SLide Seminar:

To be GIST or not to be GIST…

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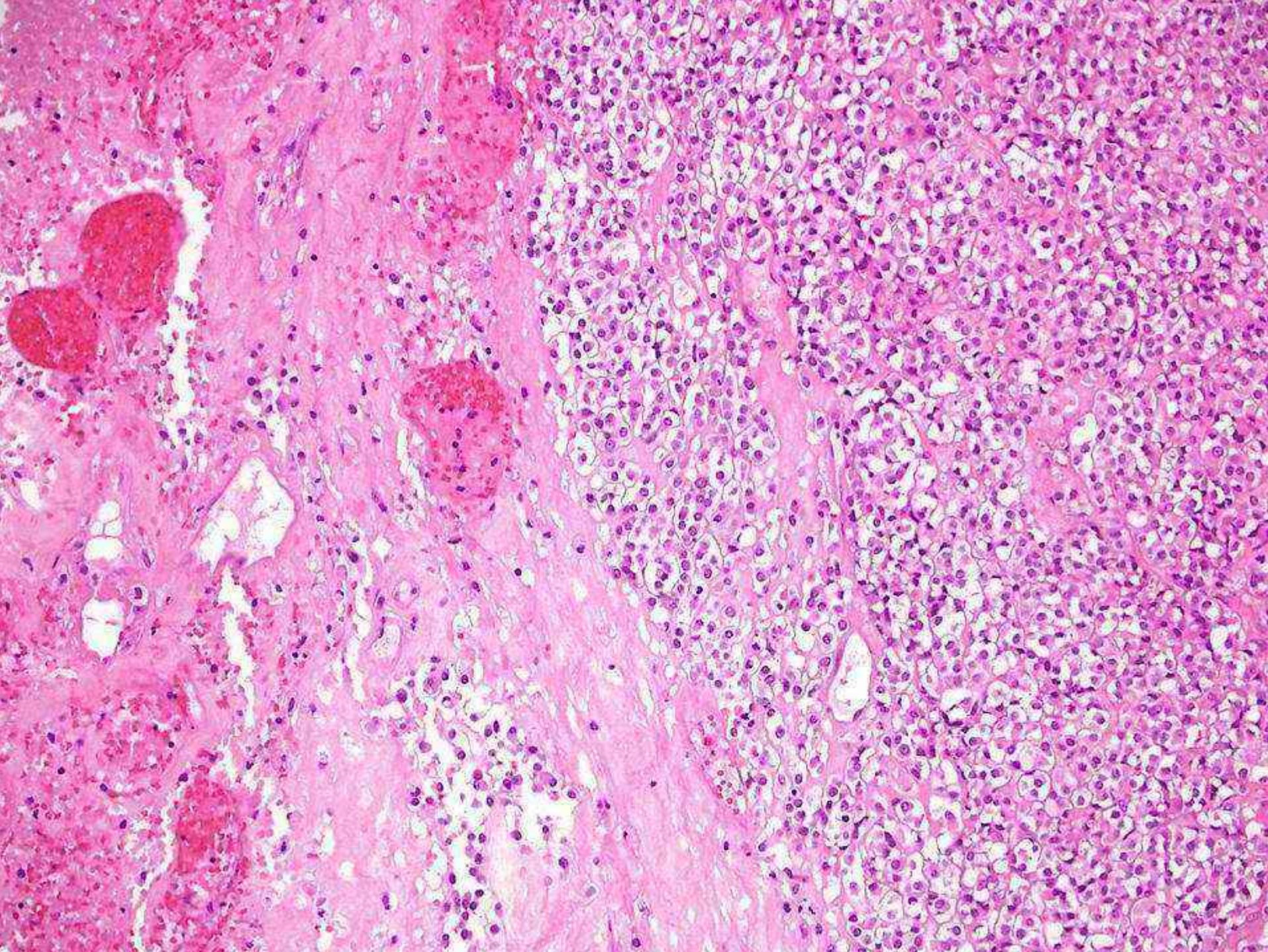
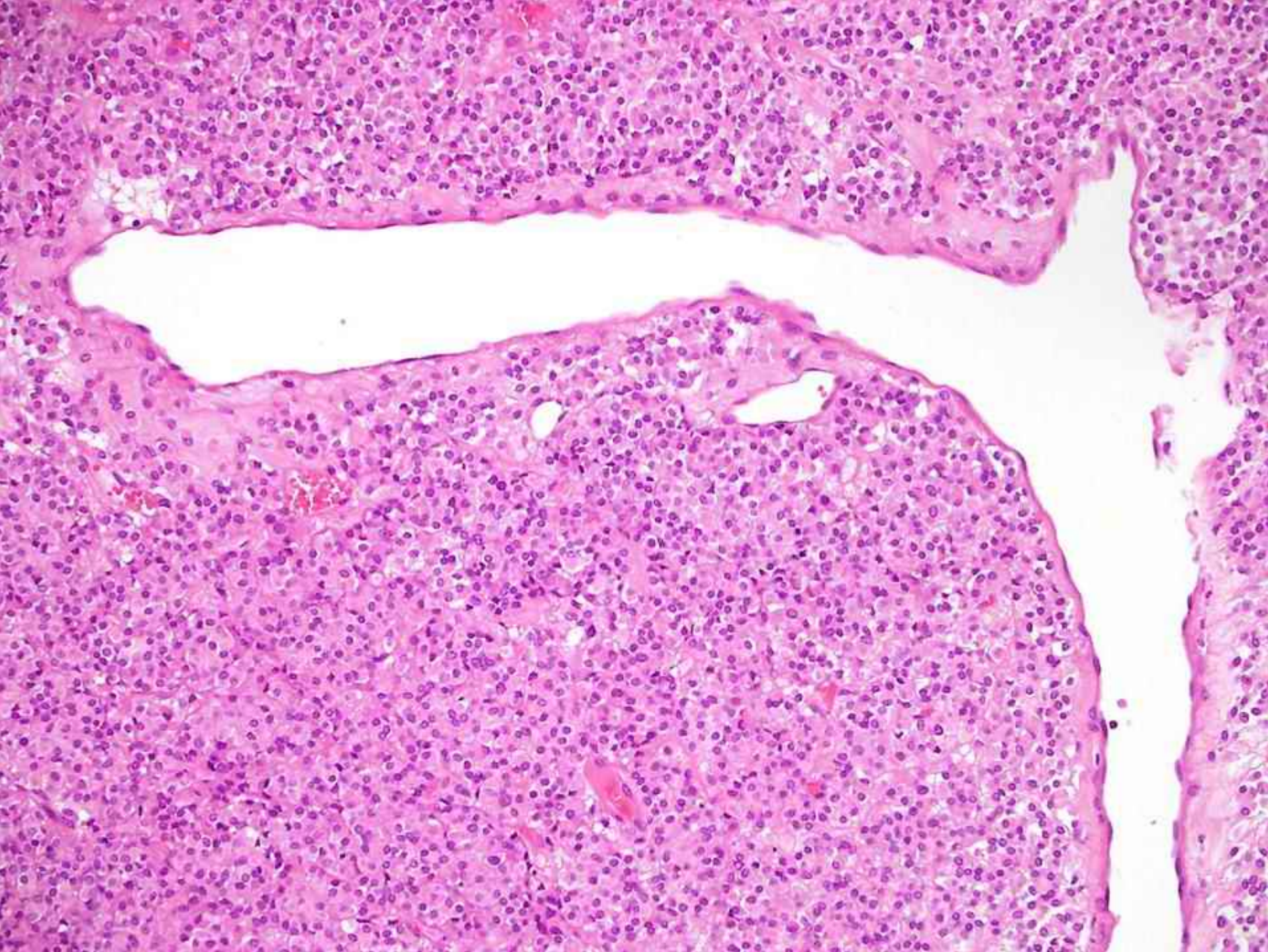
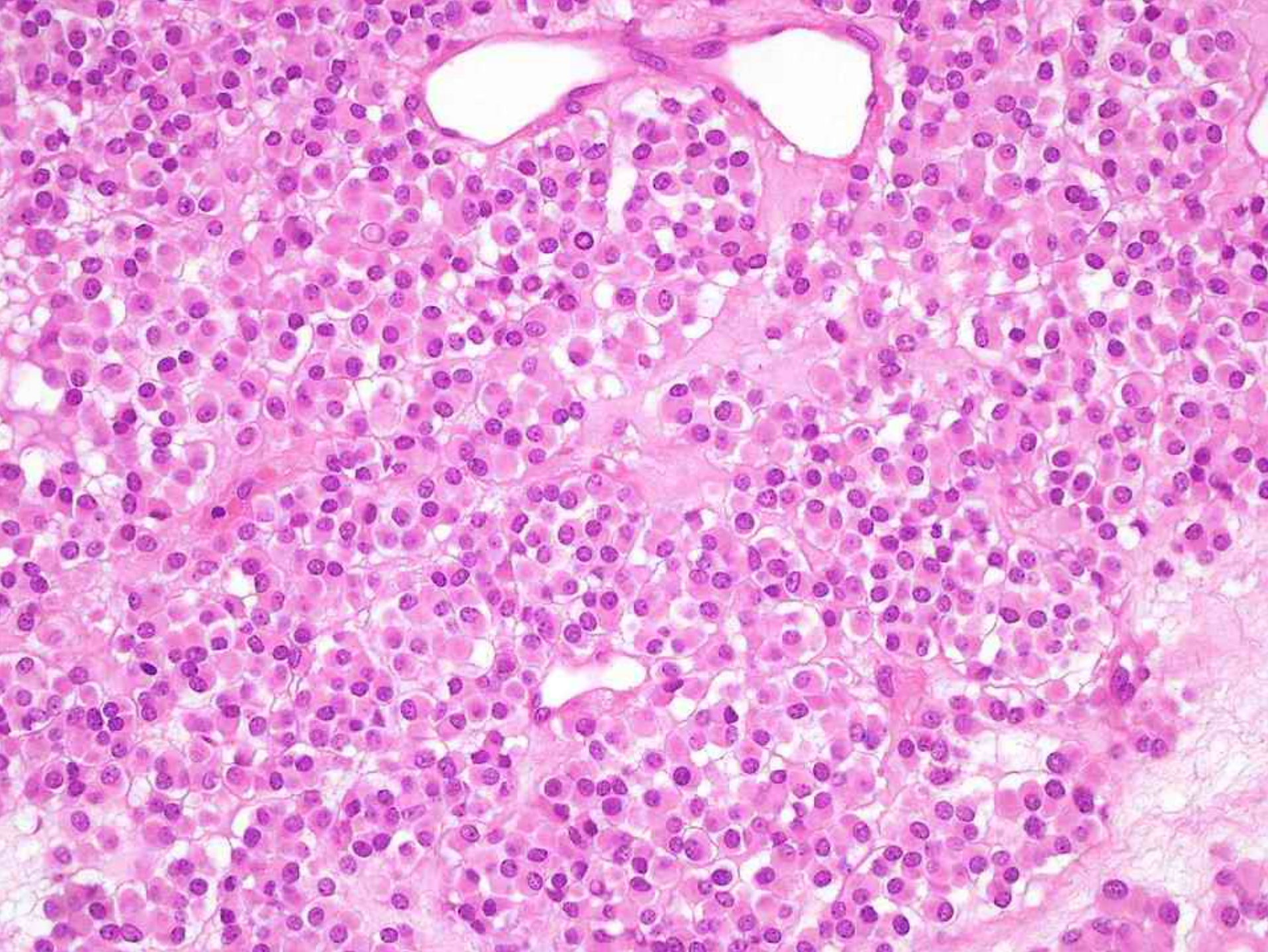
Treviso, ITALY

