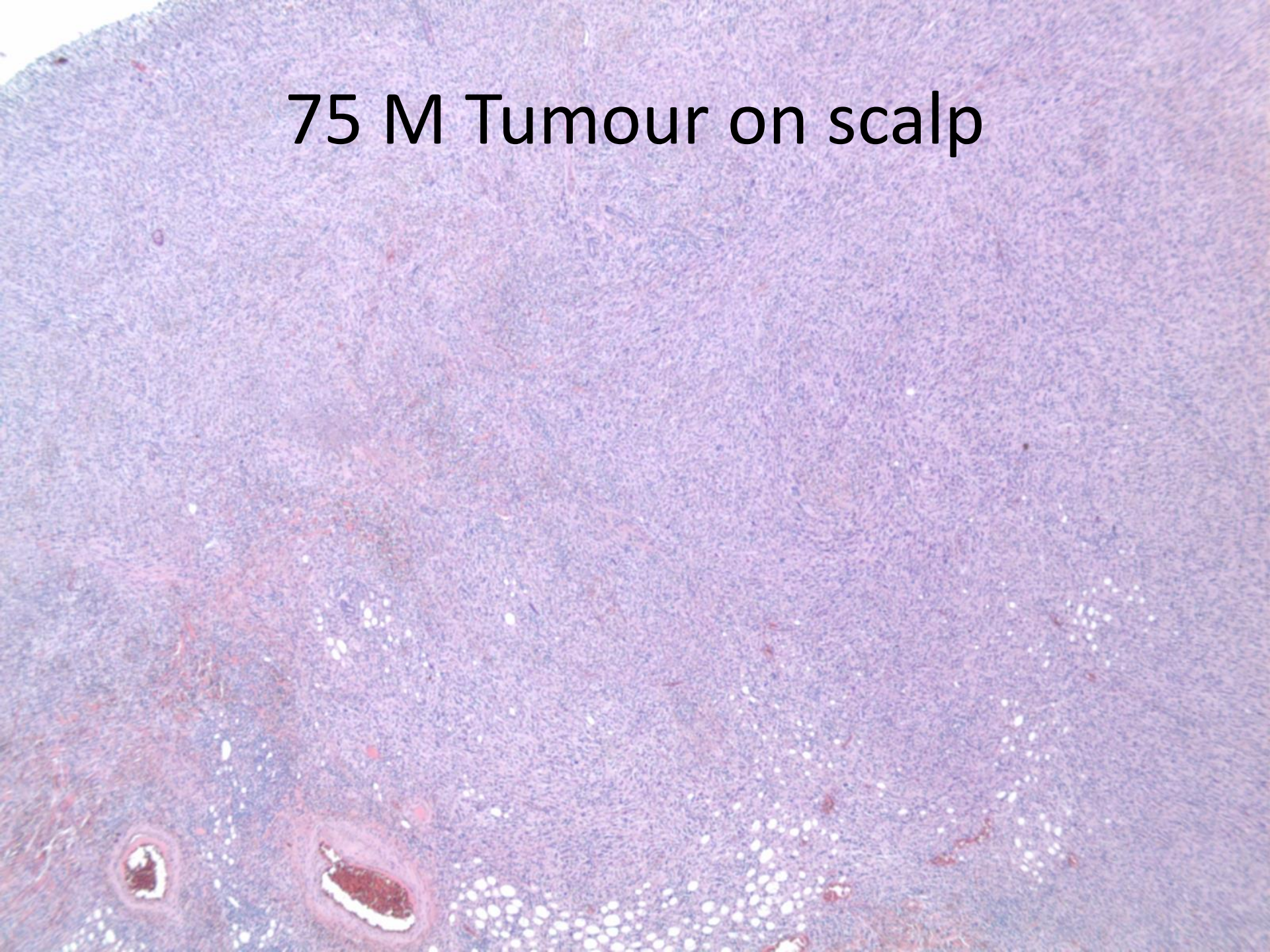
AFX- cytology

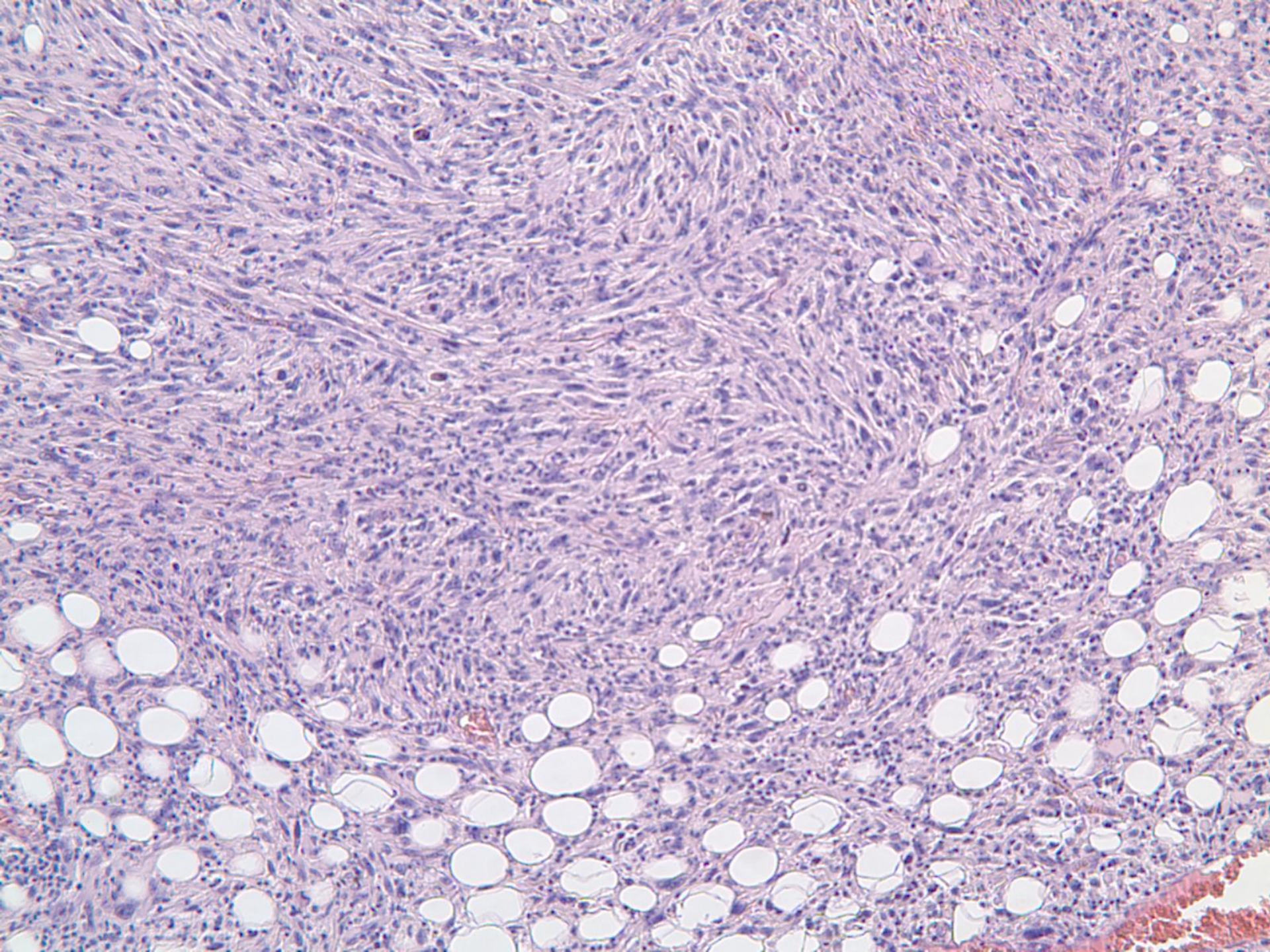
- Tumour cell; high grade atypia with pleomorphic cell, atypical xanthomatous cells and spindle cells in varying proportion

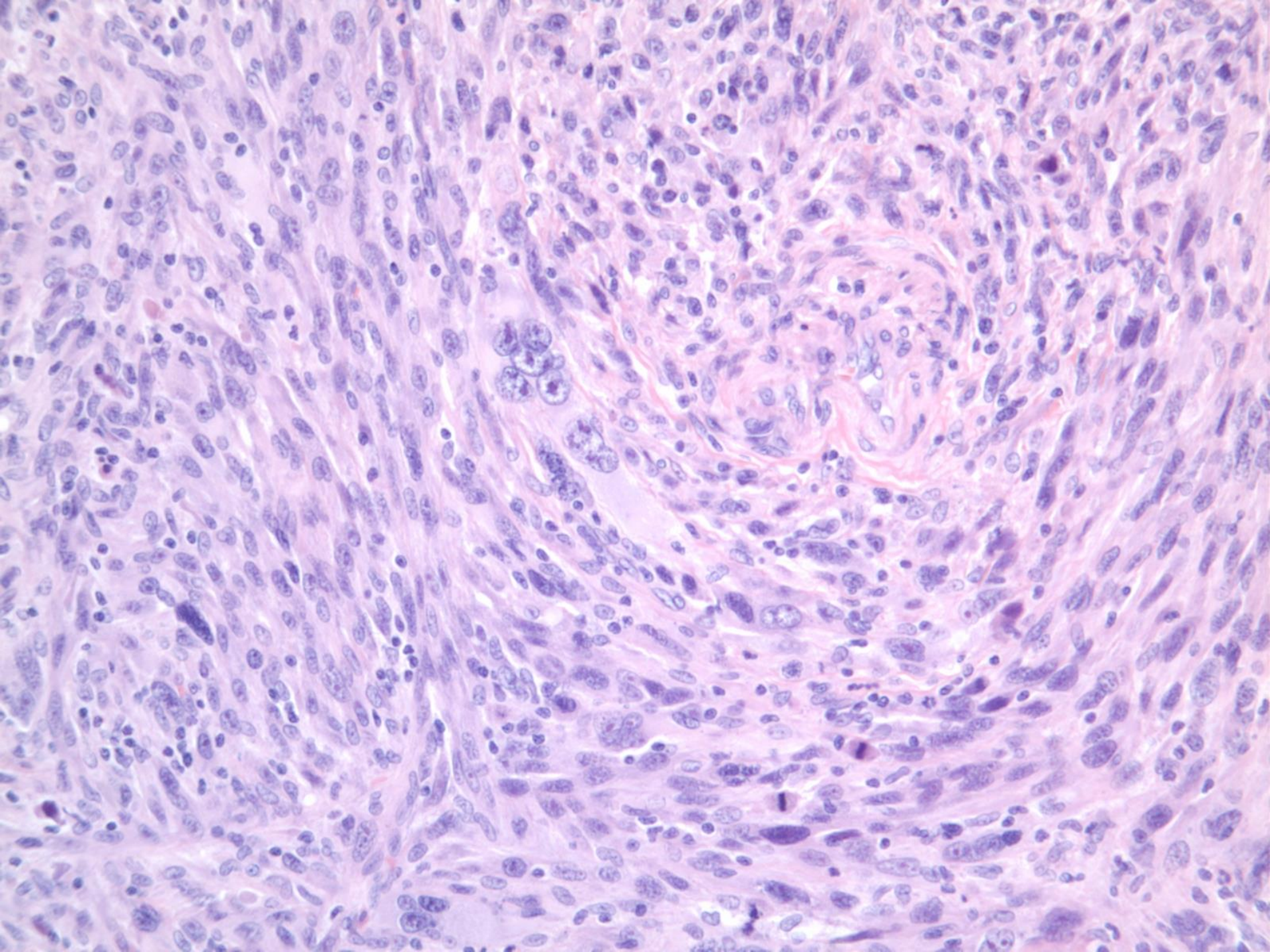
AFX

- Architecture
  - Circumscribed with pushing margin
  - No subcutaneous fat extension
  - No vascular invasion
  - No Tumour necrosis

75 M Tumour on scalp







AFX VS PDS

- Atypical FibroXanthoma [AFX]- considered benign
- Pleomorphic Dermal Sarcoma [PDS]- malignant sarcoma

AFX VS PDS

- Both terms in WHO classification of skin 2018, on following pages.

