SO-CALLED FIBROHISTIOCYTIC TUMOURS: AN OVERVIEW FOCUSSING ON LESIONS IN WHICH BIOLOGIC POTENTIAL MAY BE MISINTERPRETED

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SO-CALLED FIBROHISTIOCYTIC TUMOURS COMMONEST MISINTERPRETATIONS BENIGN LESIONS DIAGNOSED AS MALIGNANT

Cellular fibrous histiocytoma
Aneurysmal fibrous histiocytoma
Epithelioid fibrous histiocytoma
Atypical fibrous histiocytoma
Deep benign fibrous histiocytoma
(Diffuse-type giant cell tumour)
Atypical fibroxanthoma

SO-CALLED FIBROHISTICYTIC TUMOURS

MALIGNANT LESIONS DIAGNOSED AS BENIGN

Low-grade myxofibrosarcoma

Much less often a problem

SO-CALLED FIBROHISTICYTIC TUMOURS

LESIONS IN WHICH BIOLOGIC POTENTIAL IS DIFFICULT TO PREDICT

Plexiform fibrohistiocytic tumour

Angiomatoid 'MFH'

Most pursue a benign clinical course but approx. 2% (?) metastasise

CELLULAR BENIGN FIBROUS HISTIOCYTOMA

CLINICAL FEATURES

Wide age range

Peak incidence 15-45 years

Limbs > head & neck > elsewhere

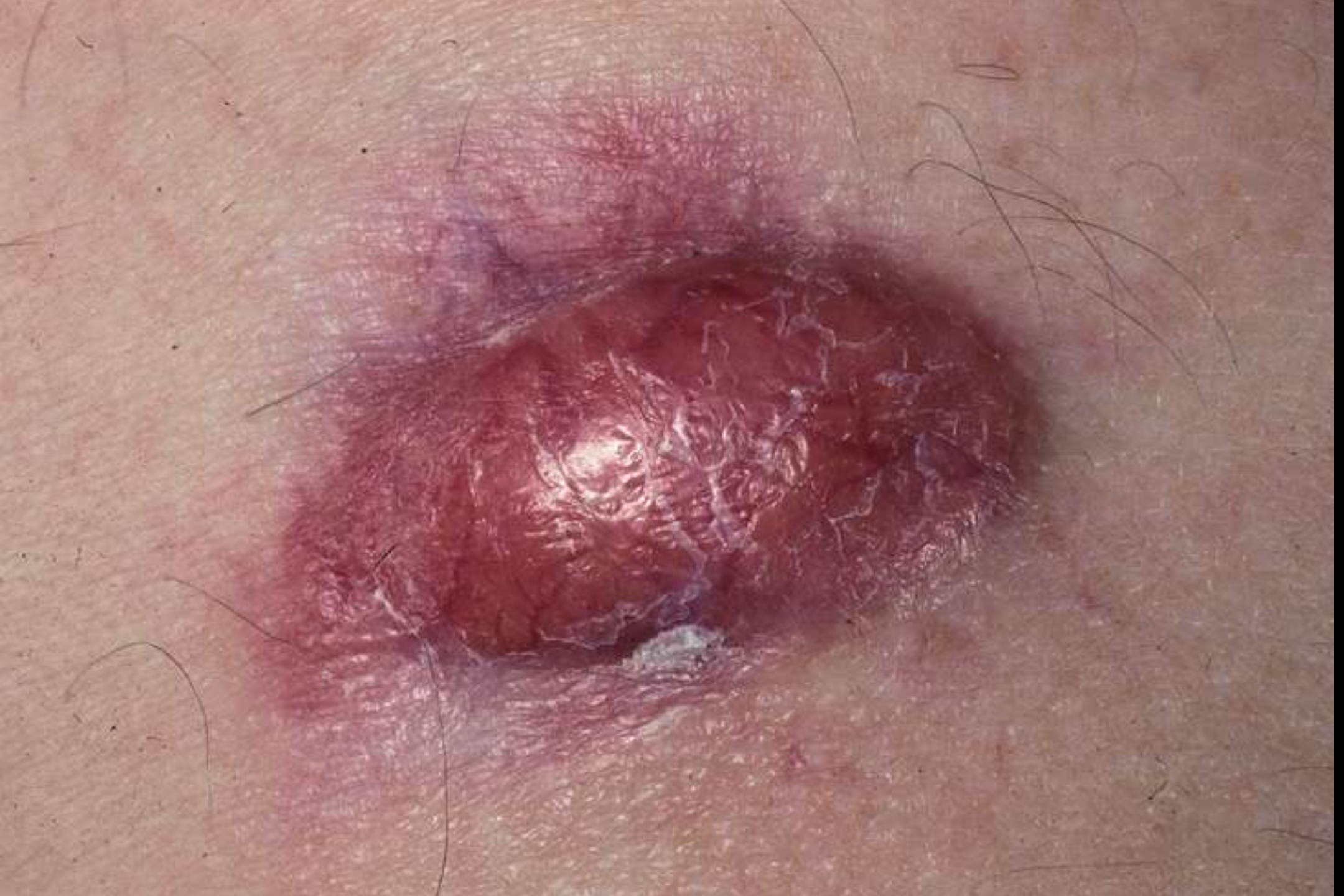
Poorly marginated nodule

Most < 3 cm

May grow rapidly

Local recurrence in 15-20%

Exceptionally metastasise



CELLULAR BENIGN FIBROUS HISTIOCYTOMA

DISTINCTIVE HISTOLOGIC FEATURES

Larger, more cellular

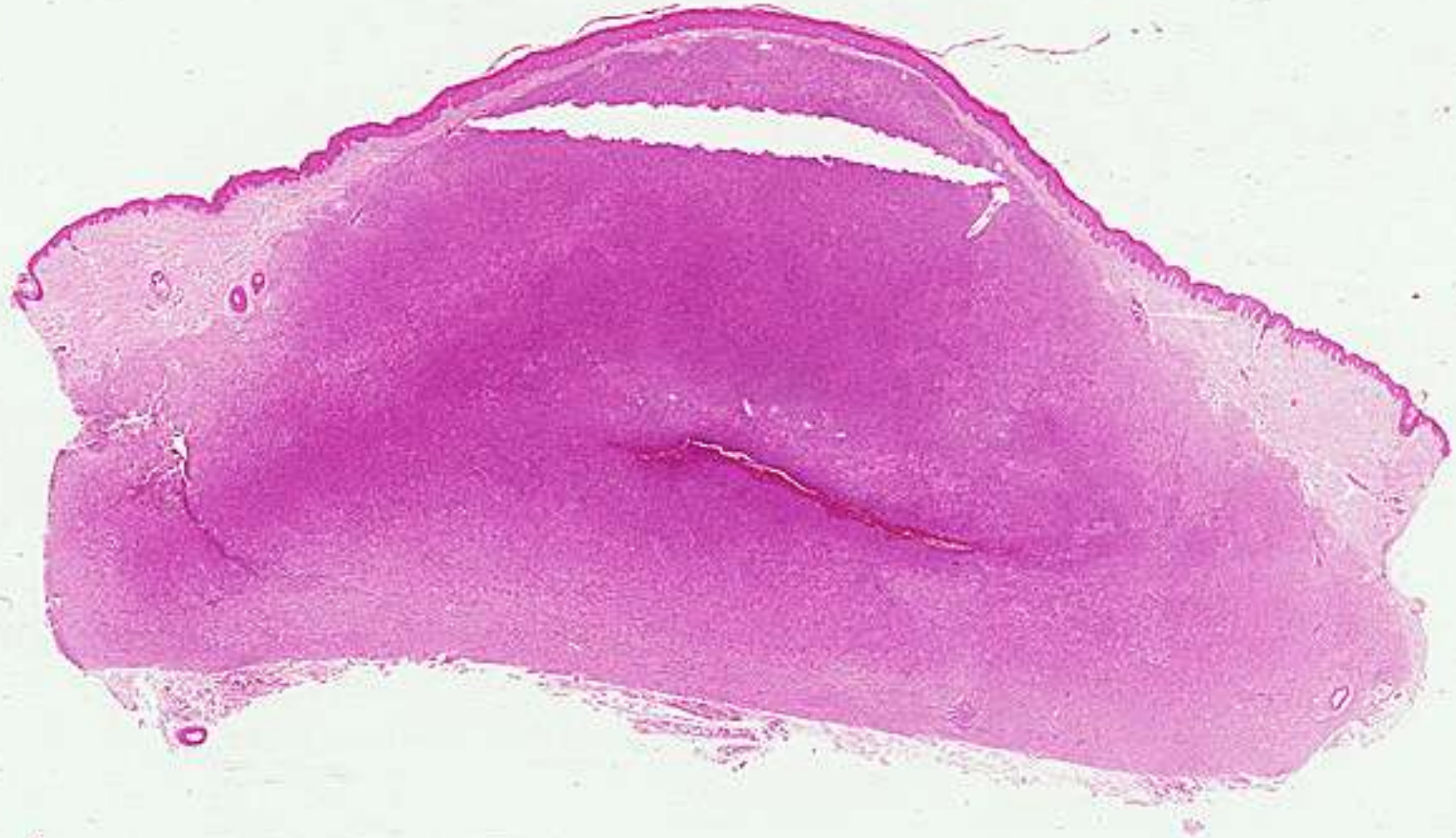
Often extends into subcutis

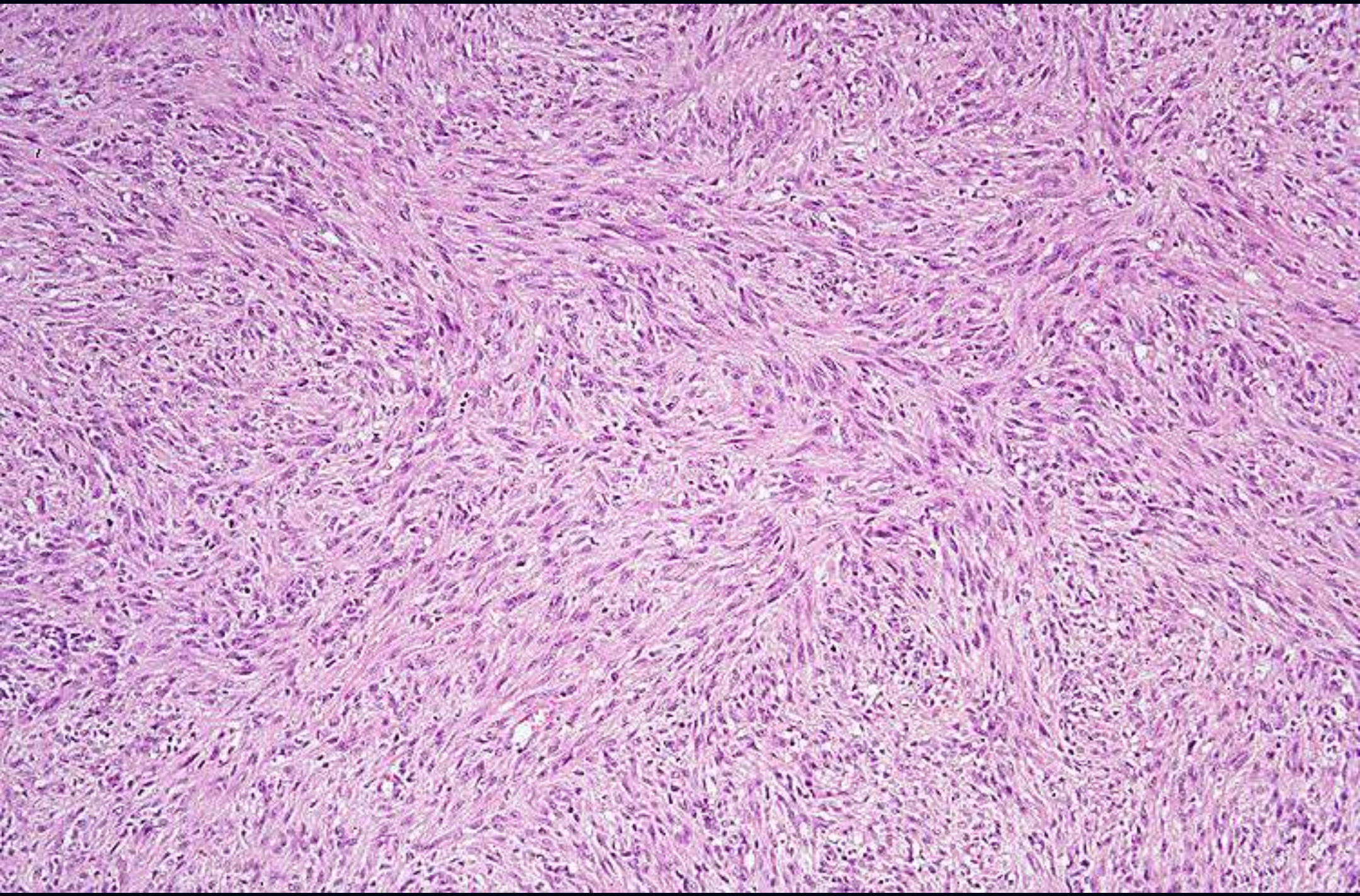
Often fascicular and ‘myoid’

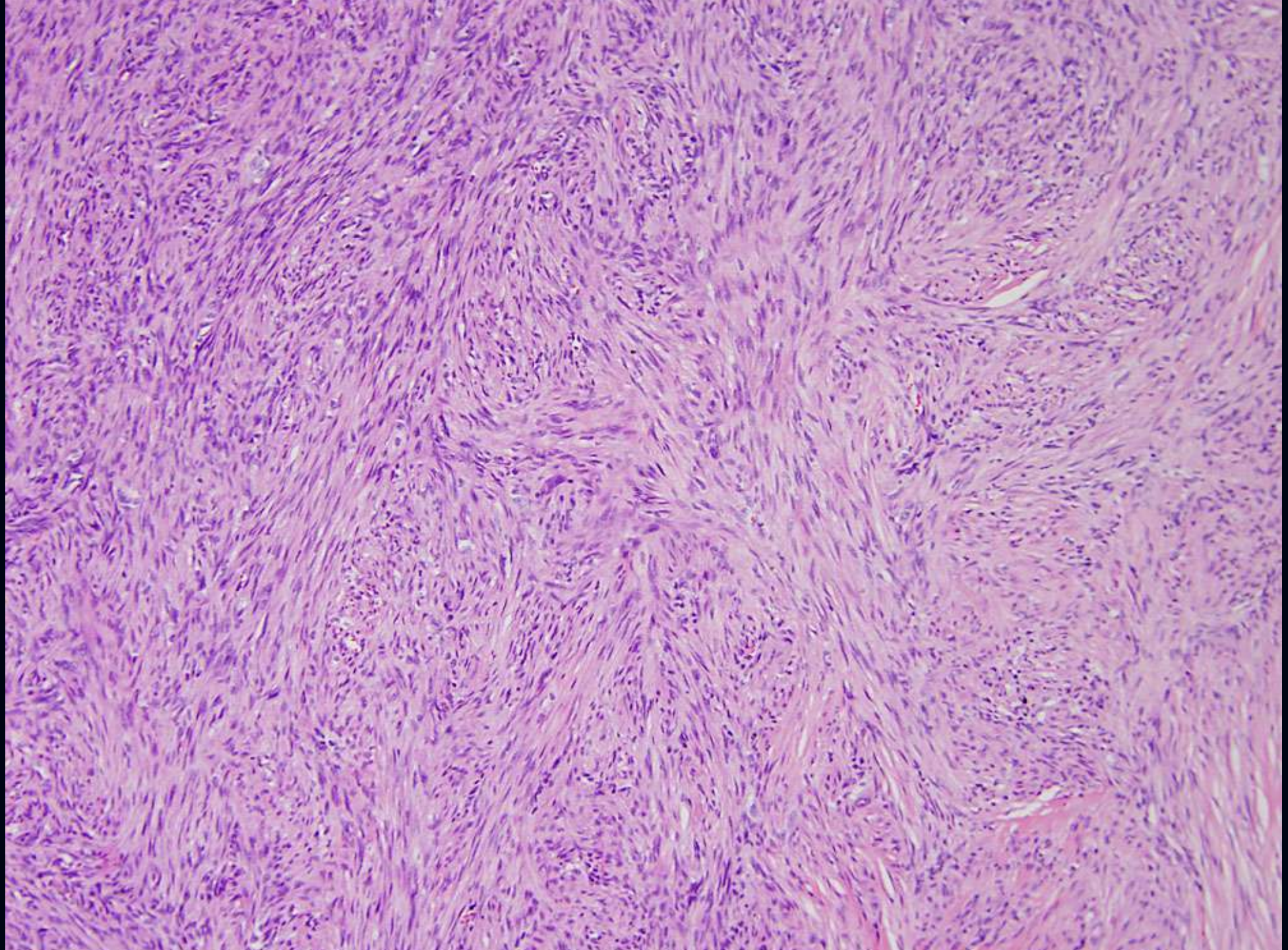
Relative paucity of giant or foamy cells