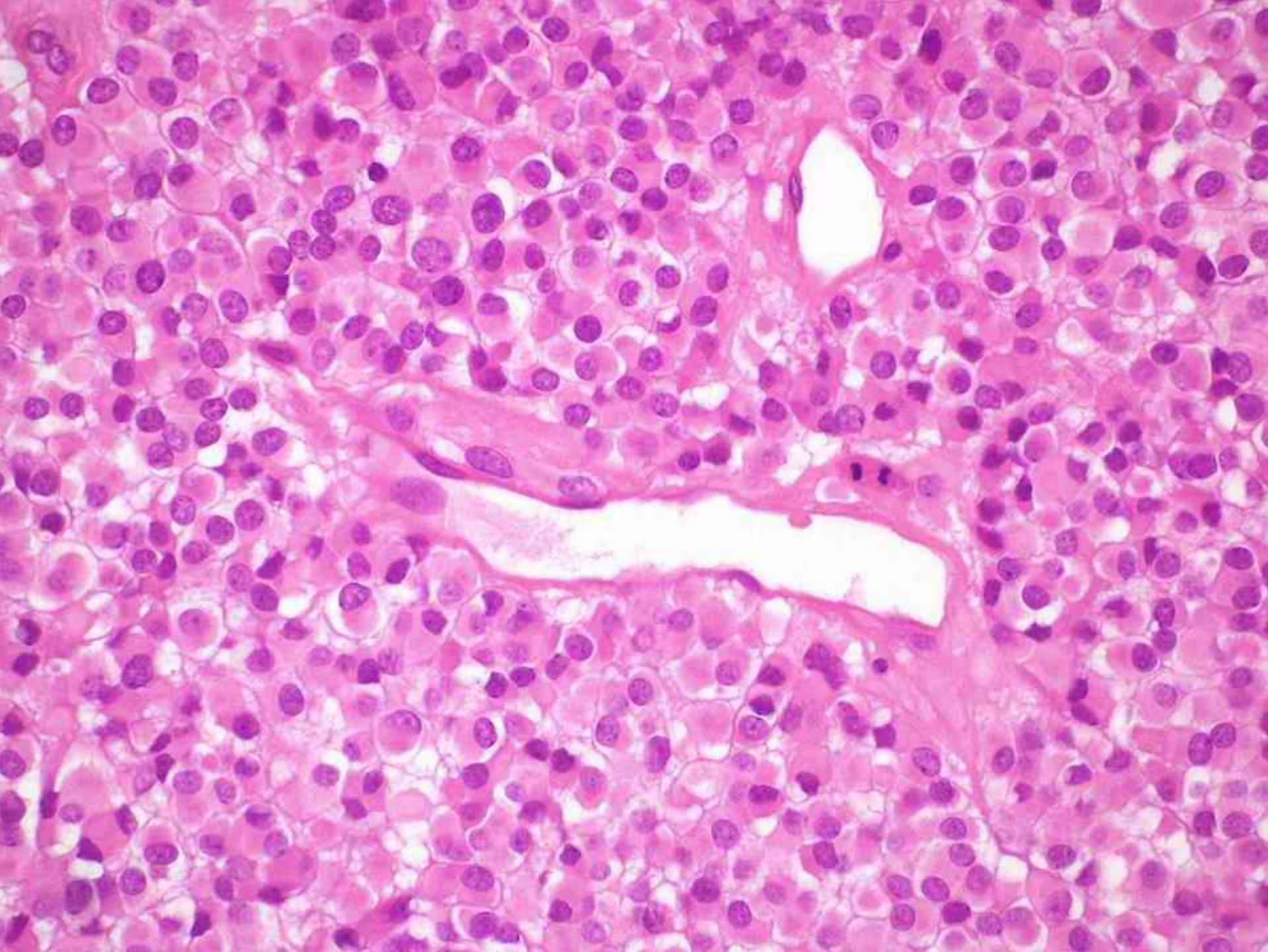
Clinical History

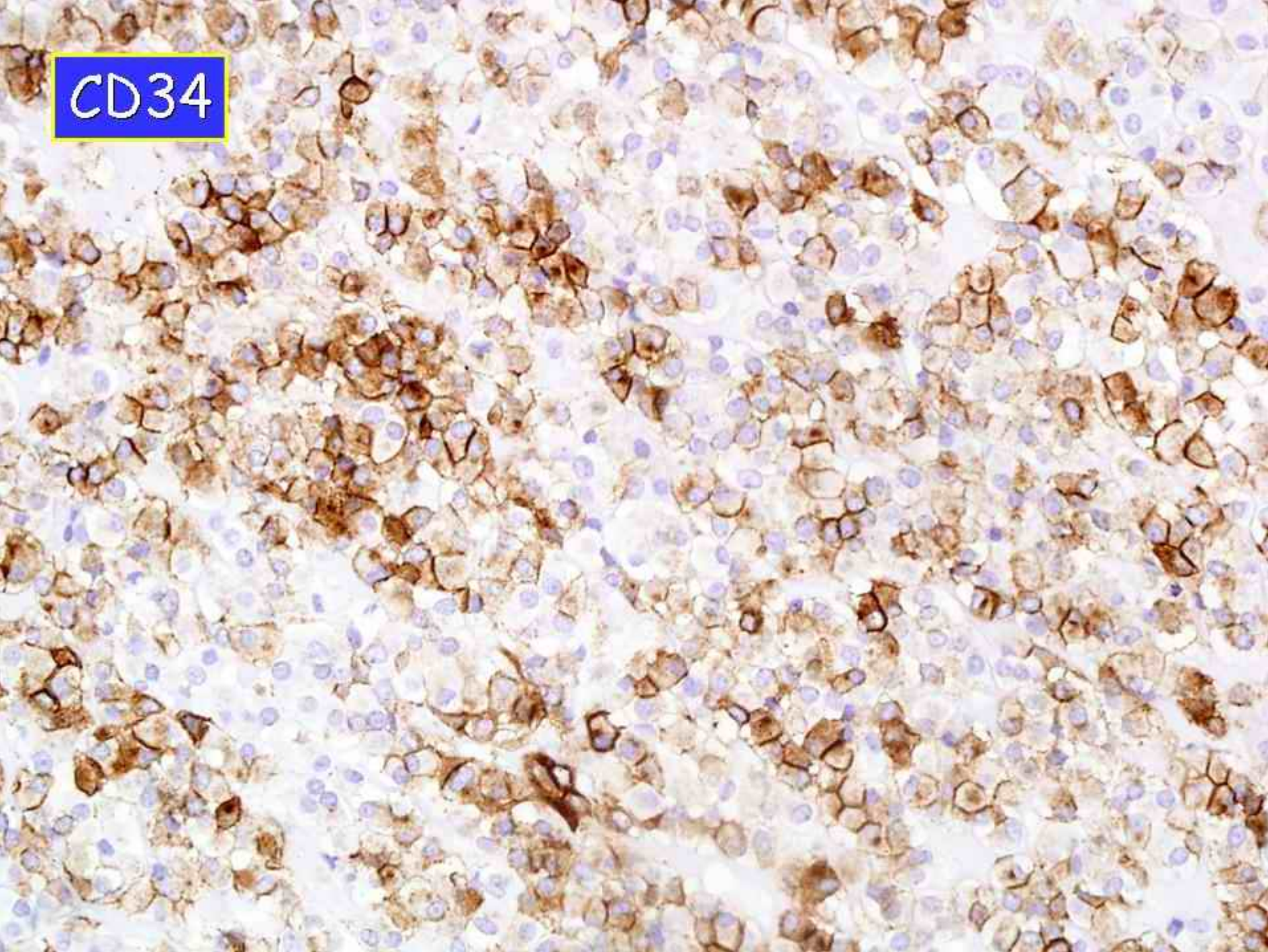
- 57 year old female
- Abdominal pain
- Multiple peritoneal masses