Pleomorphic Dermal Sarcoma

Adverse Histologic Features Predict Aggressive Behavior and Allow Distinction From Atypical Fibroxanthoma

Keith Miller, FRCPath, John R. Goodlad, MD, FRCPath,†*
and Thomas Brenn, MD, PhD, FRCPath†

(*Am J Surg Pathol* 2012;36:1317–1326)

AFX & PDS

- Same clinical picture;
- Elderly, sun damaged sites, esp. head & neck
- Raised cutaneous nodule

AFX & PDS

- Same cytology-
- Tumour cell; high grade atypia with pleomorphic cell, atypical xanthomatous cells and spindle cells in varying proportion

AFX & PDS

- Diagnosis of exclusion; rule out melanoma, carcinoma.
- Immuno. Panel; Broad spectrum cytokeratins, S100, Desmin, CD31/ERG, CD34.
- CD10 ? Useful- No

AFX VS PDS

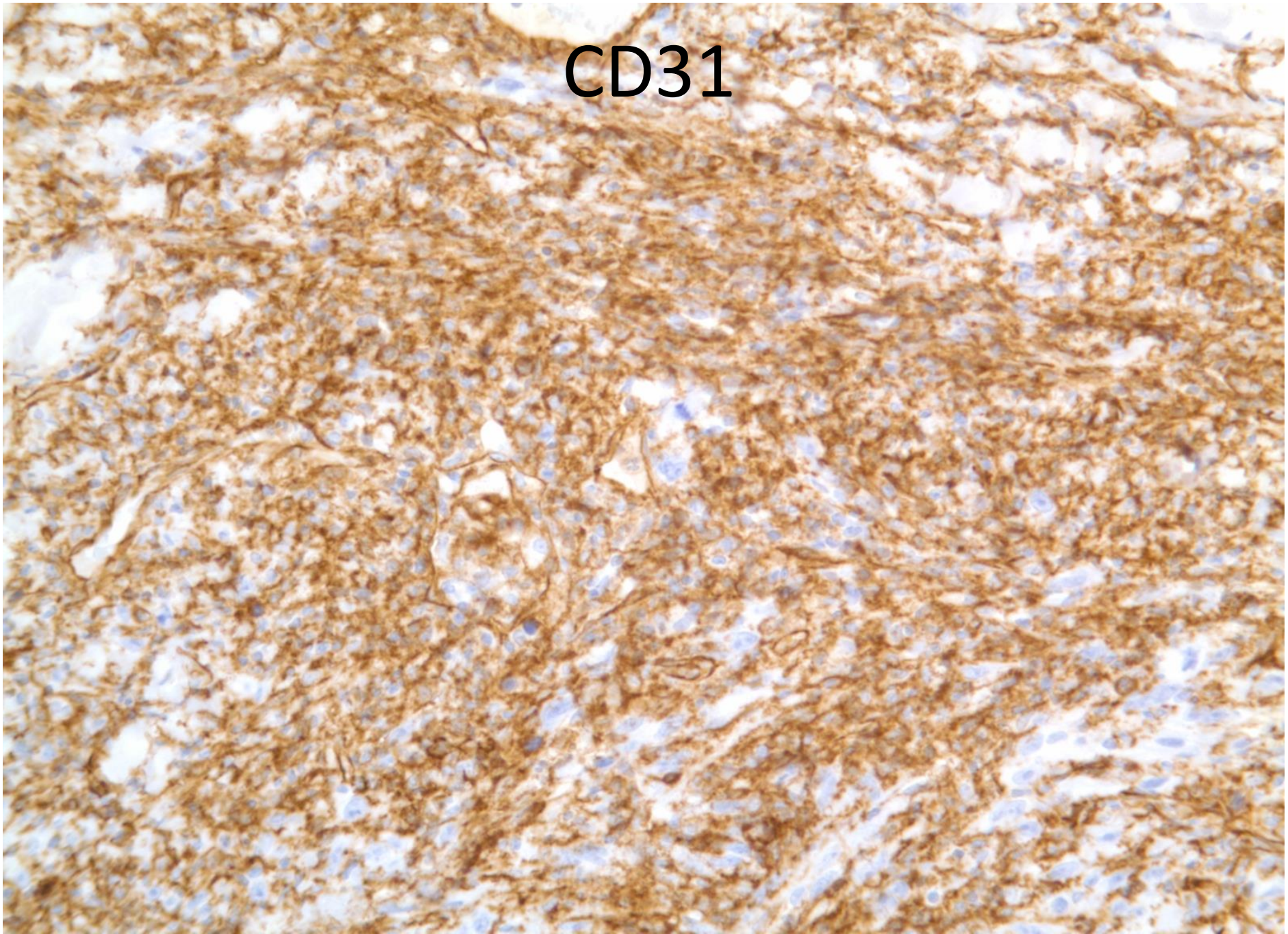
- Architecture is key- AFX if
  - Circumscribed with pushing margin Not infiltrative
  - {Minimal } NO subcutaneous fat extension { WHO definition 2018}
  - No vascular invasion
  - No Tumour necrosis
  - No Perineural invasion
- If positive for any of the above – PDS
- Cannot make distinction on biopsy.

AFX Rare variants

- Osteoclastic giant cell rich
- Granular cell
- Clear cell
- Spindle cell
- Osteoid/chondroid

PDS

- 32 cases, M > F, sun damaged site.
- Immuno;- Negative for broad spectrum cytokeratins, s100, HMB45, Desmin, CD34
- **Odd immuno findings**- SMA 70%
- CD31 -48% positive [? Histiocytes]
- Melan A- 6%
- Similar findings in AFX


CD31

CYTOKERATINS

- AE1/AE3 – broadest reactivity
  - AE3- CK- 1 -8
  - AE1 – CK 10,13,14,15,16,19
- MNF116 – CK 5,6,8,17,19
- 34 Beta E12 – CK 1,5,10,14 + other unknown.

PDS

- Follow up of 29 patients.
- 28% local recurrence [often incompletely excised].
- 10% metastasize [often to skin, but can be distant].
- Rare disease related mortality
- High grade on cytology, but low grade behaviour.

AFX vs PDS

- ? one disease process- separating early stage tumour [AFX] from late stage ones [PDS].
- Cell of origin; unknown, but hotly debated.

AFX PDS

Thanks to Arno Rutten Friedrichshafen

AFX

- Beware if not sun damaged site
- If has any aggressive features –'Pleomorphic dermal sarcoma'

Case 9

- 25 F, ? Haemangioma on leg

Case 9

- What is this?
- What should it really be called.