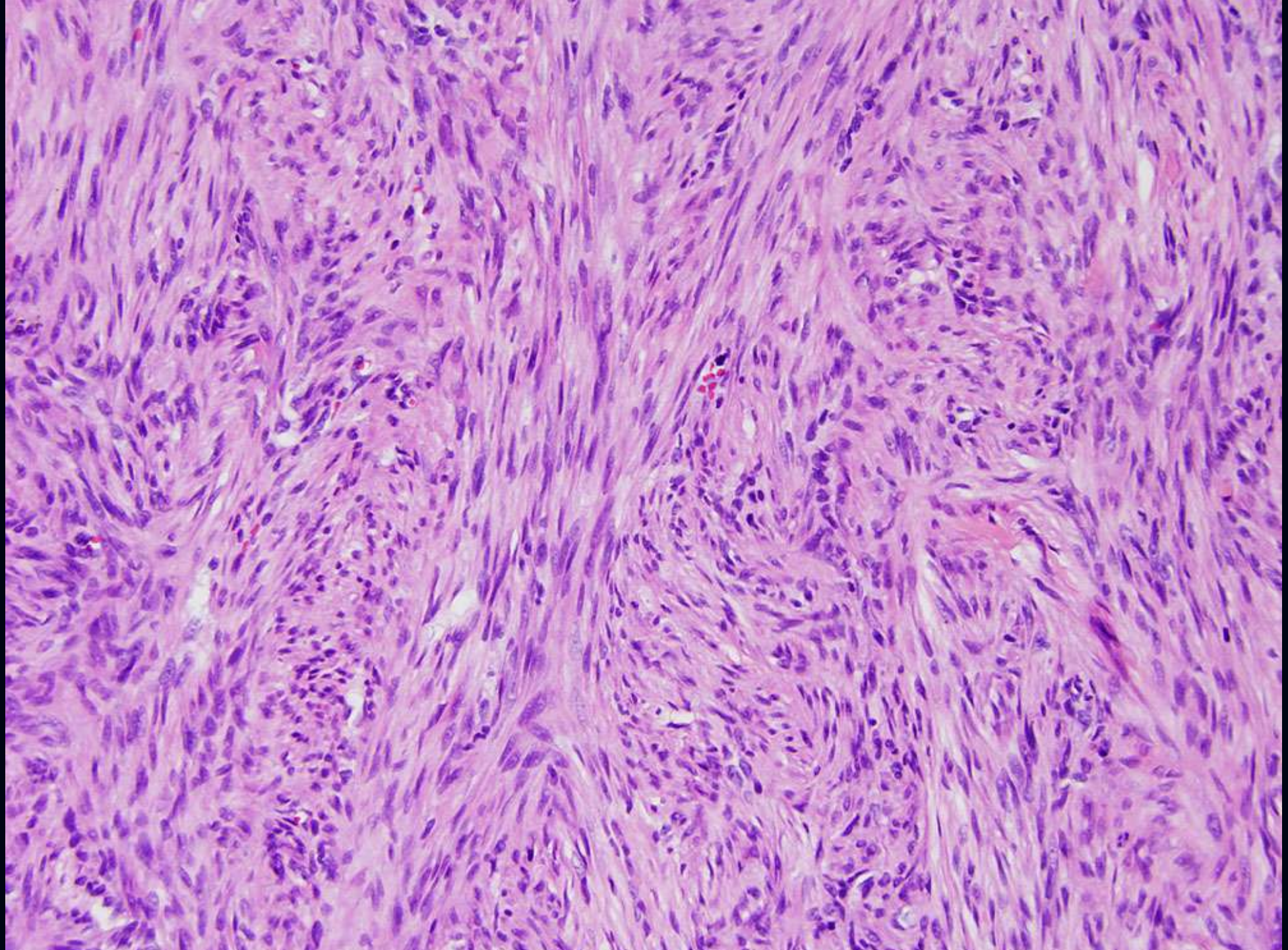
Frequent mitoses

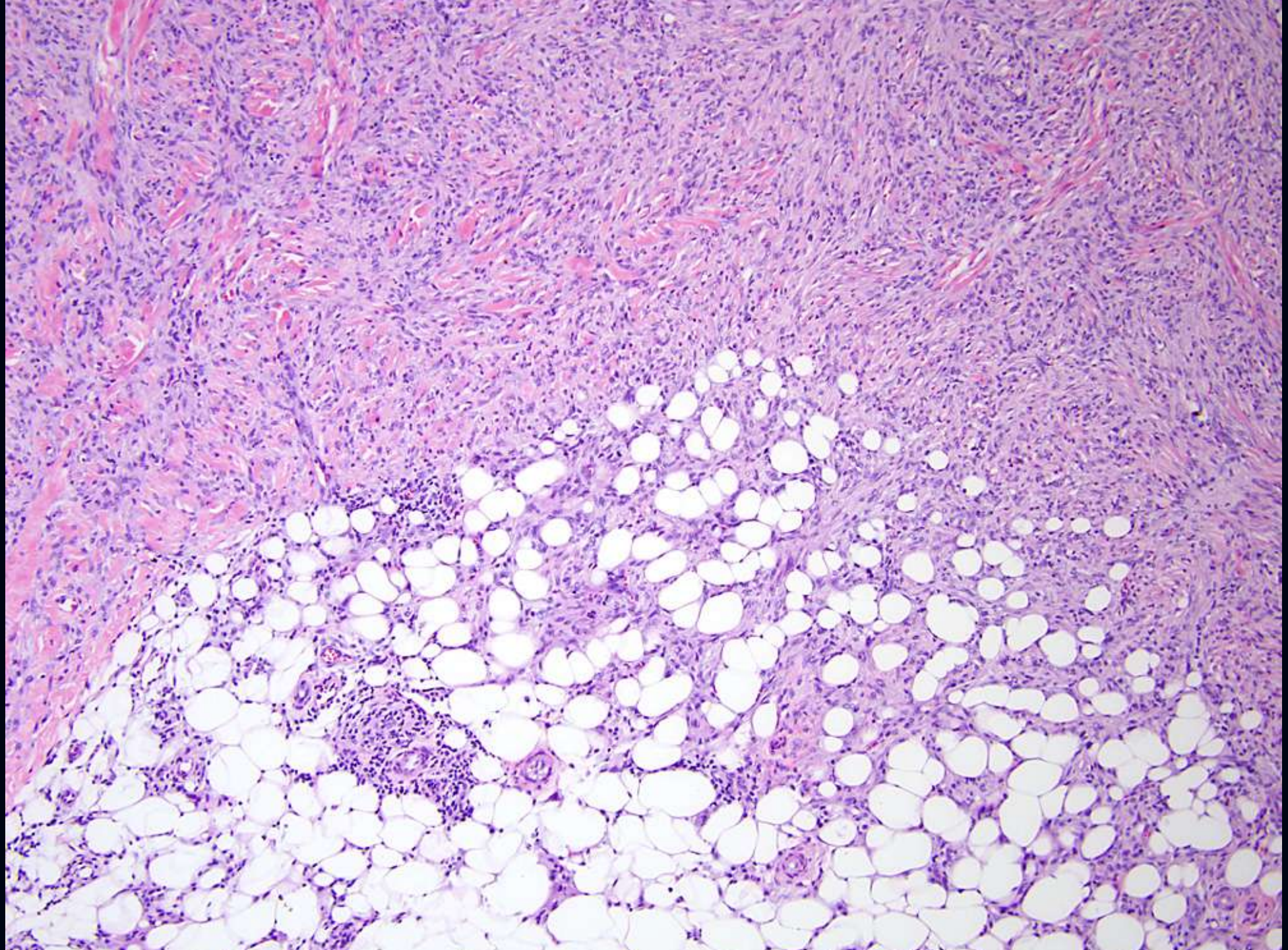
Occasional central necrosis

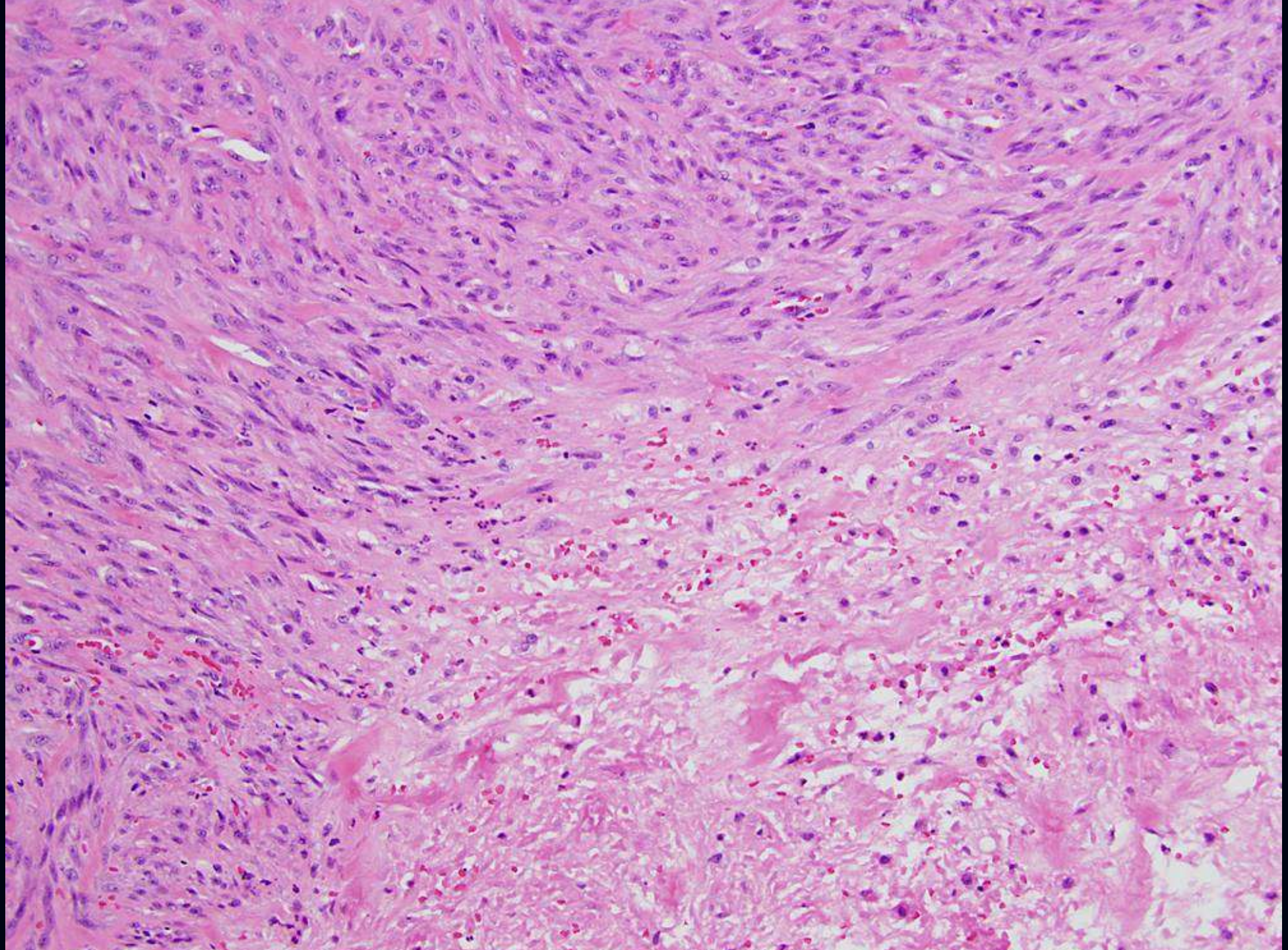


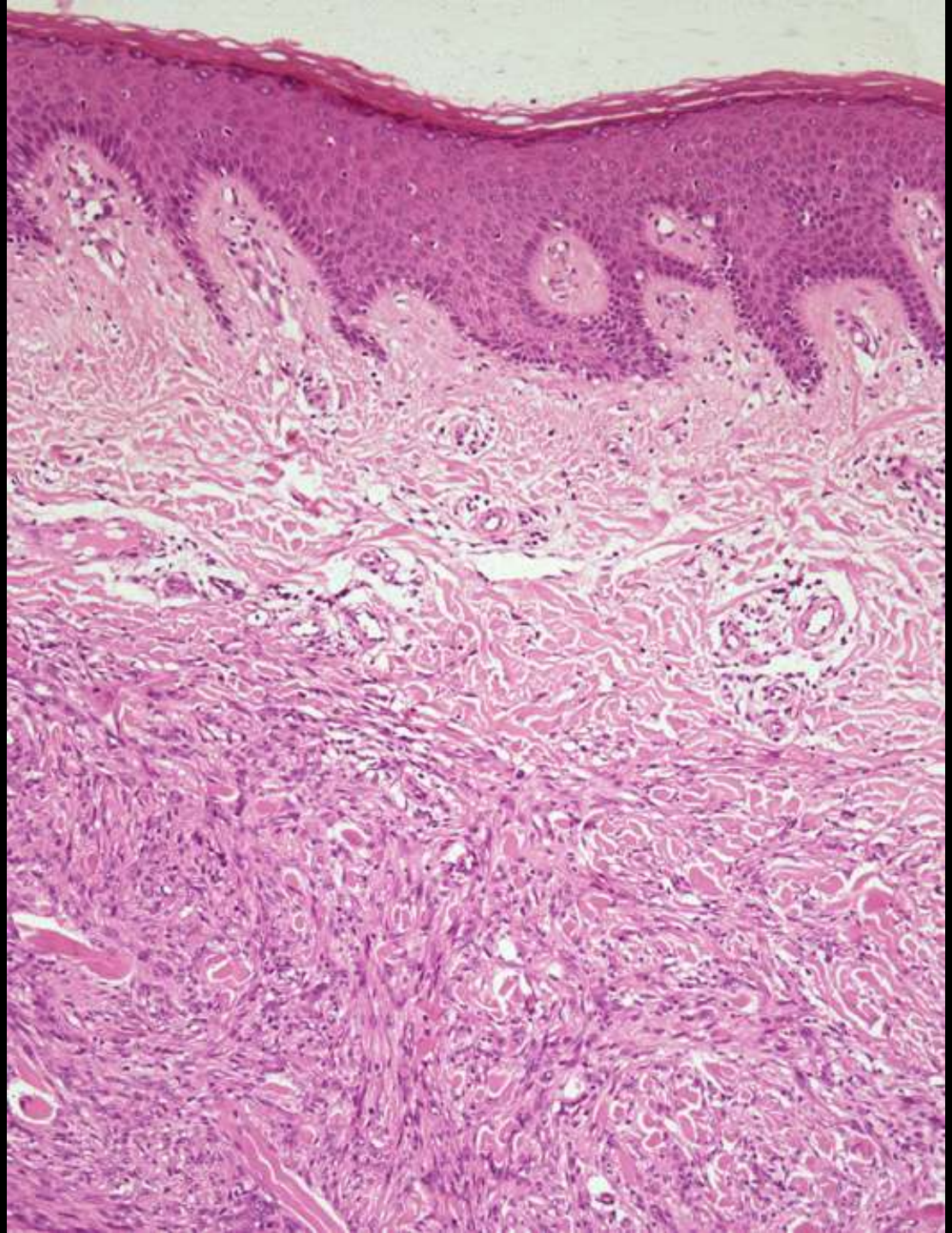


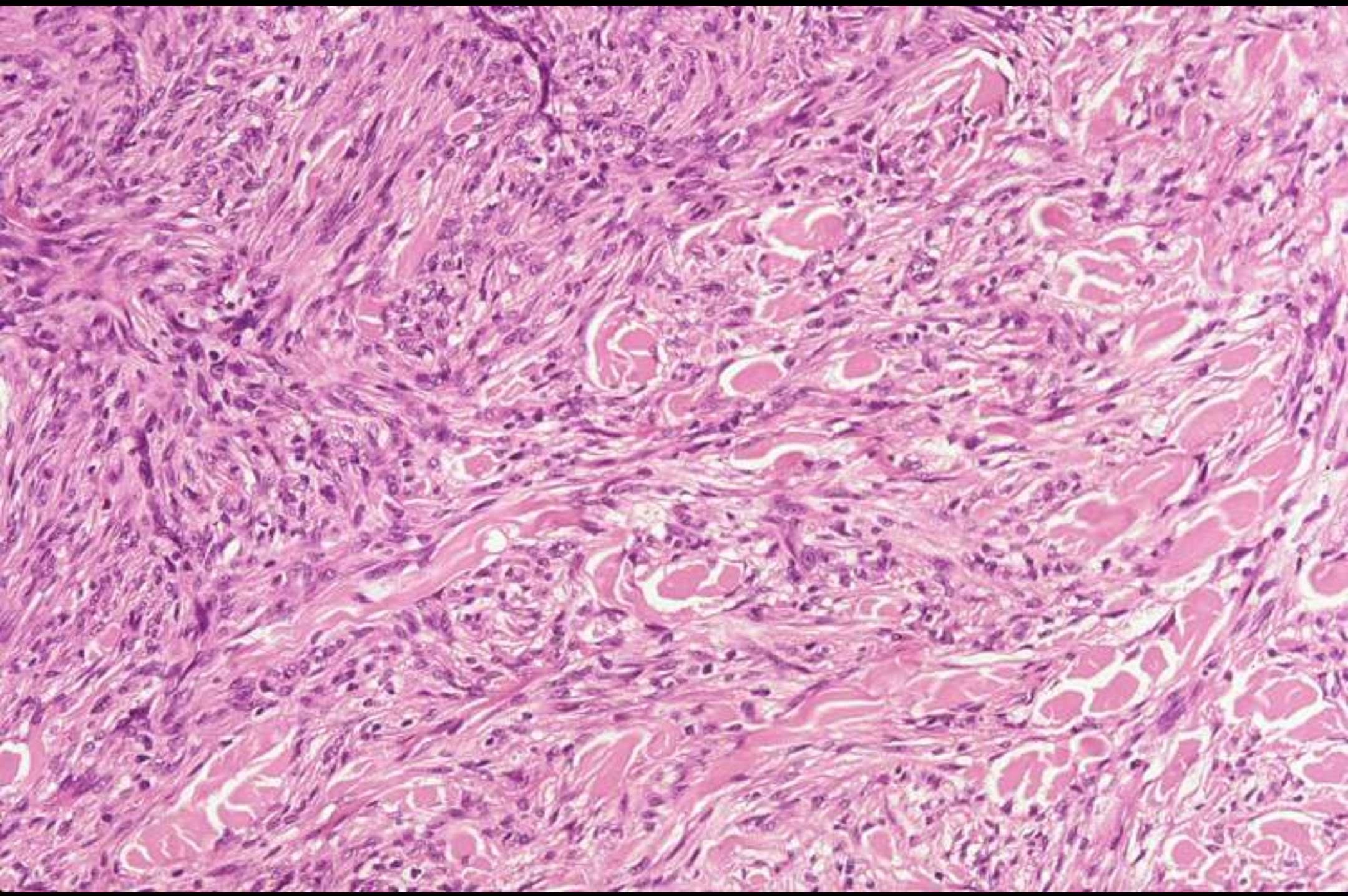


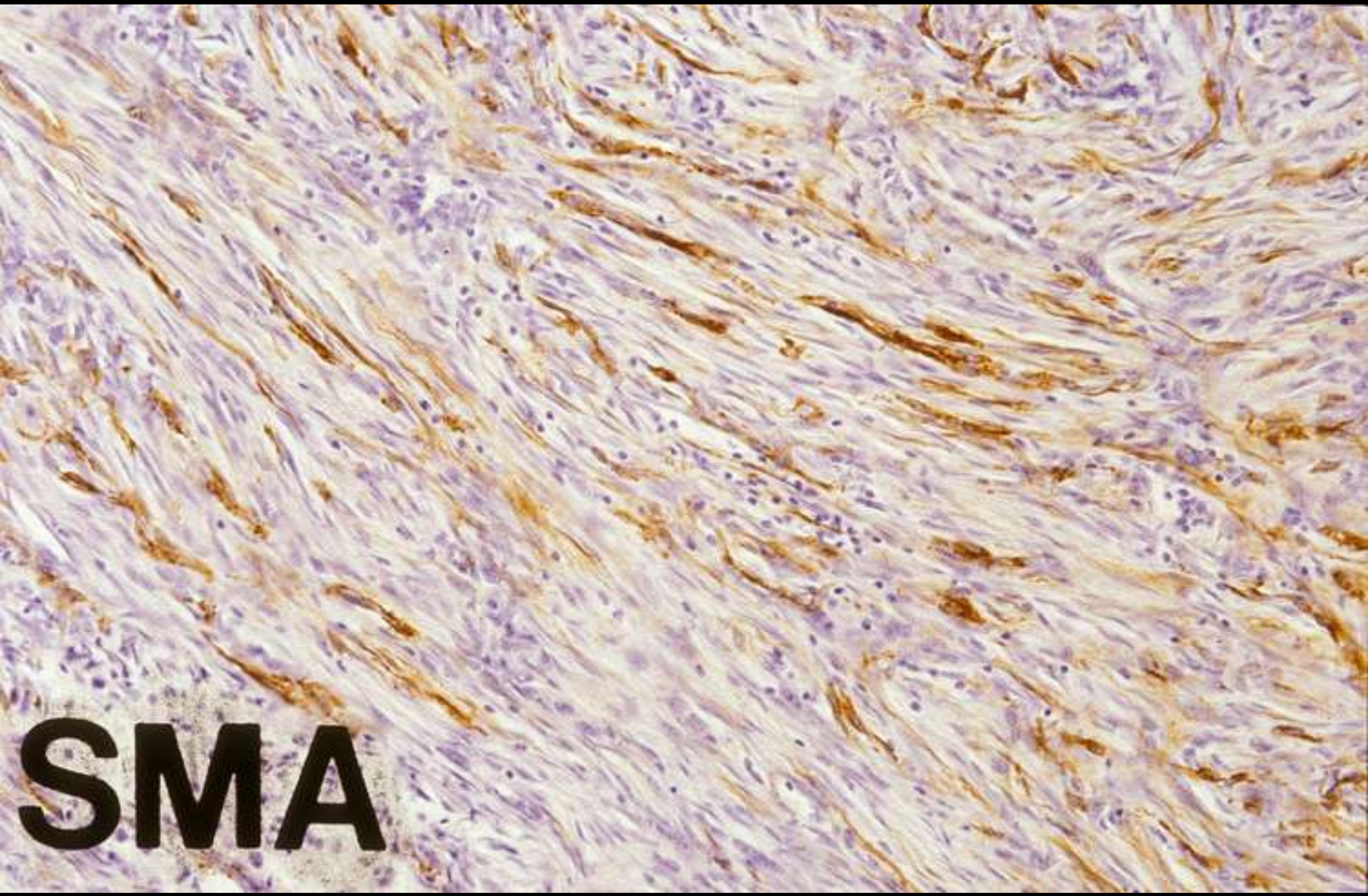








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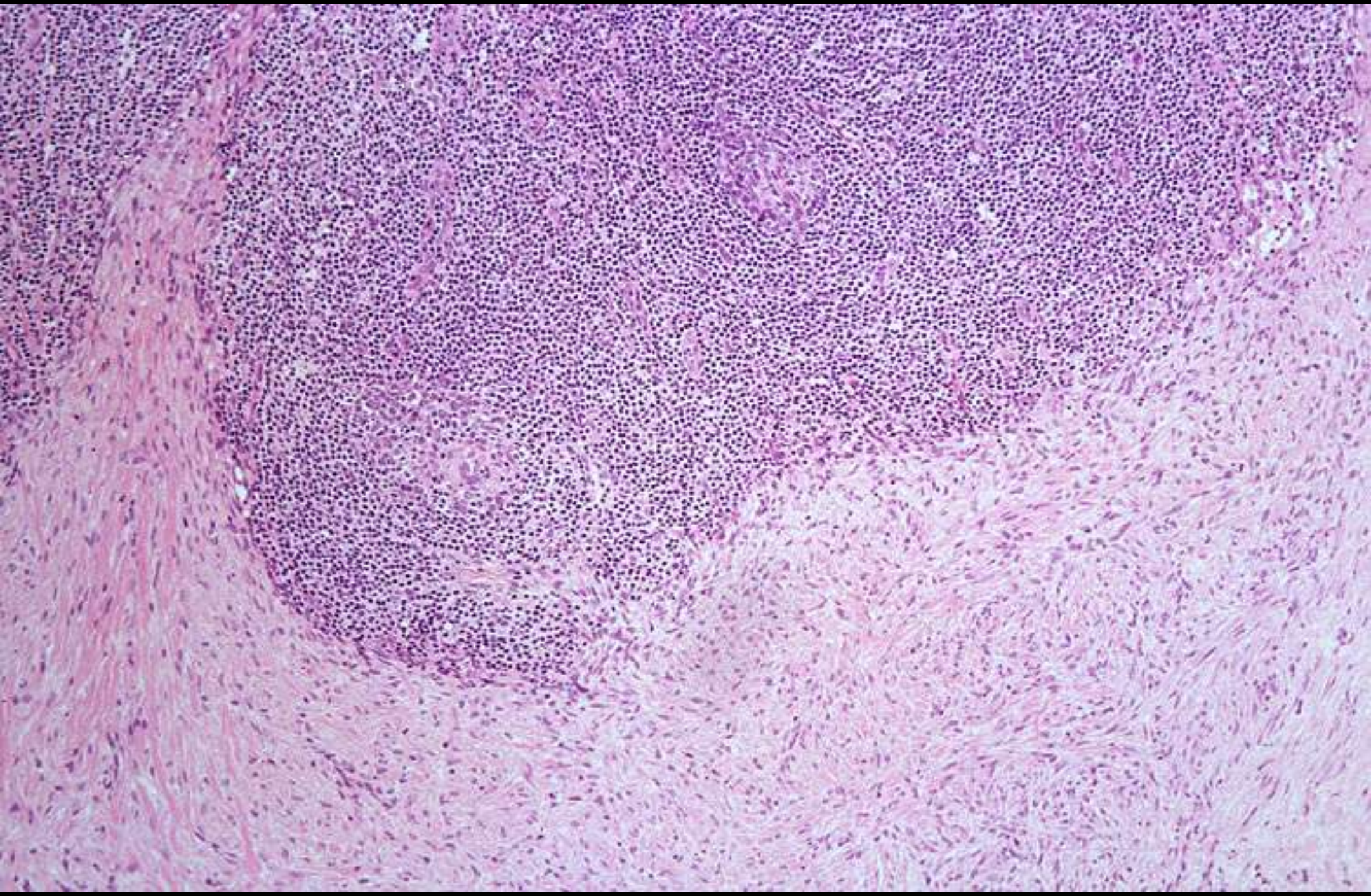
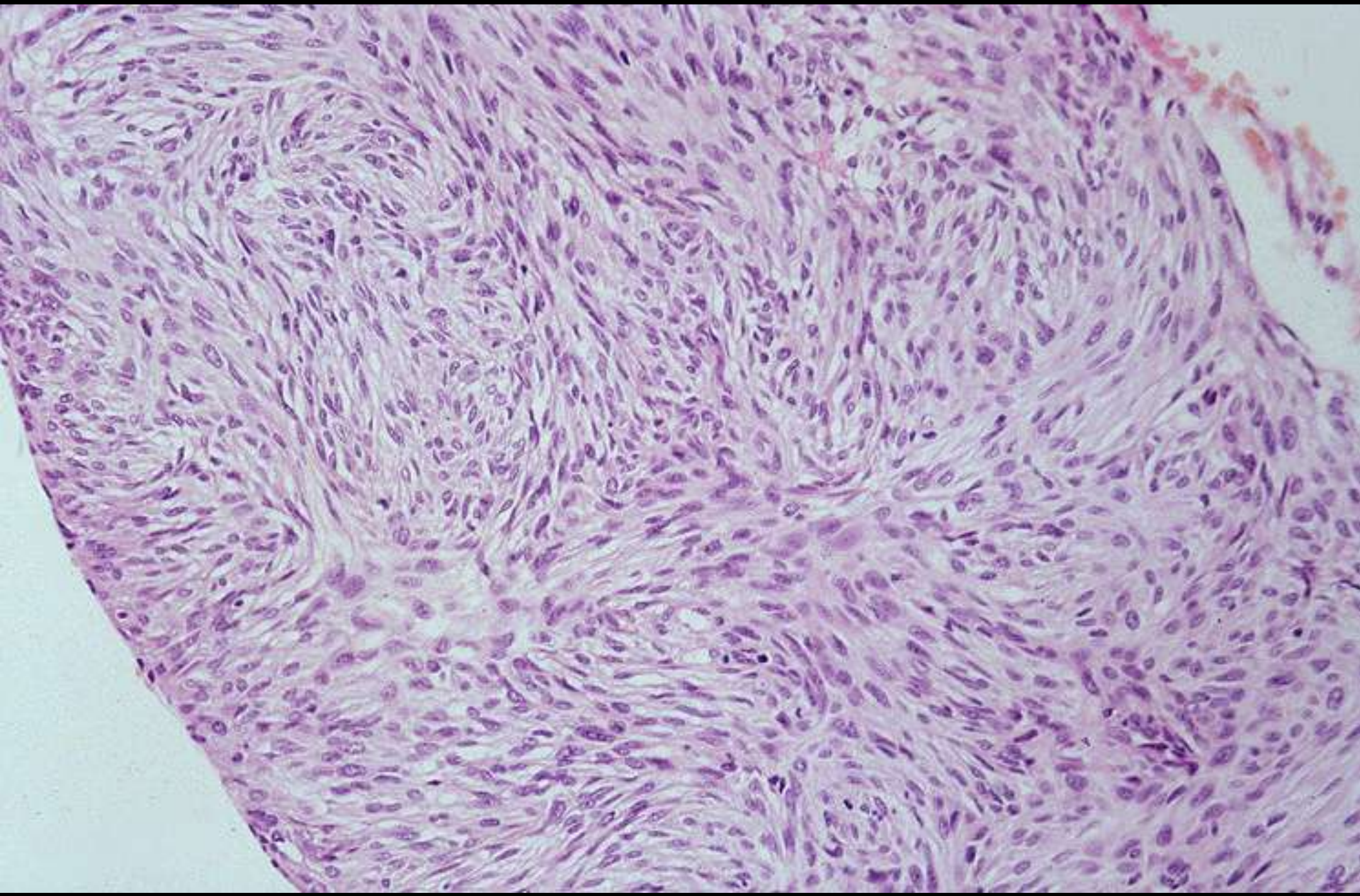
CELLULAR BENIGN FIBROUS HISTIOCYTOMA
CLINICAL RELEVANCE

Ordinary FH	**Approx. 2% recur** **Non-destructive**
Cellular FH	**15-20% recur** **Non-destructive** **Very rare metastasis**
DFSP	**30% or more recur** **Locally infiltrative** **No metastasis unless FS-DFSP**





NOTABLE FEATURES OF METASTASISING CUTANEOUS FH

- Frequently preceded by repeated local recurrence
- Predilection to spread to lymph nodes and lung
- Metastases may be delayed for many years; lung lesions may be indolent
- Metastases usually closely resemble the primary lesion

CELLULAR BENIGN FIBROUS HISTIOCYTOMA DIFFERENTIAL DIAGNOSIS

Dermatofibrosarcoma protuberans

- more basophilic
- less polymorphic
- CD34 positive

Cutaneous “leiomyosarcoma”

- cigar-shaped nuclei
- infiltrative dermal growth
- desmin positive (in skin)

ANEURYSMAL BENIGN FIBROUS HISTIOCYTOMA

CLINICAL FEATURES

Approx. 5% of cutaneous FH

Adults; peak 20-40 years

Females slightly > males

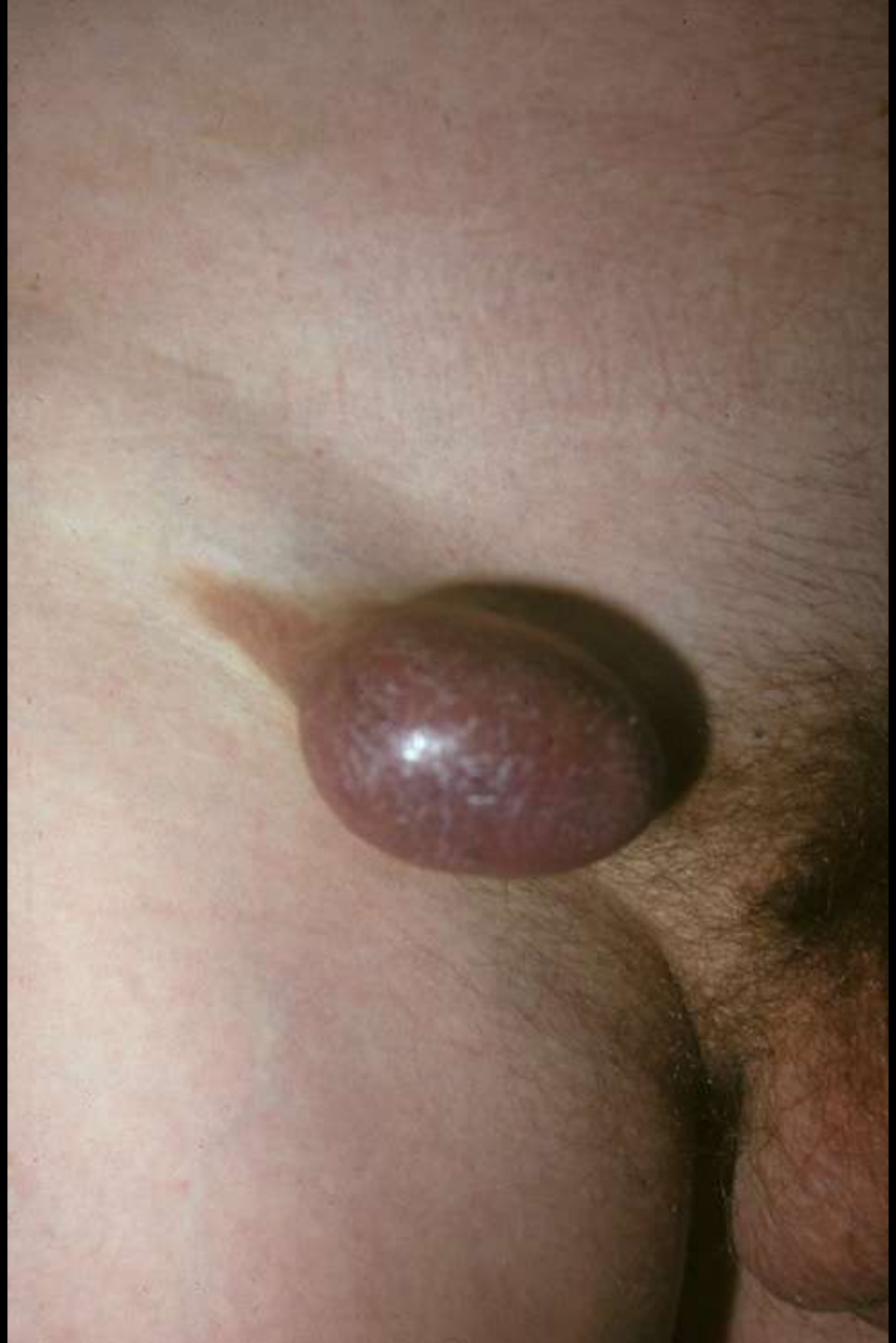
Lower limb ++ > trunk > elsewhere

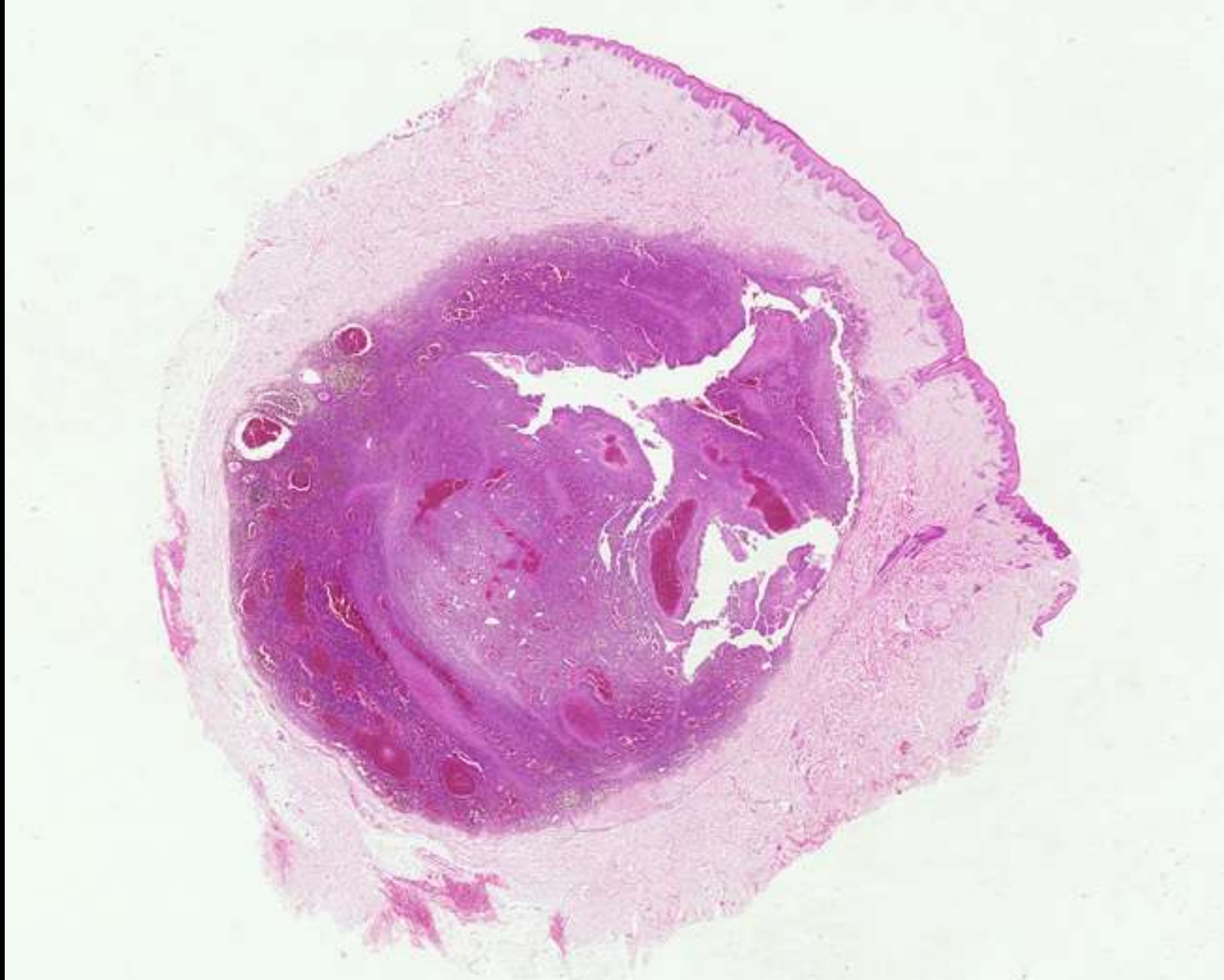
Red / brown nodule up to 2-3 cm

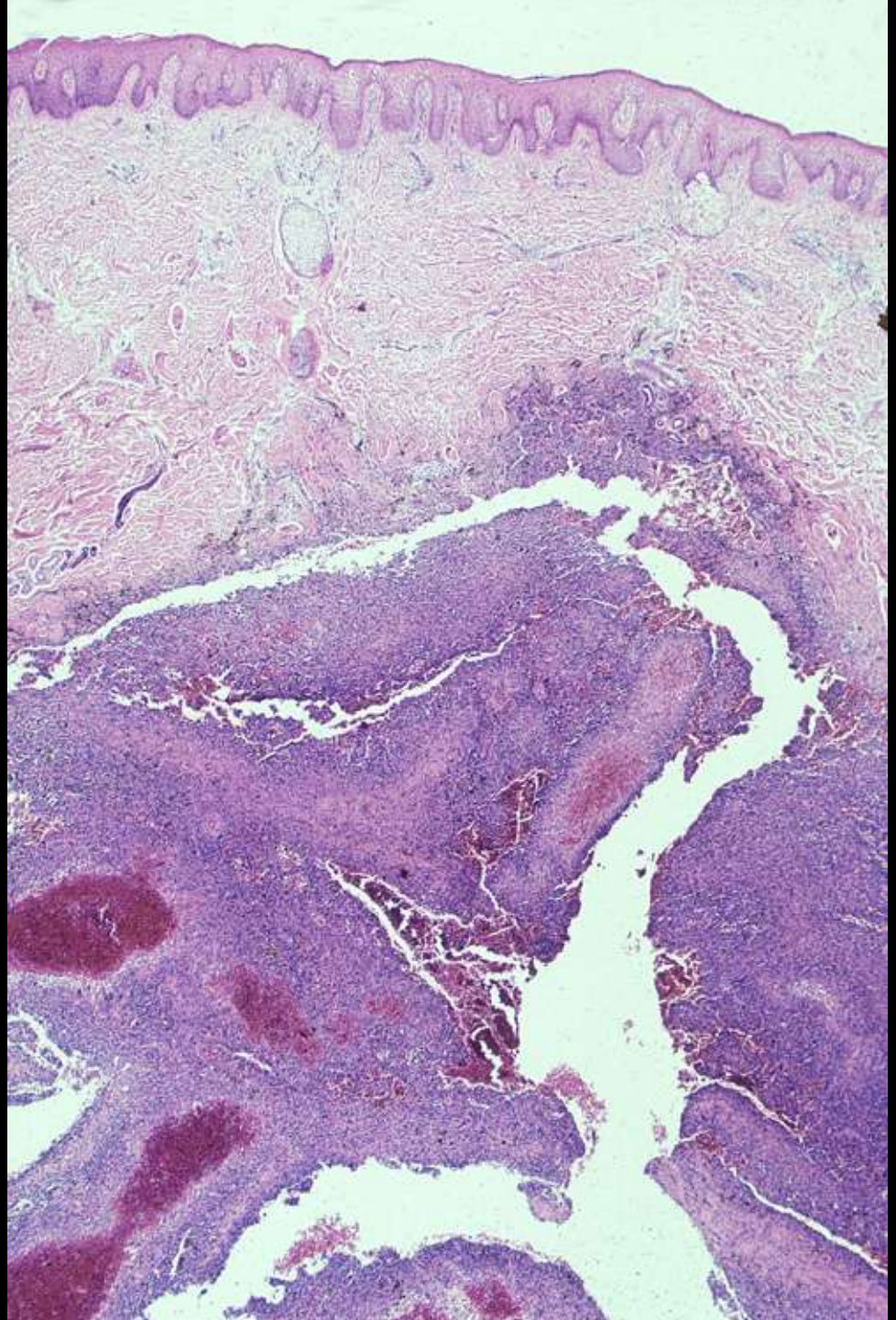
Occasional rapid growth / pain

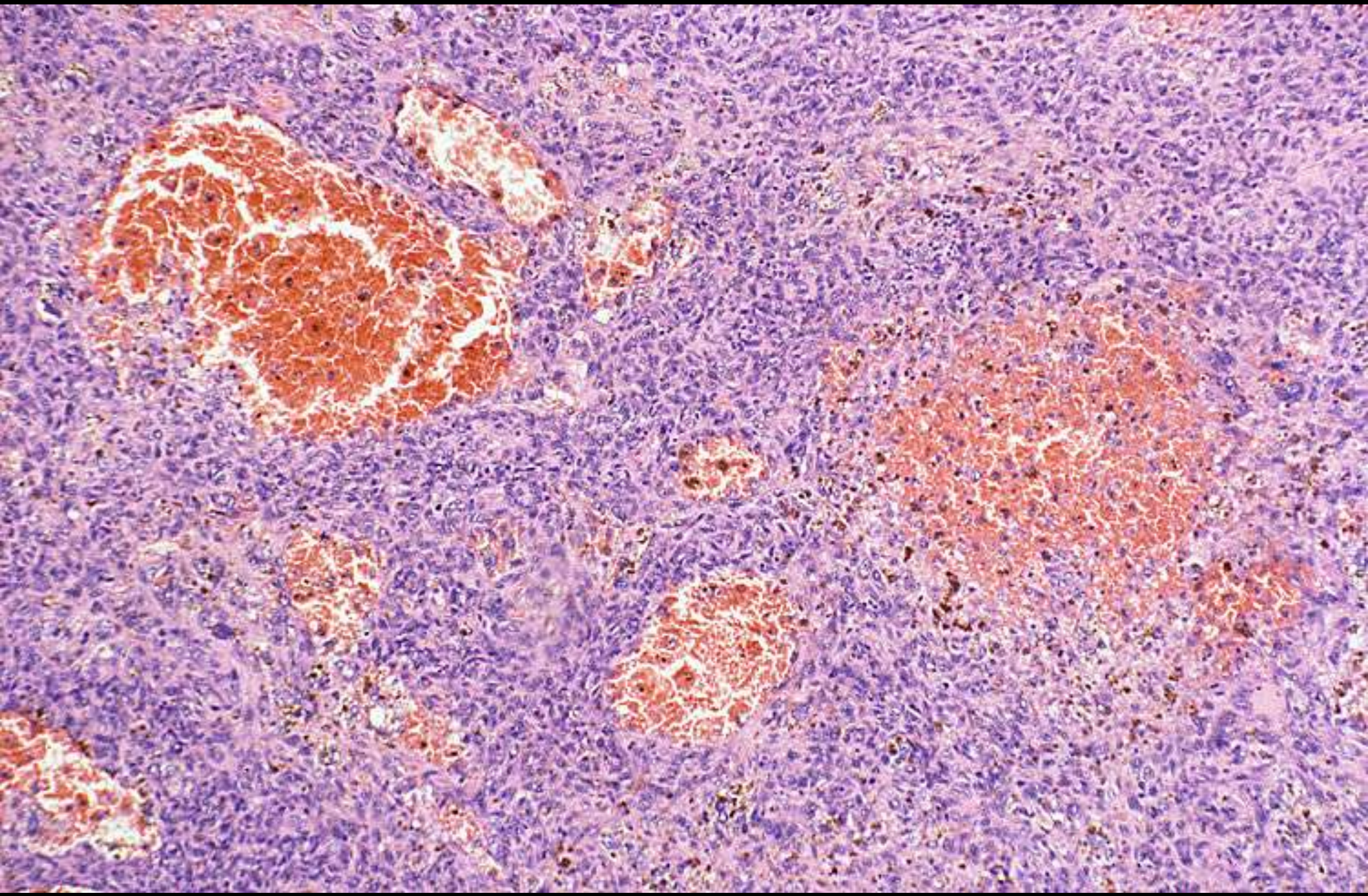
15-20% local recurrence

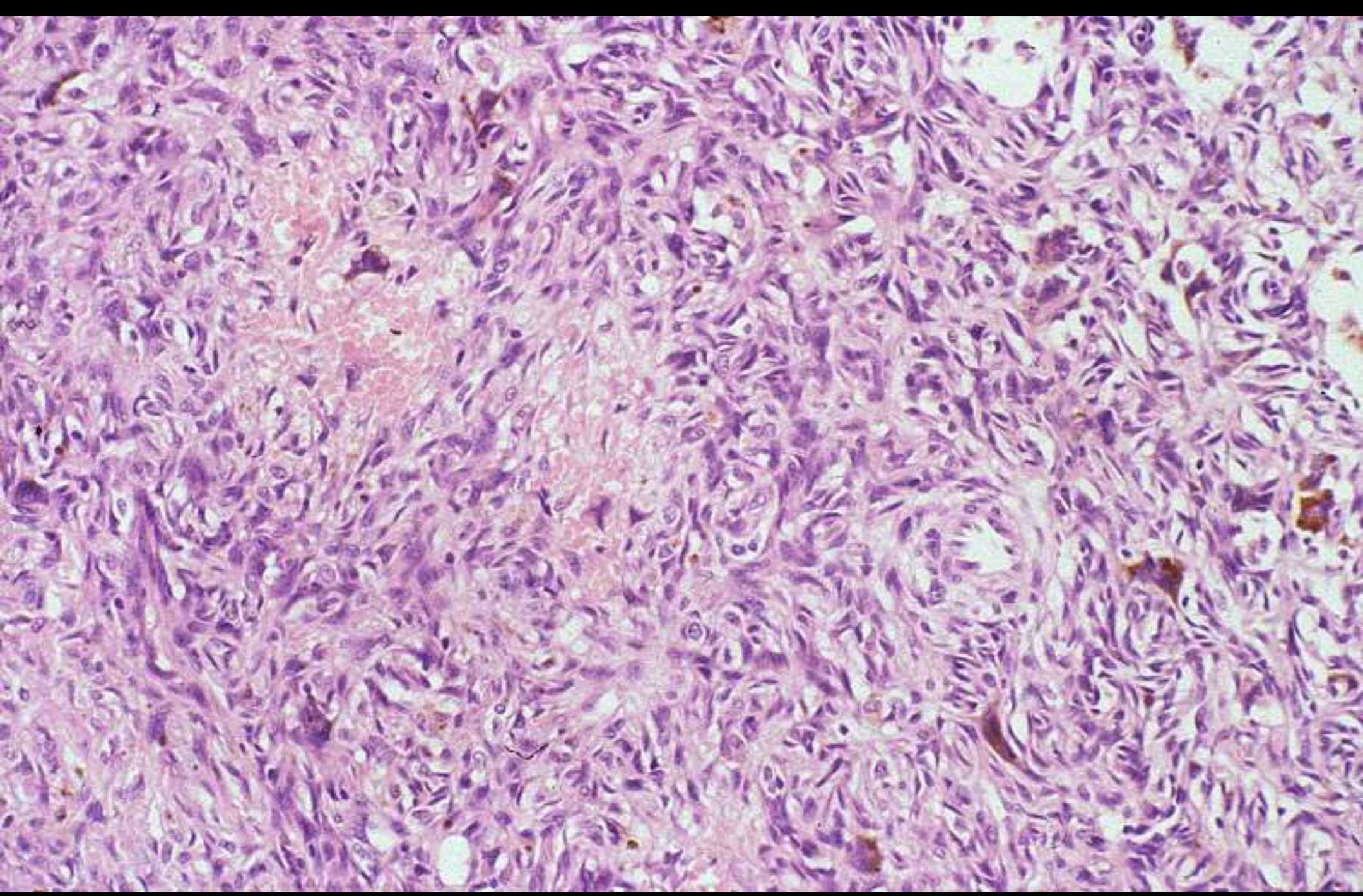
Rare metastasis

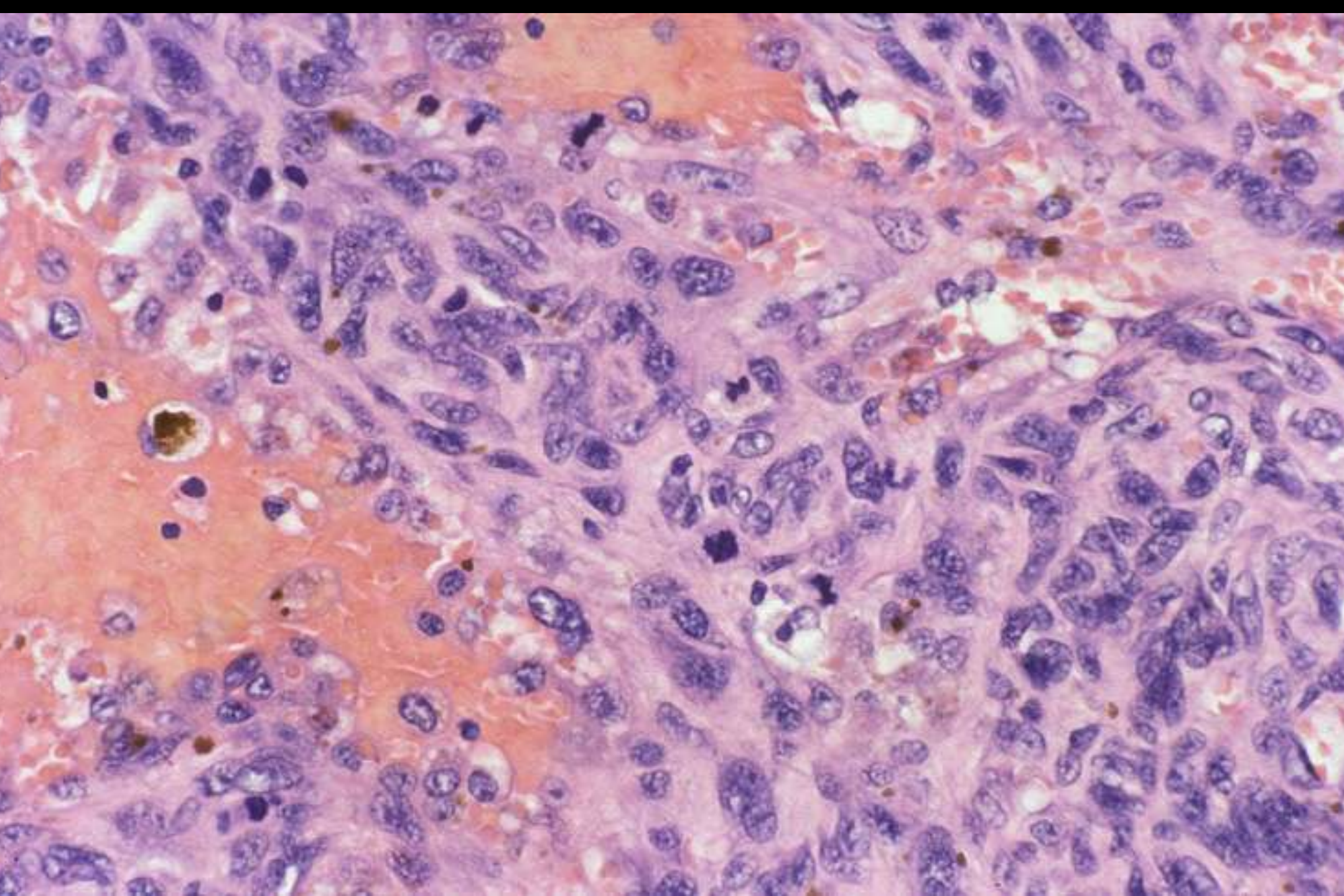


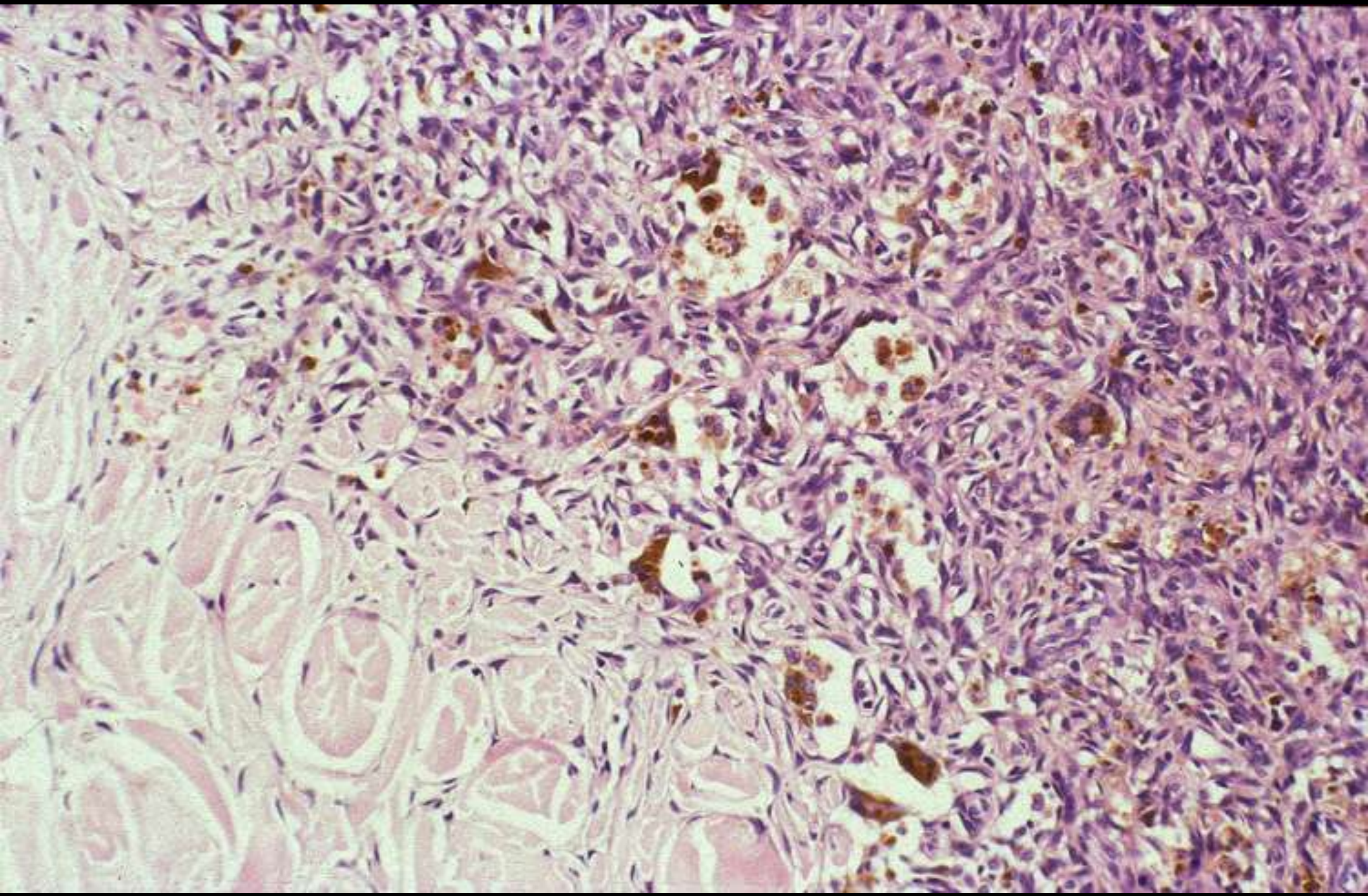












ANEURYSMAL BENIGN FIBROUS HISTIOCYTOMA DIFFERENTIAL DIAGNOSIS

Angiomatoid “MFH”
Kaposi’s sarcoma
(Spindle cell haemangioma)
(Angiosarcoma)