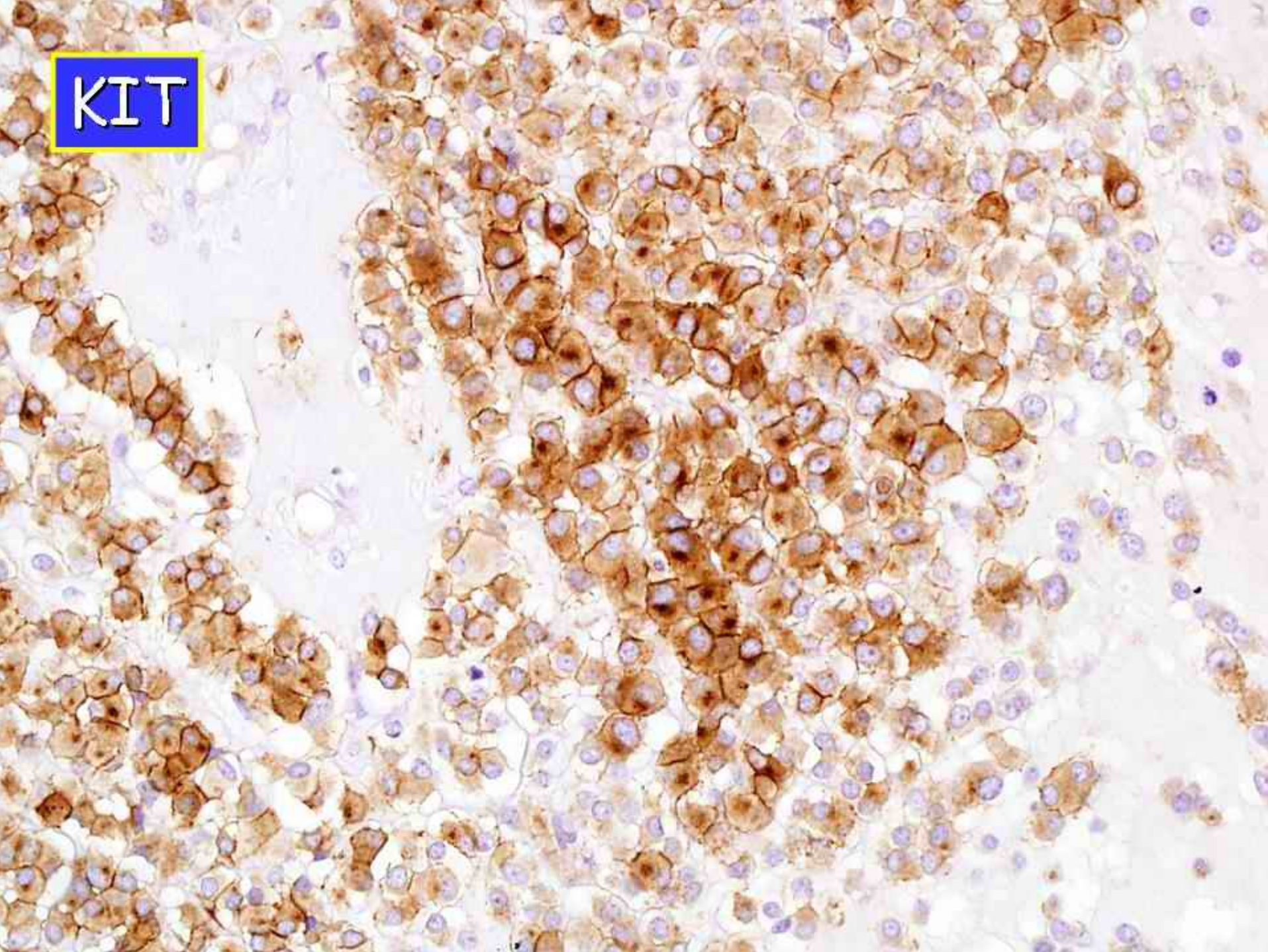


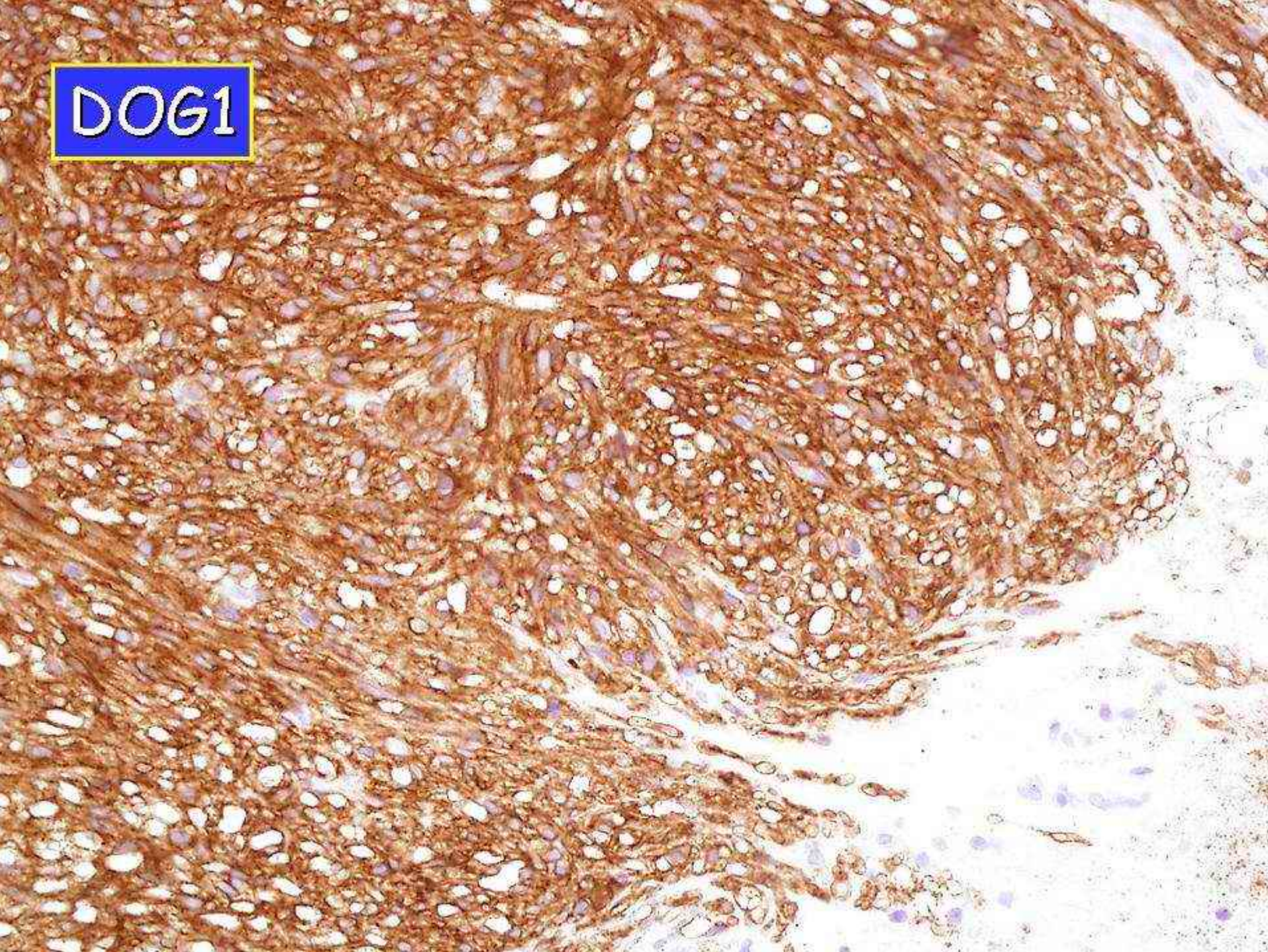






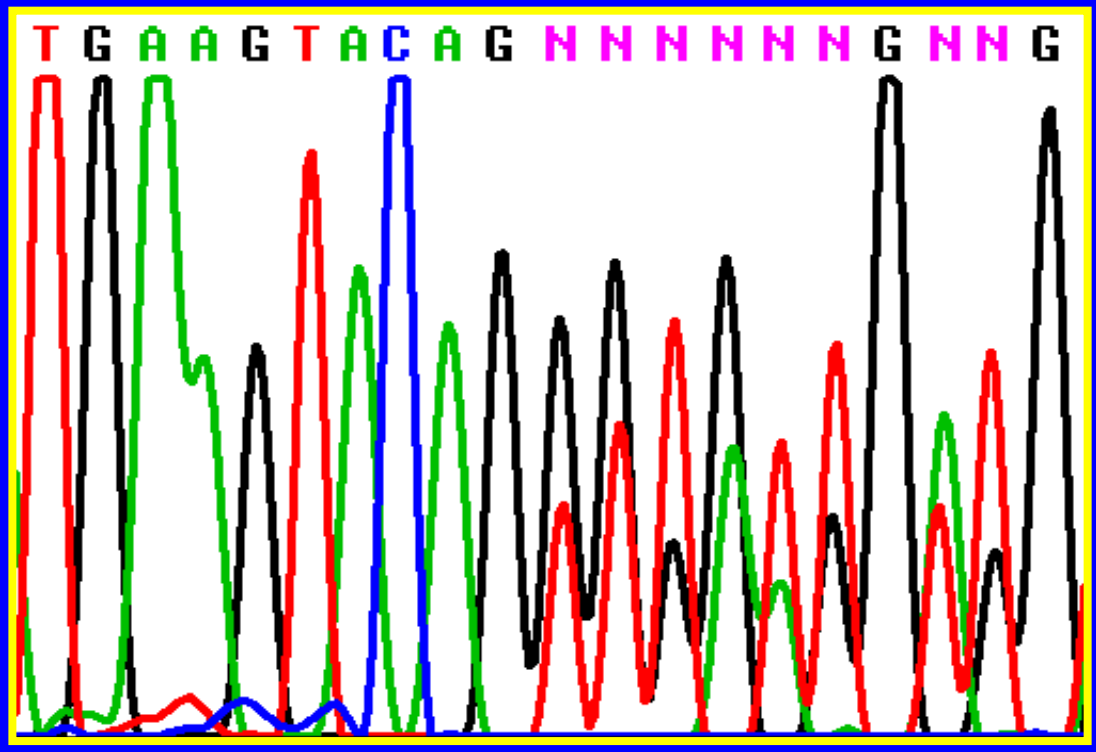

CD34


KIT


DOG1

Diagnosis

Epithelioid GIST



Case 05/15781/B4