Case 9

- Kaposi Sarcoma
- Named after Moritz Kaposi, real name Moritz Kohn

Case 10

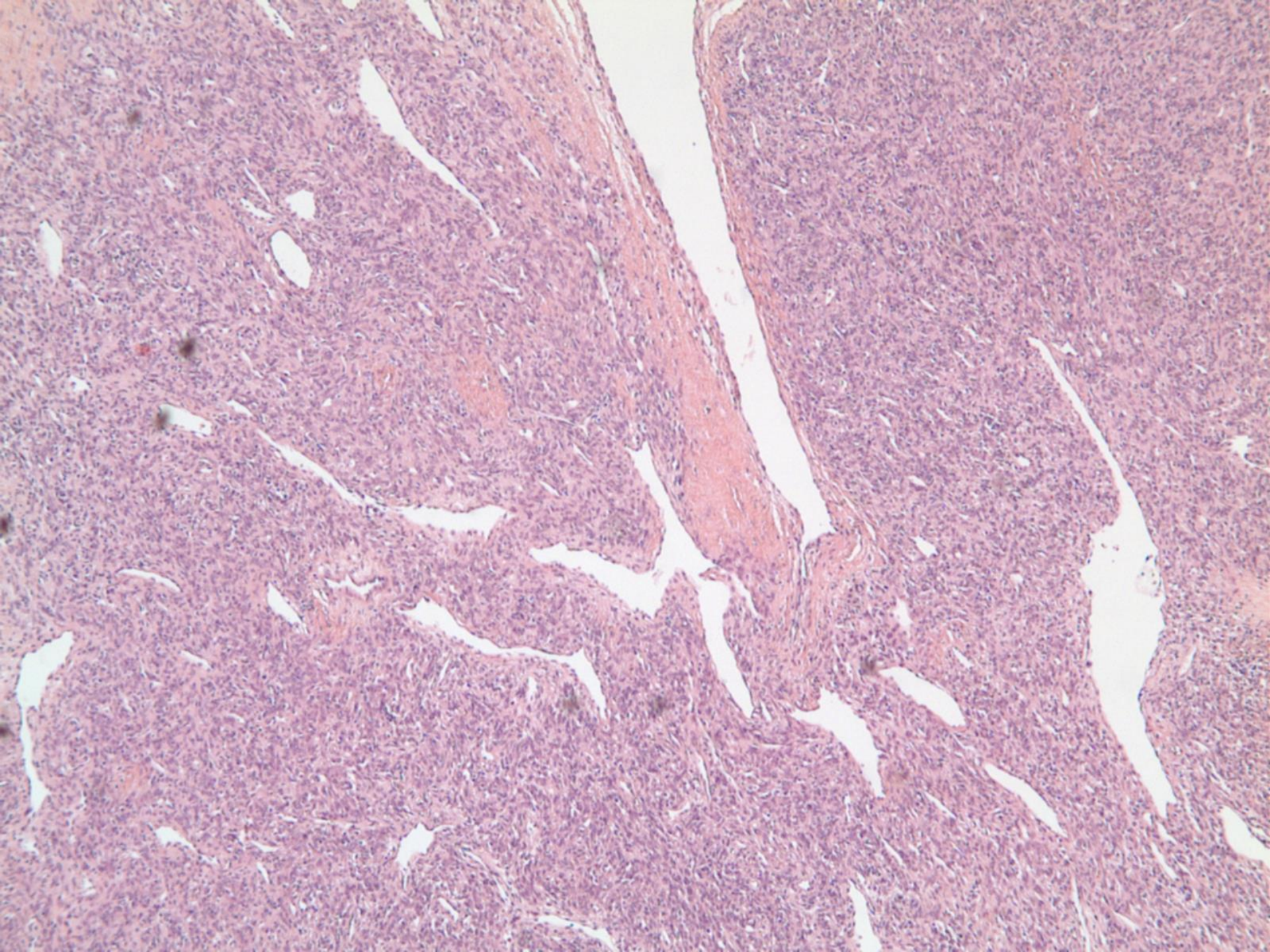
- 30M, ? Haemangioma s/c on arm

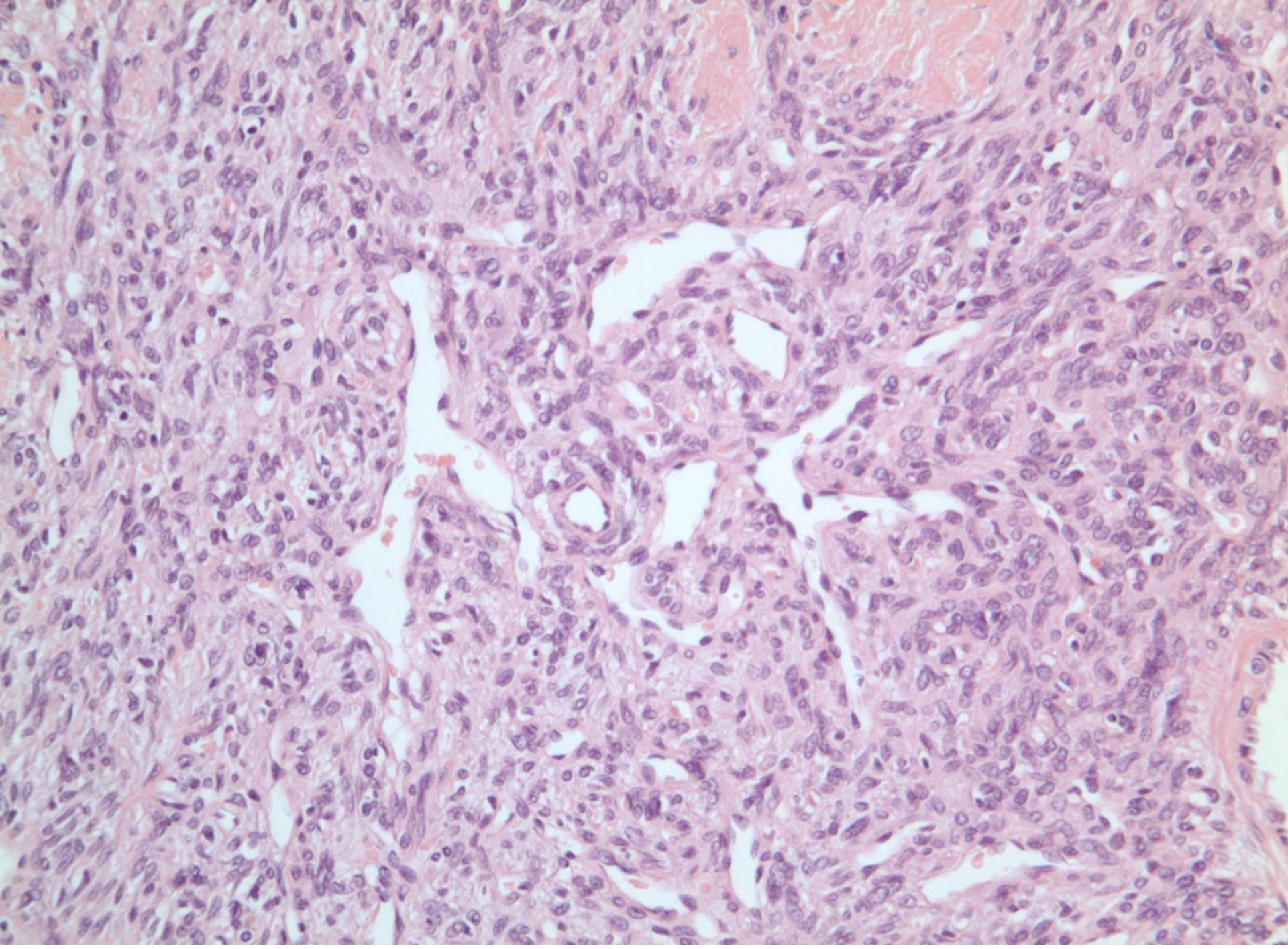
Case 10

- Variable appearance
- In-part- haemangiopericytoma like with small cells
- Foci with bundles of spindle cells with more abundant cytoplasm; odd almost chondroid matrix.

Solitary myofibroma

- Benign
- In young children, can be multifocal ‘infantile myofibromatosis’
- Often secondary changes; hyalinisation, necrosis
- Can see vascular invasion.
- Easy to call malignant





Haemangiopericytoma
HPC

- Once a common soft tissue tumour.
- Now considered a morphological appearance only.

HPC

- Differential diagnosis

Haemangiopericytoma-like pattern

- Solitary Fibrous Tumour, SFT
- Myopericytoma
- Myofibroma
- Infantile Fibrosarcoma
- Synovial sarcoma
- Round cell liposarcoma
- Endometrial stromal sarcoma

Case 11

- 30 Male lump on ankle

Case 11

- Clear/pale spindle cells.
- Organised pattern

Clear cell sarcoma of tendon and aponeuroses

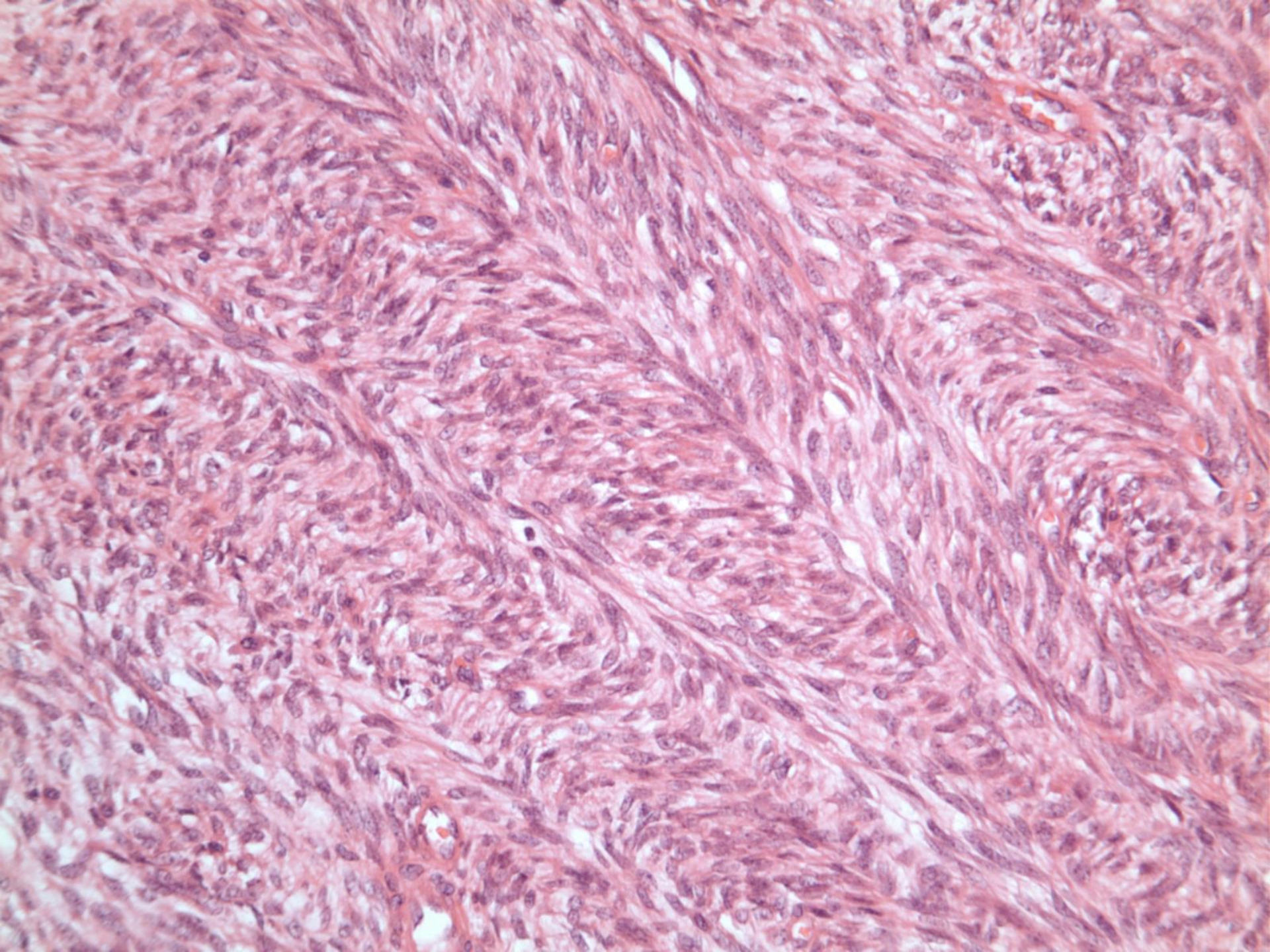
- Usually deep, often peripheral site related to tendons etc in young age.
- Now reported in bowel and skin
- Immuno, same as melanoma
- Has characteristic genetics t11:22
- EWS/ATF1 fusion . Can use FISH for EWRS1

Case 12

- 30 M Lump on chest

Fibrosarcomatous appearance

- Fascicles of spindle cells. Zig-zag pattern; ‘herringbone’
- Cellular ++, with little matrix
- Oval hyperchromatic nuclei, but uniform
- Little pale indistinct cytoplasm.



Fibrosarcomatous appearance

- Differential diagnosis;
  - MPNST
  - Synovial sarcoma
  - Fibrosarcoma
  - Clear cell sarcoma
  - LMS, high grade
  - RMS-spindle cell variant
  - Less likely;
    - melanoma,
    - carcinoma.

Synovial sarcoma

- Immuno; focal C.K., EMA positive. CD56 diffuse.
- Negative CD34 plus others
- FISH/PCR t(X;18) translocation
- Note Calcification. Quite common.
- New immuno- TLE1 – supposably specific

Case 13

- 80 Male Lump on neck

Pleomorphic Lipoma VS Liposarcoma

- Name any useful features?

Pleomorphic Lipoma

- Morphological overlap.
- Diagnosis by; Clinical ;ie age, sex,site
- Immuno; MDM2 lacking
- Cytogenetics or FISH has 13q deletion, no MDM2 amplification. [latter seen in liposarcoma].

Case 14

- 30M, Multiple Lumps and bumps for years. This one increasing in size.

Neural

- Spindle cells with small buckled nuclei.
- Nuclei have tapered end.
- Cytoplasm, pale and poorly defined.
- Variable collagenous to myxoid stroma.
- Schwannoma;
  - Nuclear palisading
  - Thick walled vessels.

Malignant change in Neurofibroma

- What to look for.