CELLULAR / ANEURYSMAL VARIANTS OF BENIGN FIBROUS HISTIOCYTOMA

WORRISOME FEATURES

Frequently large size

Cellularity

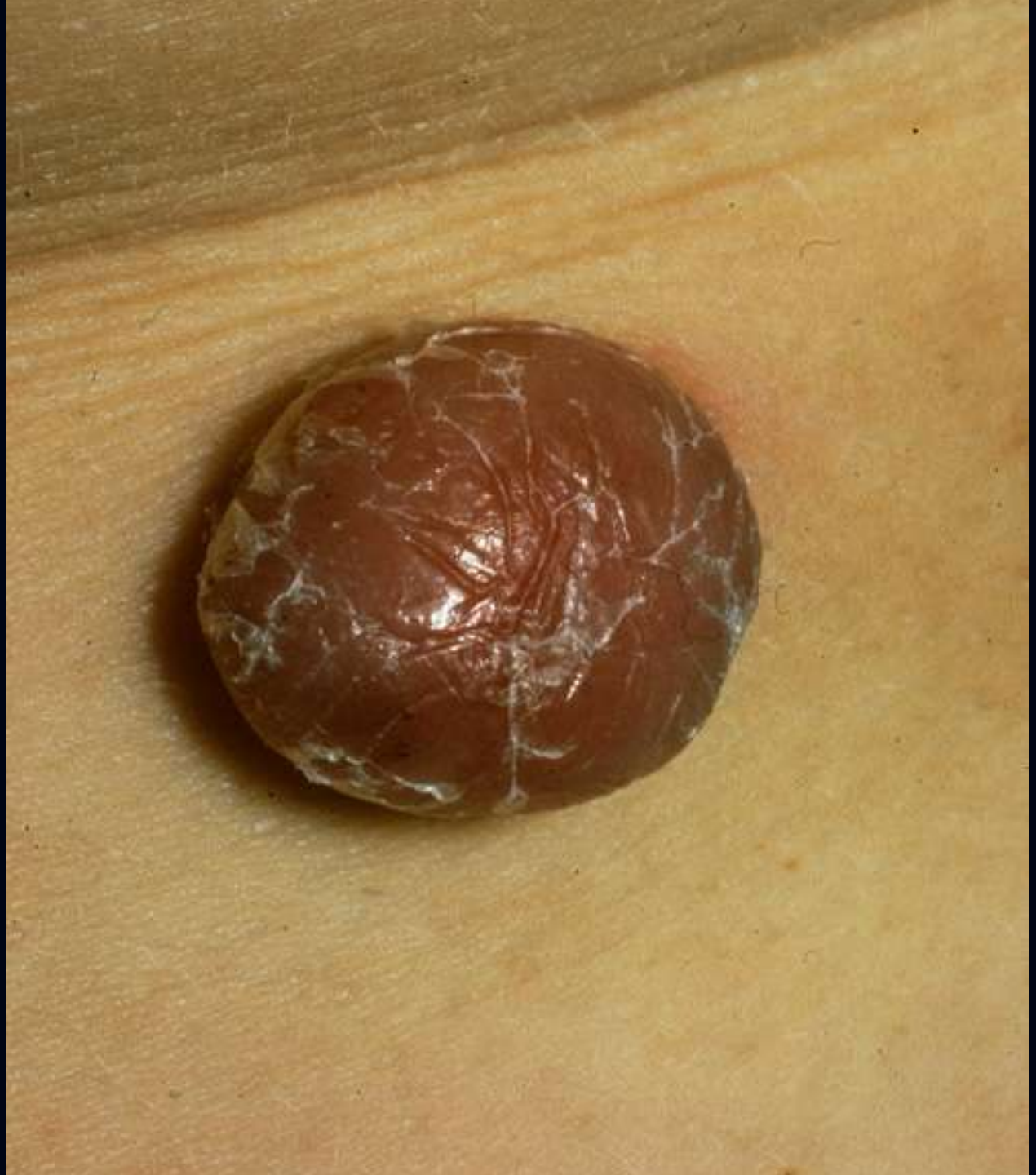
Relatively high mitotic rate

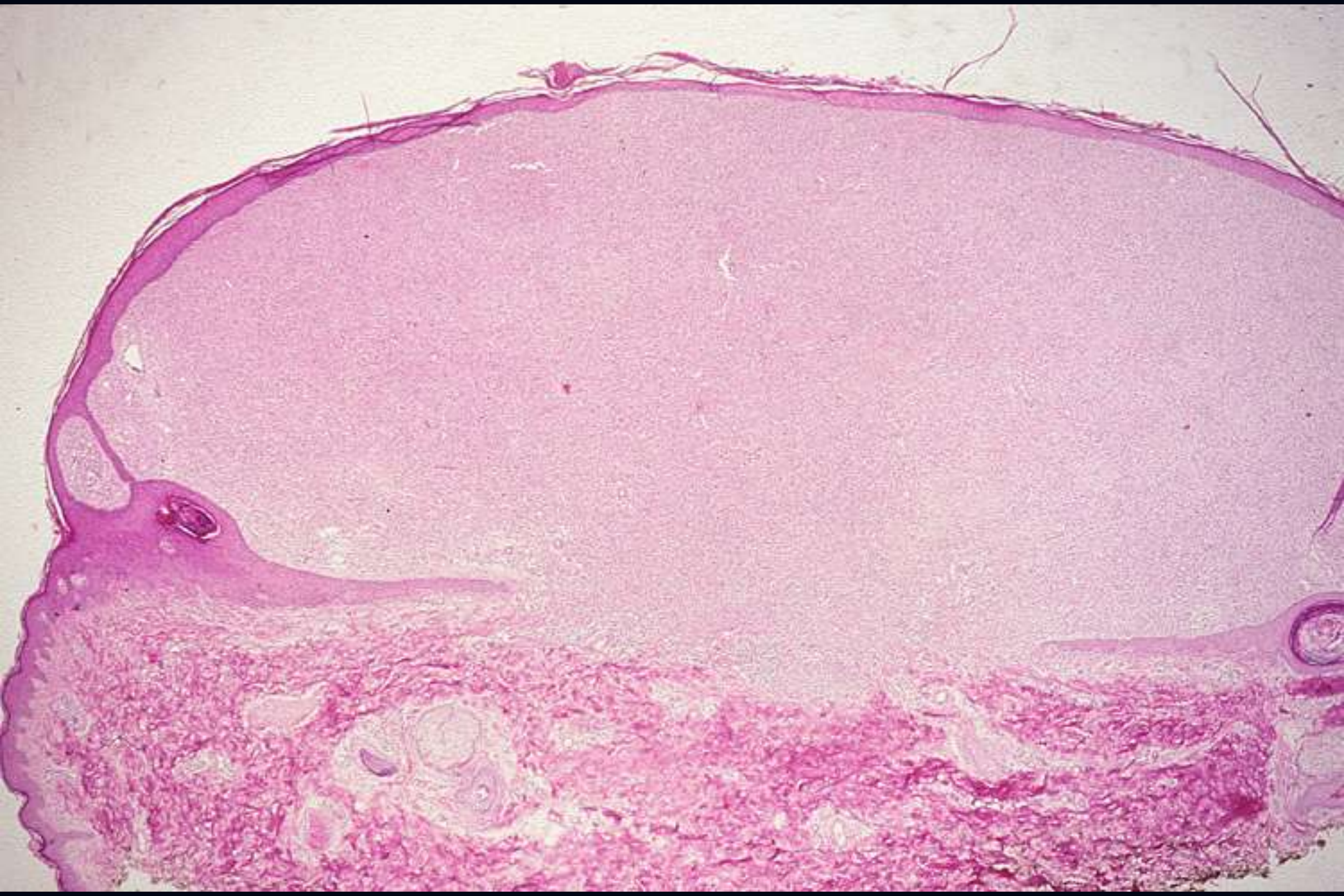
Focal necrosis in 10-15%

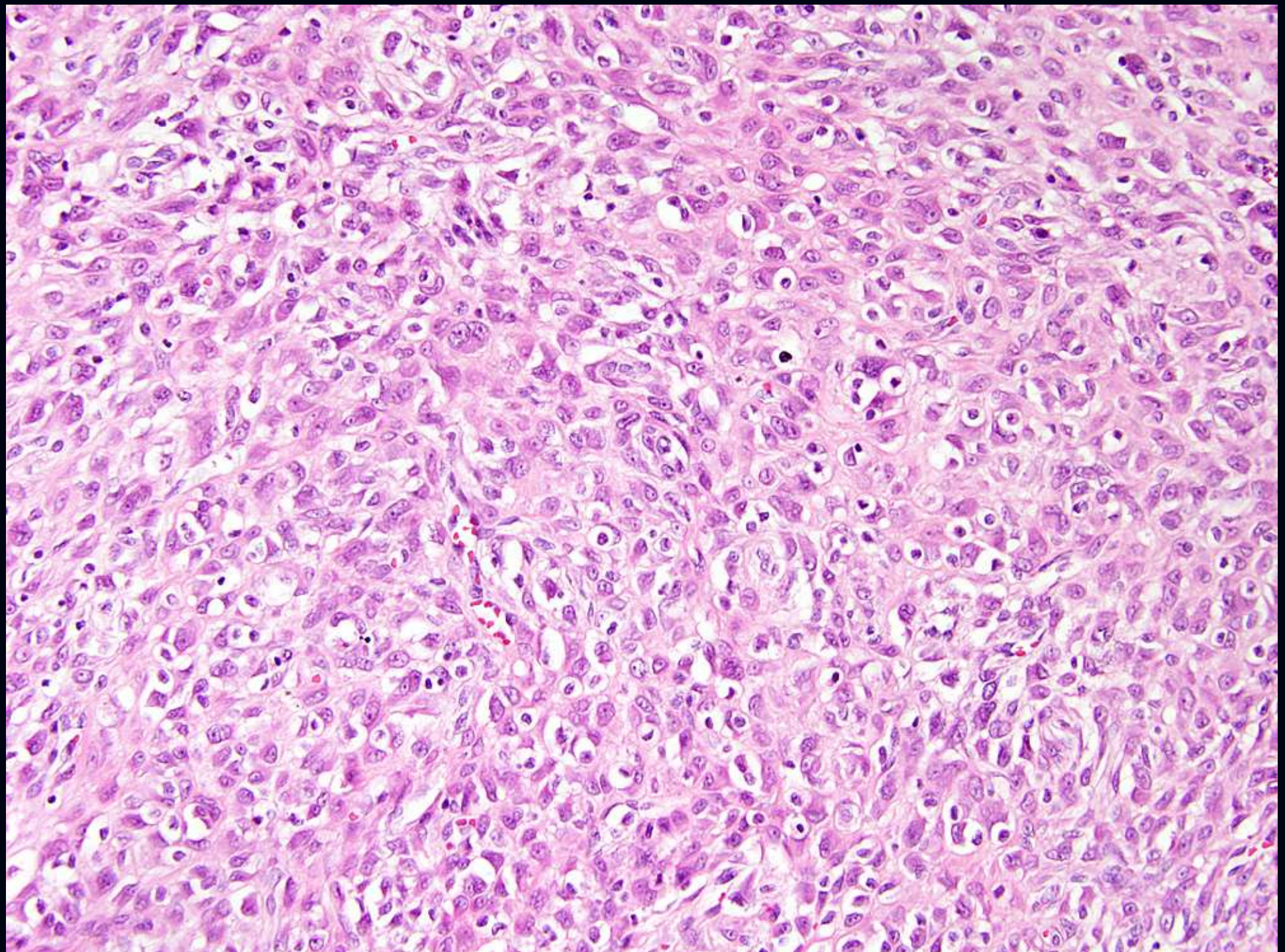
EPITHELIOID BENIGN FIBROUS HISTIOCYTOMA

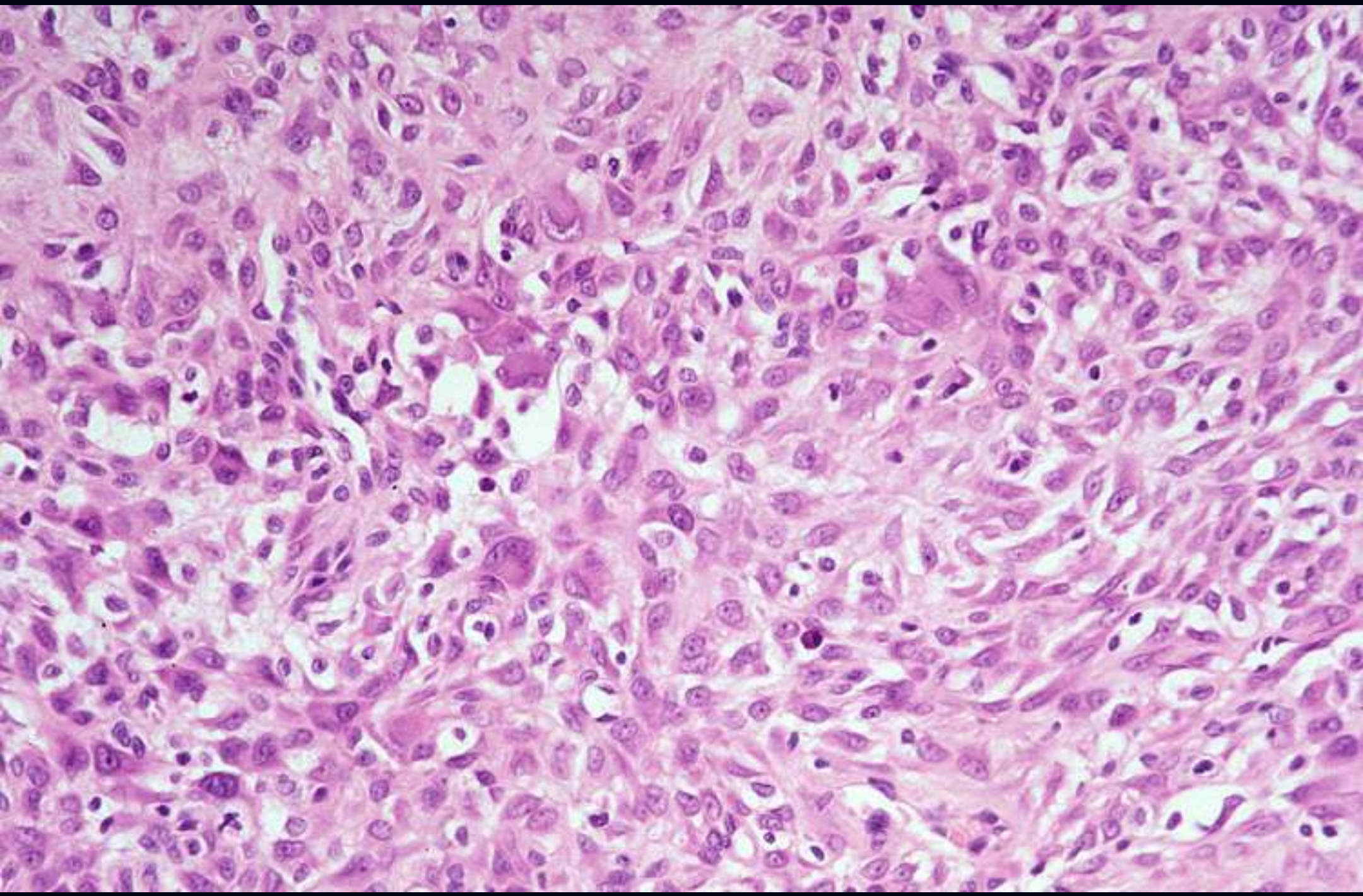
Less than 2% of cutaneous FH
Clinically similar to ordinary FH
BUT
Usually polypoid / exophytic
Frequent collarette
At least 50% of cells epithelioid
Polygonal / eosinophilic / binucleate cells
Often prominent vessels

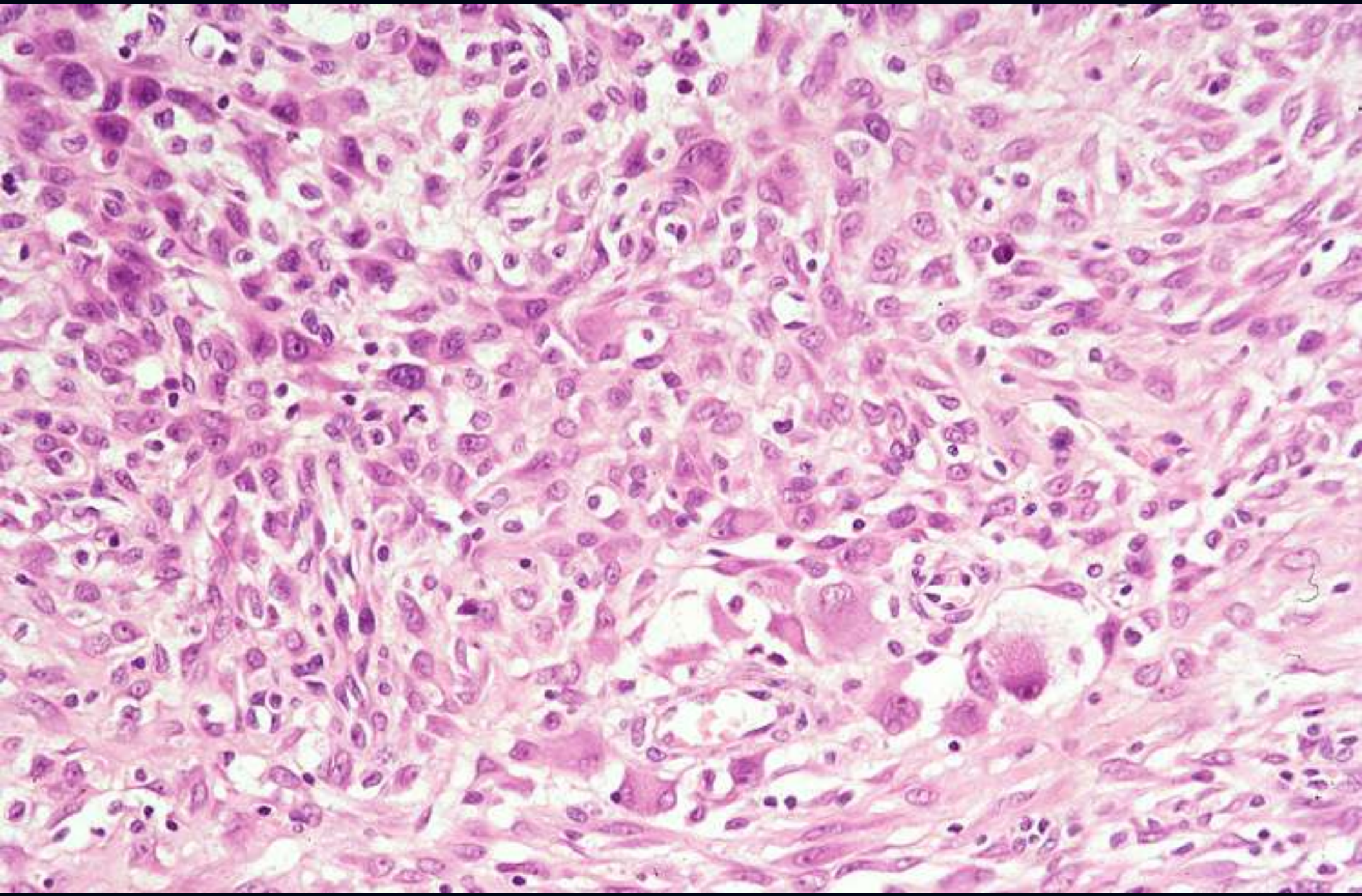
Local recurrence uncommon

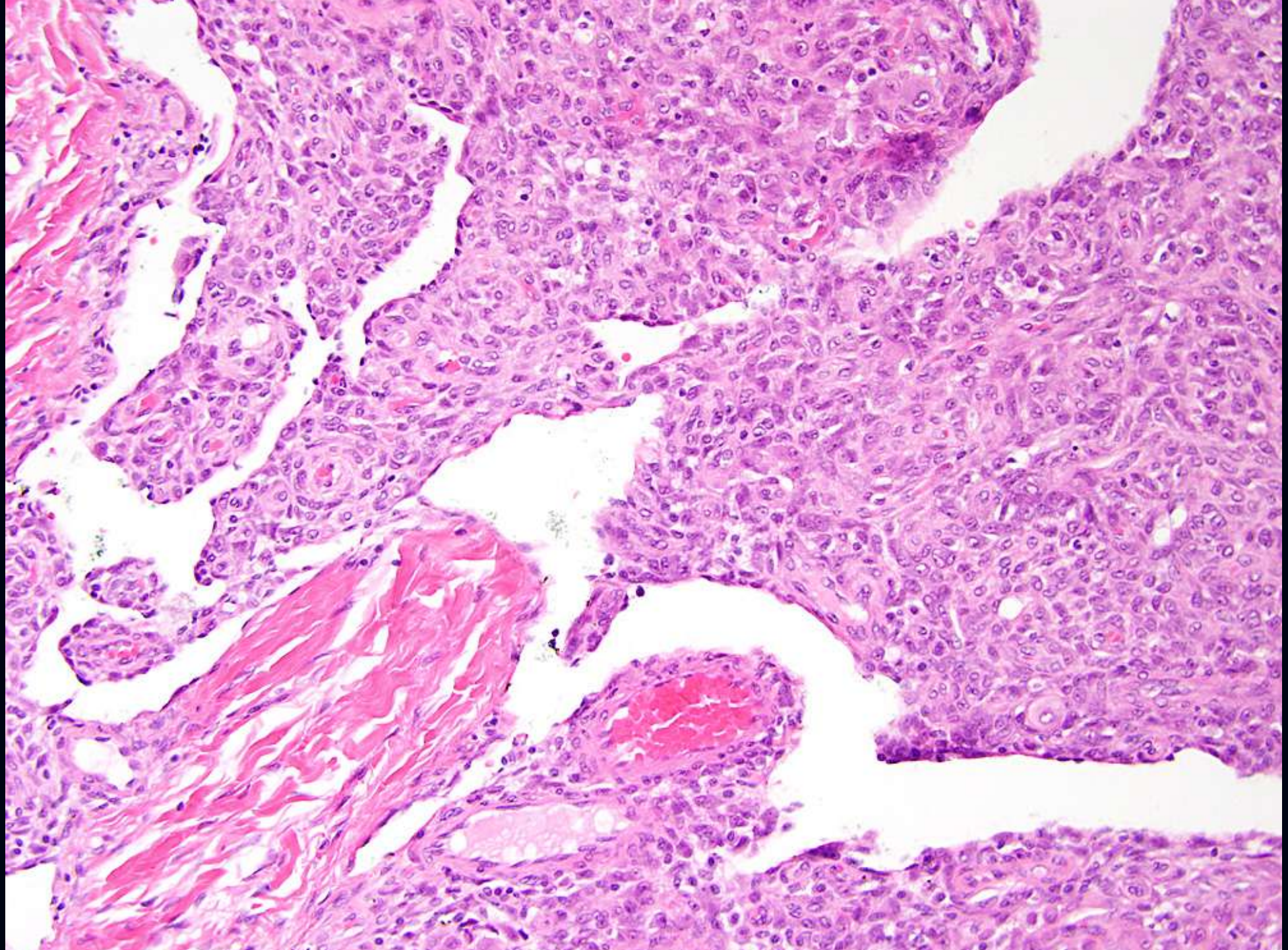


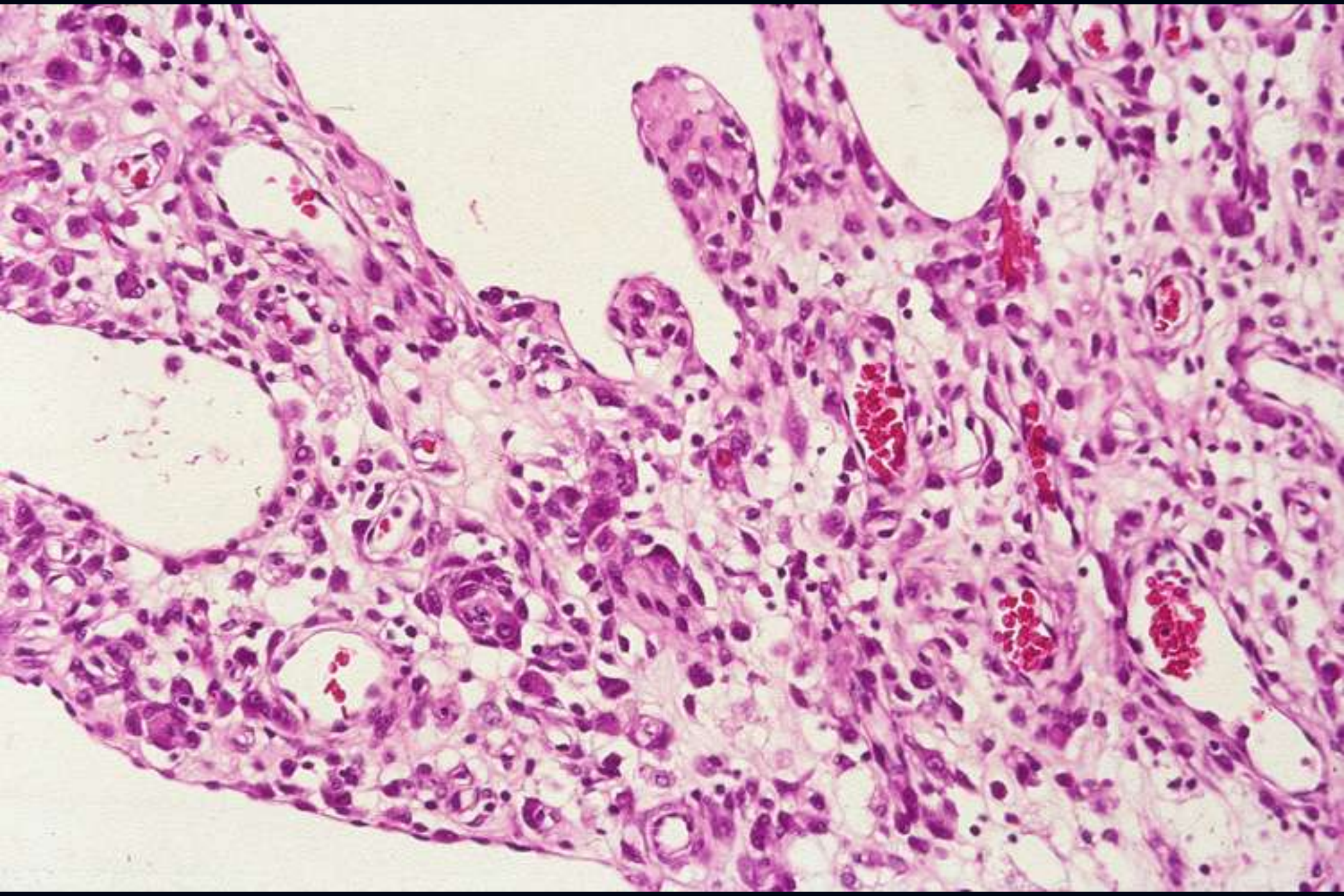


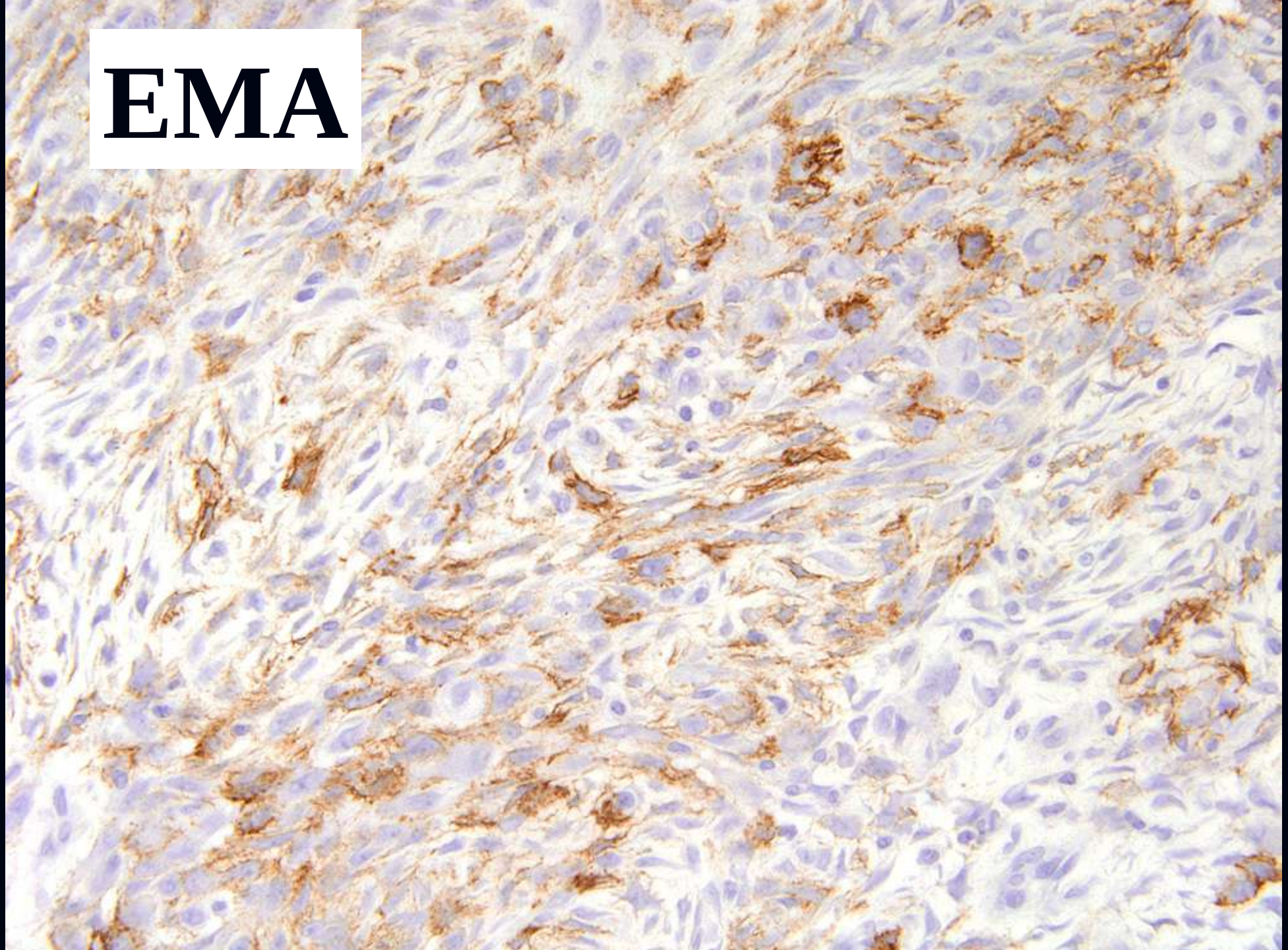








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EPITHELIOID BENIGN FIBROUS HISTIOCYTOMA DIFFERENTIAL DIAGNOSIS

Spitz naevus
Juvenile xanthogranuloma
Malignant melanoma
Epithelioid sarcoma
Epithelioid vascular tumour

ATYPICAL (PSEUDOSARCOMATOUS) FIBROUS HISTIOCYTOMA

CLINICAL FEATURES

Less than 2% of cutaneous FH

Adults; peak 20-40 years

Equal sex incidence

Limbs ++ > Elsewhere

Nodular / polypoid

10-15% local recurrence

Rare metastasis

(a.k.a. ‘dermatofibroma with monster cells’)

ATYPICAL ('PSEUDOSARCOMATOUS') FIBROUS HISTIOCYTOMA

MORPHOLOGIC FEATURES

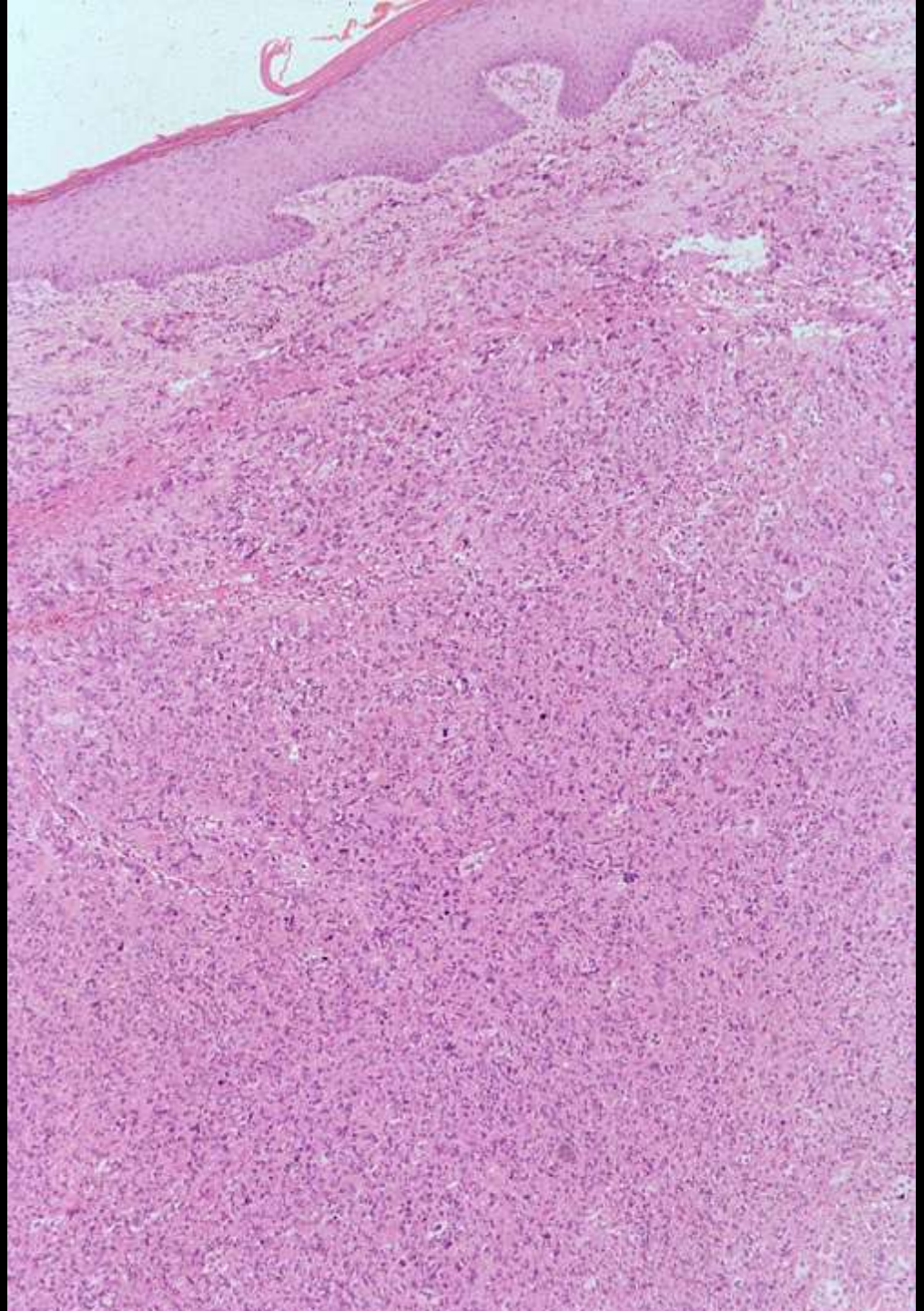
Similar to usual FH

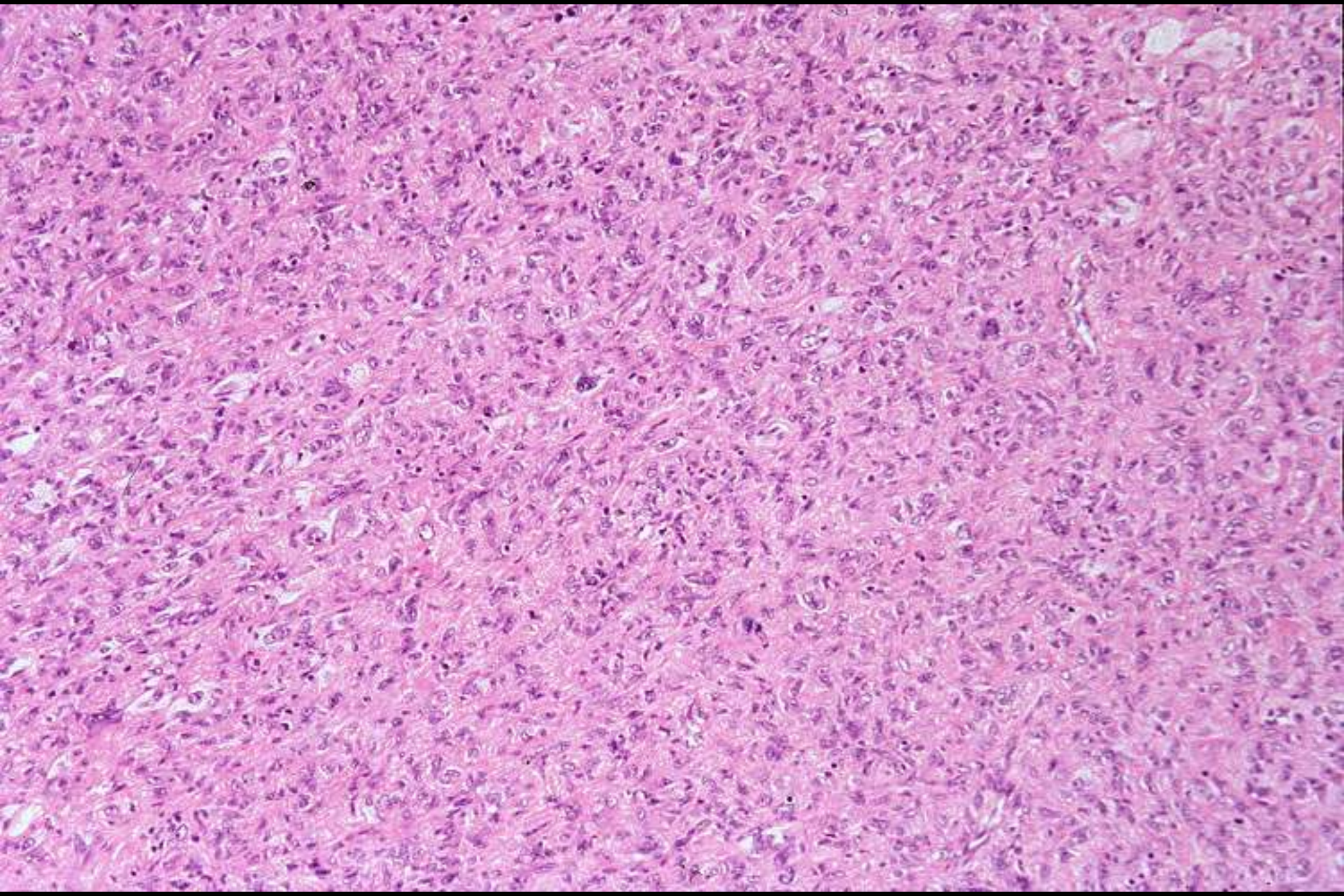
EXCEPT

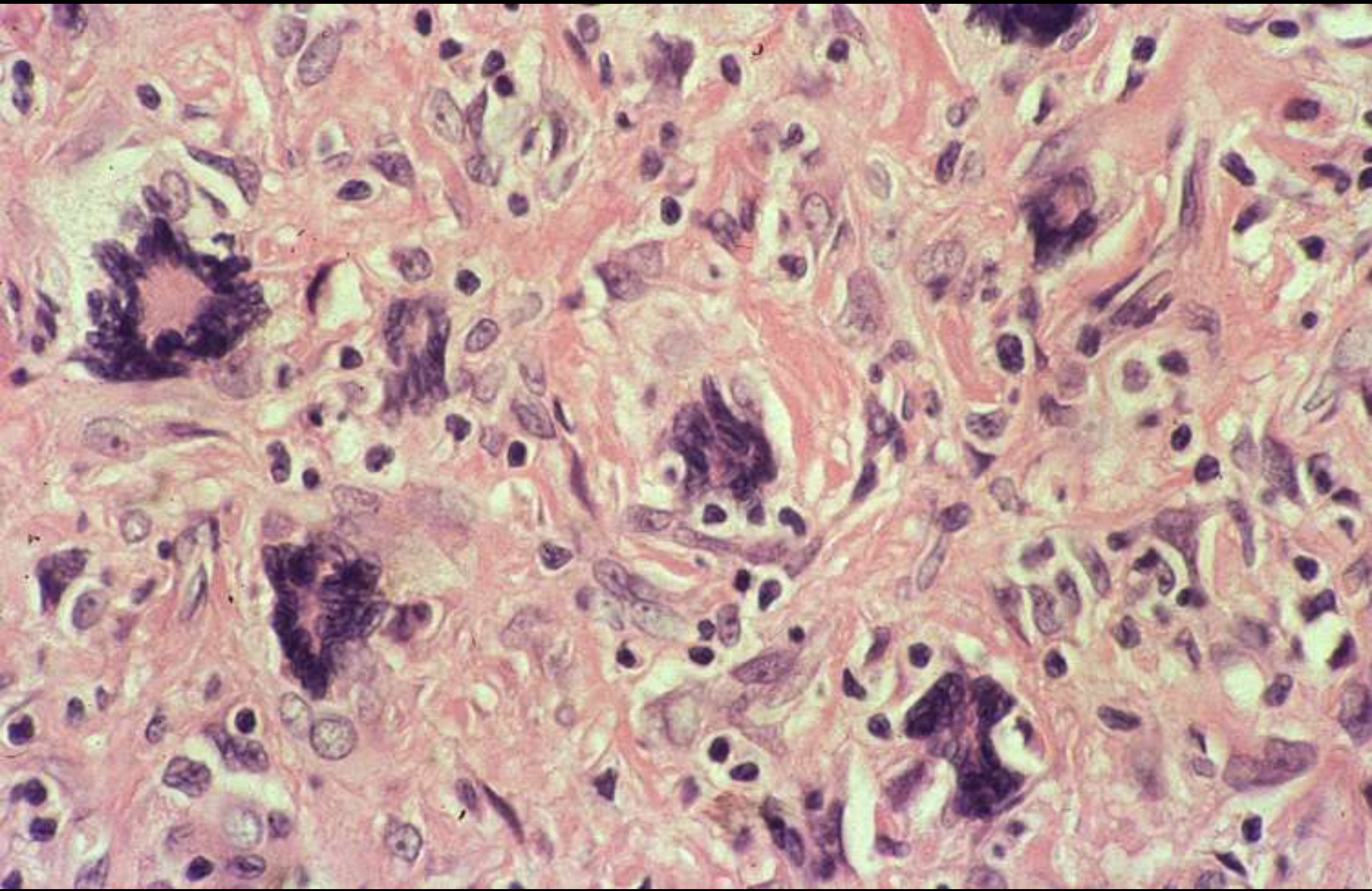
Scattered large bizarre pleomorphic cells (often multinucleate / foamy)