Exon 11 del WK 557-558

WT	KPMYEVQWKVVEEING
05/15781/B4	KPMYEVQ--VVEEING

Molecular Classification

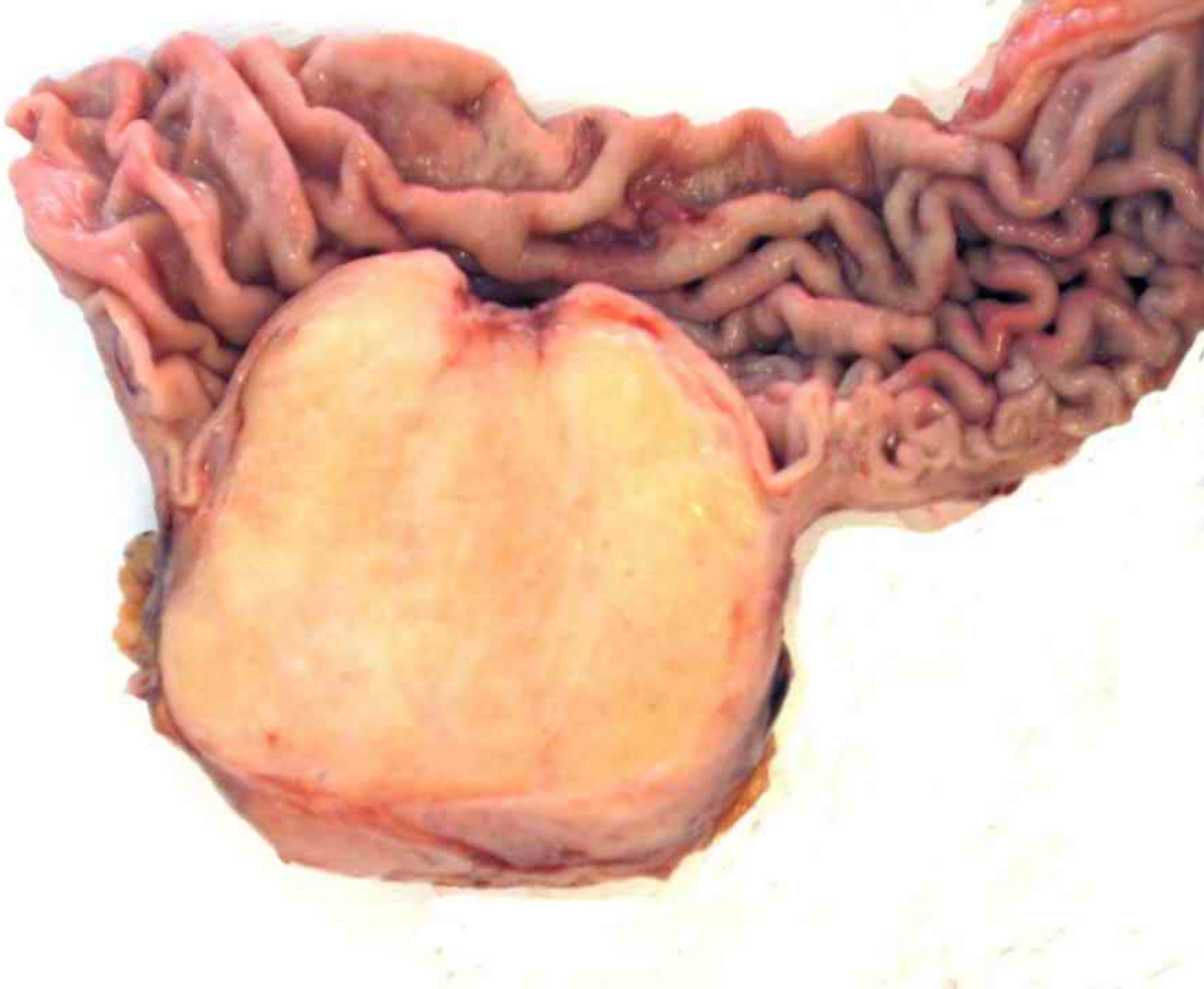
	Frequency	IV sensitivity	Objctive Response	Progressive Disease
KIT Ex 8	< 1%	Yes	-	-
KIT Ex 9	10%	Yes	34-40%	17%
KIT Ex 11	67%	Yes	65-67%	3%
KIT Ex 13	1%	Yes	Rr	-
KIT Ex 14	1%	Yes	Rr	-
PDGFRA 12	1%	Yes	Rr	-
PDGFRA 14	< 1%	Yes	-	-
PDGFRA 18	5%	D842V No	Rr	D842V
Wild Type	12-15%	Yes	23-40%	19%