Malignant change in Neurofibroma

- Nuclear Atypia
- Cellularity, ie back to back cells
- Mitotic activity- > 3/10 hpf.
- Necrosis
- Immuno – s100 becomes patchy or loss.
- CD34 ; in benign , has diffuse patterned positivity [Finger print]. Malignant, usually negative.
- P16 loss often with malignant change
- K67 – benign , 5%, malignant 10%

Atypical neurofibromatous neoplasms of uncertain biological potential [ANNUBP]

- Nuclear atypia
- High cellularity
- Loss of neurofibroma architecture [herringbone, storiform, loss of cd34 network]
- +/- mitotic activity .1/50, but<3/10 hpf

Hum Pathol. 2017 September ; 67: 1–10. doi:10.1016/j.humpath.2017.05.010.

HISTOPATHOLOGIC EVALUATION OF ATYPICAL NEUROFIBROMATOUS TUMORS AND THEIR TRANSFORMATION INTO MALIGNANT PERIPHERAL NERVE SHEATH TUMOR IN NEUROFIBROMATOSIS 1 PATIENTS – A CONSENSUS OVERVIEW

Markku M. Miettinen, MD[1], Cristina R. Antonescu, MD[2], Christopher D. M. Fletcher, MD[3], Aerang Kim, MD[4], Alexander J. Lazar, MD[5], Martha M. Quezado, MD[1], Karlyne M. Reilly, PhD[6], Anat Stemmer-Rachamimov, MD[7], Douglas R. Stewart, MD[8], David Viskochil, MD[9], Brigitte Widemann, MD[10], and Arie Perry, MD[11]

If only nuclear atypia

- Atypical Neurofibroma - benign

Published in final edited form as:

Am J Surg Pathol. 2016 April ; 40(4): 479–489. doi:10.1097/PAS.0000000000000564.

Loss of H3K27me3 Expression Is a Highly Sensitive Marker for Sporadic and Radiation-induced MPNST

Carlos N. Prieto-Granada, MD[*,†], Thomas Wiesner, PhD[‡], Jane L. Messina, MD[†], Achim A. Jungbluth, MD[*], Ping Chi, MD, PhD[‡,§,‖], and Cristina R. Antonescu, MD[*]

[*]Department of Pathology, Memorial Sloan Kettering Cancer Center

[§]Department of Medicine, Memorial Sloan Kettering Cancer Center

[‡]Department of Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center

69% of MPNST's showed loss.

Diagnostic Criteria for NF1

Diagnostic Criteria for NF1

- **Neurofibromatosis 1 is diagnosed in an individual with two or more of the following signs or factors:**
- Six or more café au lait macules: >5mm in greatest diameter in prepubertal individuals; . 15mm in greatest diameter in postpubertal individuals
- Two or more neurofibromas of any type or one plexiform neurofibroma
- Freckling in the axillary or inguinal region
- Optic glioma
- Two or more Lisch nodules (iris hamartomas)
- A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex with or without pseudoarthrosis.
- First-degree relative (parent, sibling, offspring) with neurofibromatosis 1 by the above criteria

Case 15

- 40 M. Testicular swelling

Case 15

- Differential Diagnosis
- How to make diagnosis

Spindle cell variant of well Differentiated liposarcoma

- Can be very spindly, easy to confuse with fibroblast and neural
- Favoured sites- retroperitoneal and paratesticular [as extension of retroperitoneum]
- CD34 and often desmin positive. S100 neg in spindle cells.

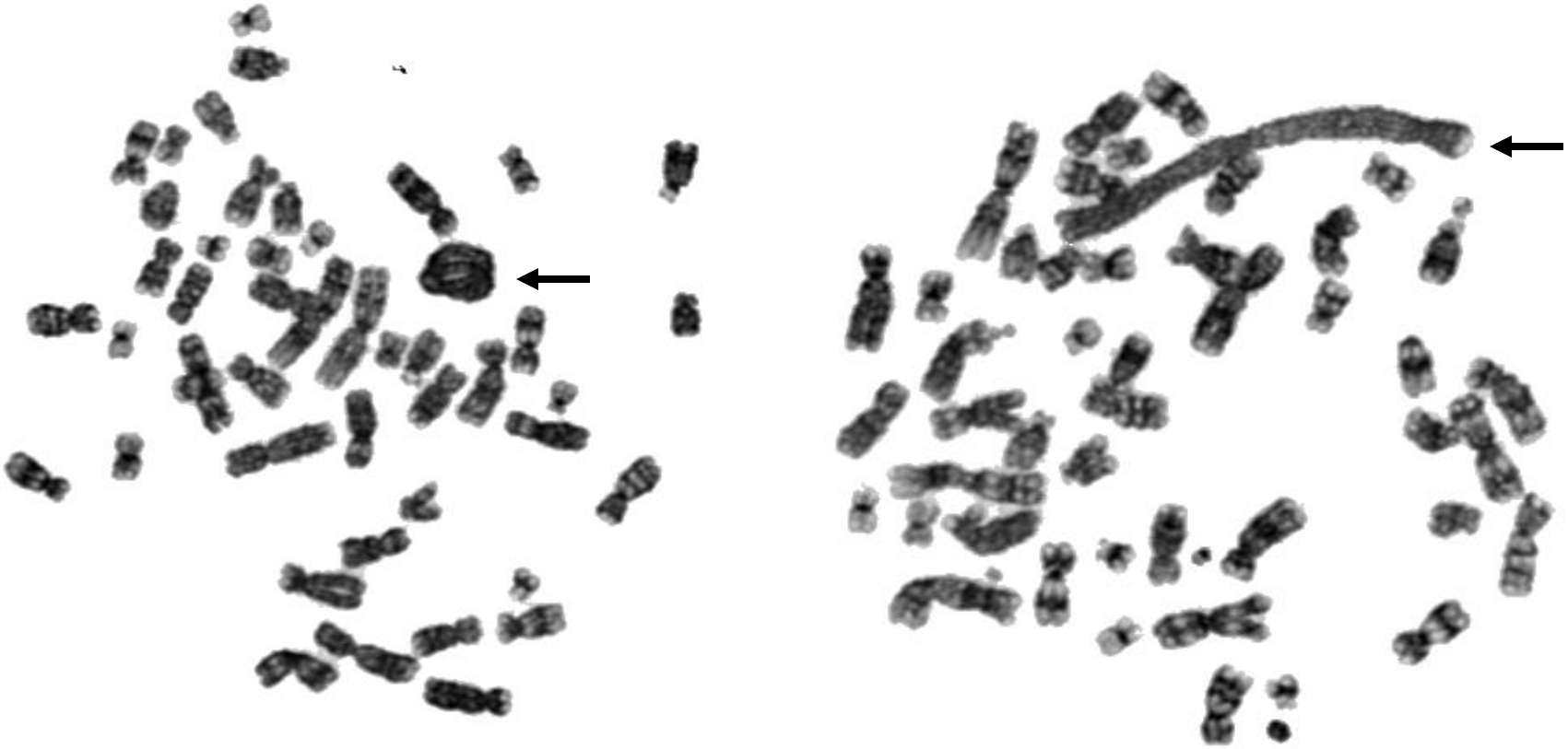
Spindle cell fatty Tumours

- BENIGN
  - Spindle cell lipoma
  - Pleomorphic lipoma
  - Cellular angiofibroma
  - Mammary-type myofibroblastoma
- MALIGNANT
  - Well diff. Liposarcoma
    - Spindle cell
    - Sclerosing
    - Inflammatory

Spindle cell fatty Tumours

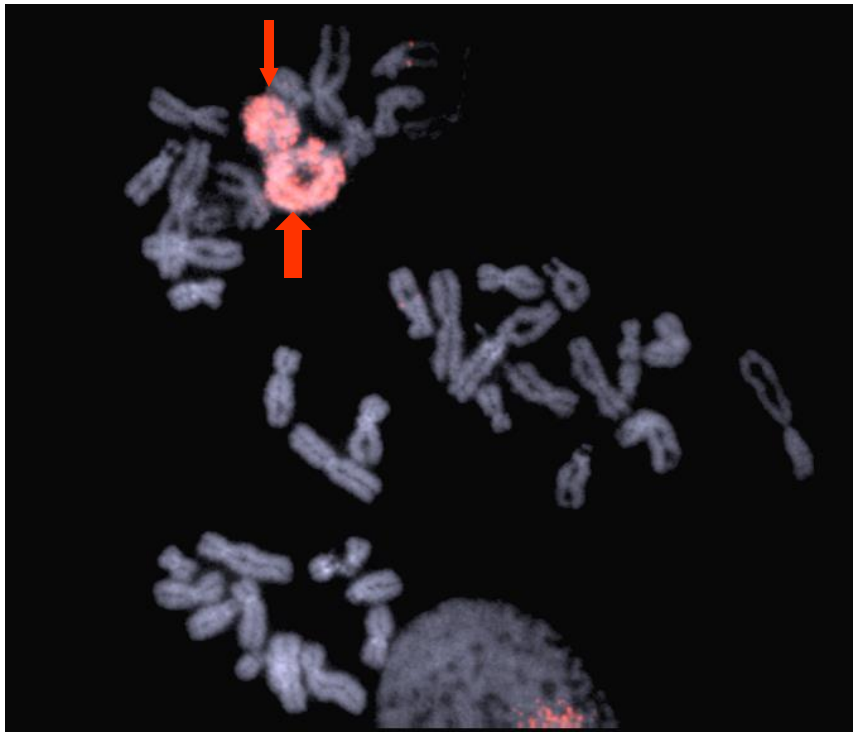
- Can be difficult to separate. Both can be cytologically bland or show nuclear atypia.
- FISH for MDM2 and 13q very helpful

Well-differentiated liposarcoma (WDLPS) with supernumerary rings and giant chromosomes

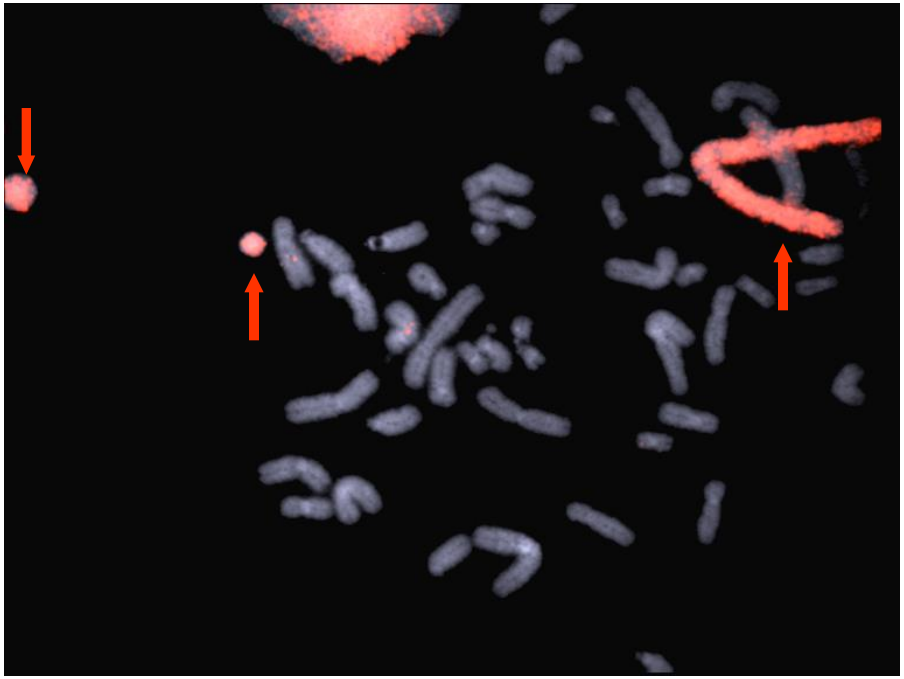


Amplification of 12q13~15:
MDM2, also *CDK4*, *SAS*, *HMGA2*, not *CHOP*

MDM2 amplification in WDLPS



Ring (12)