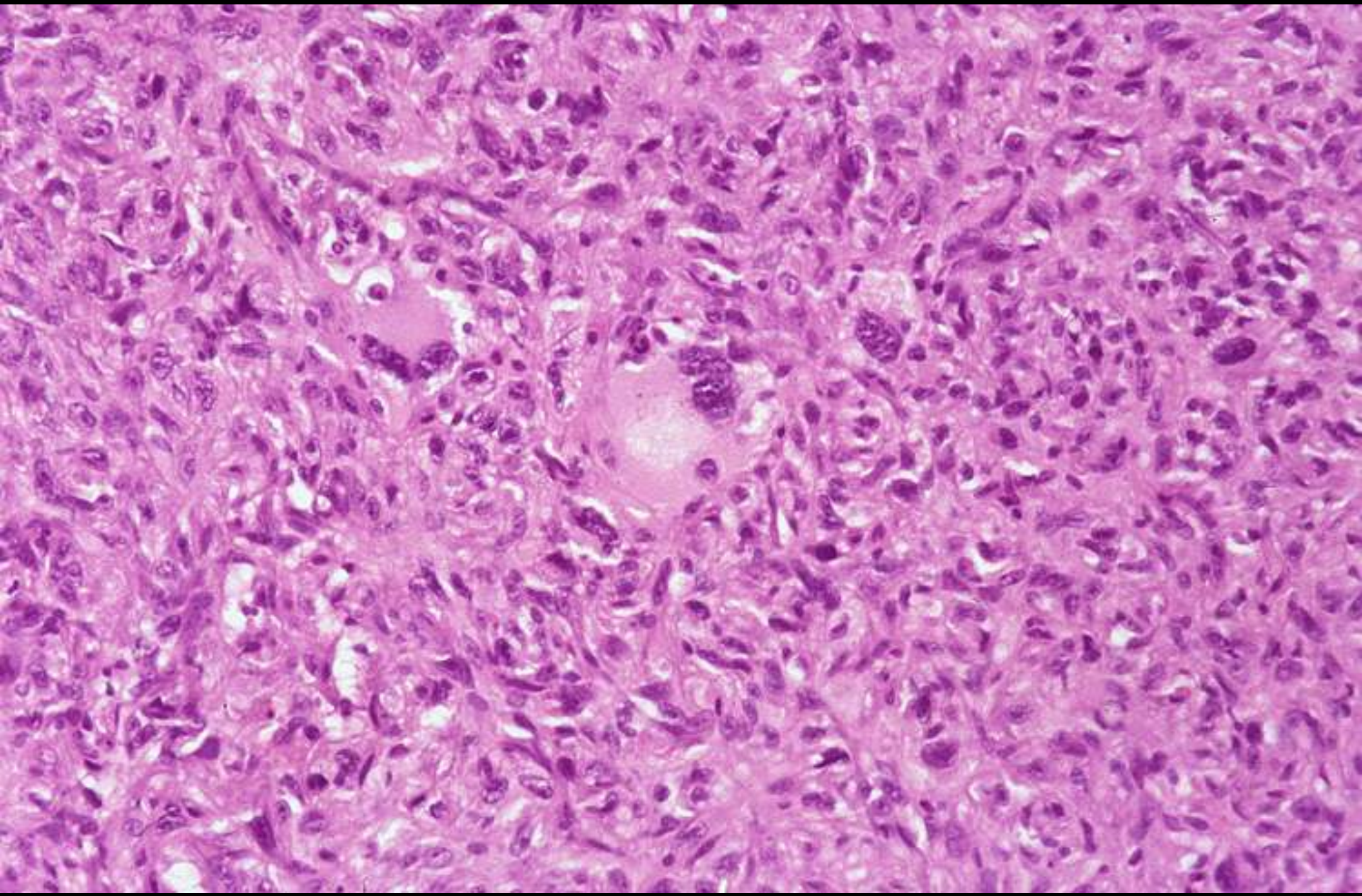
30% have atypical mitoses

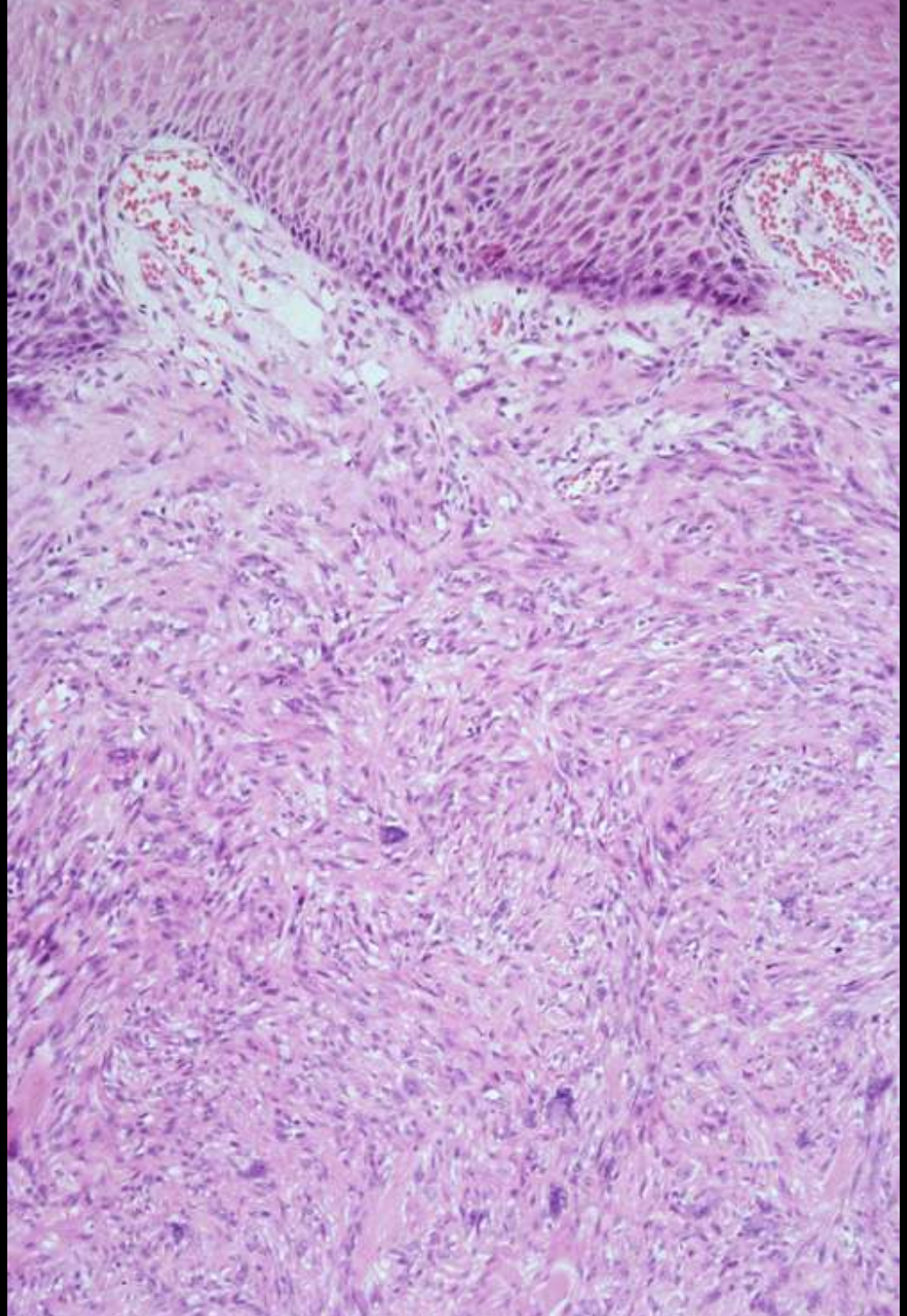
10% have necrosis

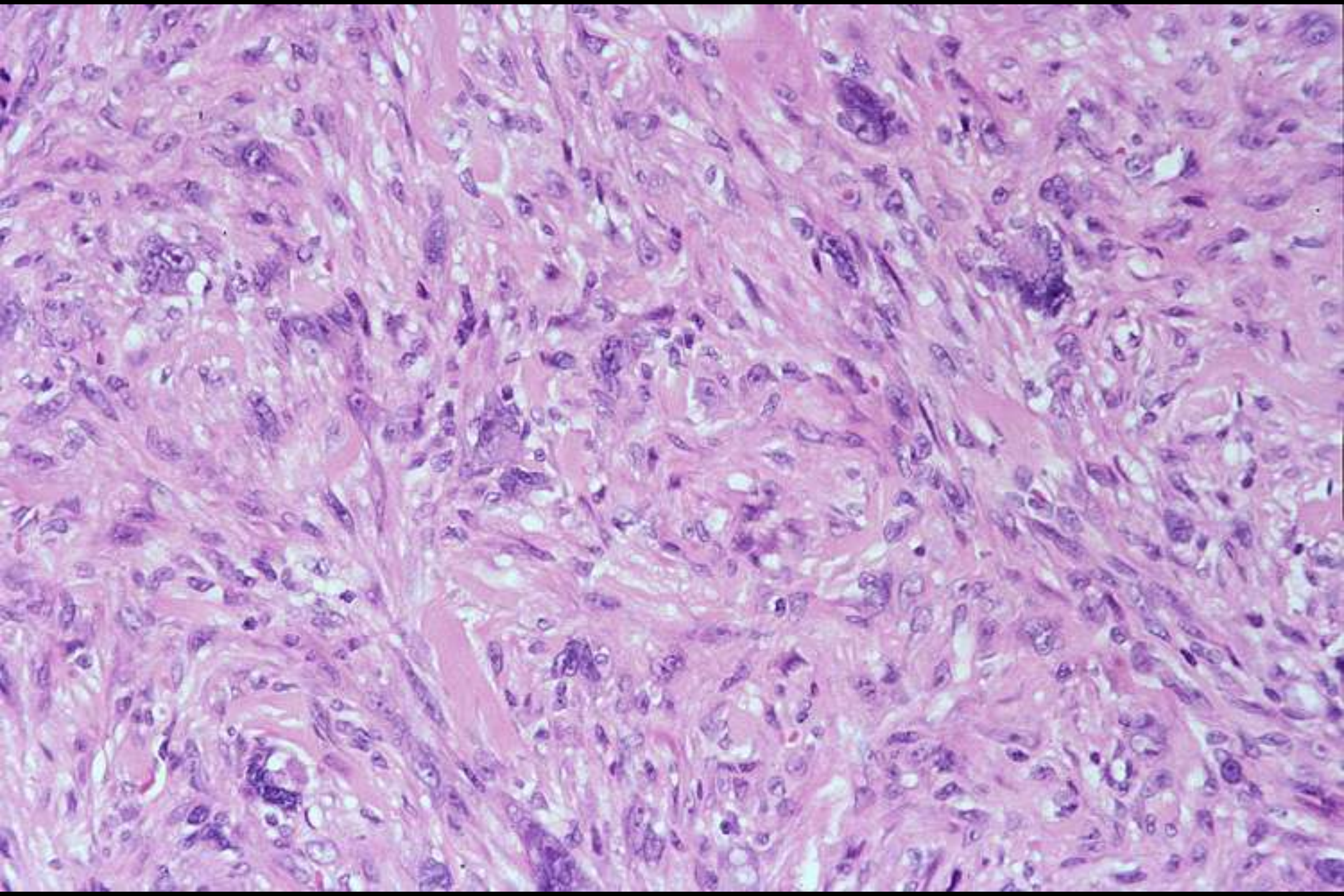


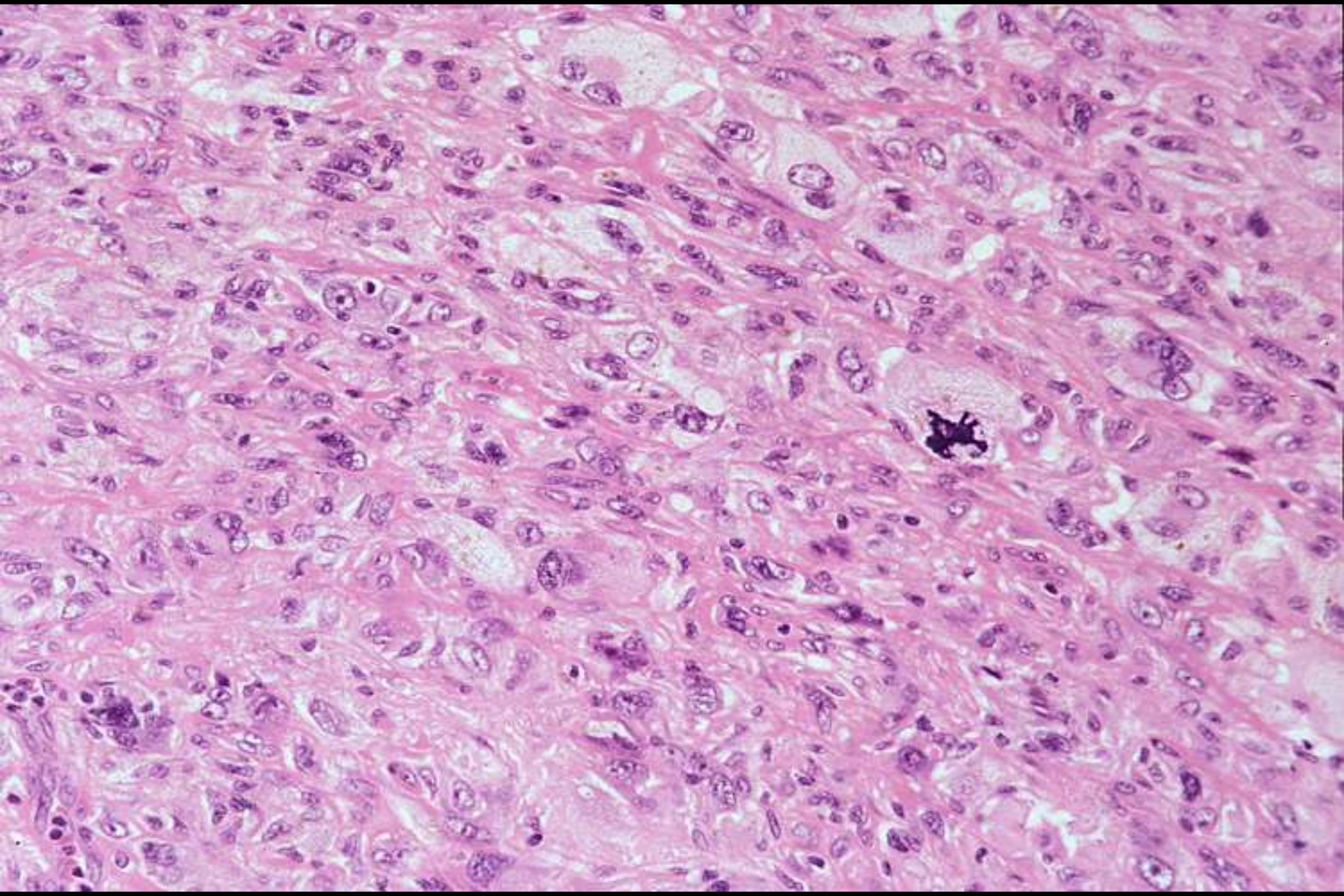


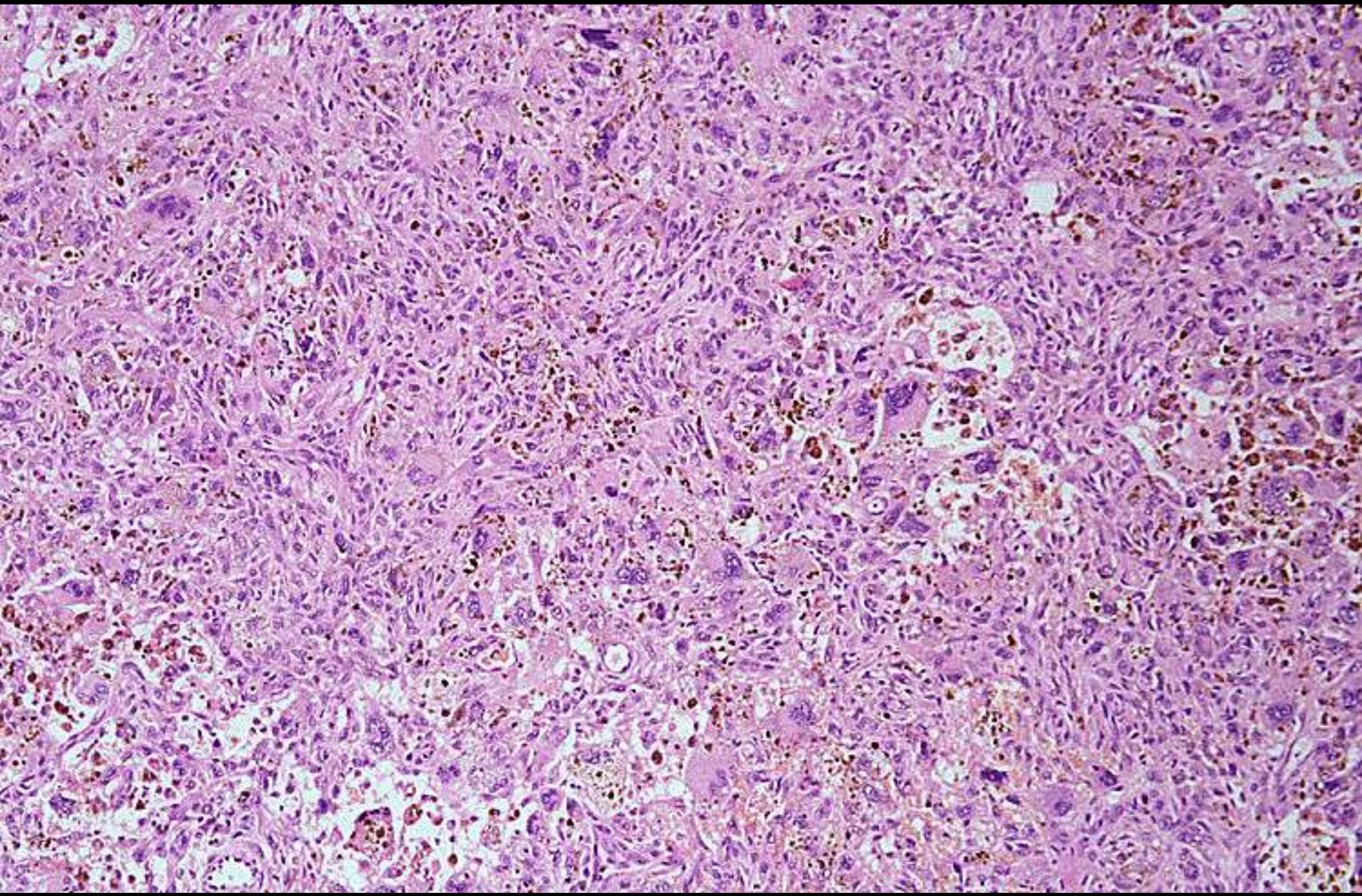


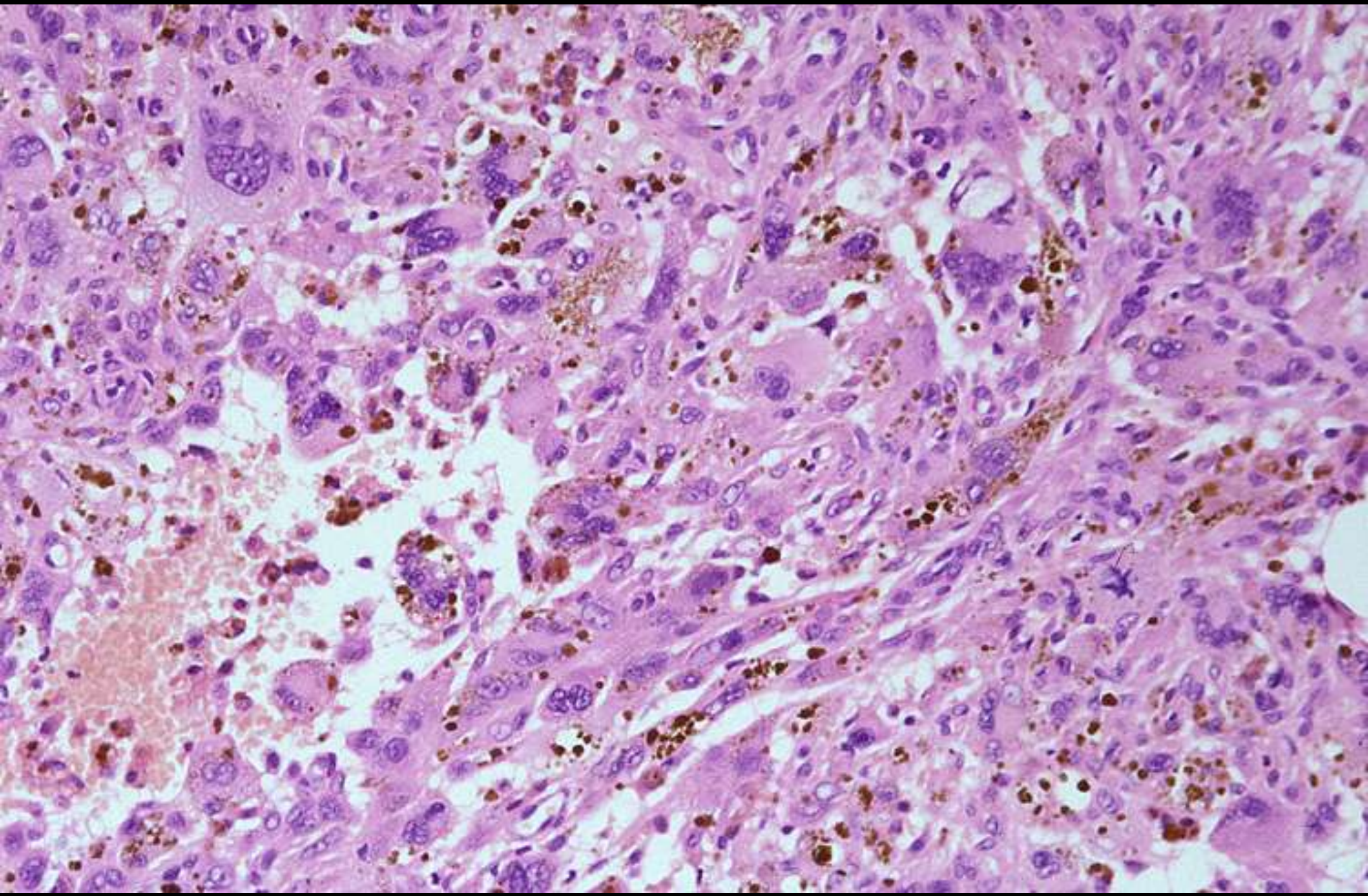












ATYPICAL FIBROUS HISTIOCYTOMA
DIFFERENTIAL DIAGNOSIS

Atypical fibroxanthoma
Pleomorphic sarcoma (“MFH”)
(Sarcomatoid SCC)
(Metastasis)

ATYPICAL FIBROXANTHOMA

'…histologically bizarre tumor usually found in sun-damaged skin of elderly persons… had been initially misdiagnosed as a variety of sarcomas or carcinomas…benign behavior of these lesions is documented. It is suggested that AFX represents a reactive or reparative process in previously damaged dermis.'

Kempson & McGavran
Cancer 1964; 17:1463-1471

ATYPICAL FIBROXANTHOMA

‘…one may speculate that it represents part of a spectrum of reactive processes…. The series of 140 cases….appears to further establish AFX as a mesenchymal proliferation of the dermis characterized by a bizarre and pleomorphic sarcoma-like histologic appearance but but with a disposition to benign biologic behaviour.’

Fretzin & Helwig

Cancer 1973; 31:1541-52

ATYPICAL FIBROXANTHOMA

‘It is histologically indistinguishable from pleomorphic forms of malignant fibrous histiocytoma. From a conceptual point of view, we regard it as a superficial form of that tumor which, by virtue of its superficial location, almost invariably pursues a benign course.’

Enzinger & Weiss, 1st Edn, 1983

‘ATYPICAL FIBROXANTHOMA’ WITH METASTASIS

‘Factors that portend aggressive behavior and metastasis are vascular invasion, recurrence, deep tissue invasion, tumor necrosis…..’

Helwig & May
Cancer 1986; 57:368-376

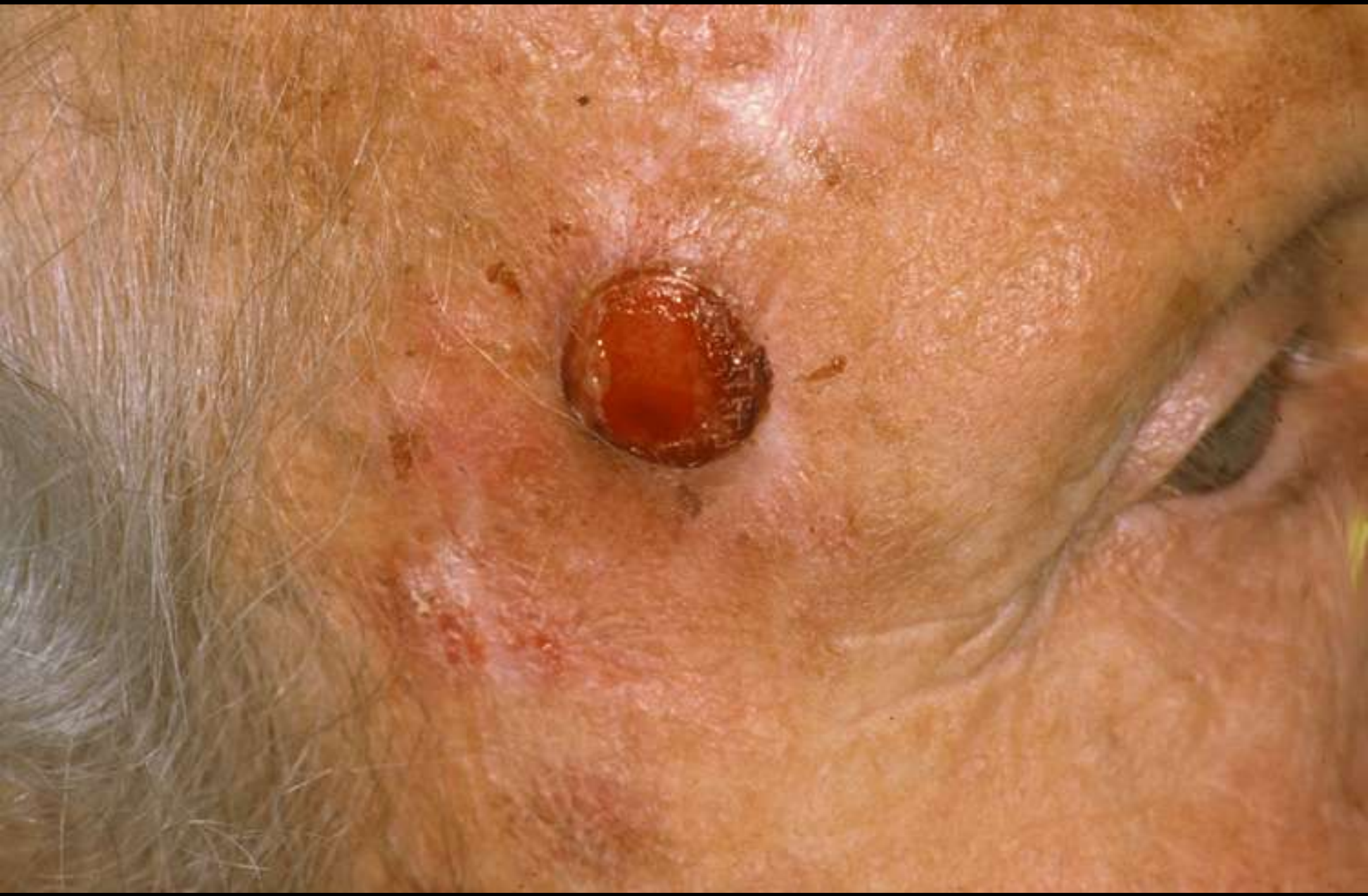
ATYPICAL FIBROXANTHOMA PROBLEMS

- Diagnostic criteria
- Cases in the pre-immuno era
- Shave biopsies
- Rare keratin-negative cases of spindle cell SCC with ulceration

ATYPICAL FIBROXANTHOMA
CLINICAL FEATURES

Mainly elderly patients
Males > females
Head and neck++ / limbs rare
Rapidly enlarging exophytic
Sometimes multiple / asynchronous