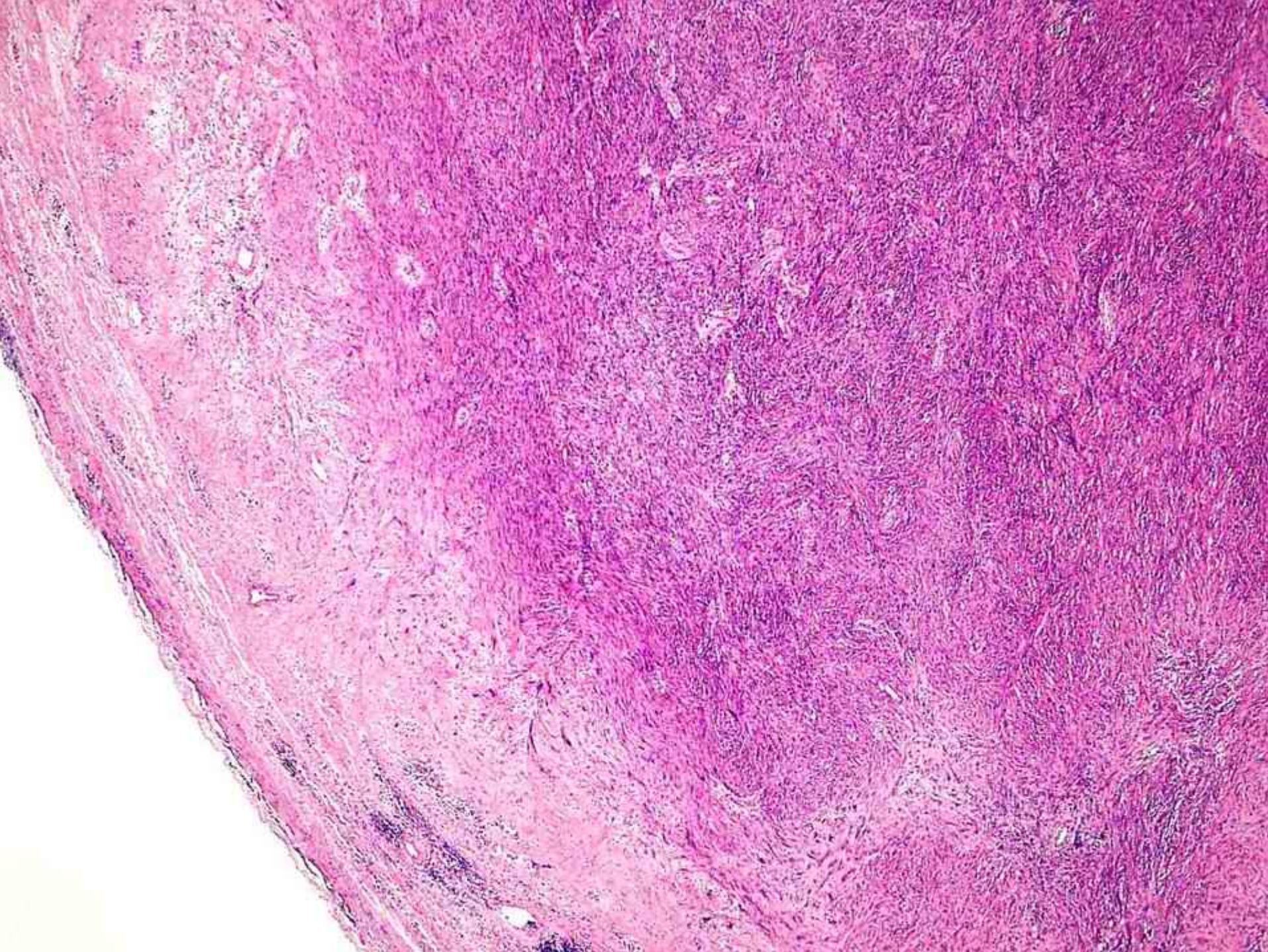
ESMO Guidelines on STT Sarcoma and GIST

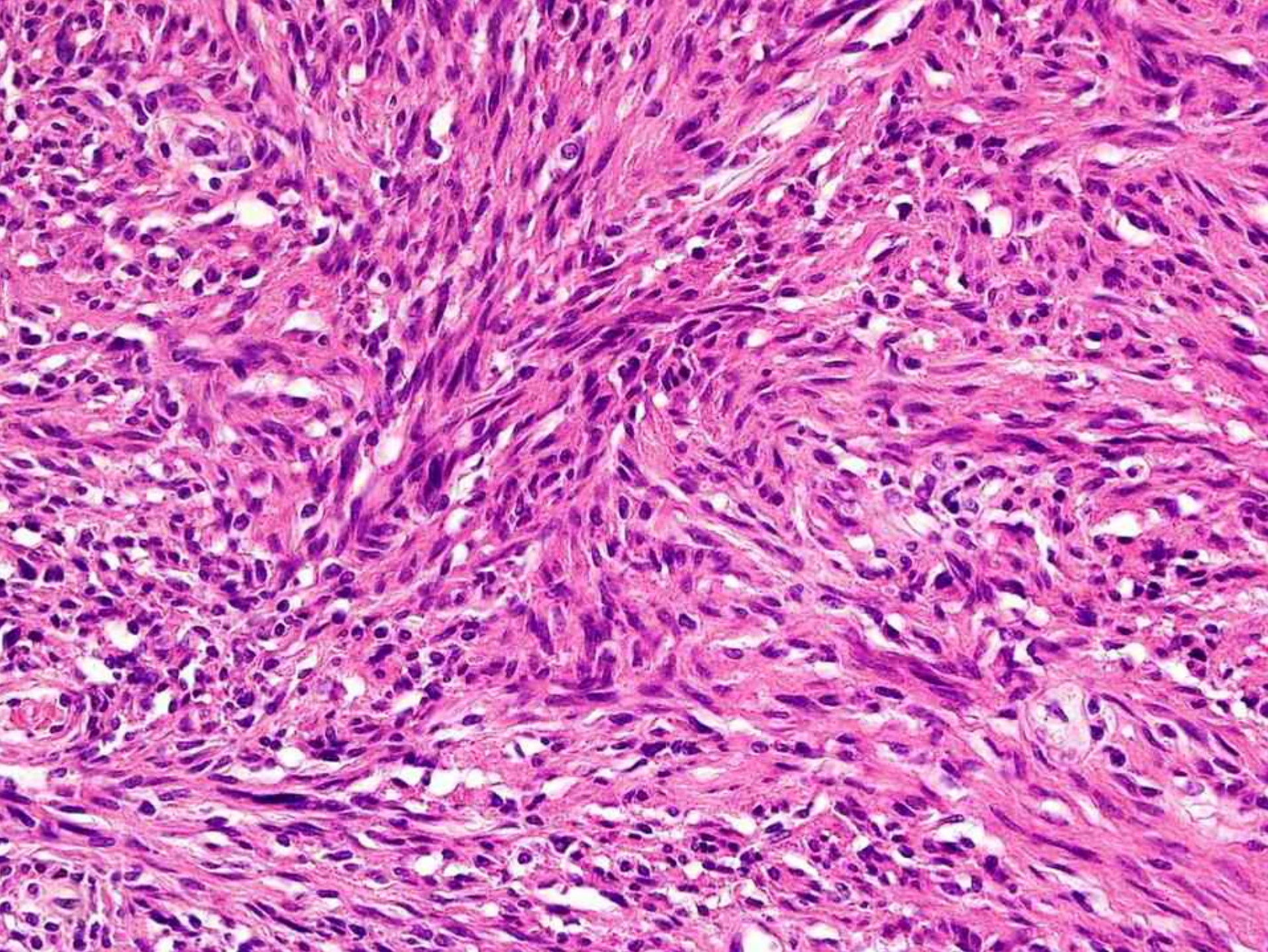
- KIT/PGFRA molecular analysis strongly recommended
- Reference lab
  - Expertise in mesenchymal neoplasm and molecular testing
  - Avoid nice molecular diagnosis on the wrong tumor