Giant markers and rings

NB rings seen in lipomas but no *MDM2*

Case 16

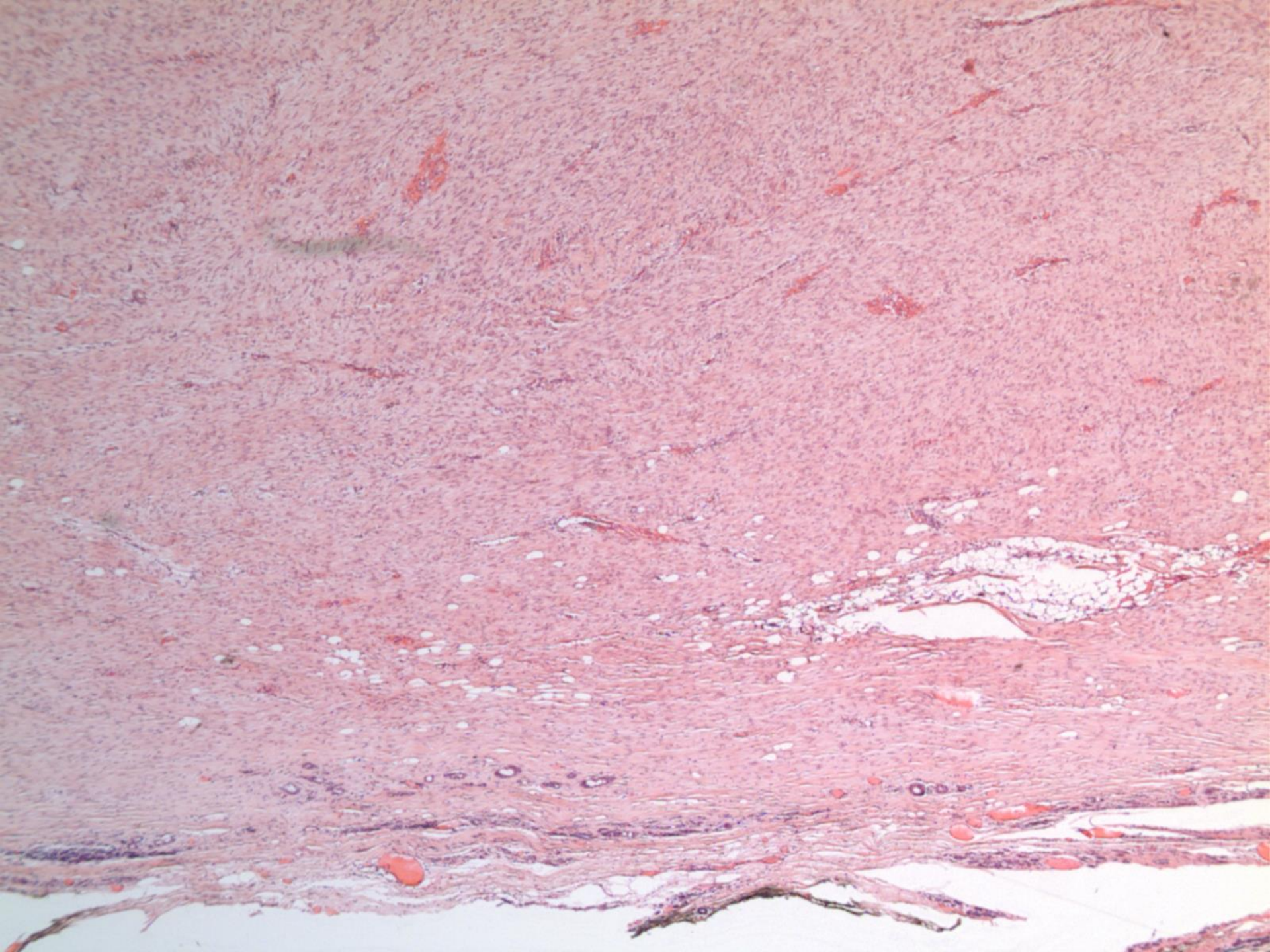
- 70 M, metastatic colorectal carcinoma to liver, resected. Mass noted adjacent to pancreas

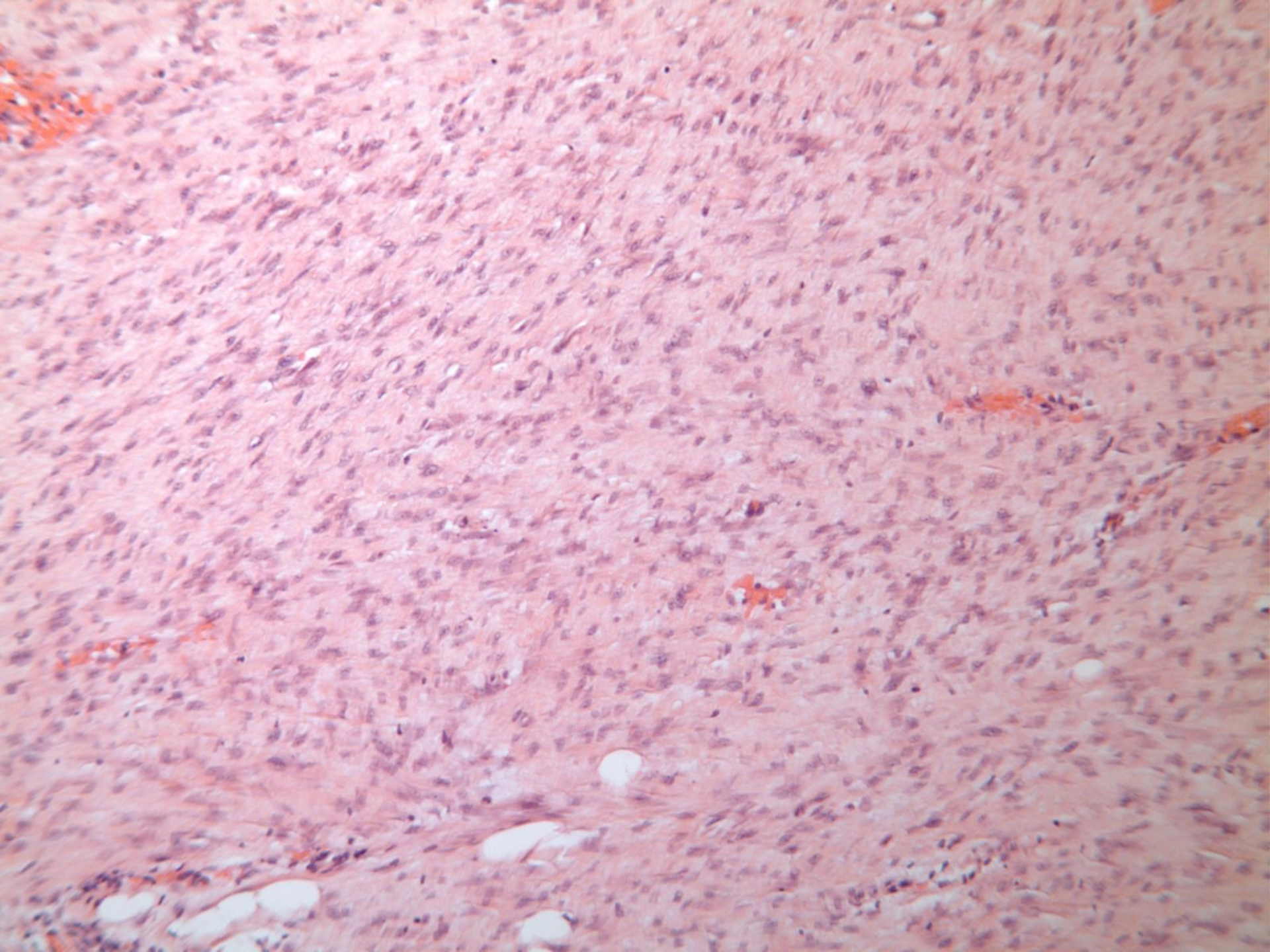
Fibromatosis

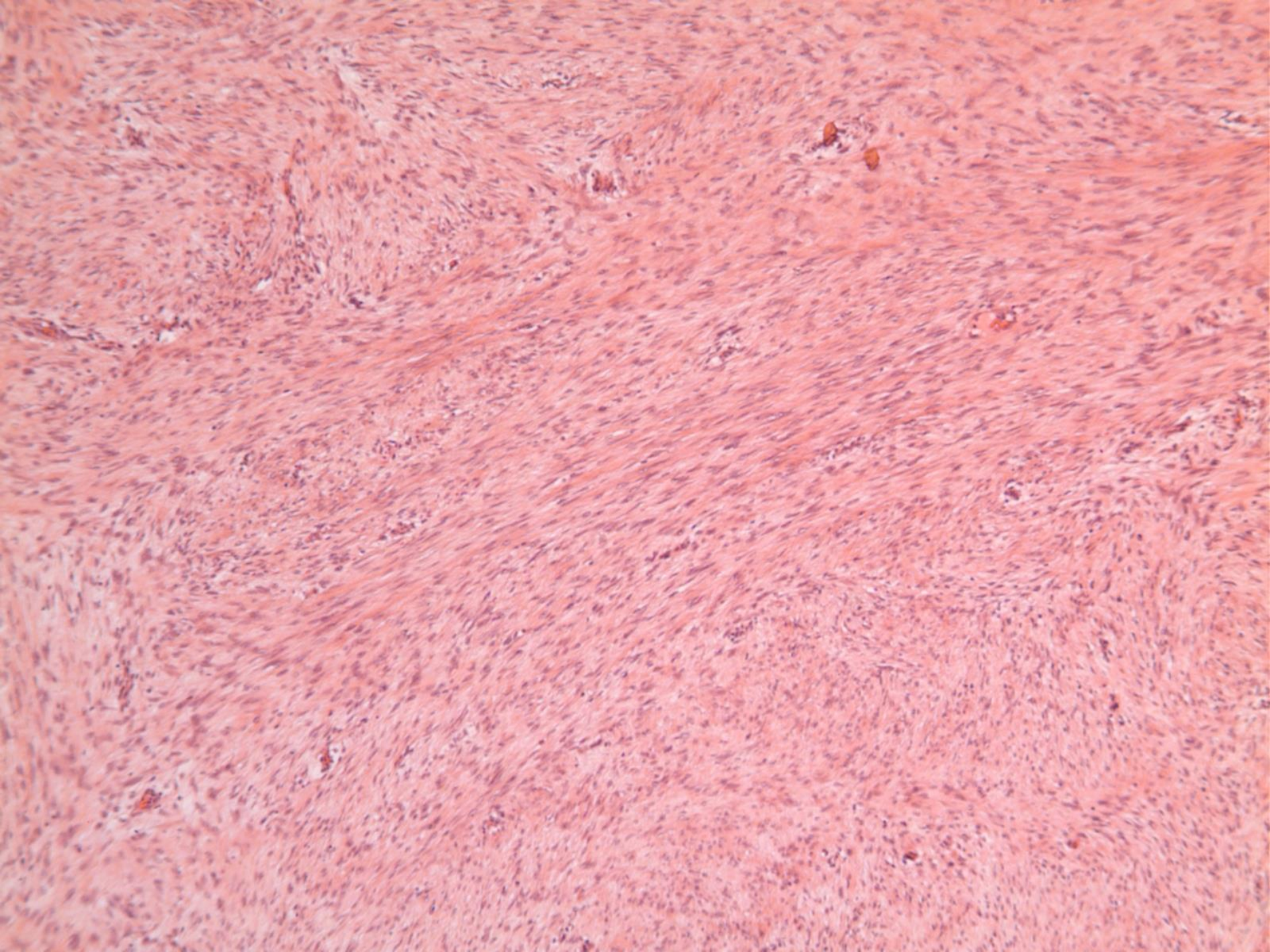
- Characteristic long fascicles of spindle cells. Spindle cells have small elongated nuclei, often wavy.
- Stroma, usually collagenous, can be focally myxoid or keloidal. Infiltrative and entraps structures
- Lymphoid aggregates at periphery common.
- Intra. Abdo. Cases often quite myxoid.