Recurrence infrequent
No metastasis if carefully diagnosed



ATYPICAL FIBROXANTHOMA

MORPHOLOGIC FEATURES

Arise in actinically damaged skin

Usually very cellular / mitotic

Variably pleomorphic / bizarre

Often ulcerated

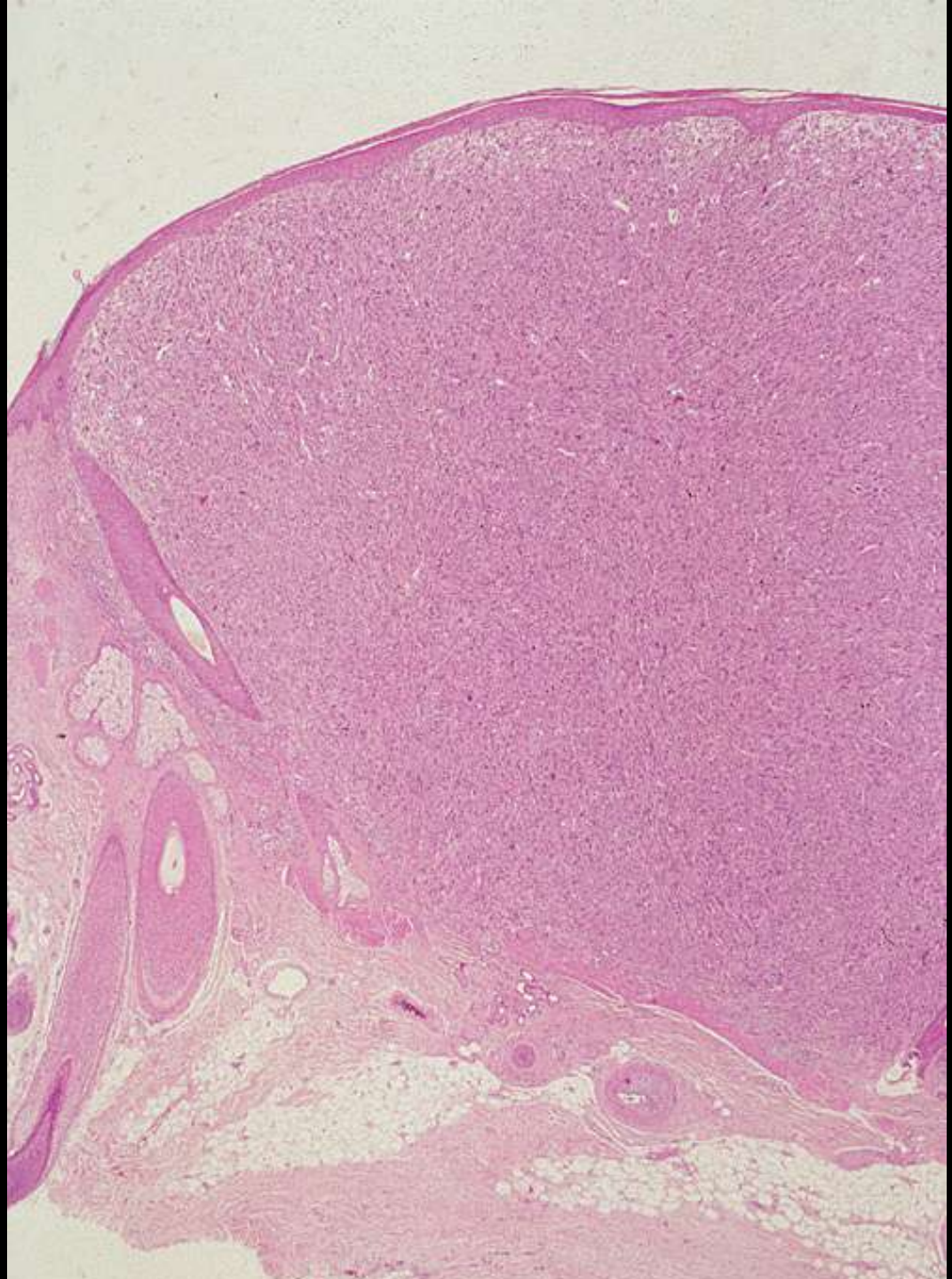
Frequent collarette

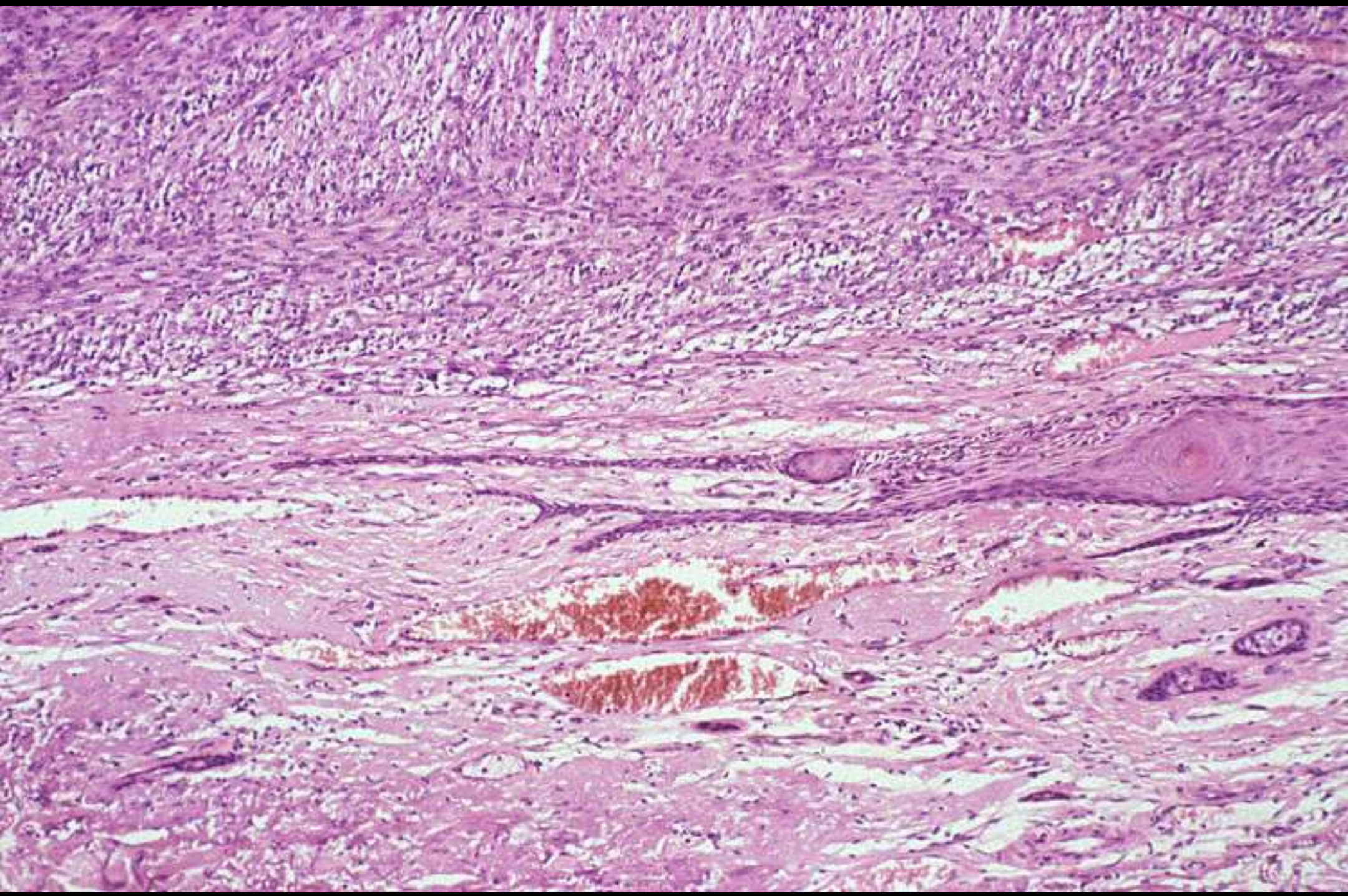
Usually confined to dermis

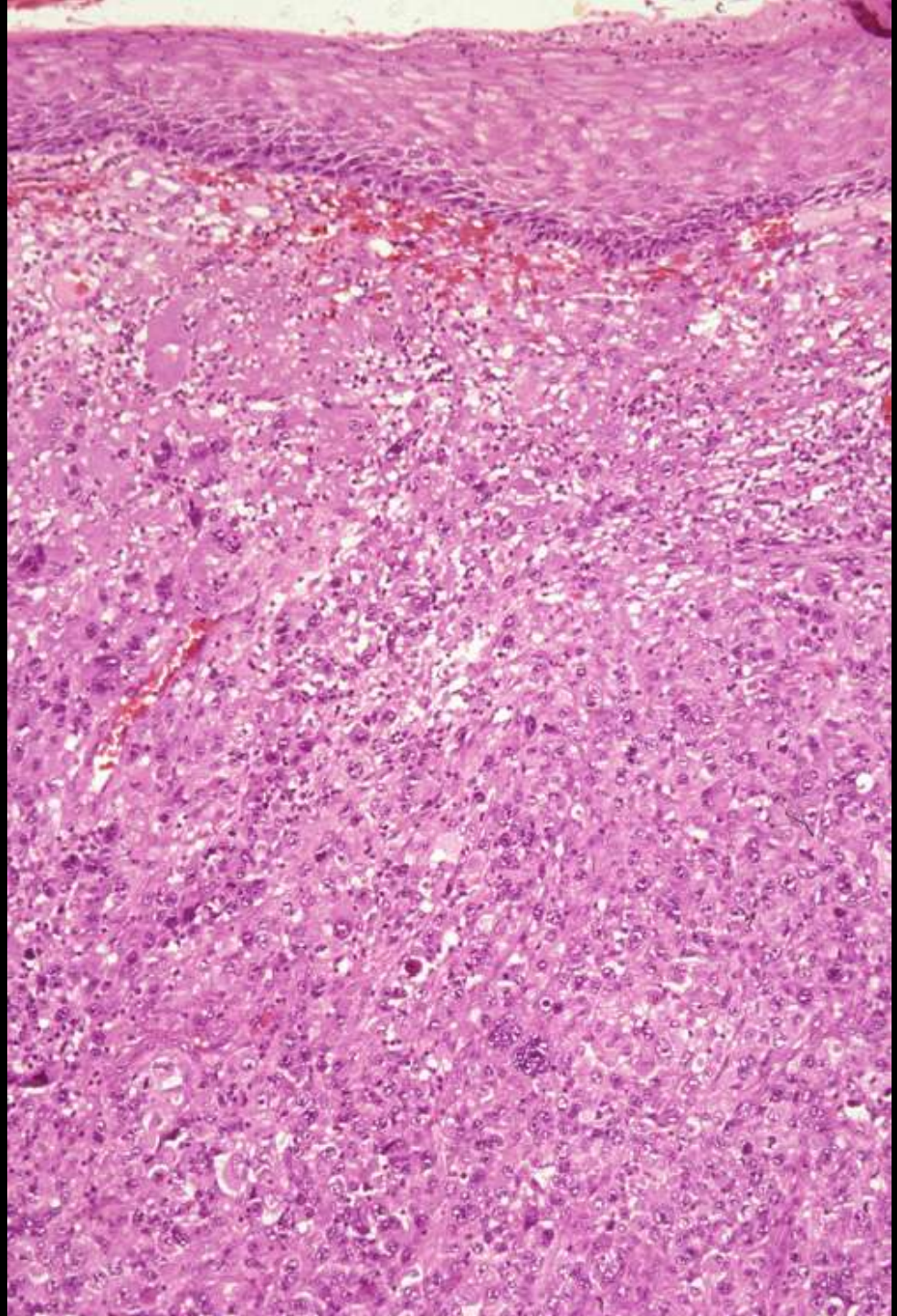
Smooth deep margin

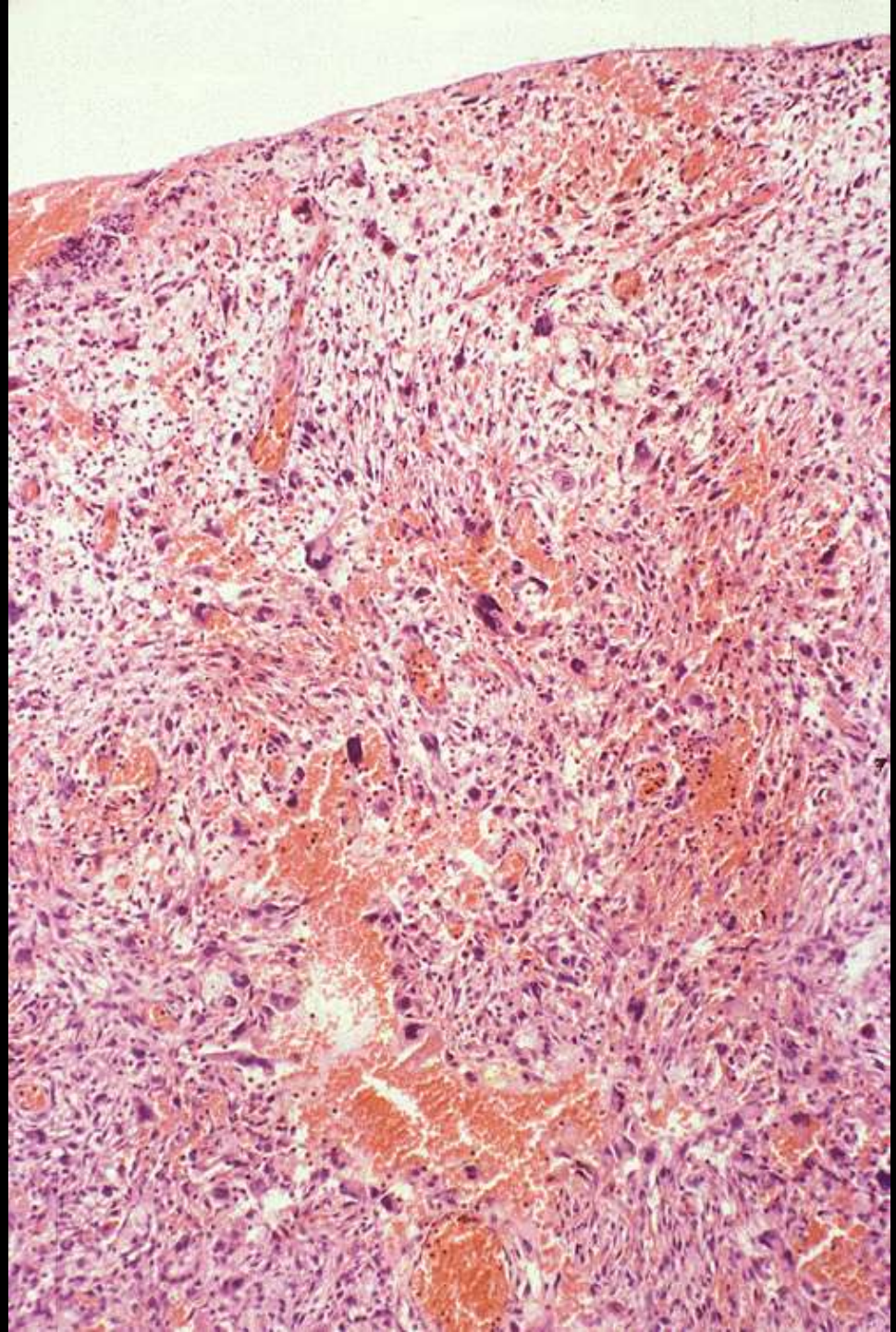
No epidermal / junctional component

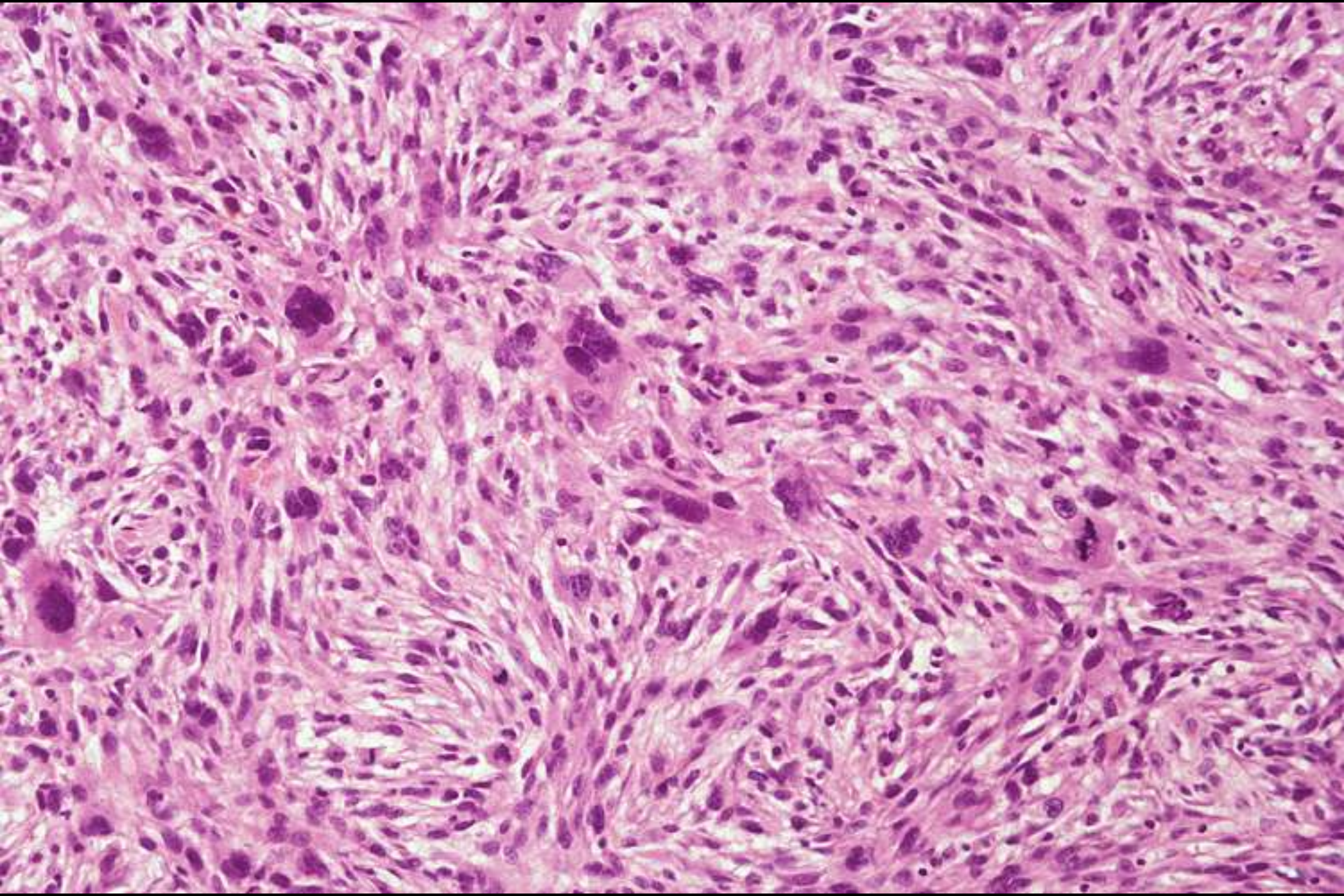
Keratin / S-100 protein / desmin negative

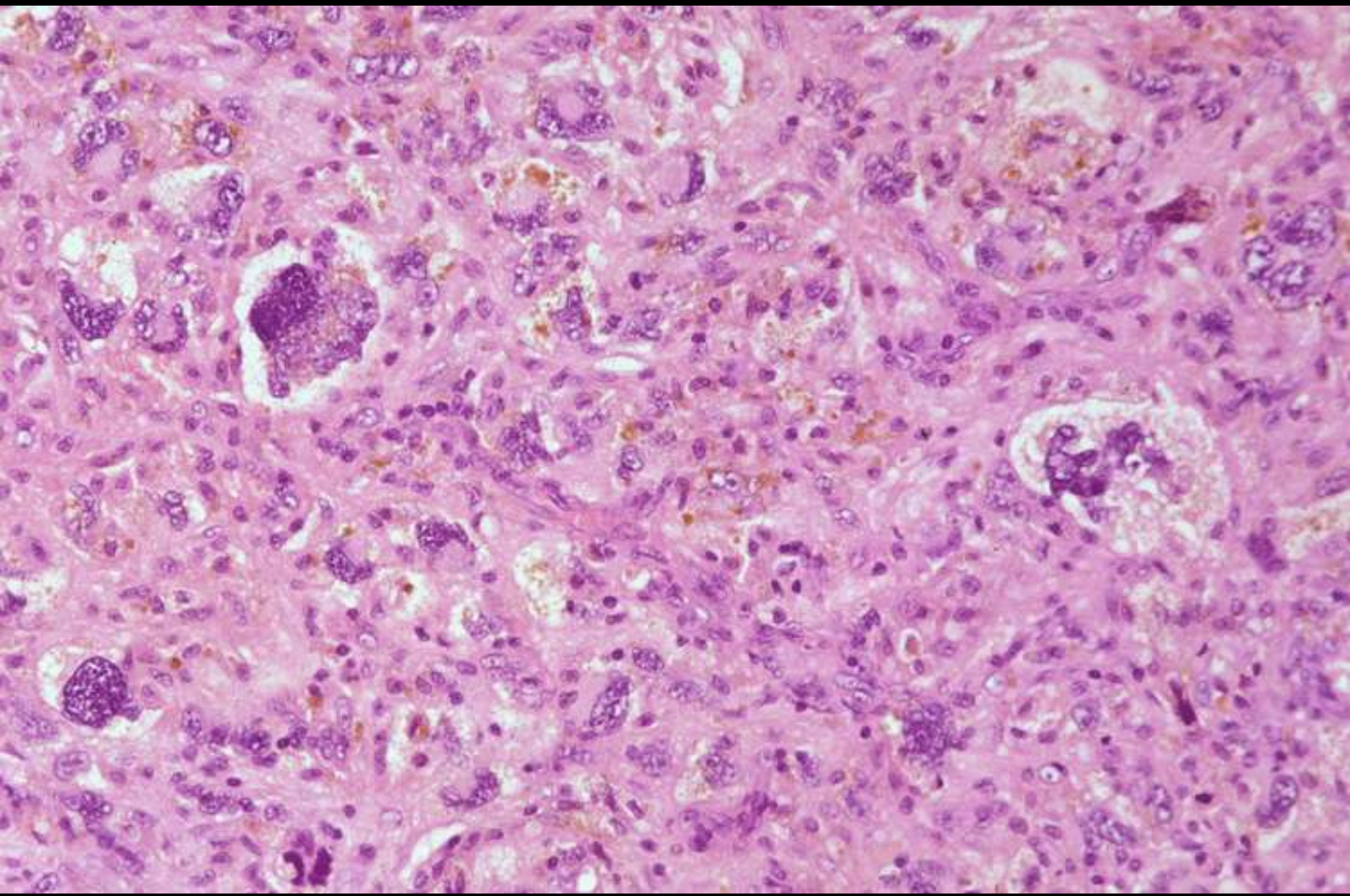


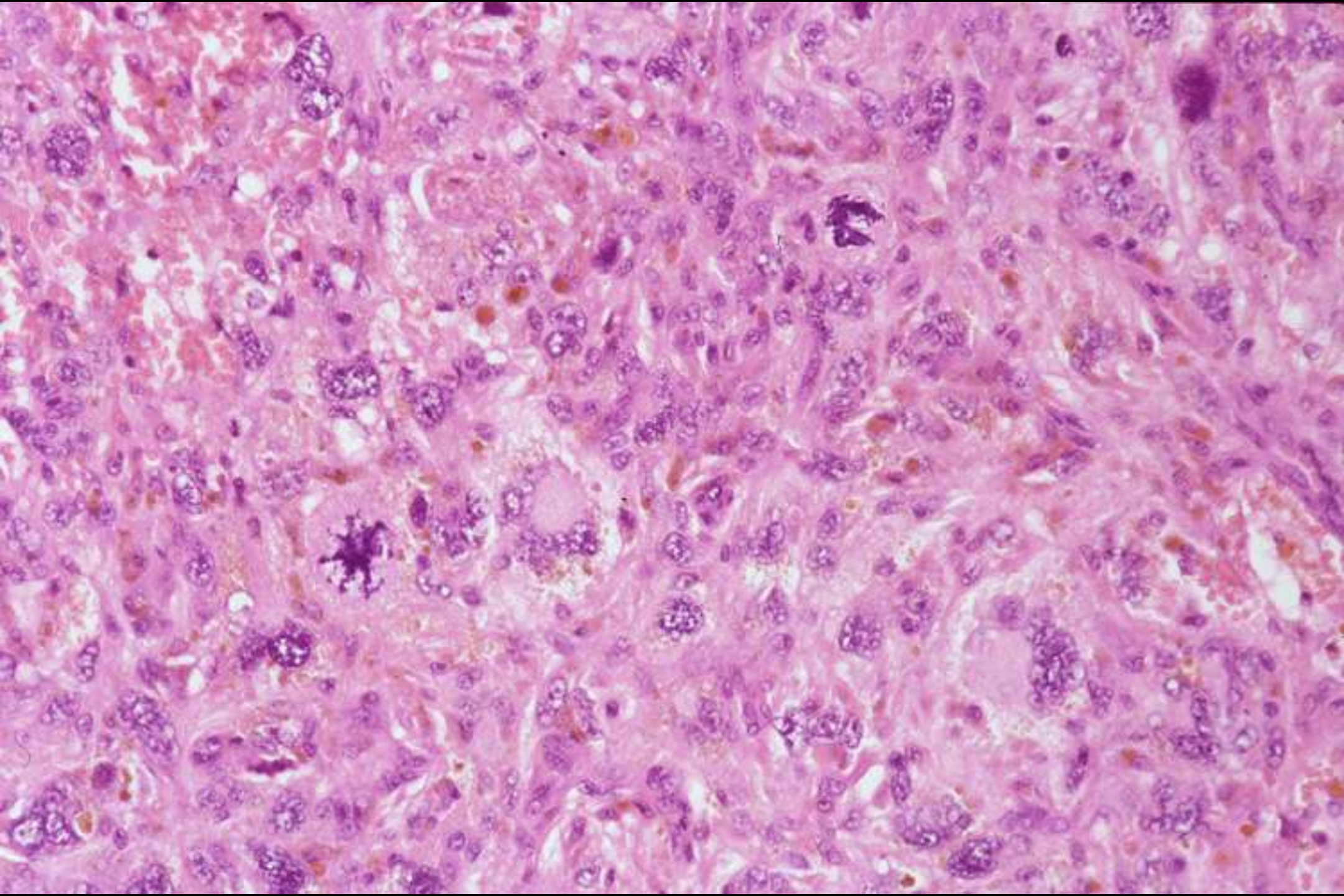


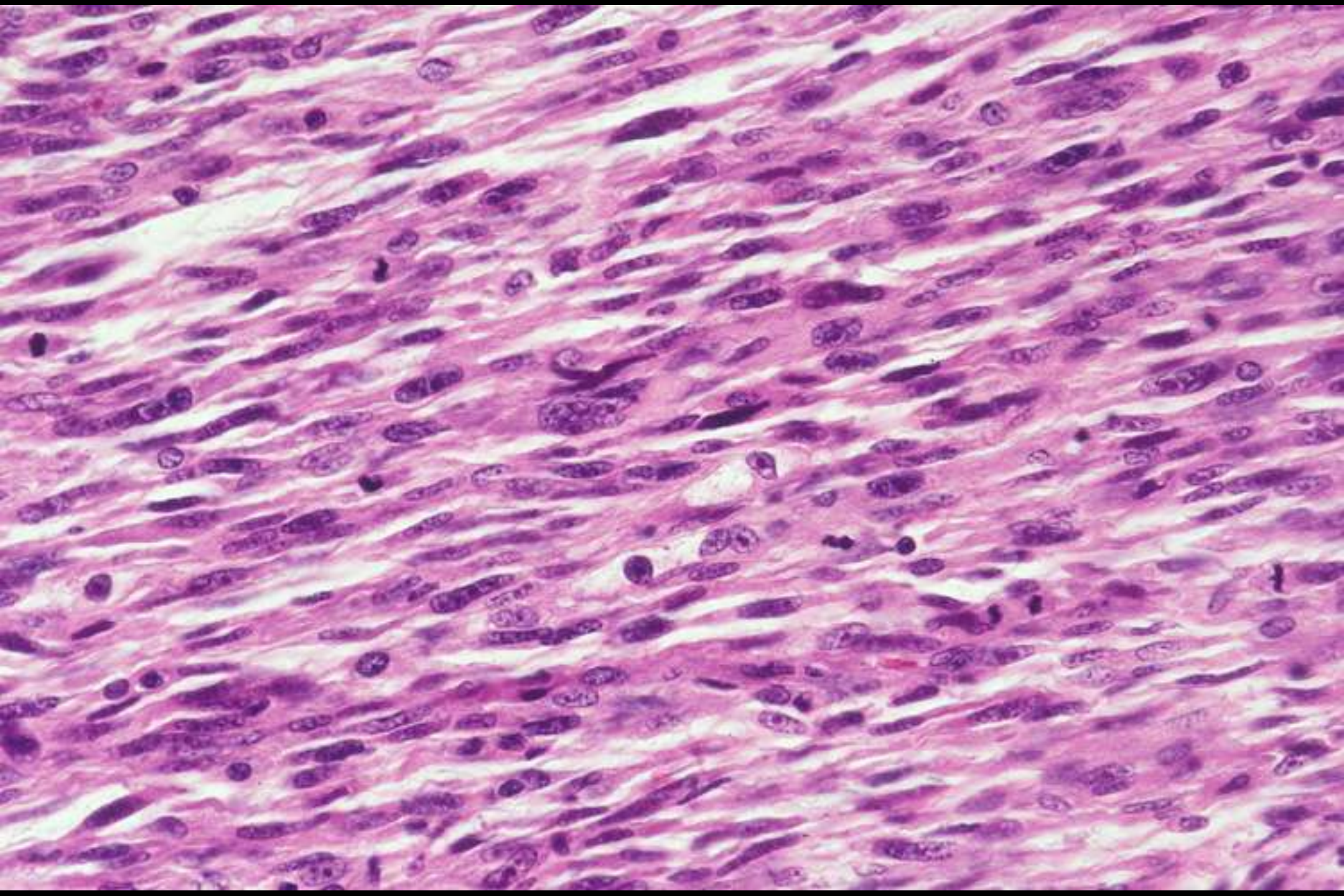


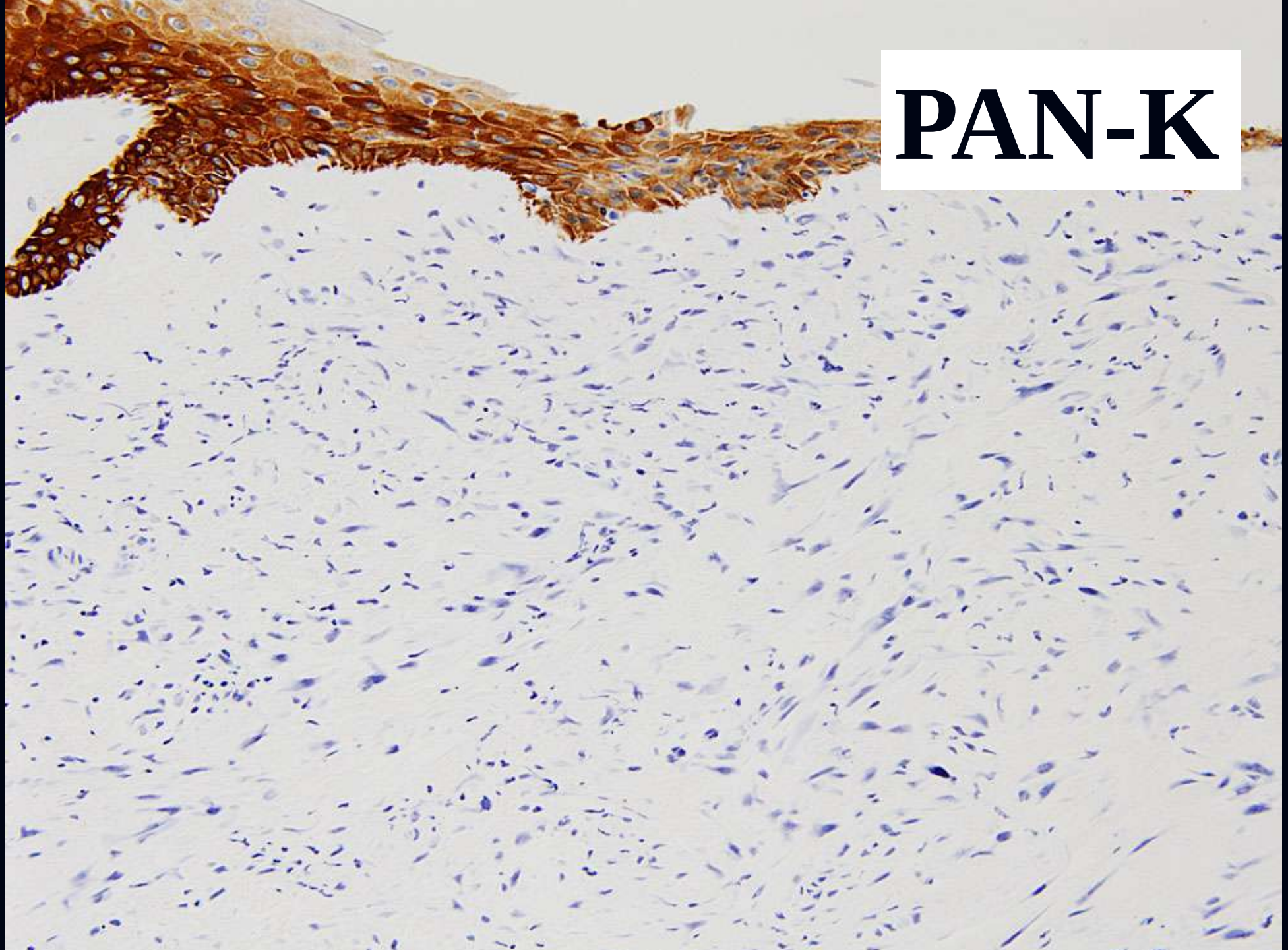








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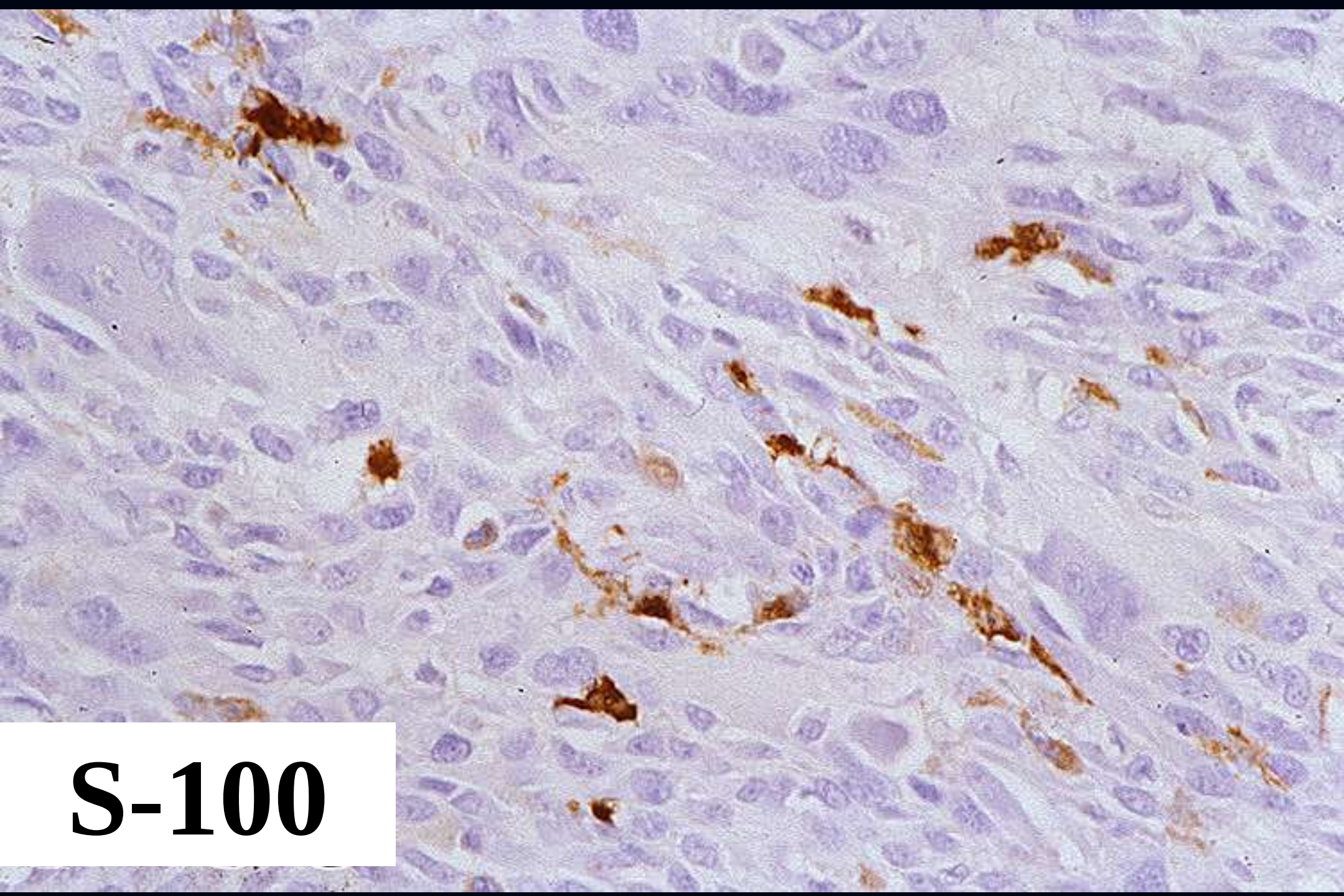
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ATYPICAL FIBROXANTHOMA
IMPORTANT CRITERIA

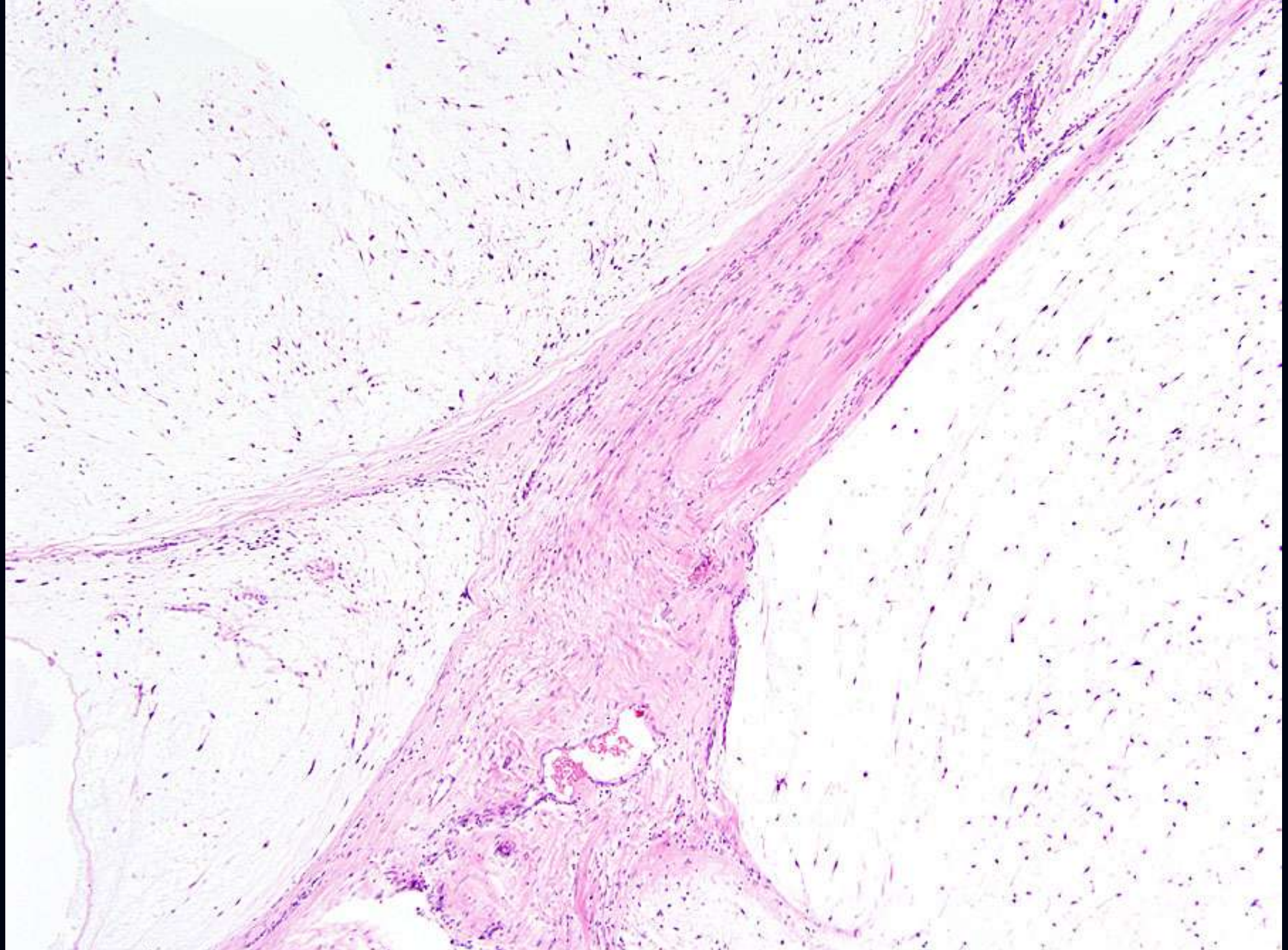
Origin in sun-damaged skin
No epidermal / junctional origin
No subcutaneous (or deeper) invasion
No necrosis (except surface)
No vascular or perineural invasion
Relevant negative immuno

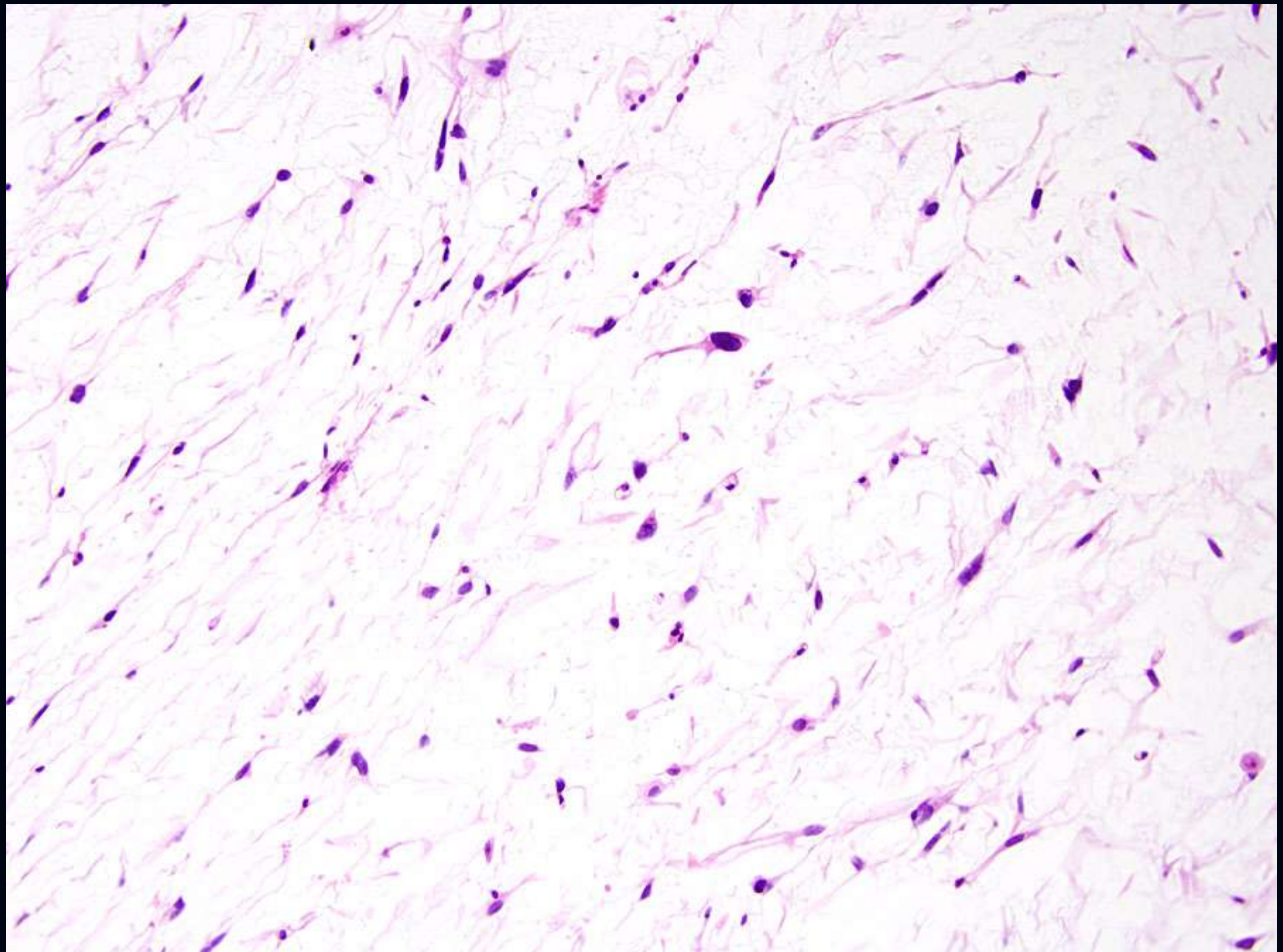
ATYPICAL FIBROXANTHOMA
CONCEPTUAL QUESTIONS

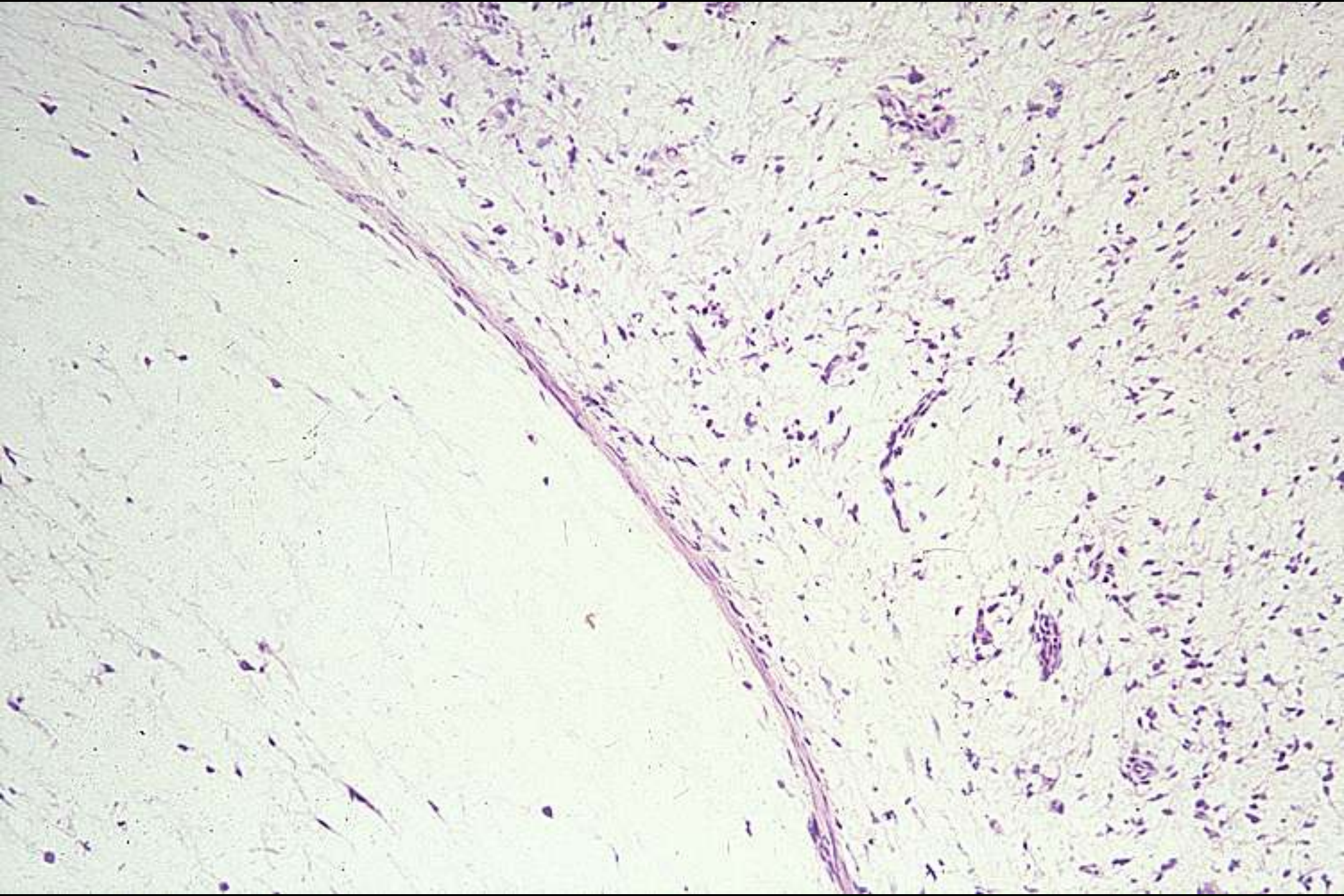
What are they ?
What is the role of U-V irradiation ?
Do they occur in young patients ?
Do they ever metastasise ?
Are they related to ‘MFH’ ?

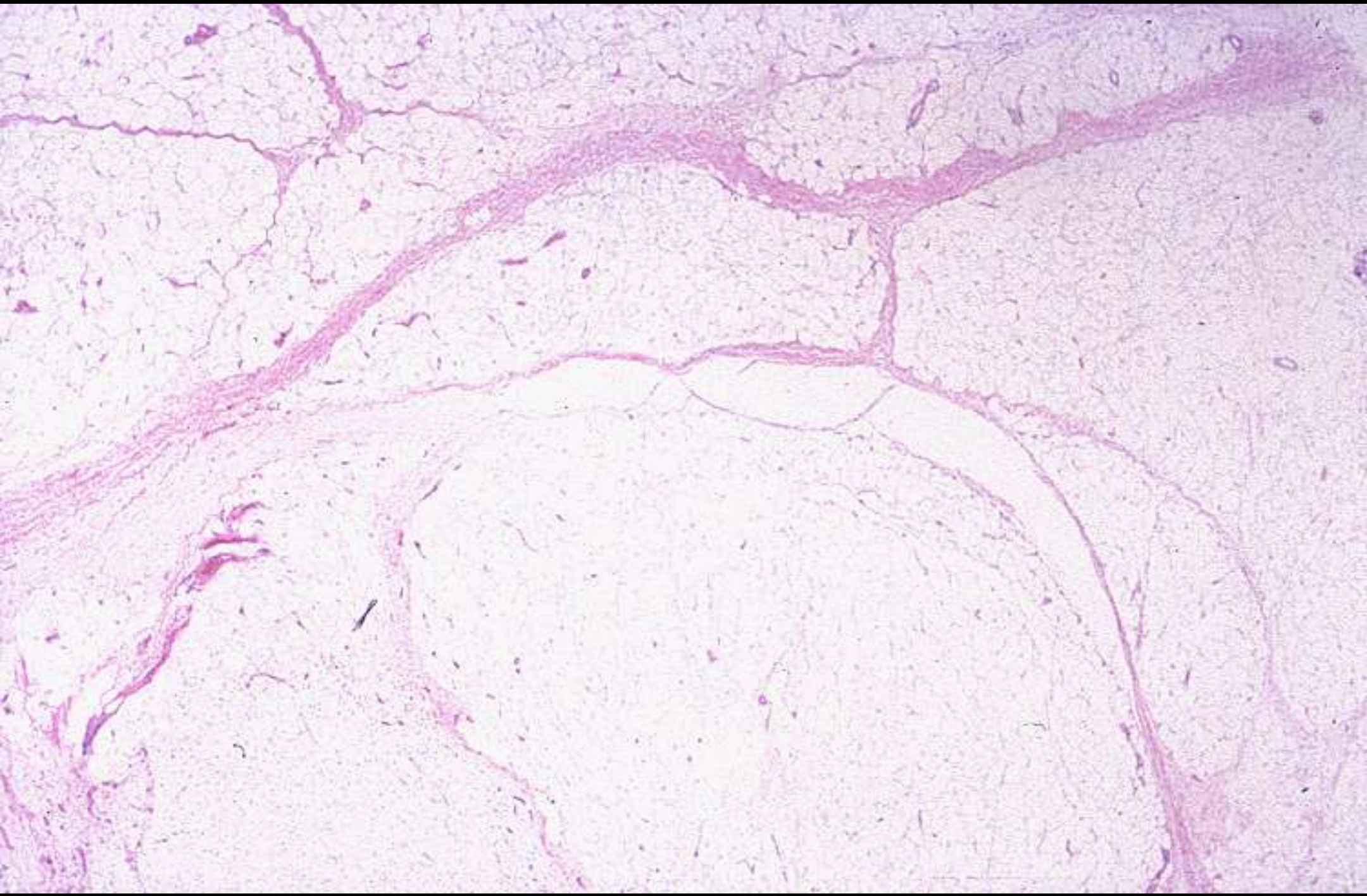
MYXOFIBROSARCOMA
(FORMERLY MYXOID 'MFH')
CLINICAL FEATURES

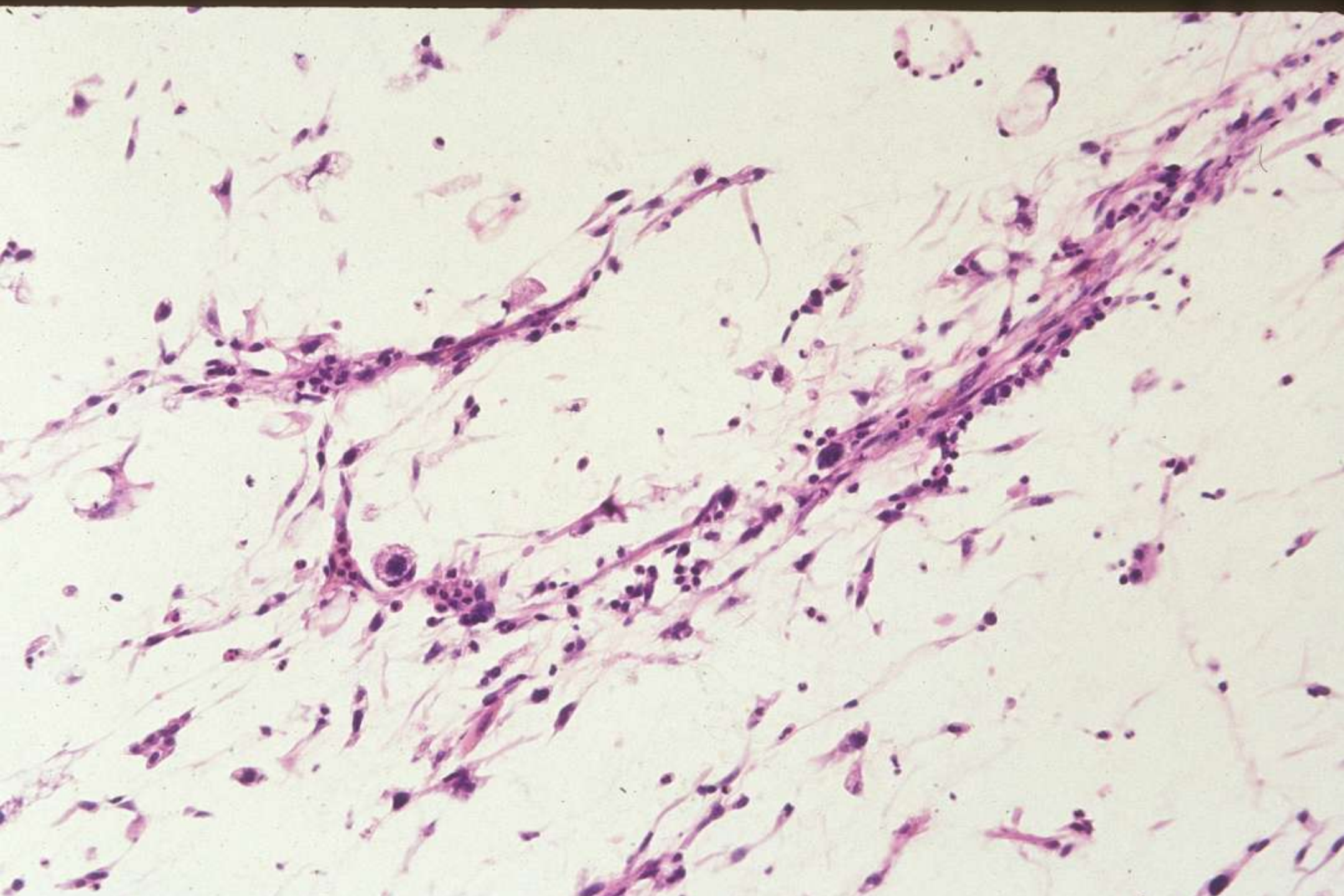
Adults; peak 50-70 years
Equal sex incidence
Lower limb > upper limb > trunk
Retroperit and head/neck rare
60-70% Subcutaneous / deep dermal
Some tendency to nodal metastasis
Survival depends on grade

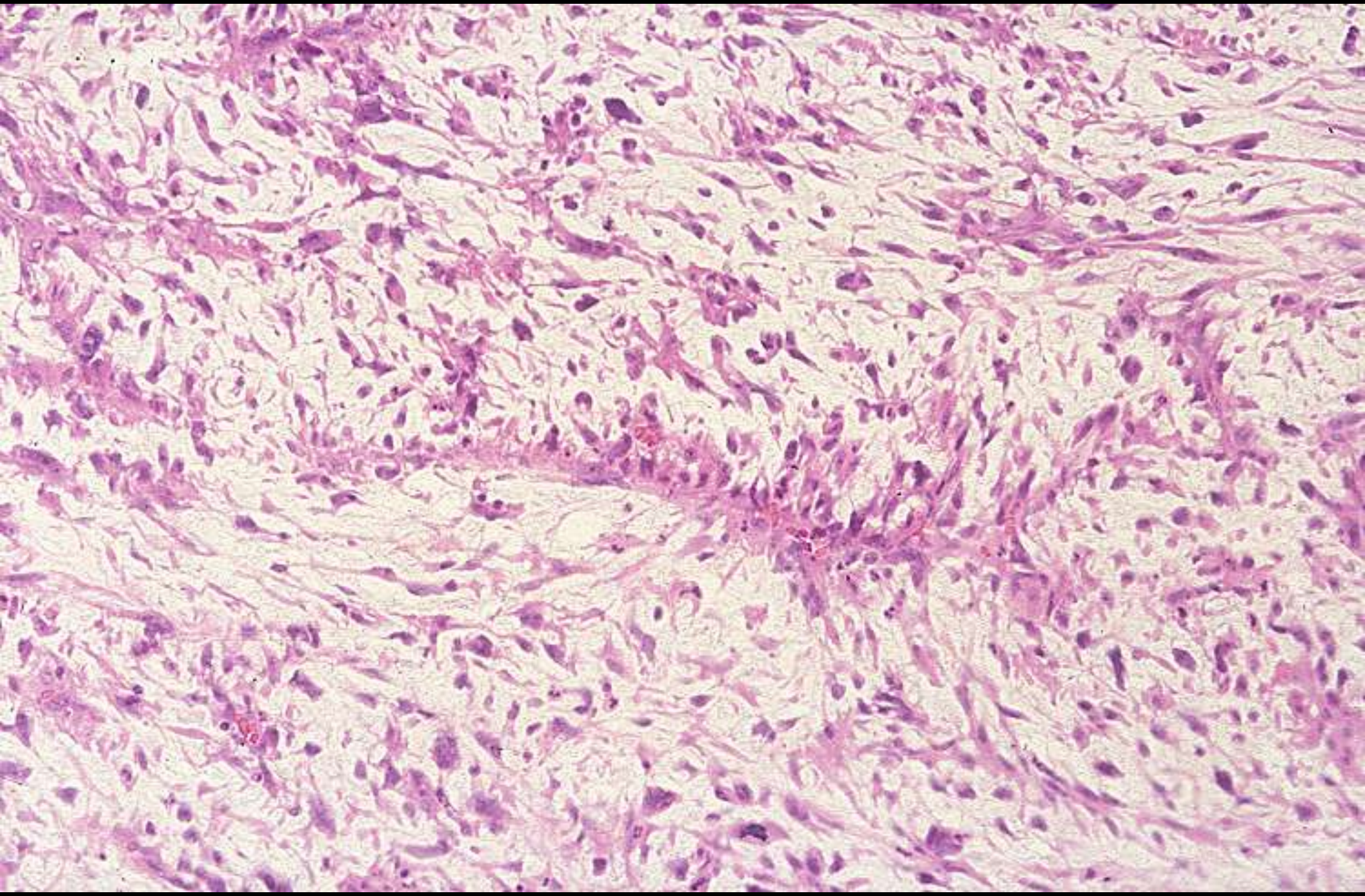


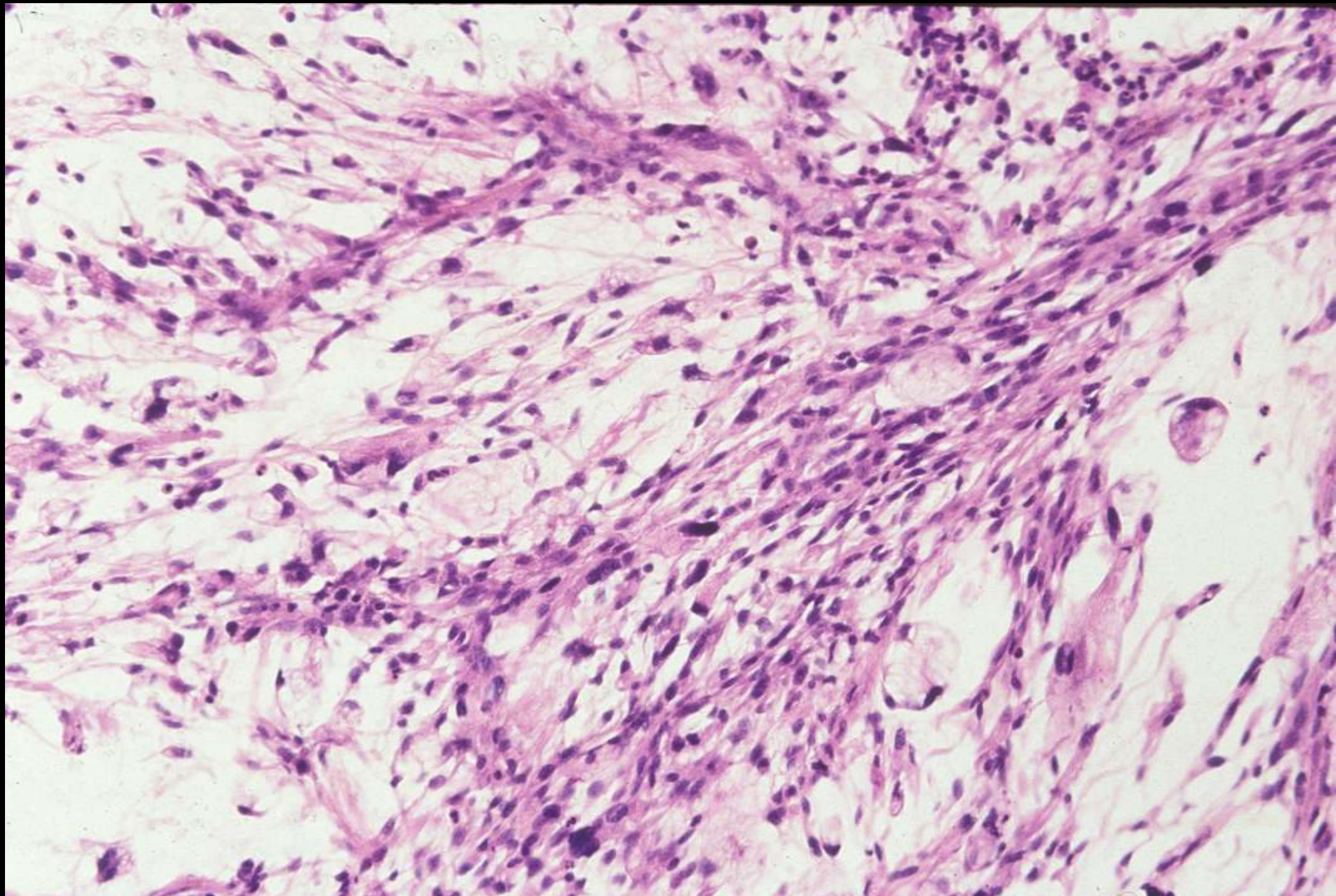


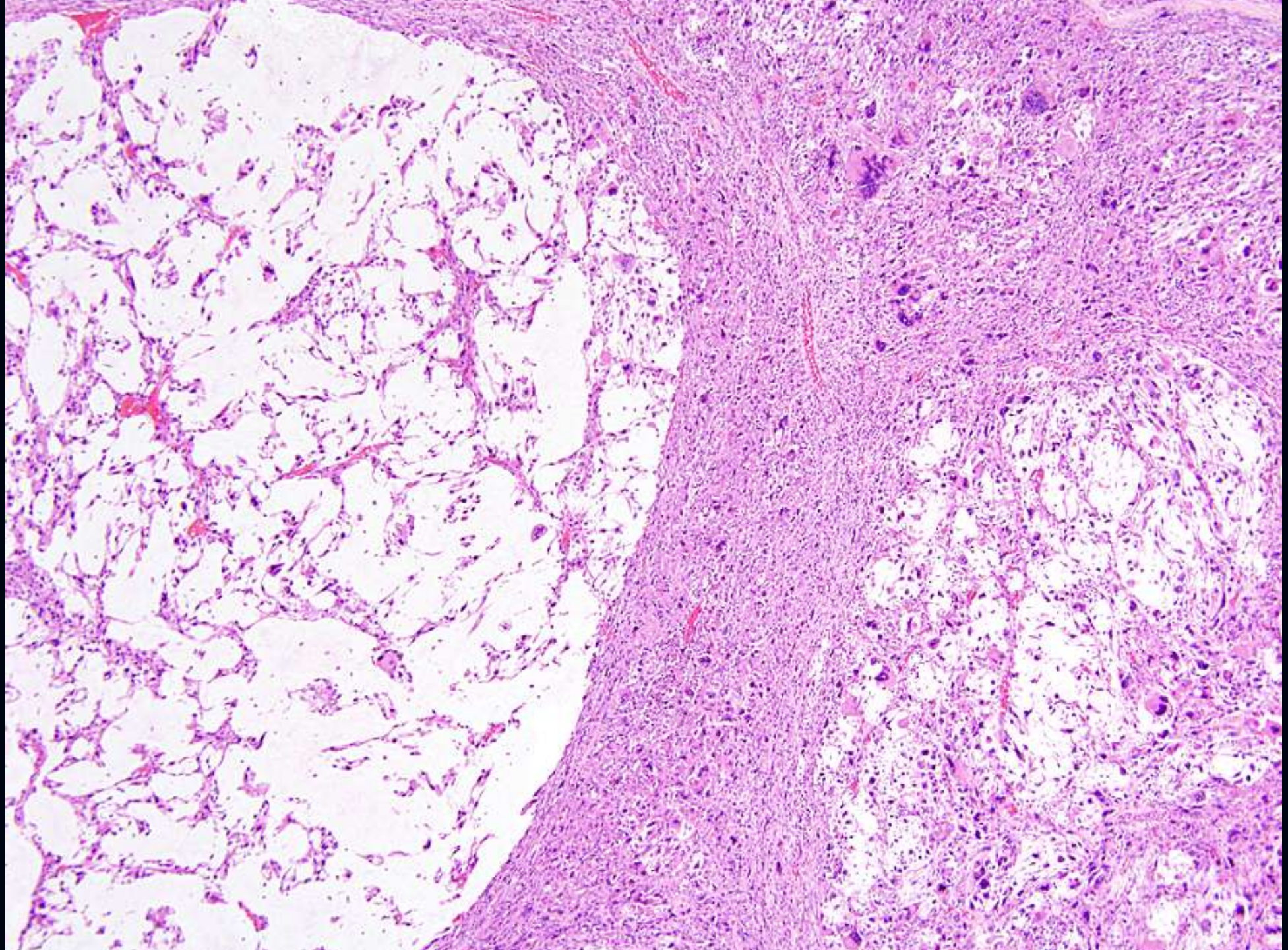


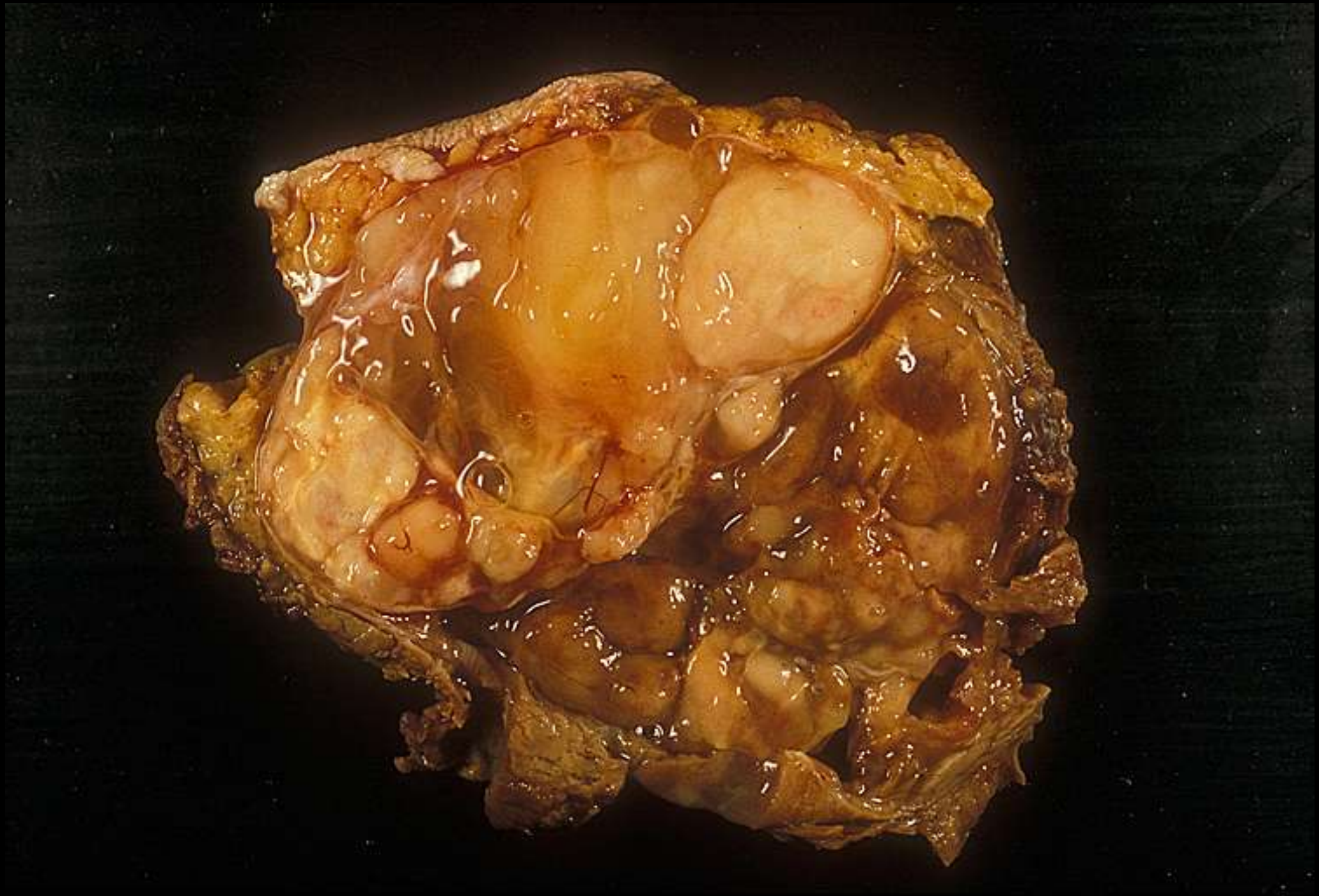












MYXOFIBROSARCOMA
METASTASES / TUMOUR-RELATED DEATHS

	Superficial	Deep
Low	0%	0%
Intermed	20%	30%
High	30%	35%

Local recurrence(s) may advance in grade

PLEXIFORM FIBROHISTIOCYTIC TUMOUR

CLINICAL FEATURES

Commonest 0-30 years

Wide age range

F > M 3:1

65% upper limb

Slowly growing dermal / subcut mass

20-30% local recurrence

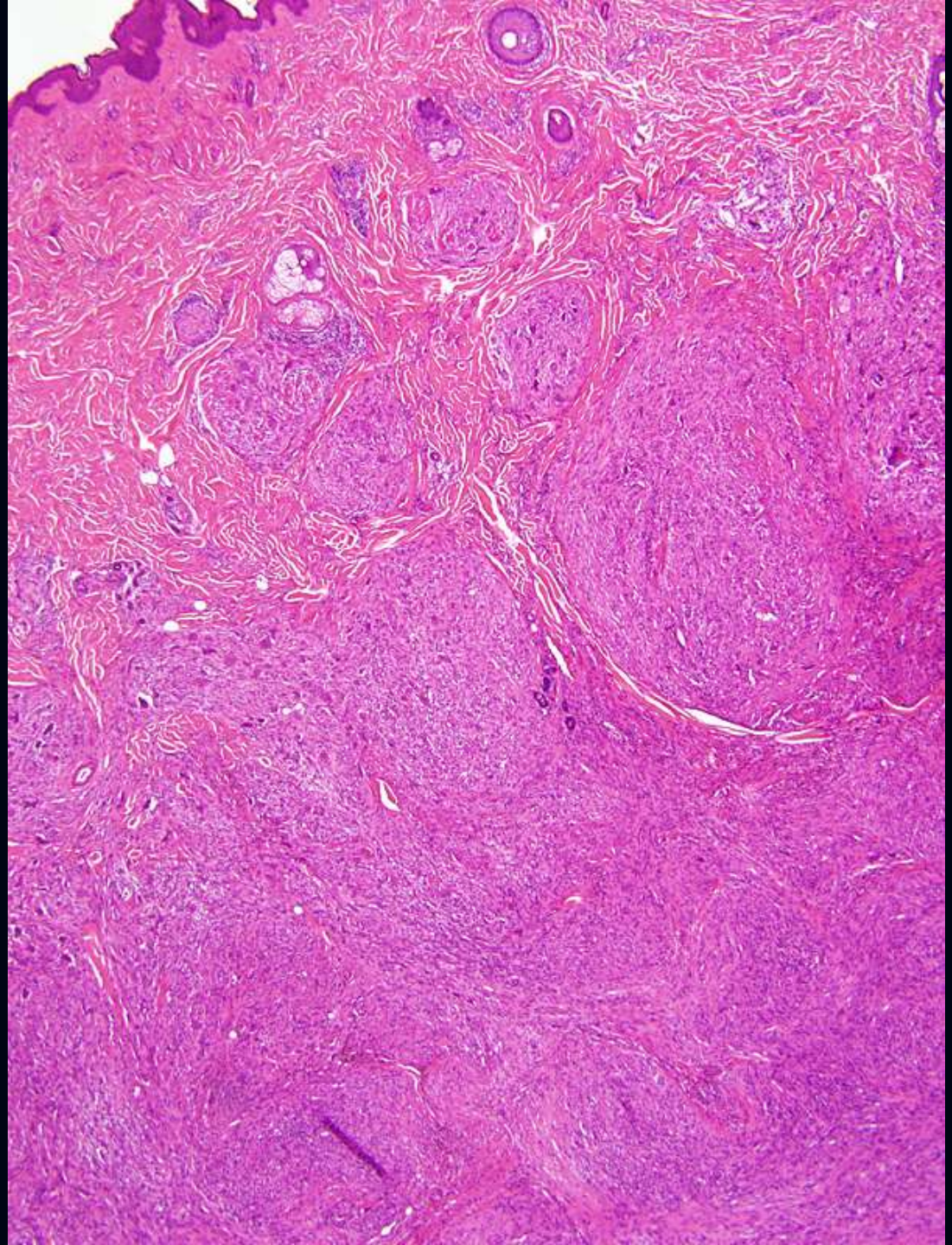
Nodal / systemic metastasis ~ 2% (? more)

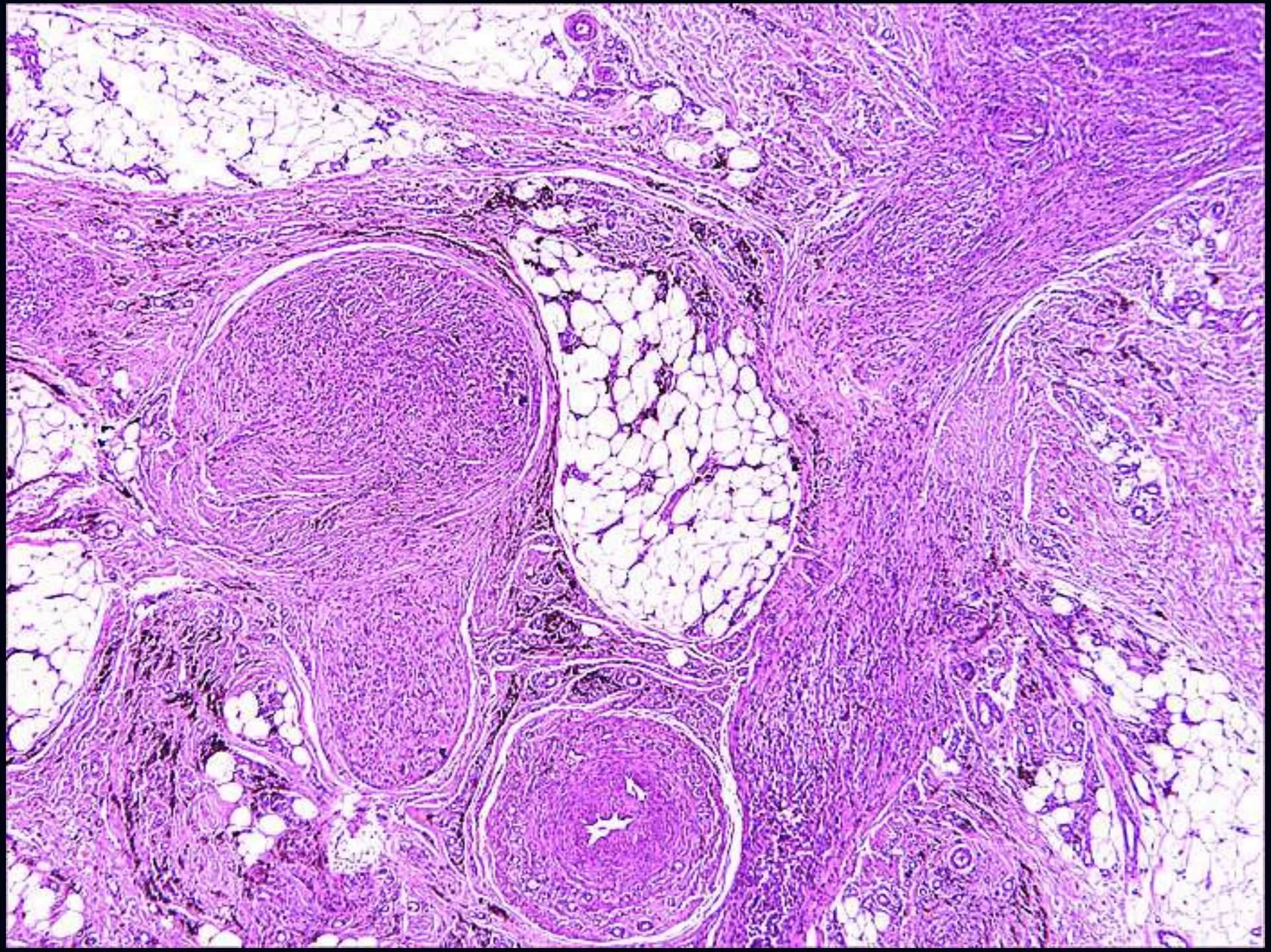
PLEXIFORM FIBROHISTIOCYTIC TUMOUR

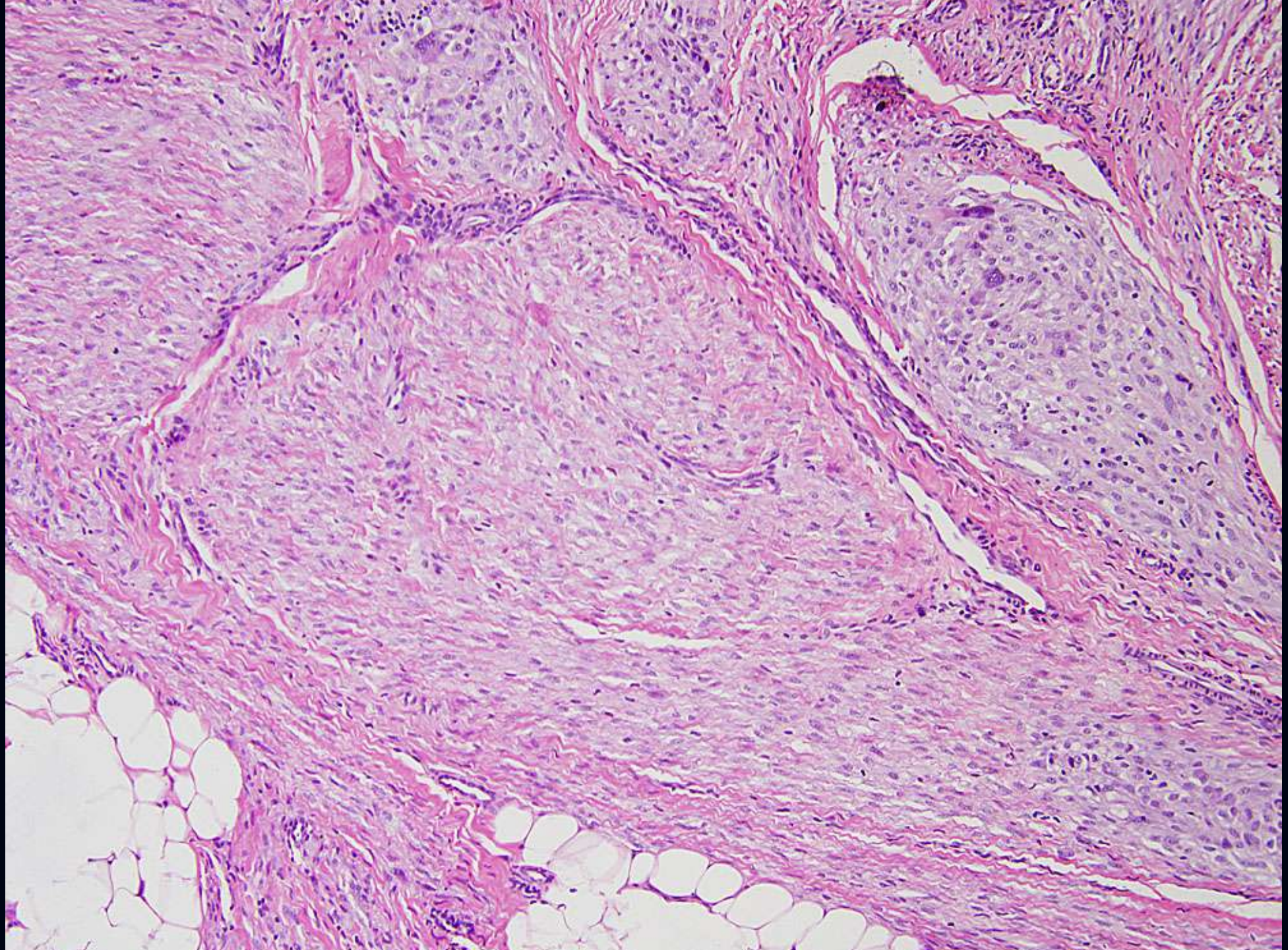
PATHOLOGIC FEATURES

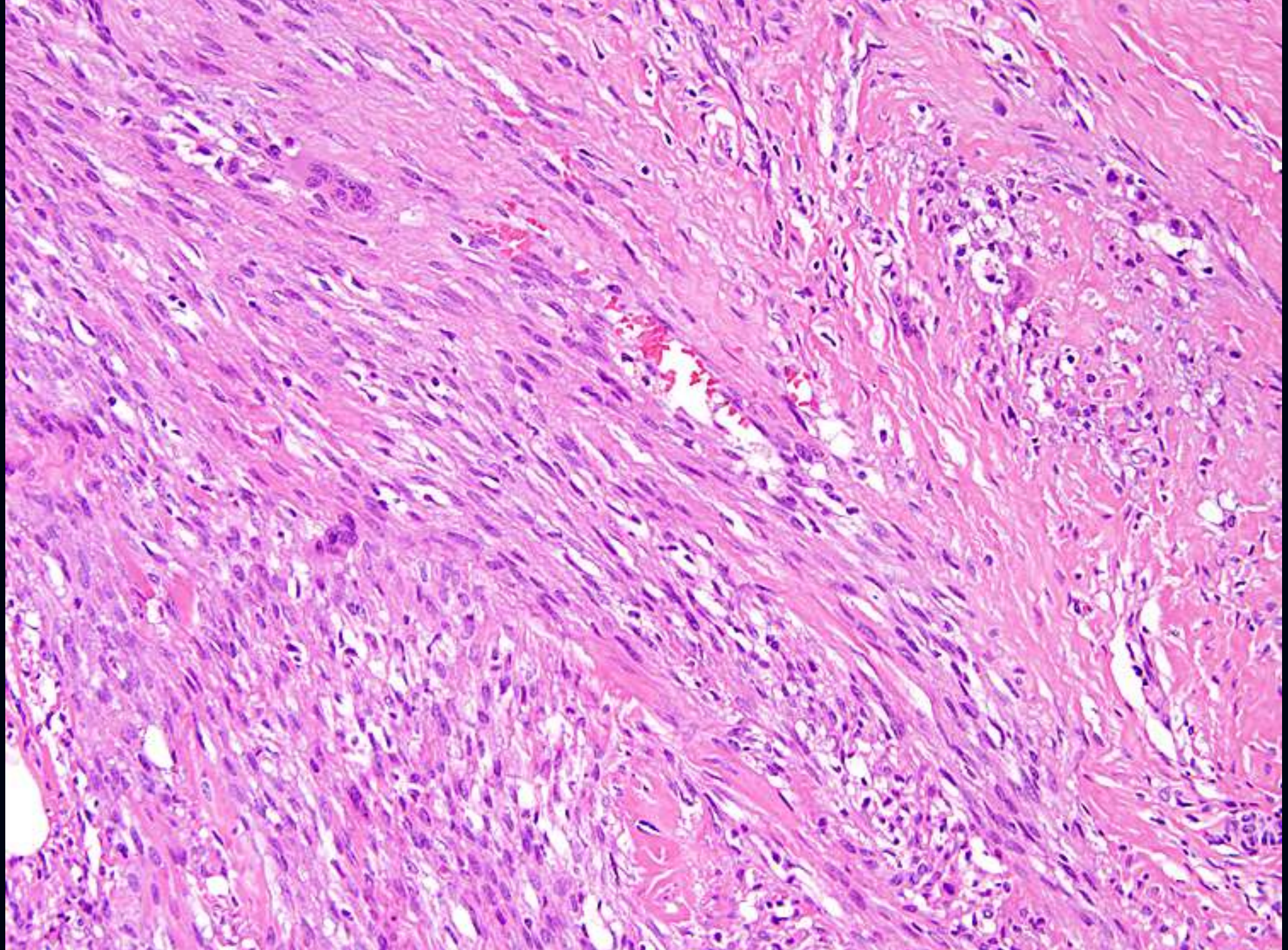
Most < 3 cm
Poorly demarcated
Centred on dermal / subcut junction
Variable proportions of:
- spindle cell fascicles
- aggregates of histiocytoid cells
Osteoclastic giant cells common