Fibromatosis

- Can be part of FAP/ Gardner's syndrome
- Infiltrative lesion
- Occasionally multi-centric.
- Can follow surgery







Fibromatosis

- Immuno; SMA and HHF35 , may show tram track appearance.
- Beta-catenin, was thought very useful and specific [80%]. Now; can be seen in phyllodes and occ. cell in spindle cell Ca, but focal.
- CD 34 - Negative
- C.K.- Negative
- C-kit /DOG1 Neg

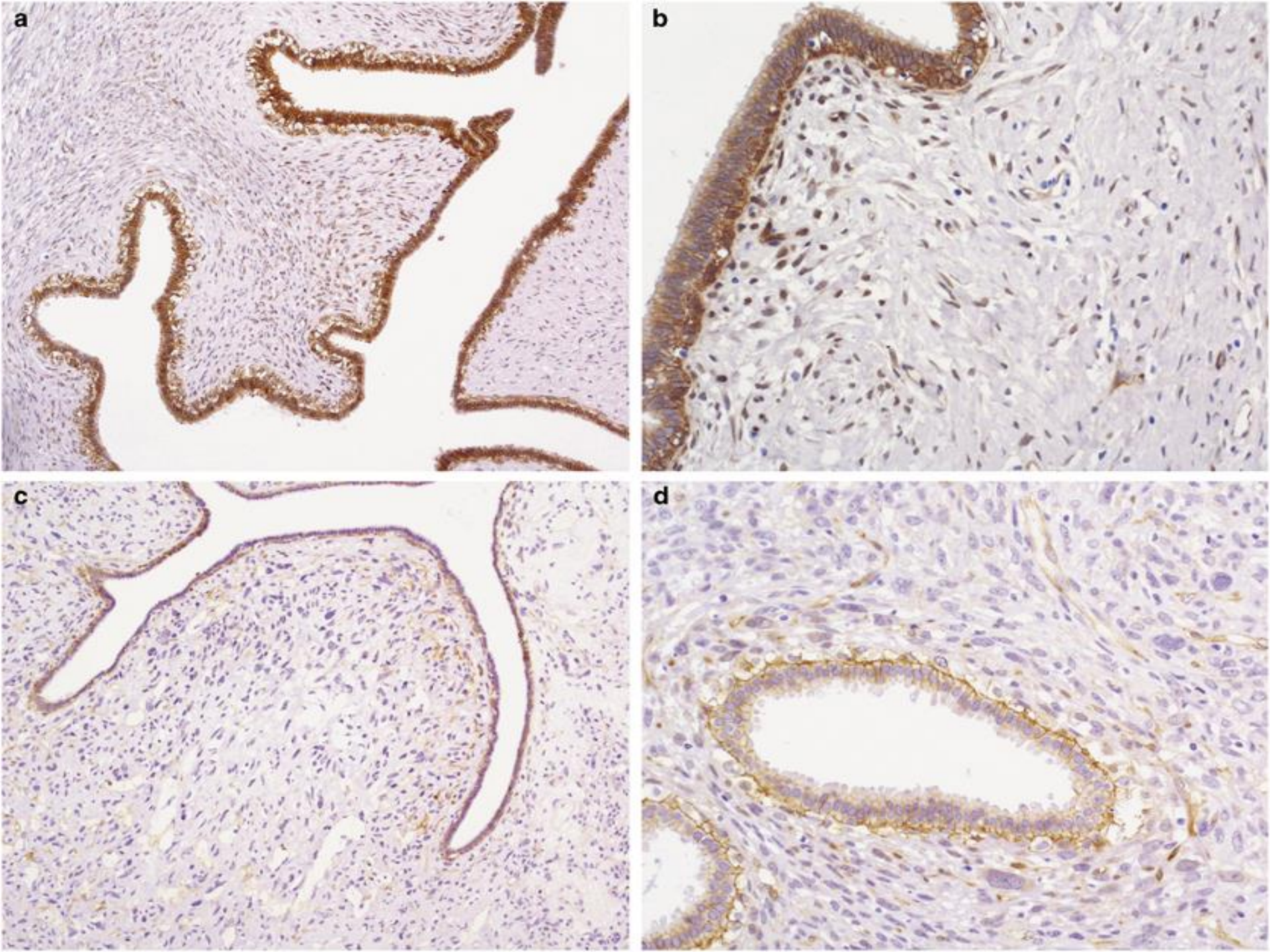
Beta- Catenin

- Involved in wnt-signalling pathway.
- Normal expression is membranous.
- With wnt activation, beta-catenin moves to cytoplasm and nucleus.
- Originally thought to be highly specific for fibromatosis.
- Now noted to be positive in other spindle tumours, but usually weak and focal

Beta-catenin

- 80- 100% Fibromatoses, [diffuse and strong]
- 90% Phyllodes Benign and 57% malignant phyllodes
  - Only cells around epithelial structures
- 23% metaplastic Ca
  - often focal, weak

  - Mod.Path, 23 1438-1448, 2010


a
b
c
d

Fibromatosis, differential

- Scar ; haemosiderin, fat necrosis, macrophages
- Low grade spindle cell carcinoma
- True sarcoma; has nuclear atypia, abnormal mitoses and necrosis. Closest mimic is low grade myofibrosarcoma. Usually occurs in muscle.

Fibromatosis

- Can be locally aggressive
- Recurs in 20%, doesn’t metastasize.

Case 17

- 40M. Tumour on small bowel.
- C-kit positive
- Comment on risk factors

Risk Factor

- You might cock it up.

Remember, Remember Melanoma

- Melanoma can appear very sarcomatous.
- Spindle cell and desmoplastic melanoma very difficult to separate from MPNST.
- Schwann cell and melanocytes share common origin from Neural crest.
- Can present as visceral tumour

Patient re-examined

- Partially regressed melanoma on back.

Case 18

- 25 Male, para-testicular mass

Case 19

- Spindle cell tumour
- Usual differential diagnosis

Spindle cell Rhabdomyosarcoma

- Distinct variant of RMS
- Often older age group, teens, M>F
- H+N, Paratesticular, but described elsewhere.
- If thinking smooth muscle or pleomorphic sarcoma NOS, remember are variants of RMS [spindle cell and pleomorphic].
- Can focally express Cytokeratin
- Add myogenin and MyoD1 to immuno panel.

Case 19

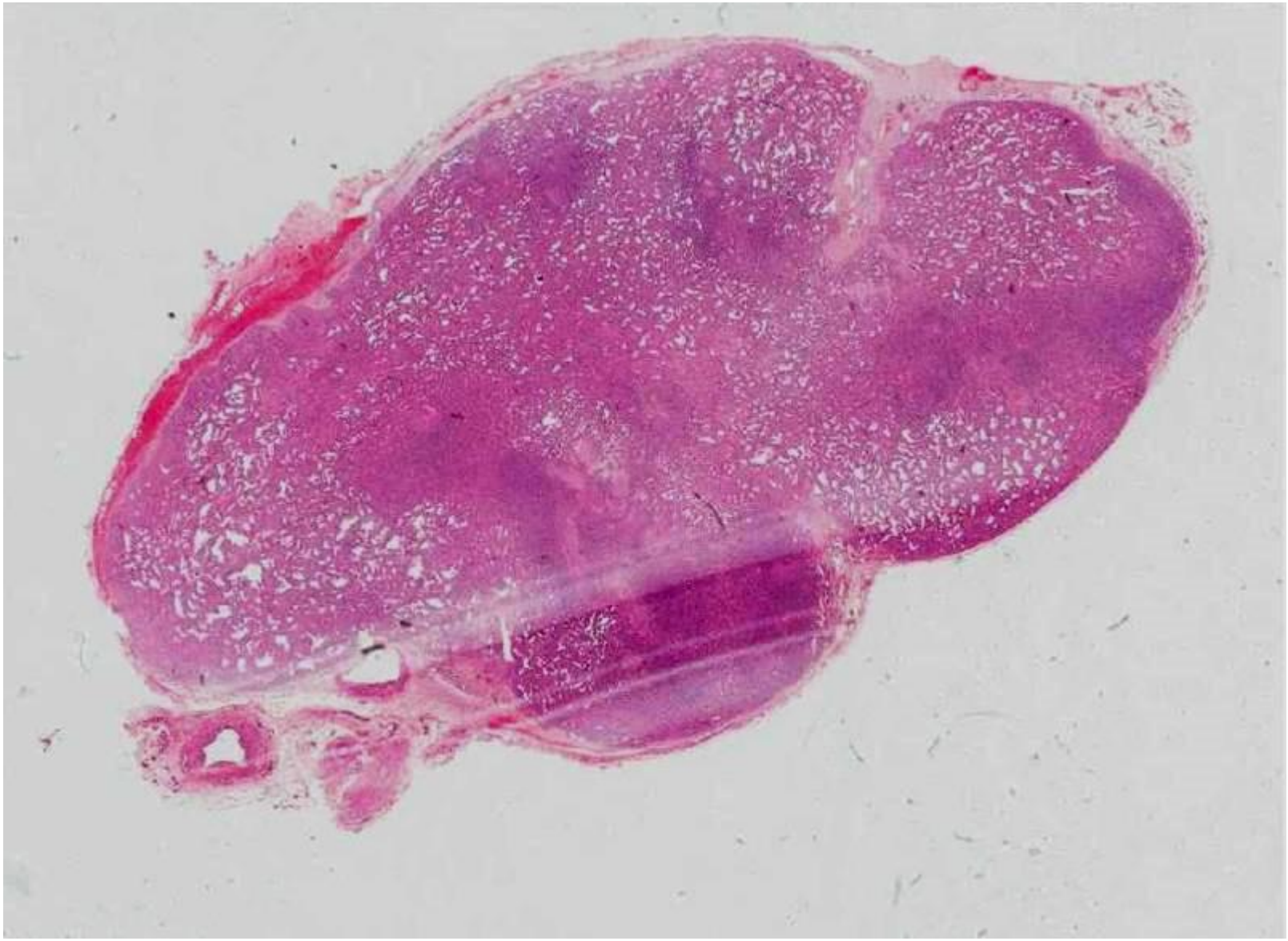
- 30 F, Multiple lumps left leg.