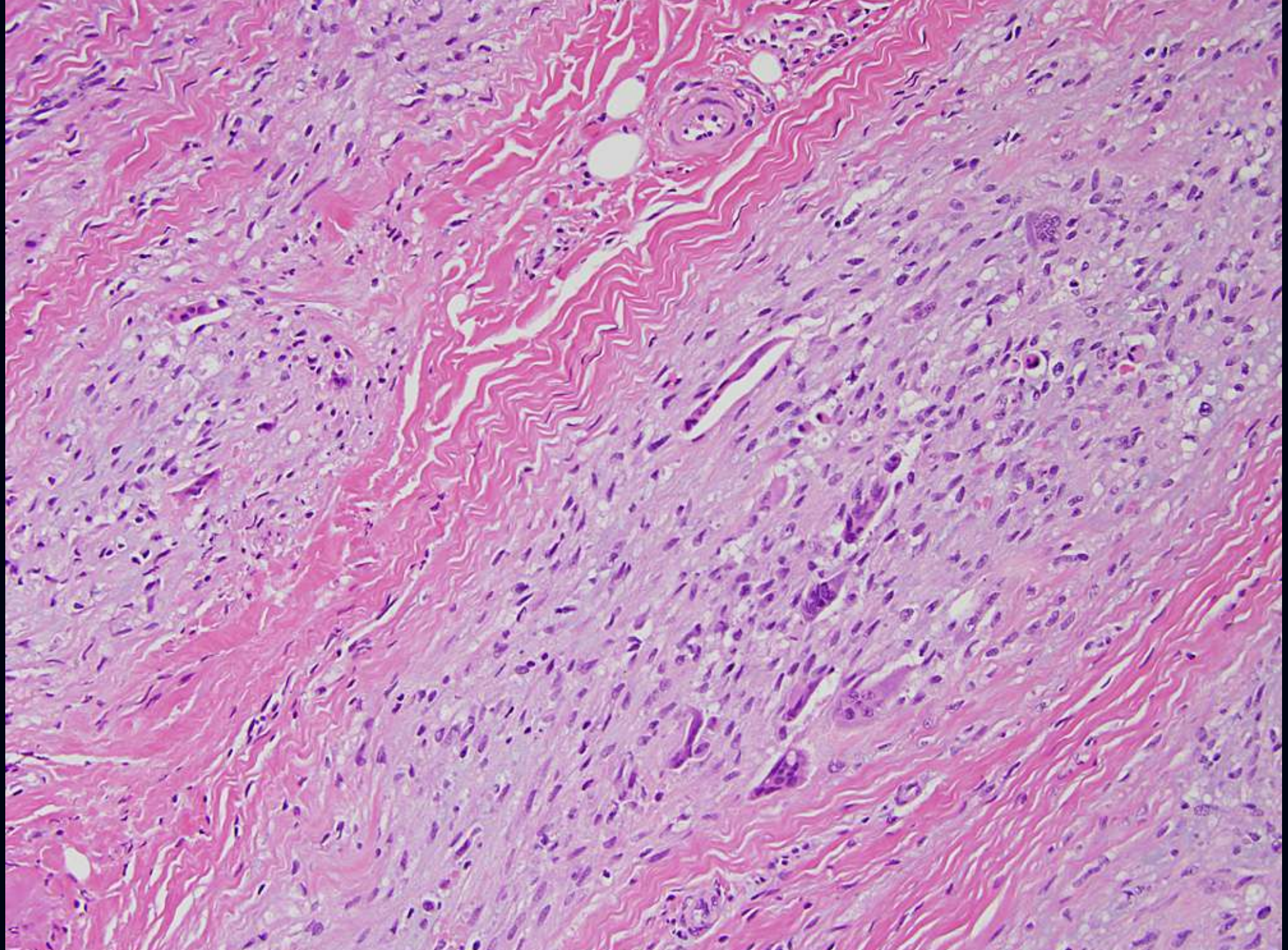
Vascular invasion ~ 30%

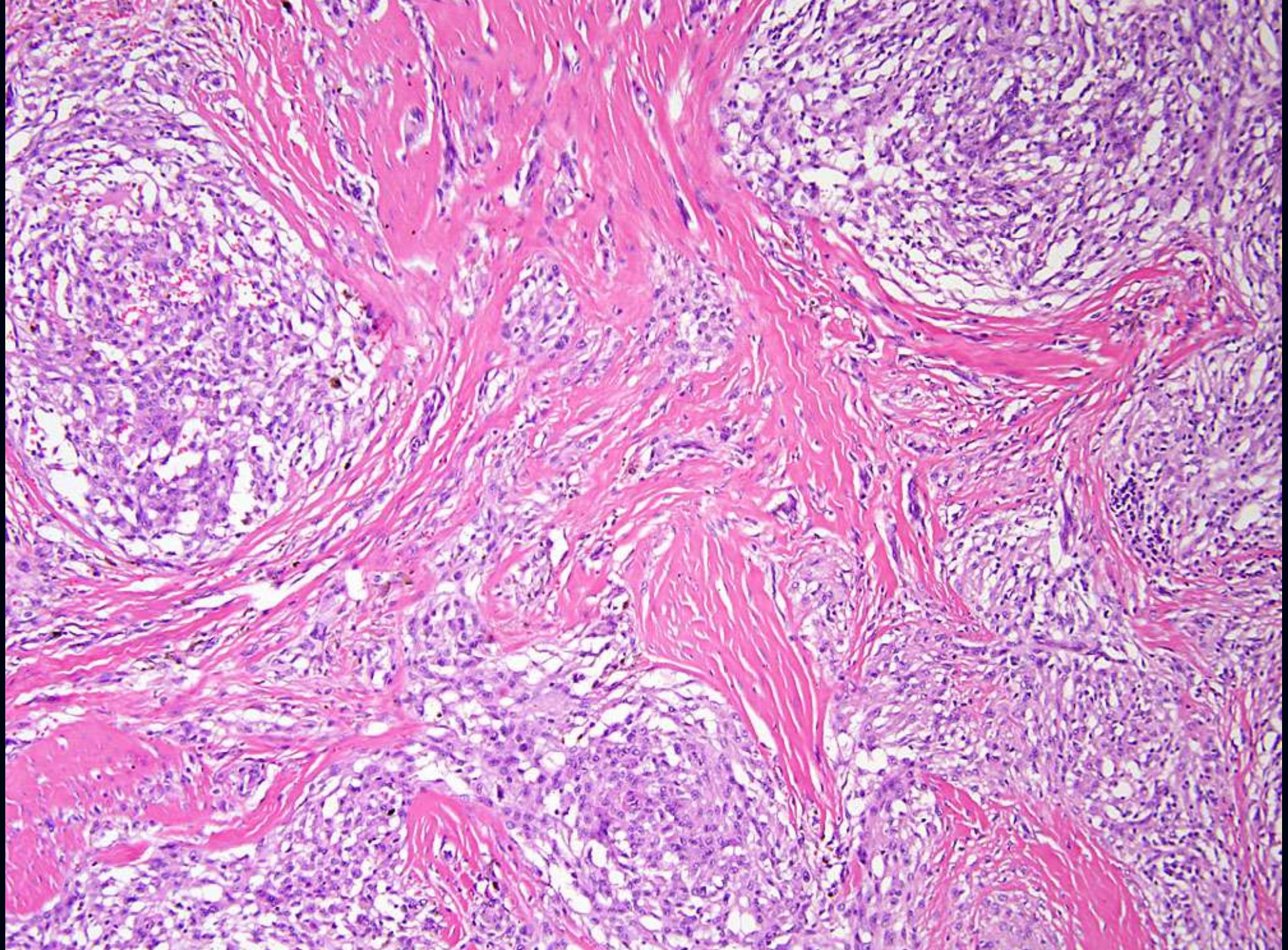


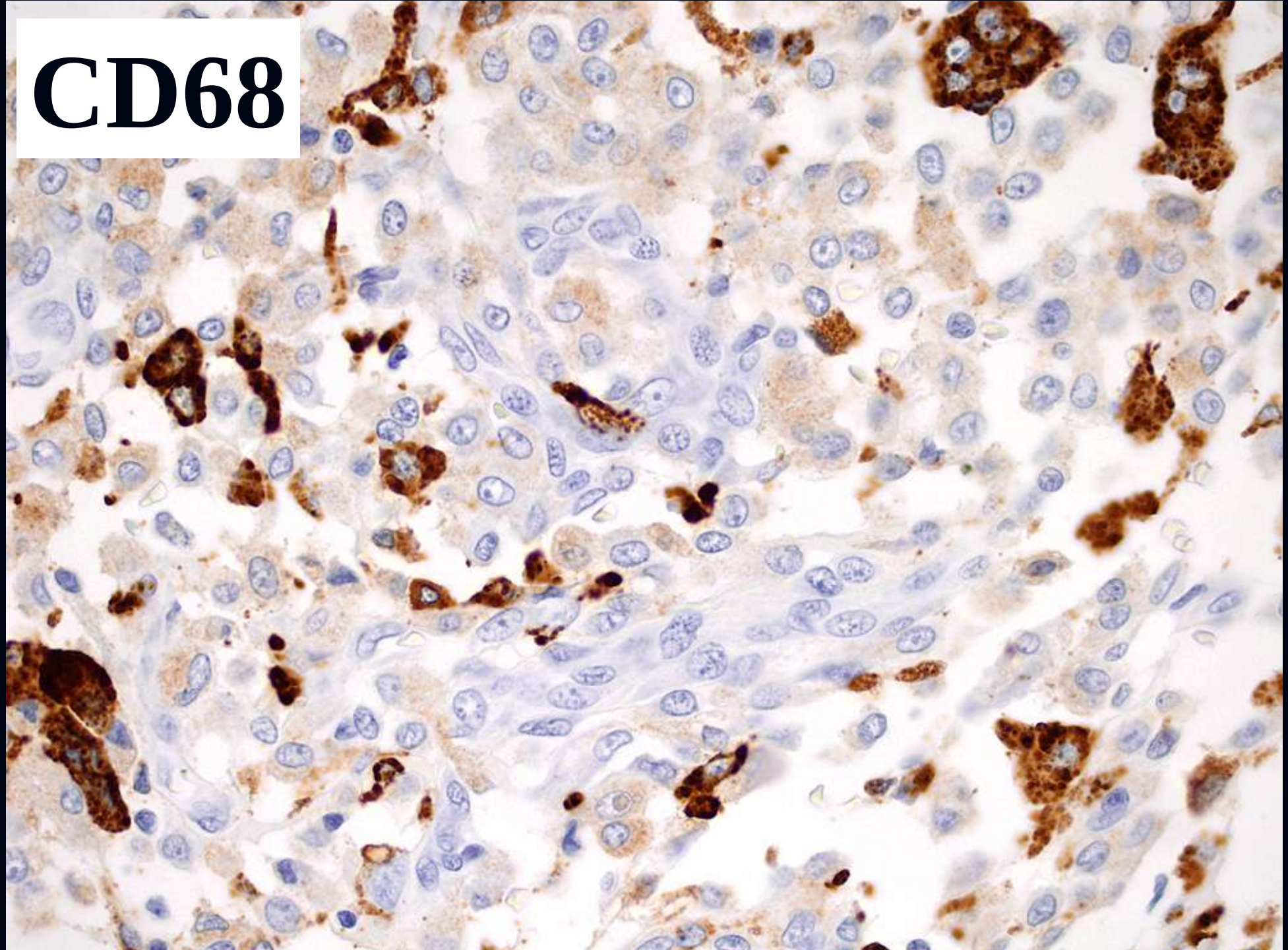








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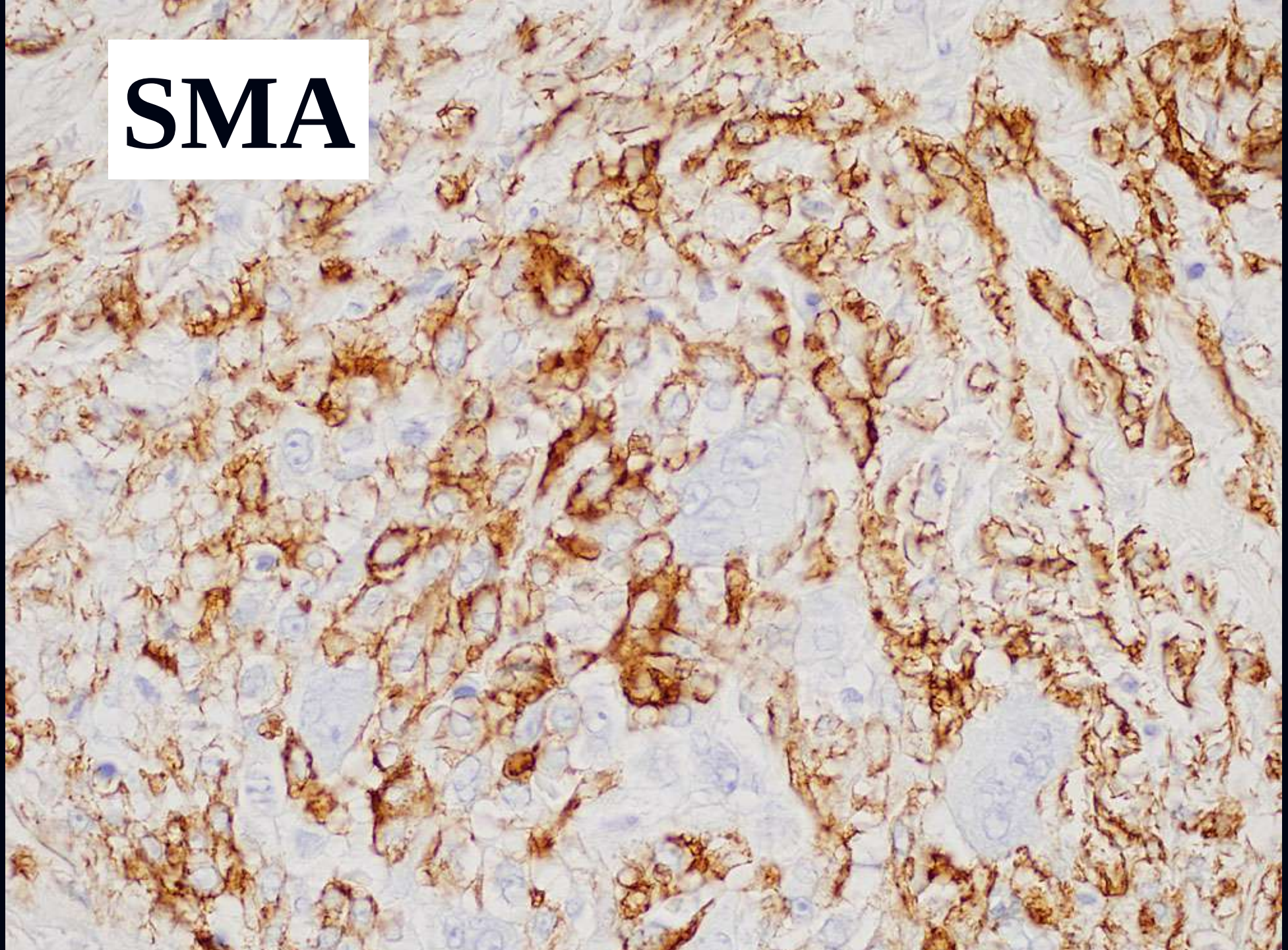
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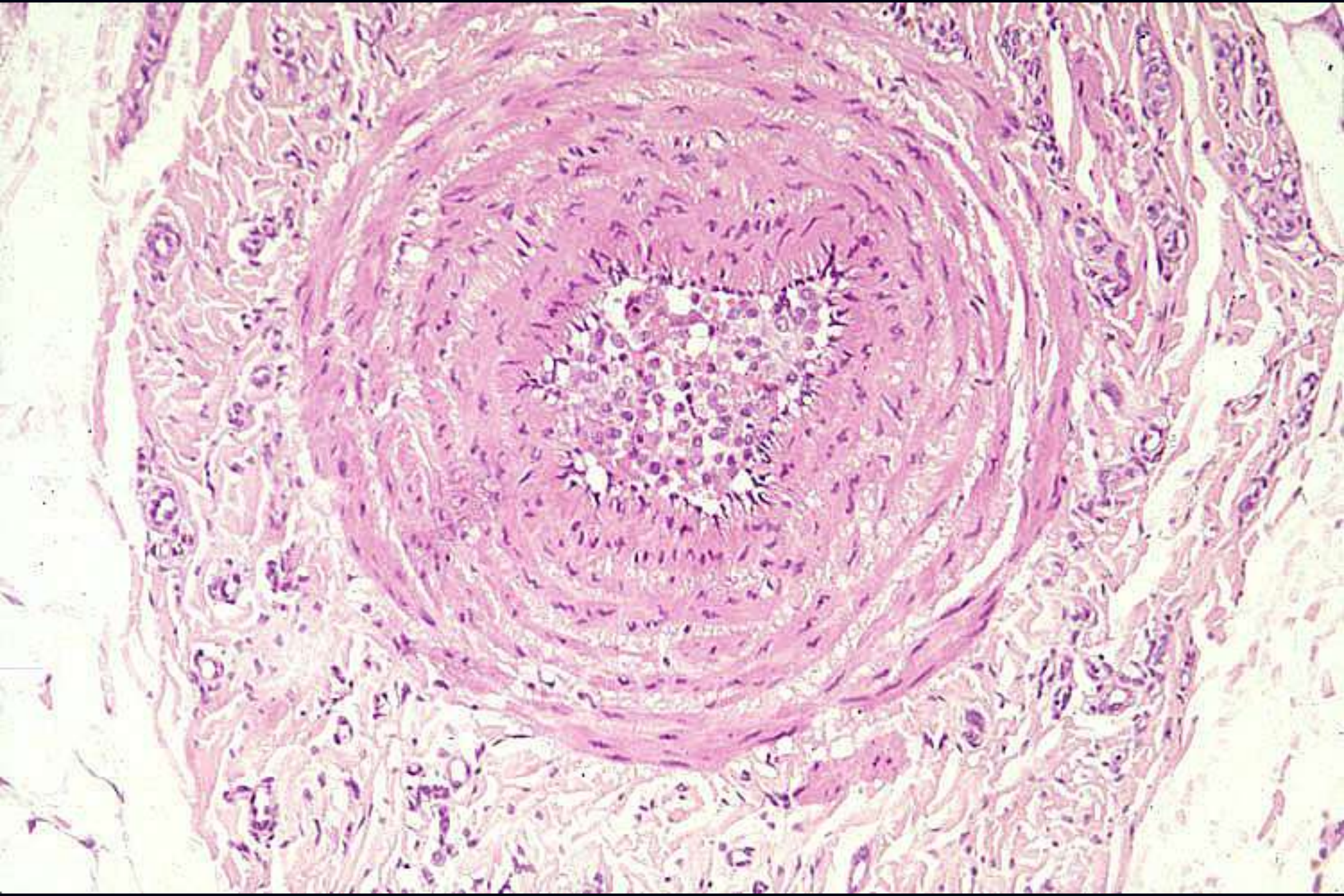
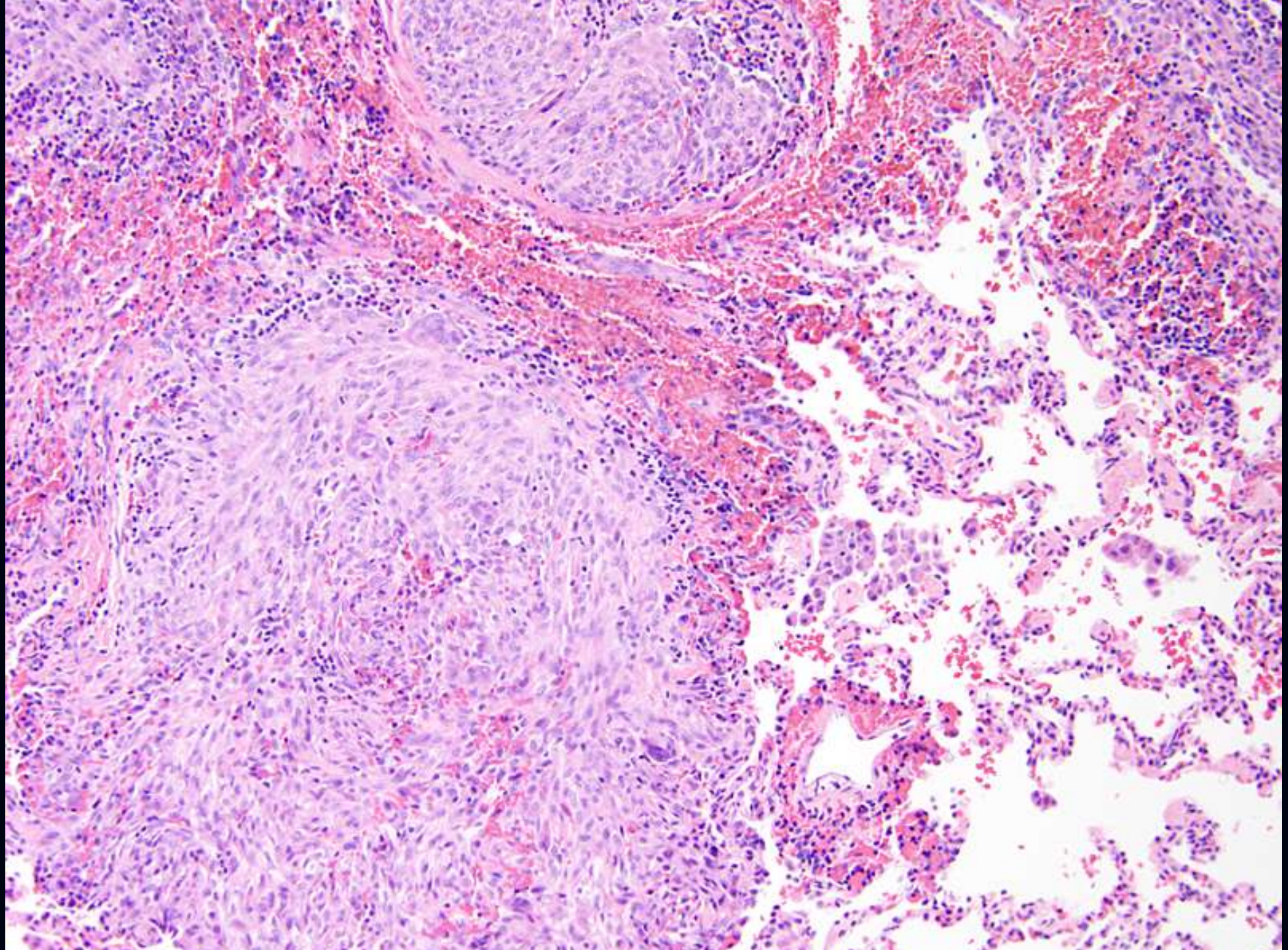




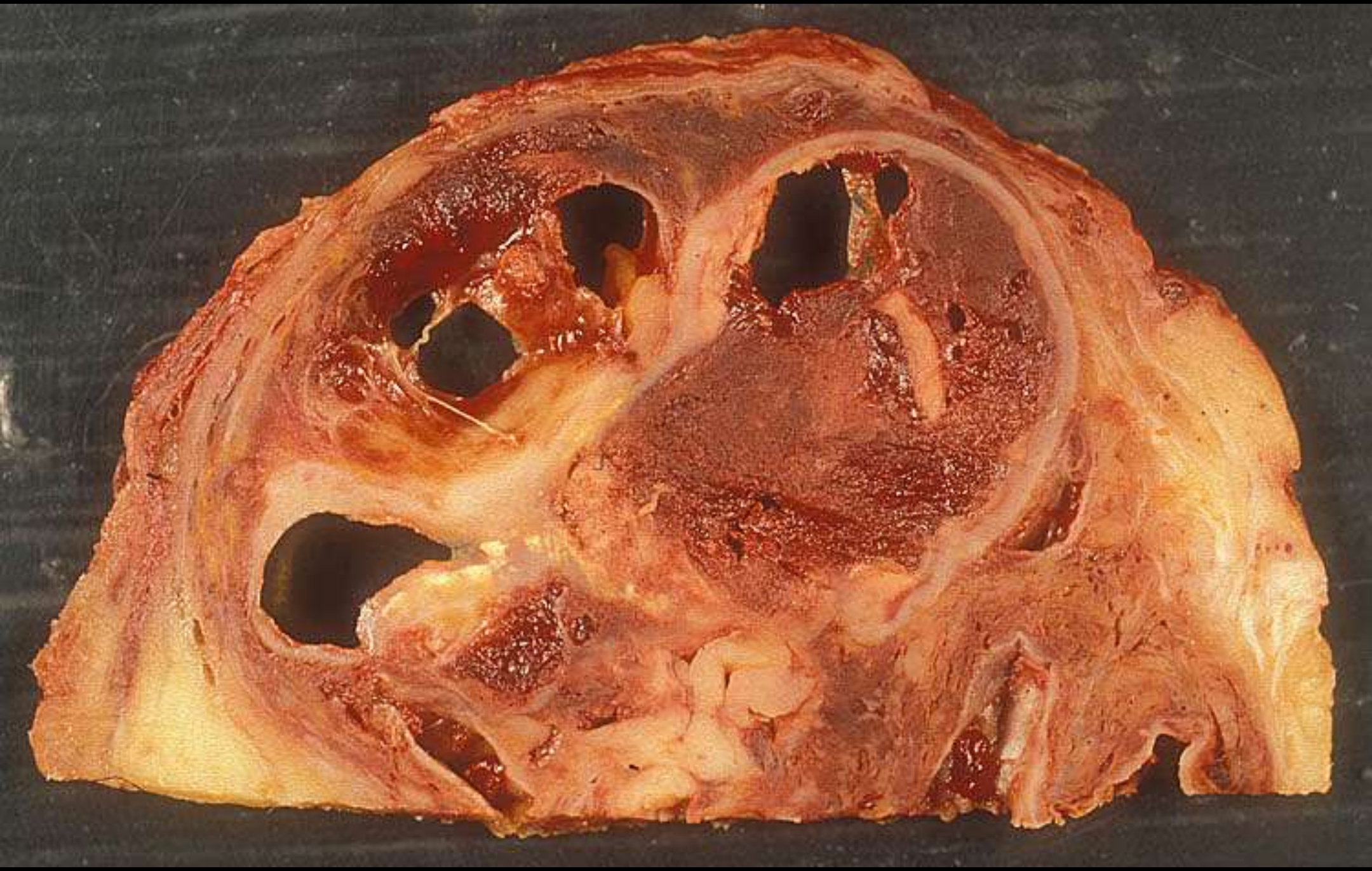
PLEXIFORM FIBROHISTIOCYTIC TUMOUR DIFFERENTIAL DIAGNOSIS

Ordinary fibrous histiocytoma
Fibromatosis
Giant cell tumour of soft tissue
(Giant cell tumour of tendon sheath)
(Granulomatous process)

SO-CALLED ANGIOMATOID 'MFH'
CLINICAL FEATURES

Children / adolescents / young adults
Equal sex incidence
Limbs > trunk
Most often subcutaneous
Slowly growing, usually < 5 cm
Often mistaken for haematoma
Systemic features in < 5%
- fever, weight loss, anaemia, ESR ↑

Local recurrence approx. 10%
Metastasis < 2%

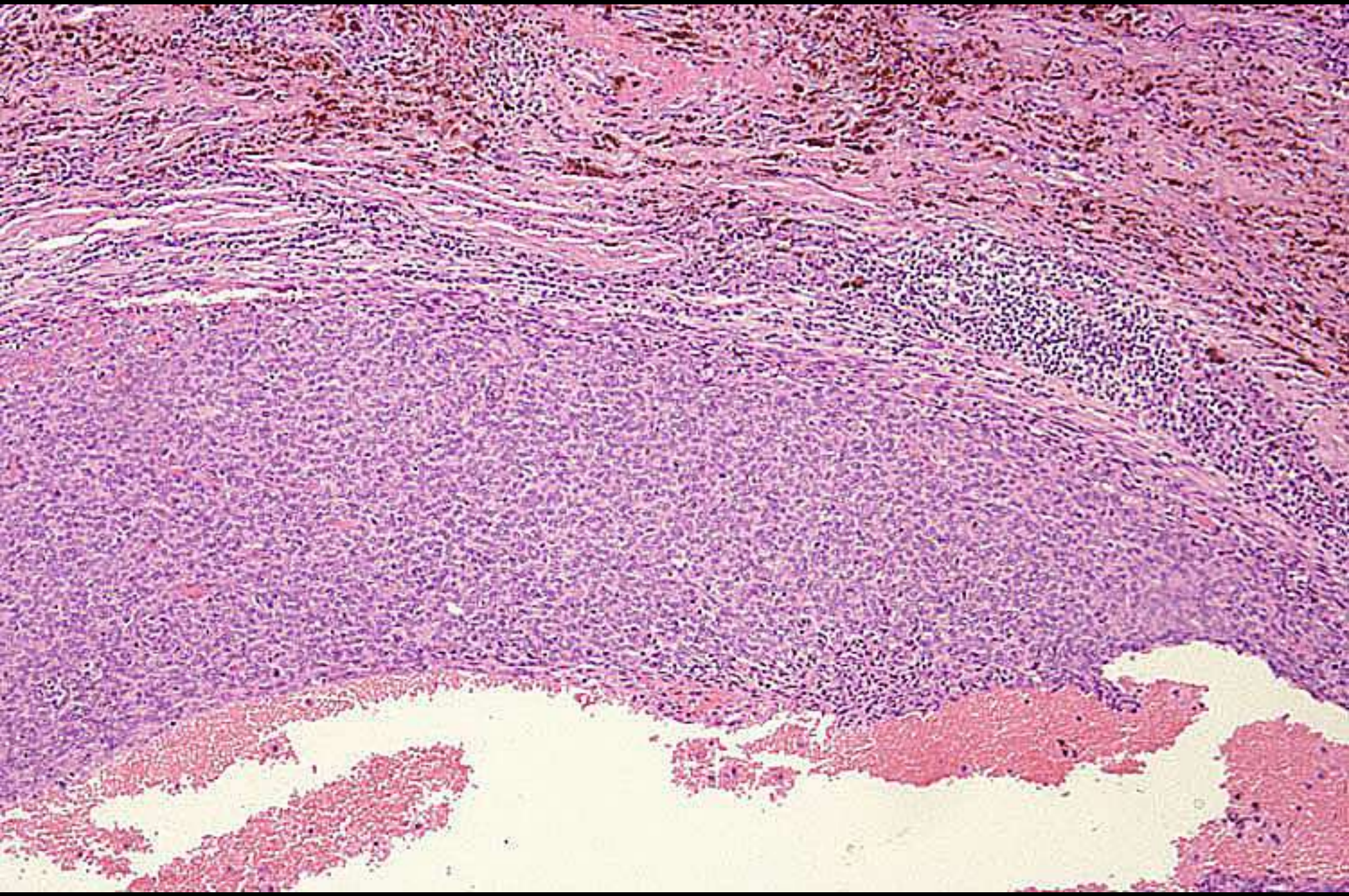


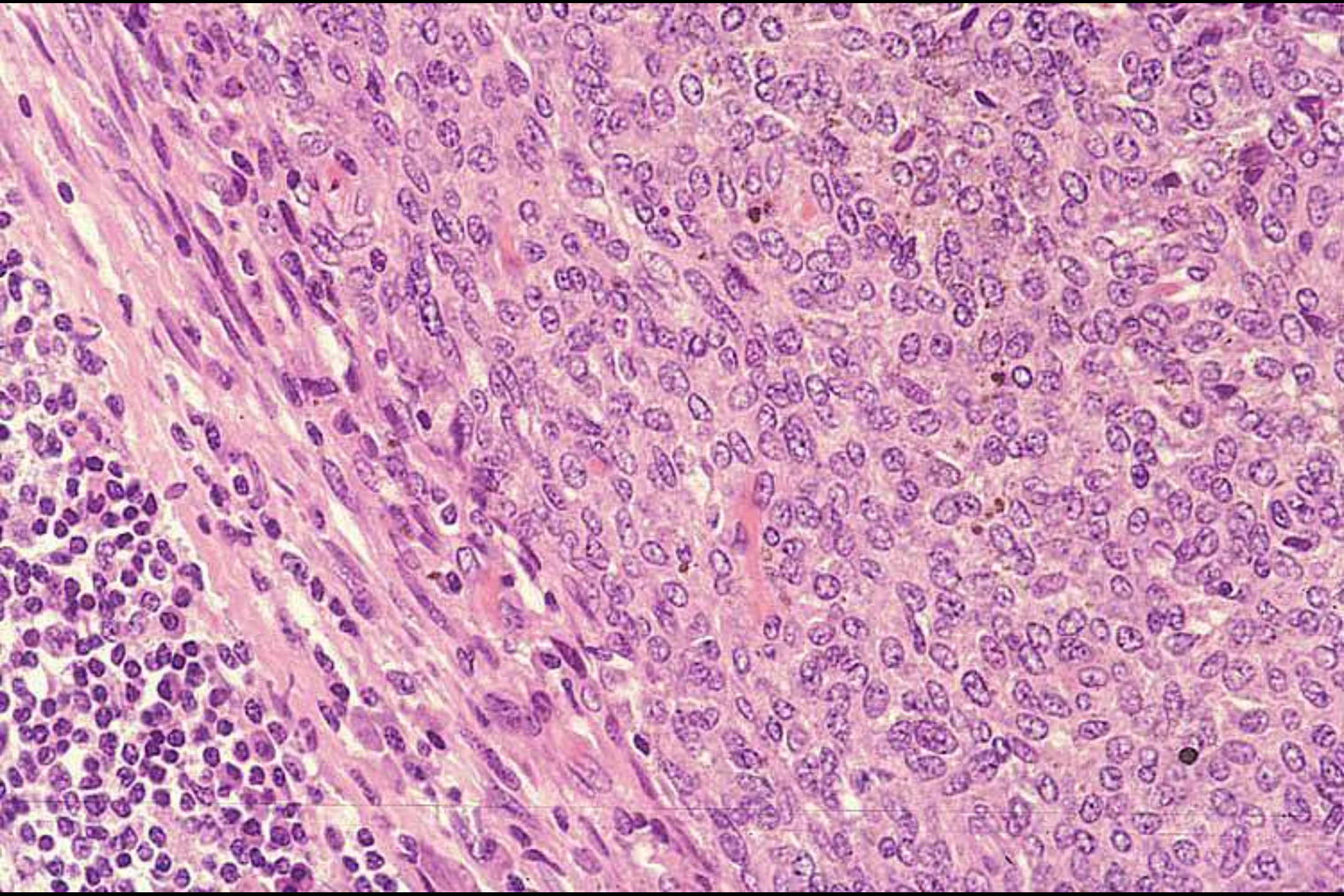
SO-CALLED ANGIOMATOID 'MFH'