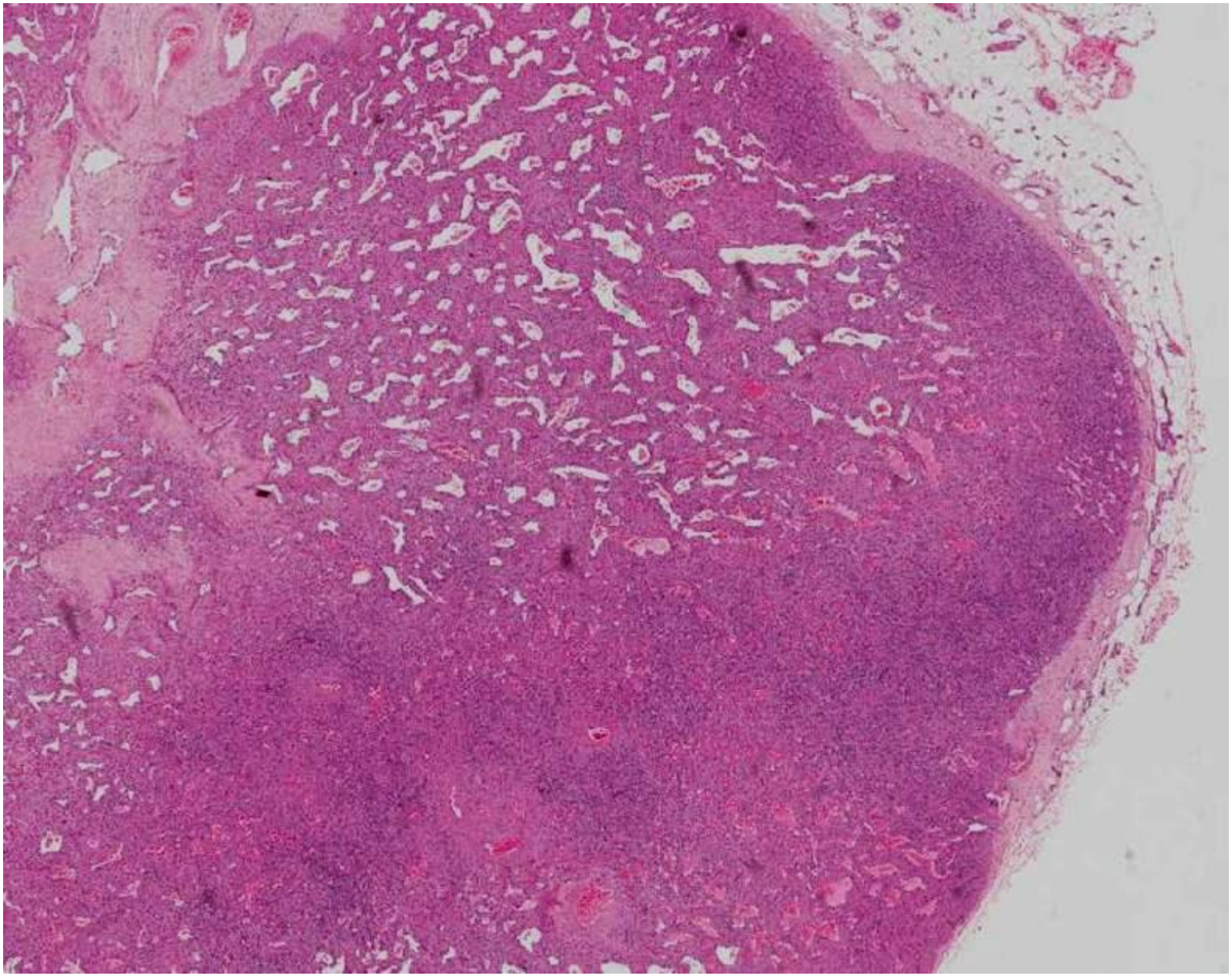
Myopericytoma

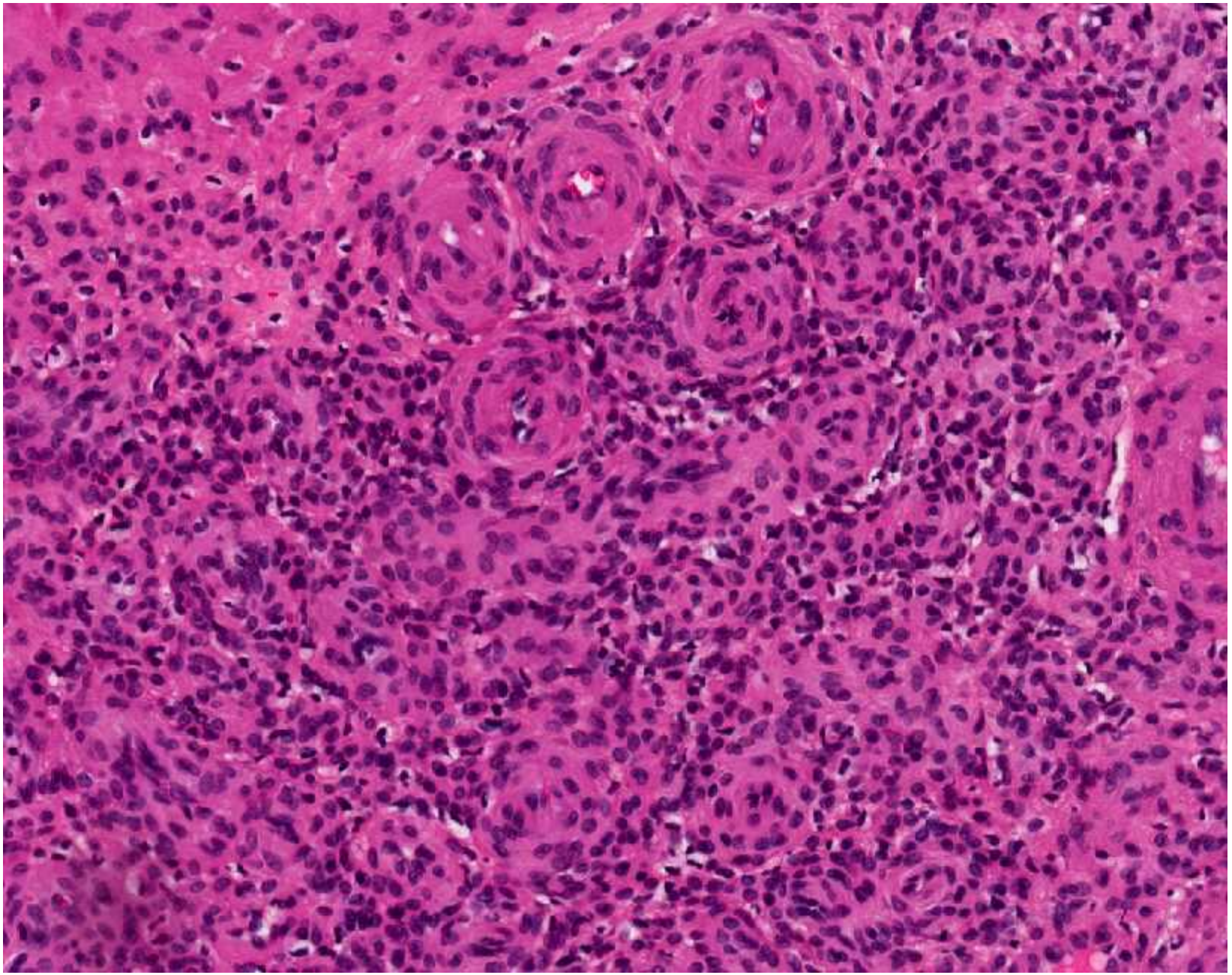
- Tumour showing differentiation towards perivascular myoid cells [Myopericytes].
- Usually subcutaneous, limbs of adults but wide variation.
- Presents as a small nodule =?-painful

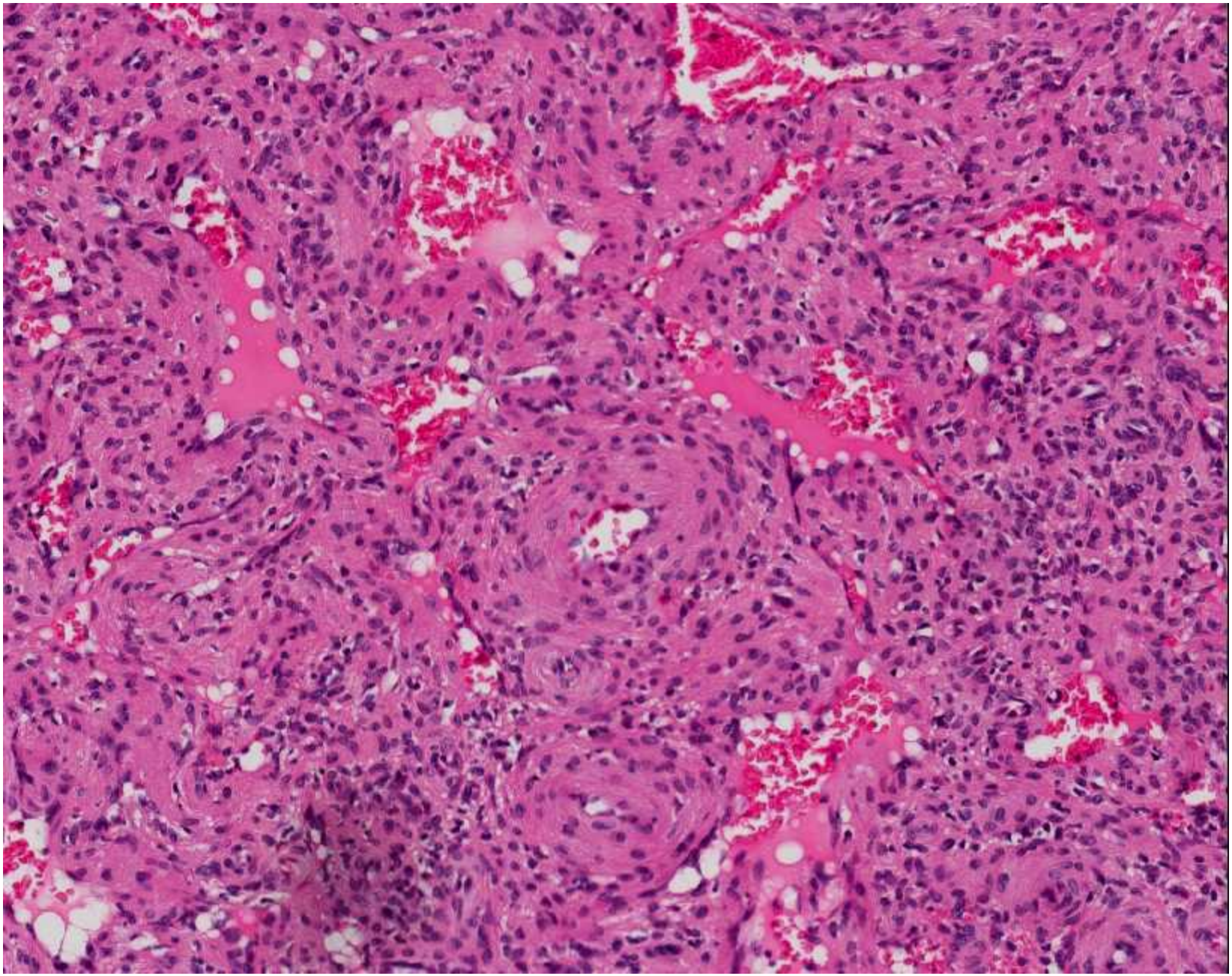
Myopericytoma

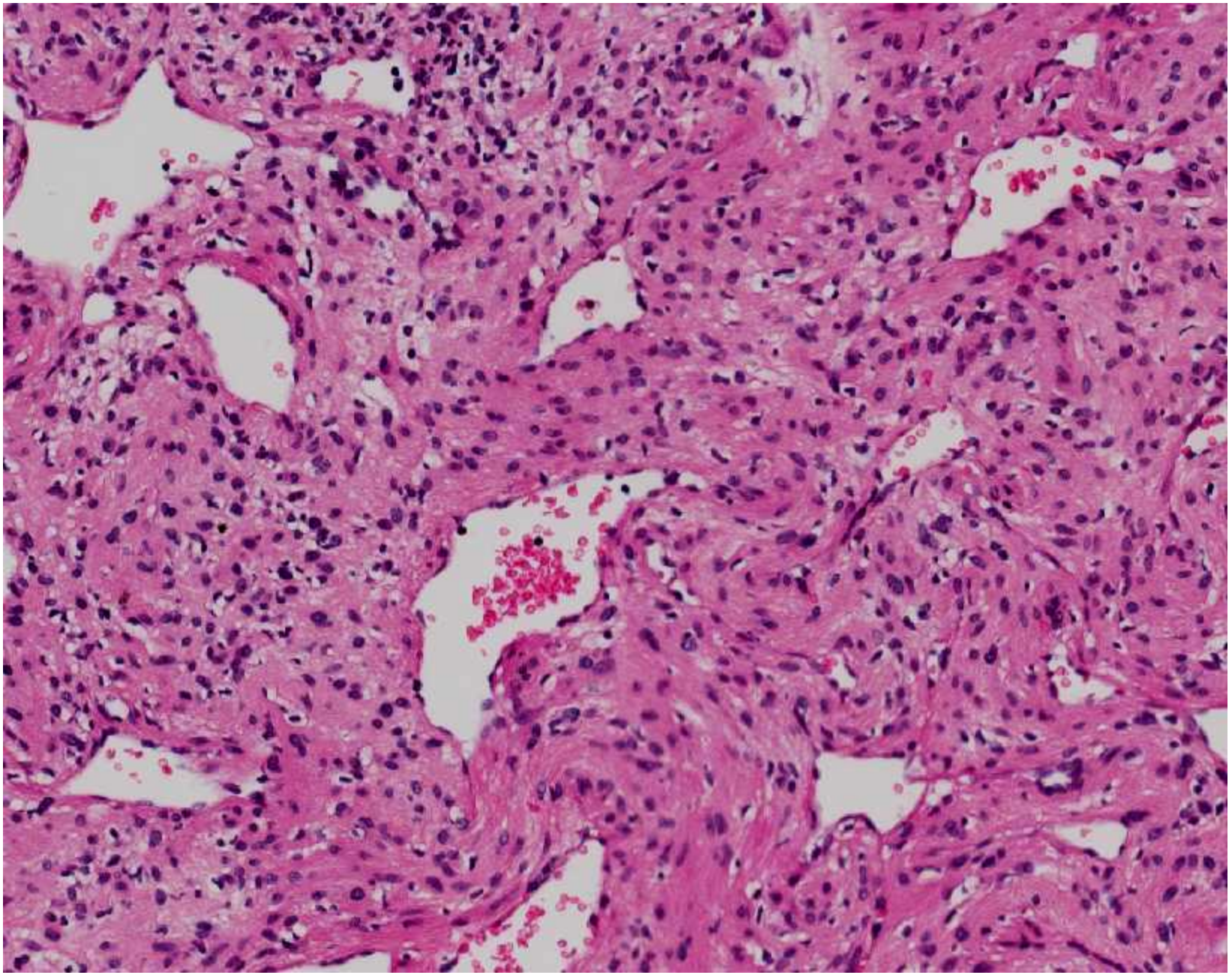
- Well circumscribed tumours
- Prominent vasculature , often gaping , branching pattern [HPC]
- Cells form concentric pattern of growth.
- Spindle to oval myoid appearing cytology
- SMA and H-caldesmon positive, but Desmin rarely positive.











Myopericytoma

- Accounts for many cases which would have been called Haemangiopericytoma [Solitary fibrous tumour accounting for most of the rest]
- Spectrum of tumours; myofibromatosis,myofibroma,glomaniopericytoma and myopericytoma, glomus
  - Granter et al; Am.J.Surg.Path.1998;22:513-525

Myopericytoma

- Most are benign
- Occasional cases are multiple within an anatomical zone.
- Rare malignant cases described, which have prominent cytological atypia.

Case 20

- 60 F. lump in kidney and liver [2002 +2012]

Spindle cell tumour

- Differential diagnosis
- Immuno

Intra. Abdo. tumour
Smooth muscle differentiation

- What should you think of?

Intra. Abdo. tumour
Smooth muscle differentiation

- Leiomyoma/Leiomyosarcoma
- GIST
- PEComa
- Myopericytoma/ angioleiomyoma/glomus
- EBV associated Smooth Muscle tumour

EBV associated SMT

- Immunosuppressed. This case had renal transplant
- Very low grade tumours.
- Often multi-centric, not metastatic.
- Use in-situ hybridisation to identify EBV [EBER]

Case 21

- 50F. Intra-abdominal mass.

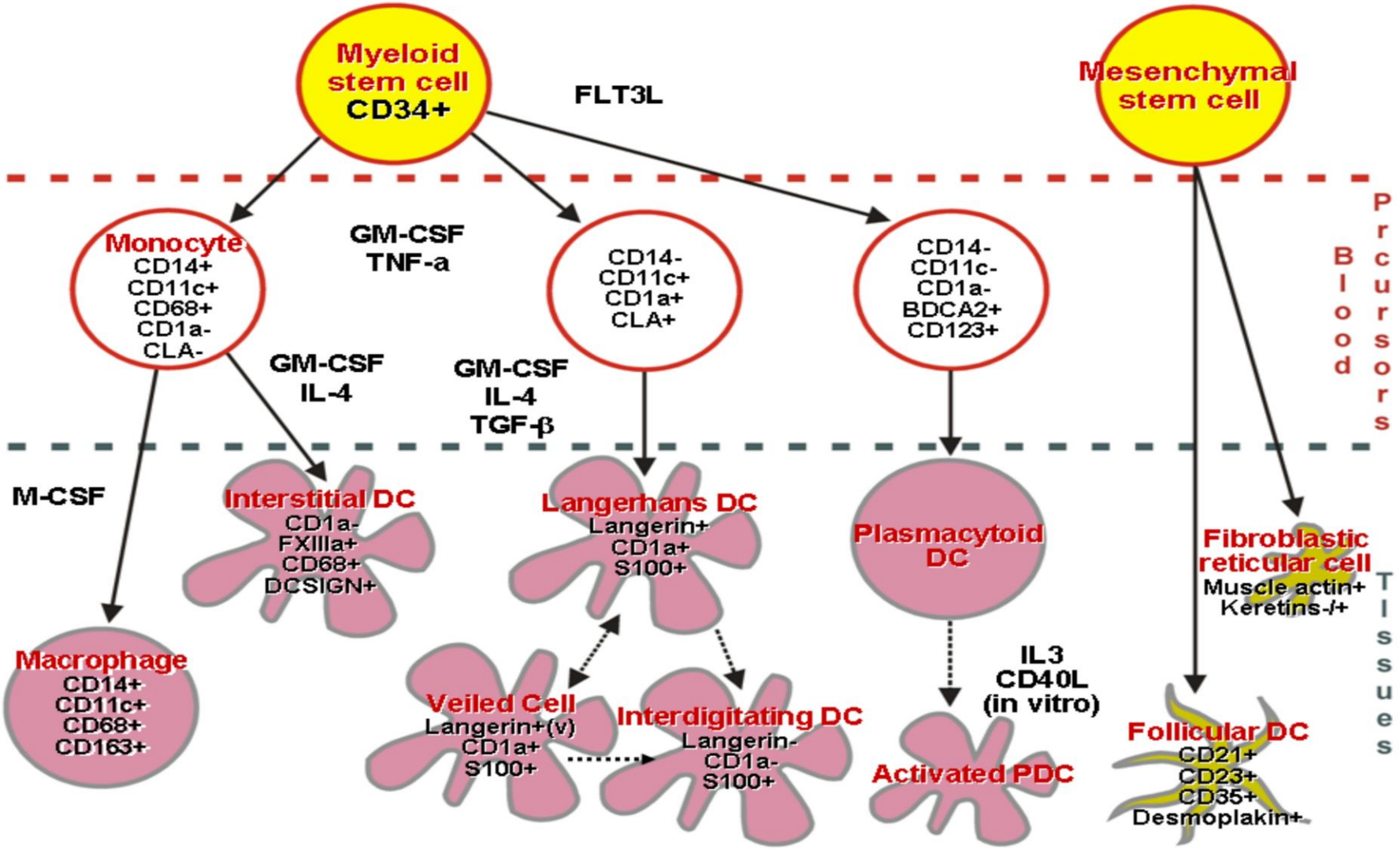
Rare causes of spindle cell tumour

- Soft tissue tumours
- Carcinoma's
- Melanoma's
- Haematopoietic system.
  - Mast cell disease
  - Histiocytic. JXG [spindle cell xanthogranuloma]
  - Follicular dendritic cells.

Follicular dendritic cell sarcoma

- Associated with Castleman's disease
- Can arise in lymph nodes. Intra. Abdo recognised site.
- Spindle cells. Often storiform or whorled pattern
- Sprinkling of lymphocytes.
- EMA, CD21, CD35 positive

Cell of origin for Histiocytic lesions From WHO classification



Take home points

- Never forget Carcinoma and Melanoma
- Very spindly- Fibrous, Neural and **Lipo.**
- Remember basic patterns; HPC, Giant cell MFH, Fibrosarcomatous, storiform.
- Remember to look for low grade areas at margins.

Take home points

- Plump spindle cells- add Rhabdo to list
- CD34 and p63 very helpful immuno.
- FISH, PCR techniques paramount
- Keep open mind, do broad immuno panel including hematopoietic; CD45, CD163, EMA,CD21 at least third line.

THE END

GOOD LUCK !