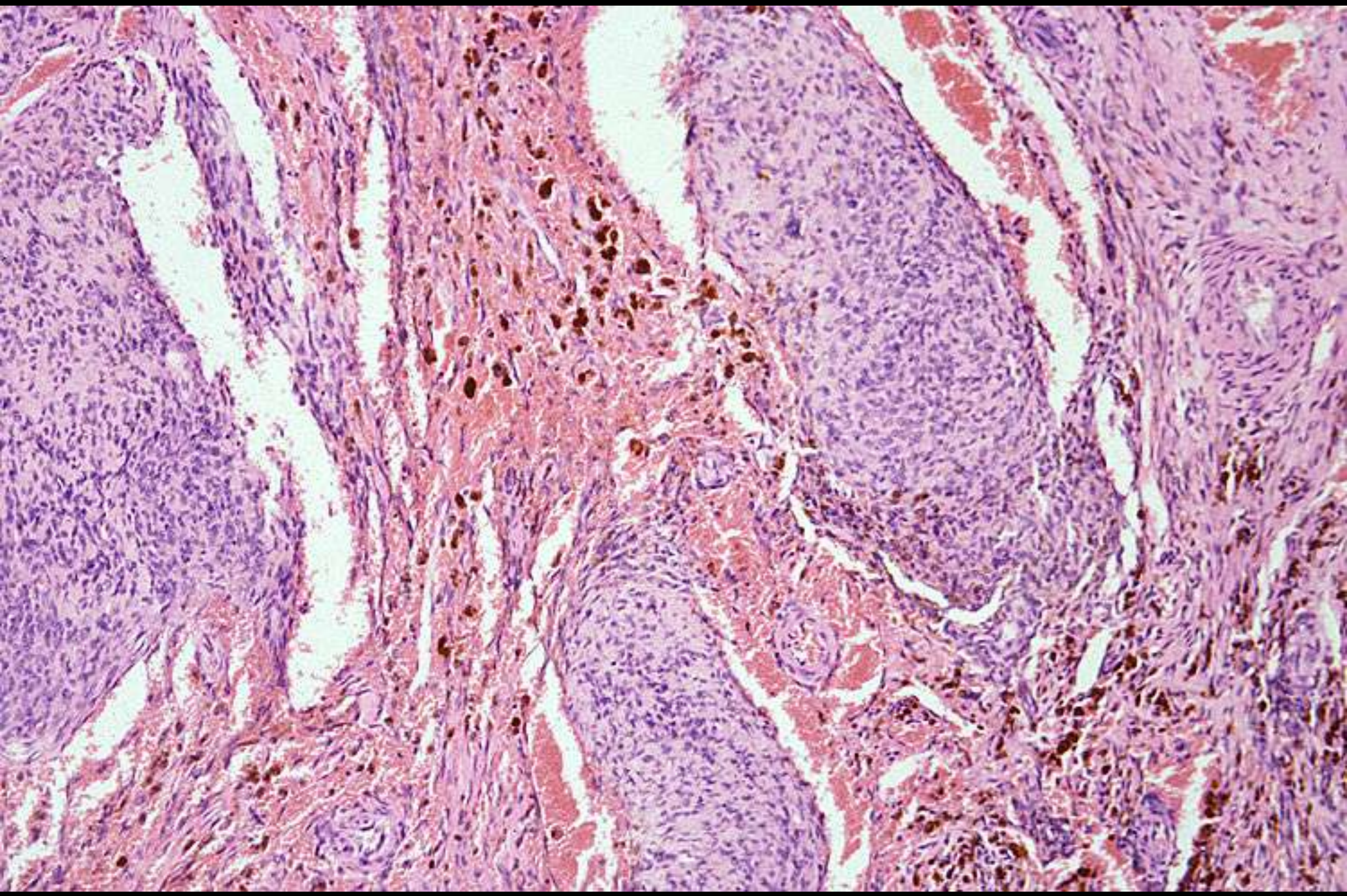
PATHOLOGIC FEATURES

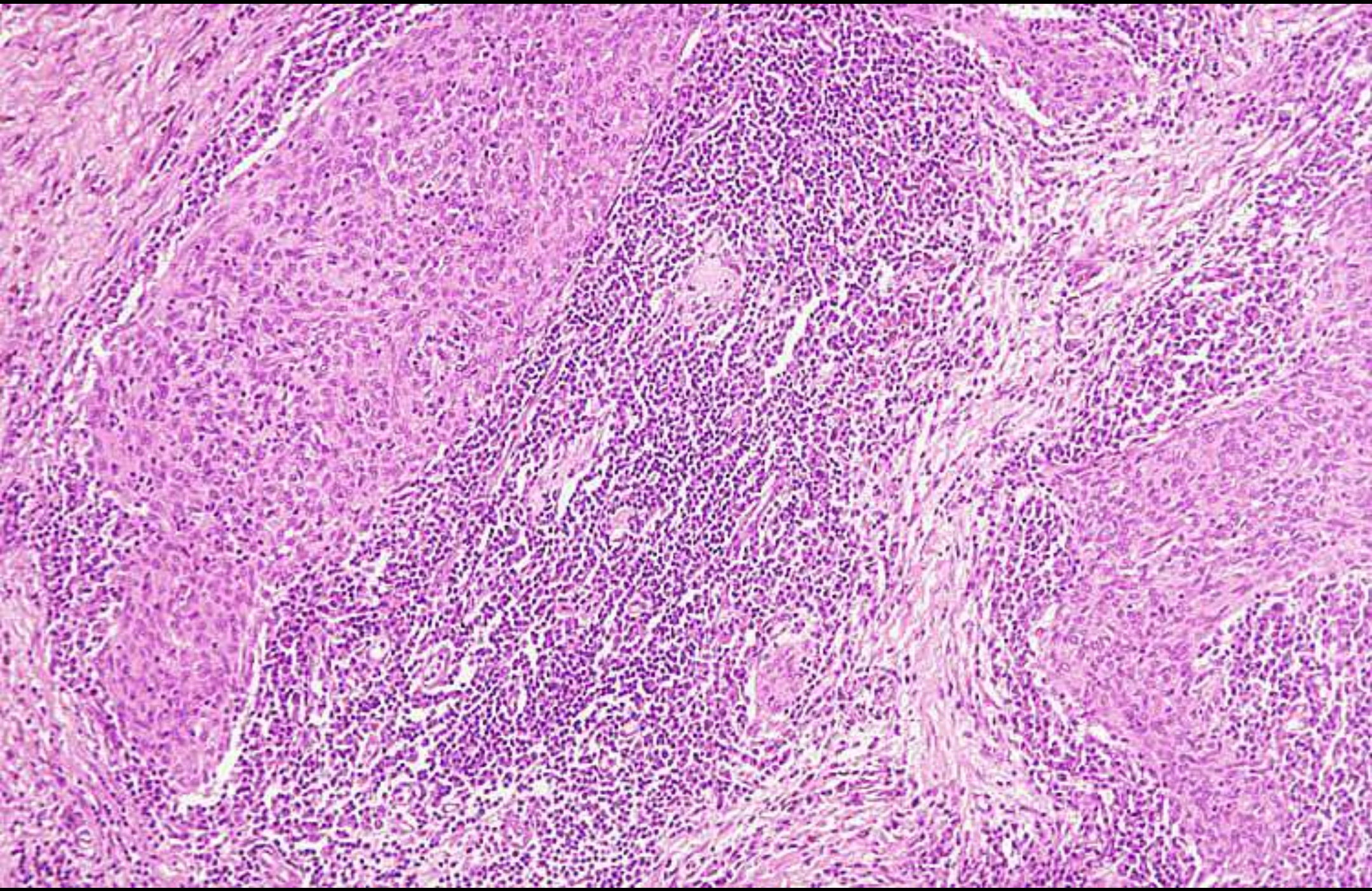
Multinodular, haemorrhagic
Nodules / sheets of
eosinophilic ovoid to spindle cells
Pleomorphism infrequent
Lymphoplasmacytic infiltrate
Dense collagenous stroma
Haemosiderin deposition
Some variability

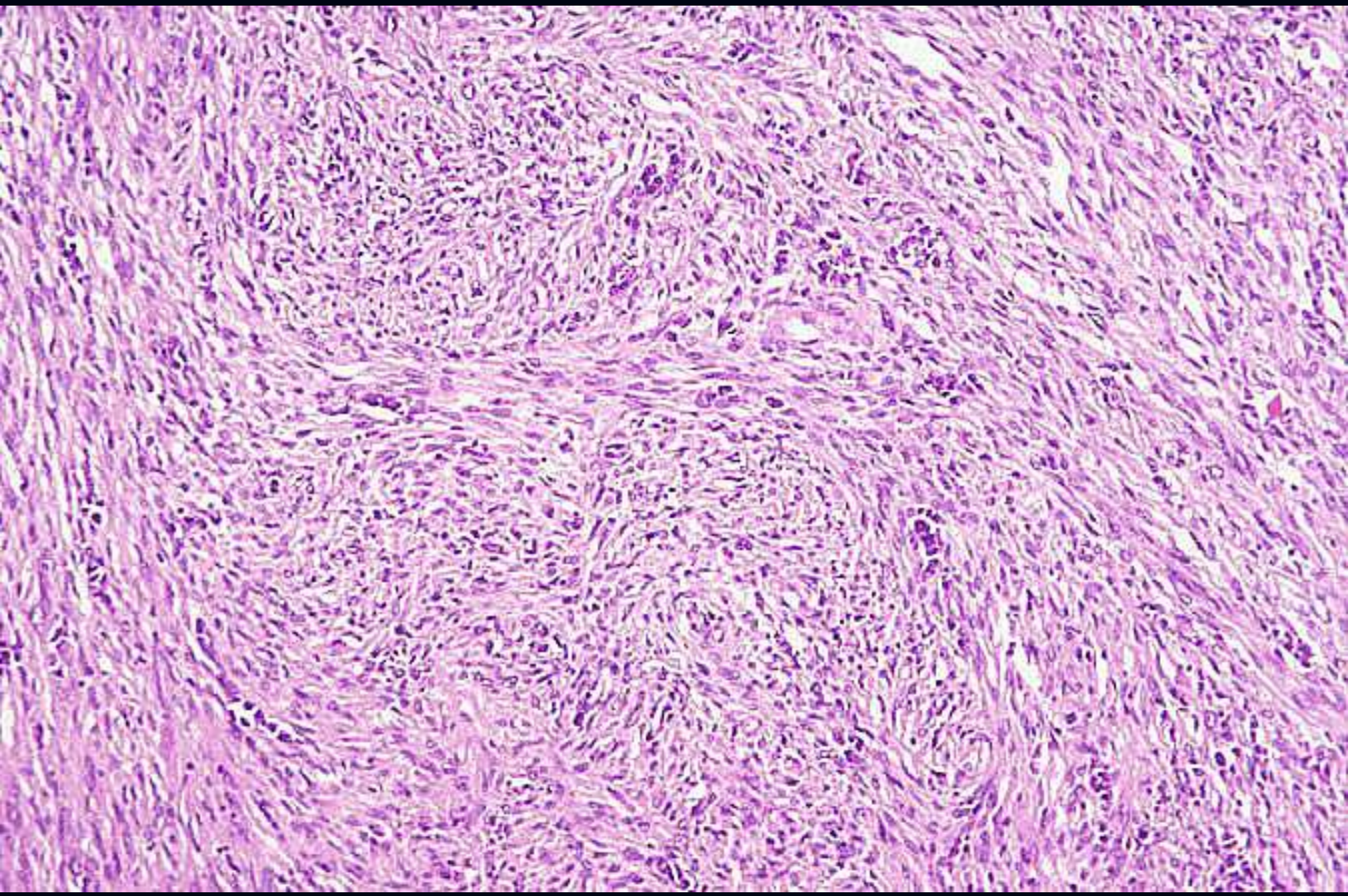
Desmin / EMA positive in 40-50%
CD68 and CD99 often positive (? significance)
Specific fusion gene(s)
Usually *EWSR1-CREB1* ; less often *EWSR1-ATF1*

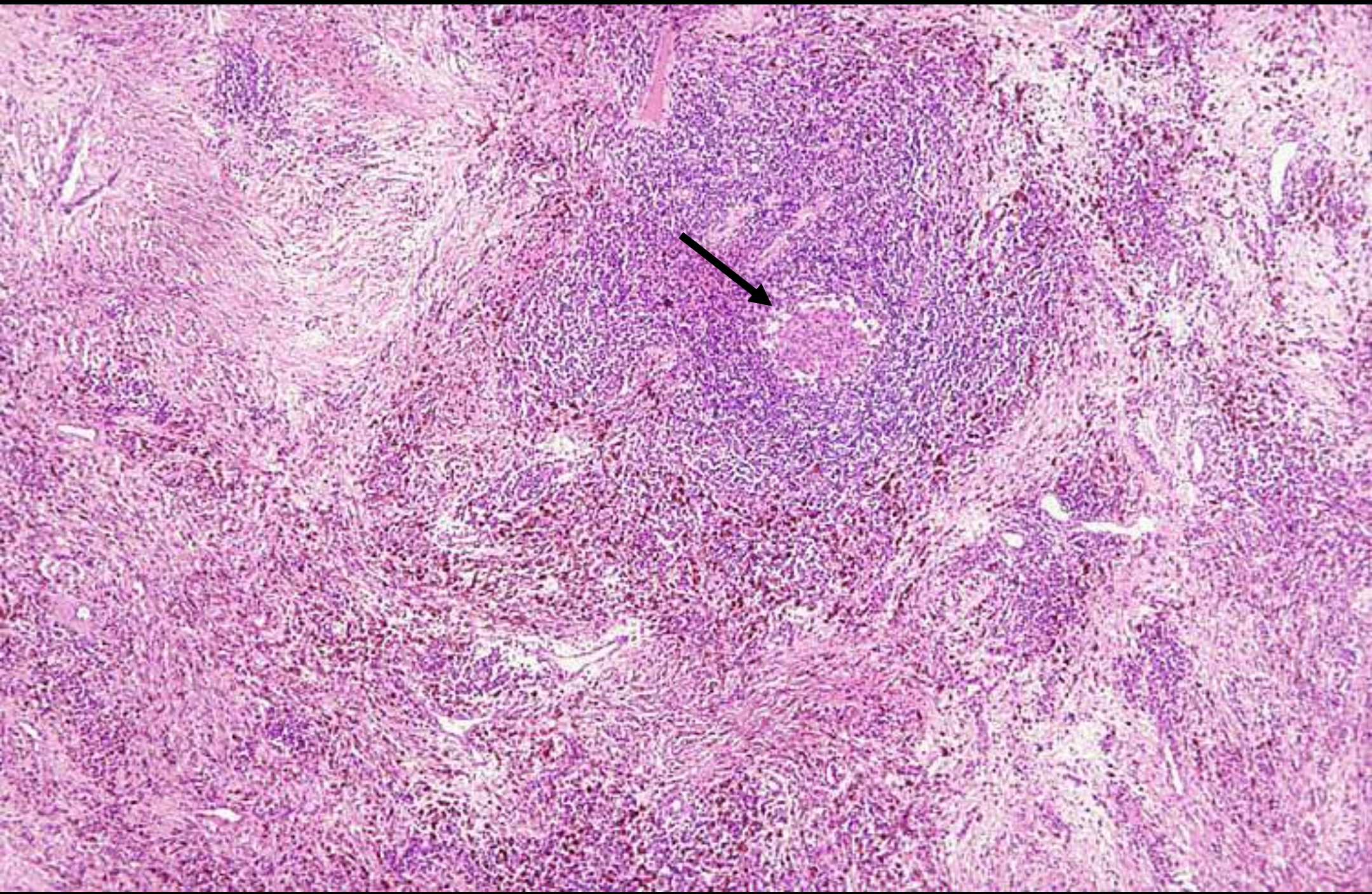


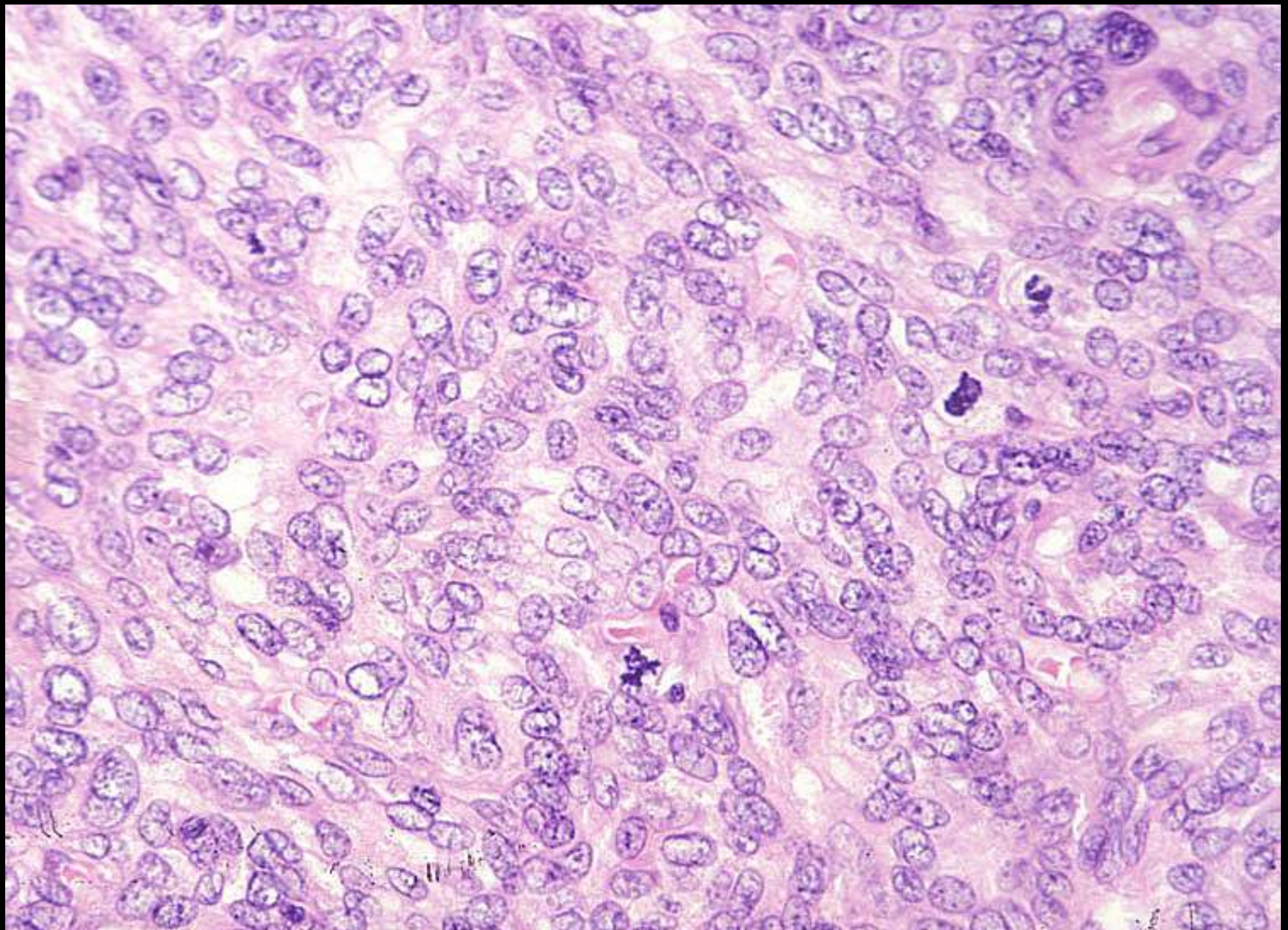


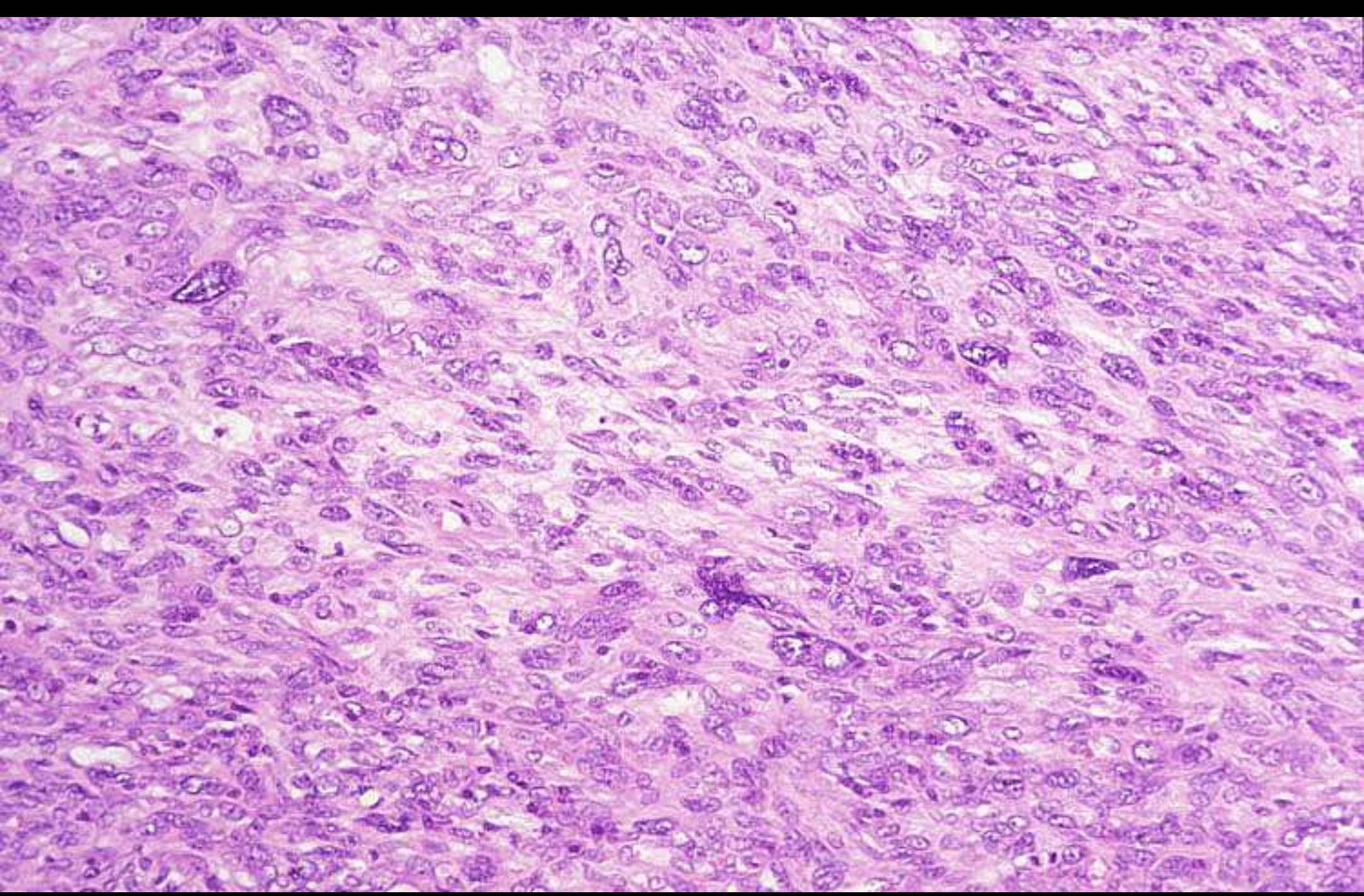


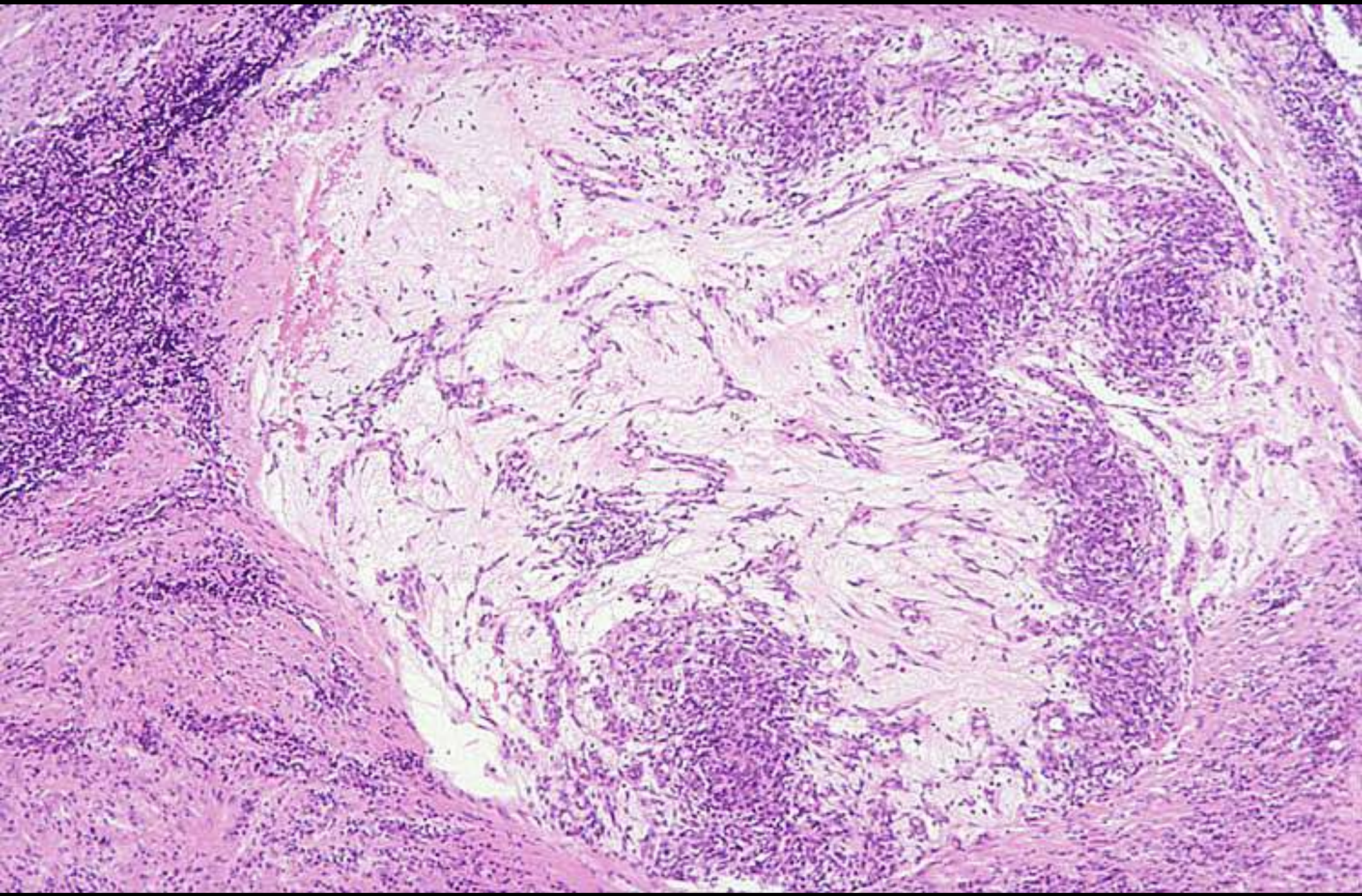


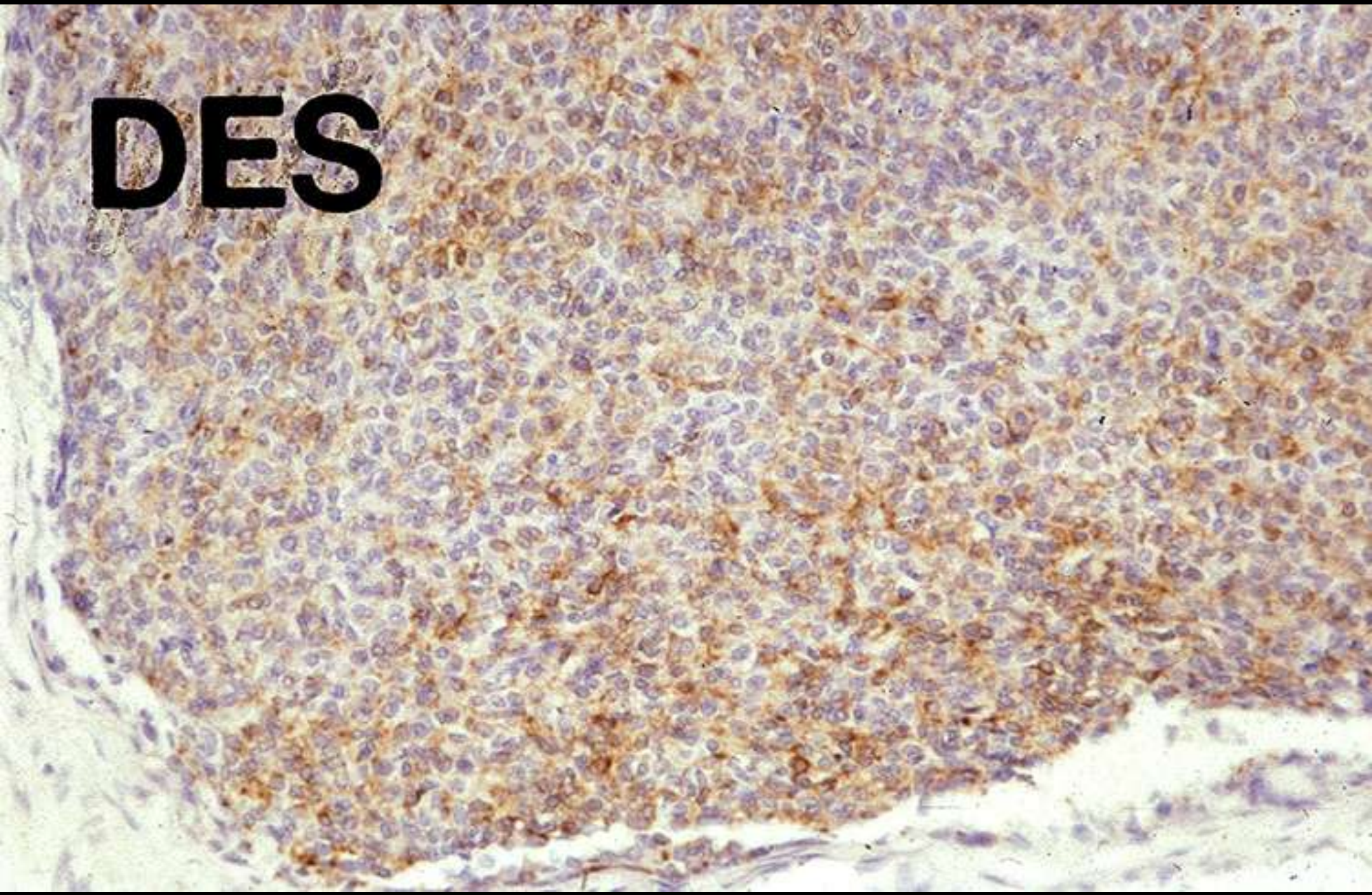








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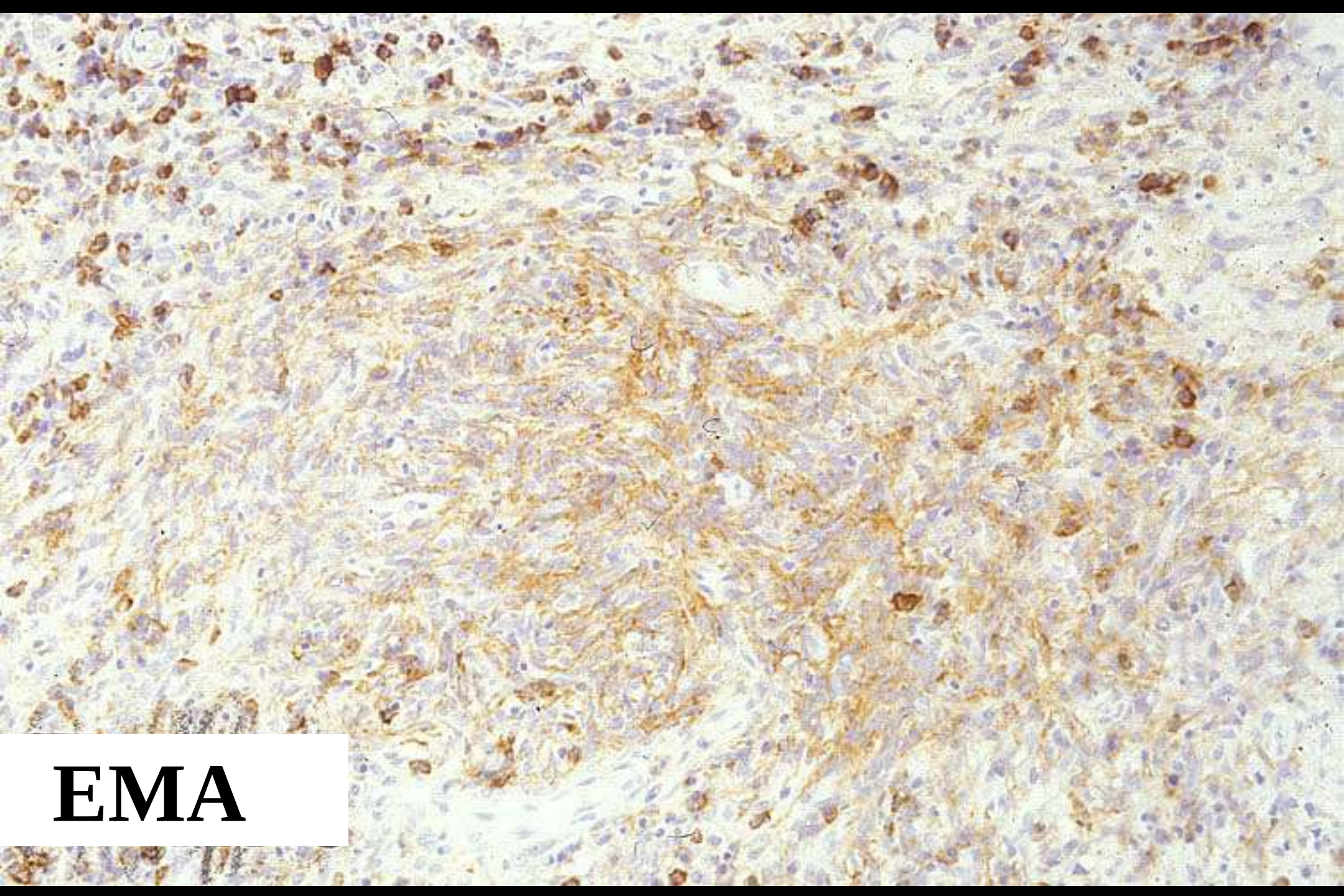
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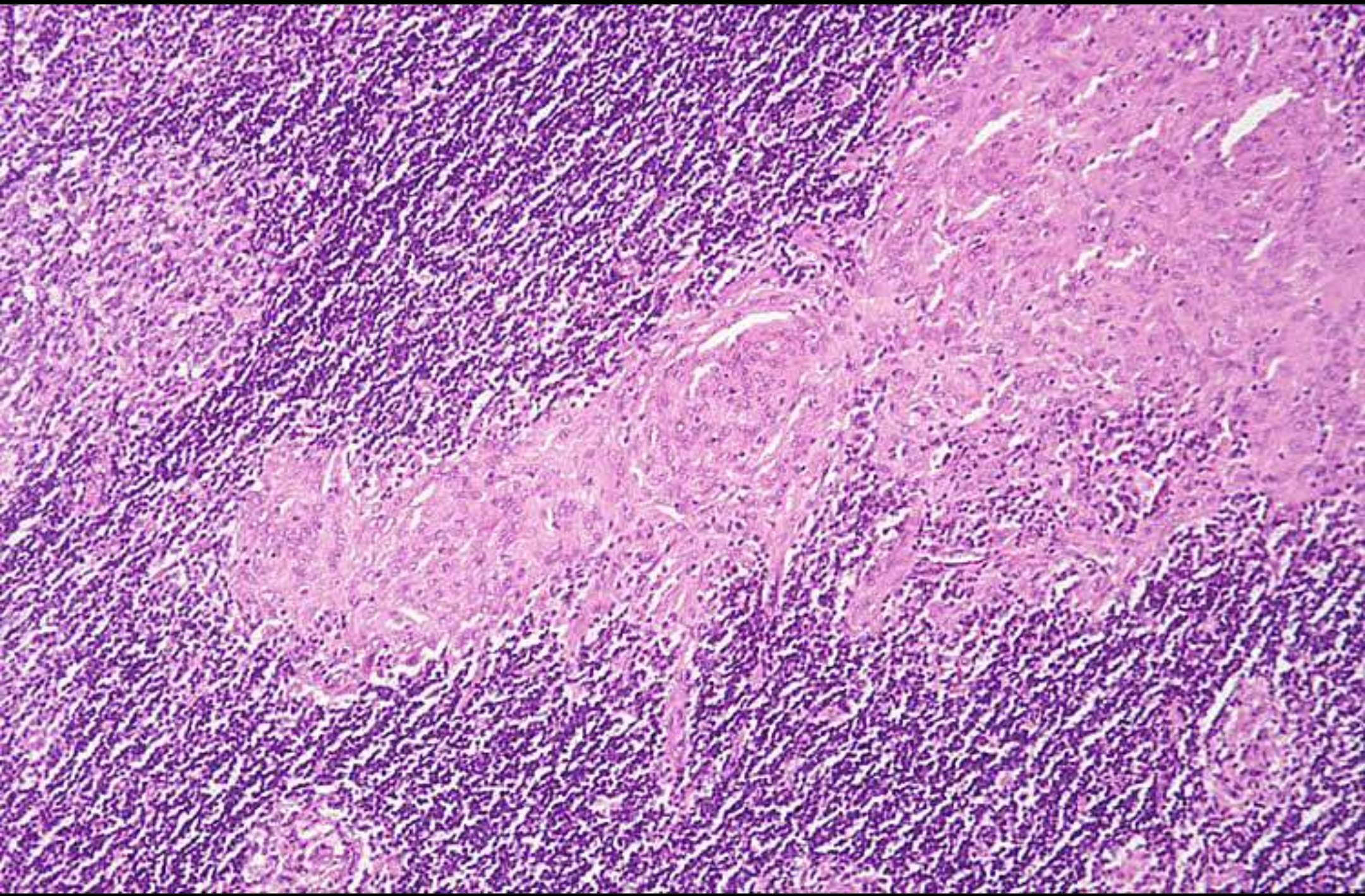

SO-CALLED ANGIOMATOID 'MFH'
DIFFERENTIAL DIAGNOSIS

Aneurysmal benign FH
Diffuse-type giant cell tumour
Organising haematoma
Dendritic cell neoplasm (?)

SO-CALLED ANGIOMATOID 'MFH'

LINE OF DIFFERENTIATION

Currently unknown

Numerous hypotheses over the years

? Myoid / perivascular differentiation

? Fibroblastic reticulum cell (or similar)

SO-CALLED FIBROHISTIOCYTIC TUMOURS

HOW TO AVOID MISINTERPRETATION ?

- Think about clinical context
- Develop understanding of natural history
- Avoid ‘knee-jerk’ response to cytologic atypia or mitoses
- Thoughtful use of immunostains
- Acknowledge uncertainty and, if required, seek consultation