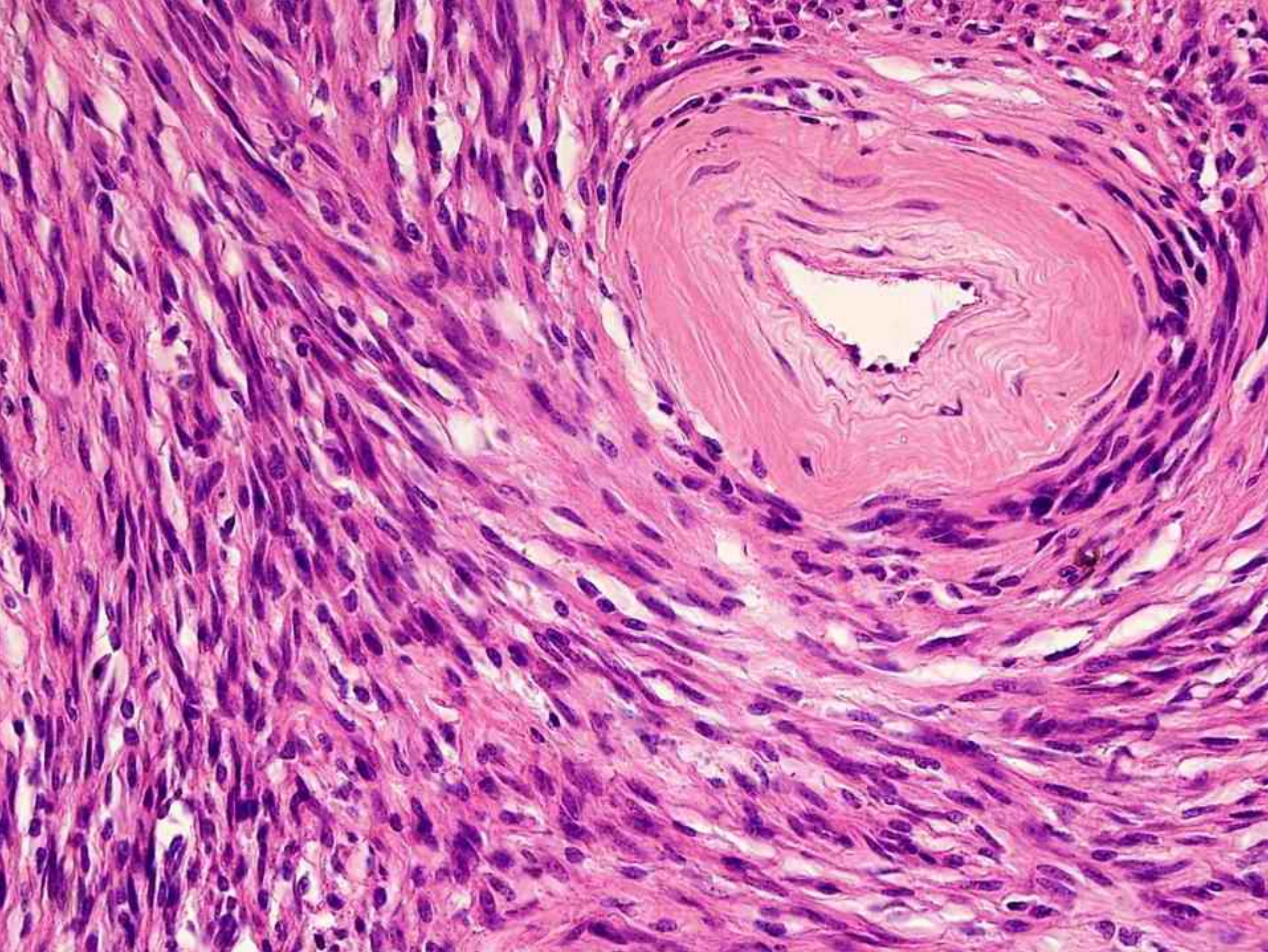
Clinical History

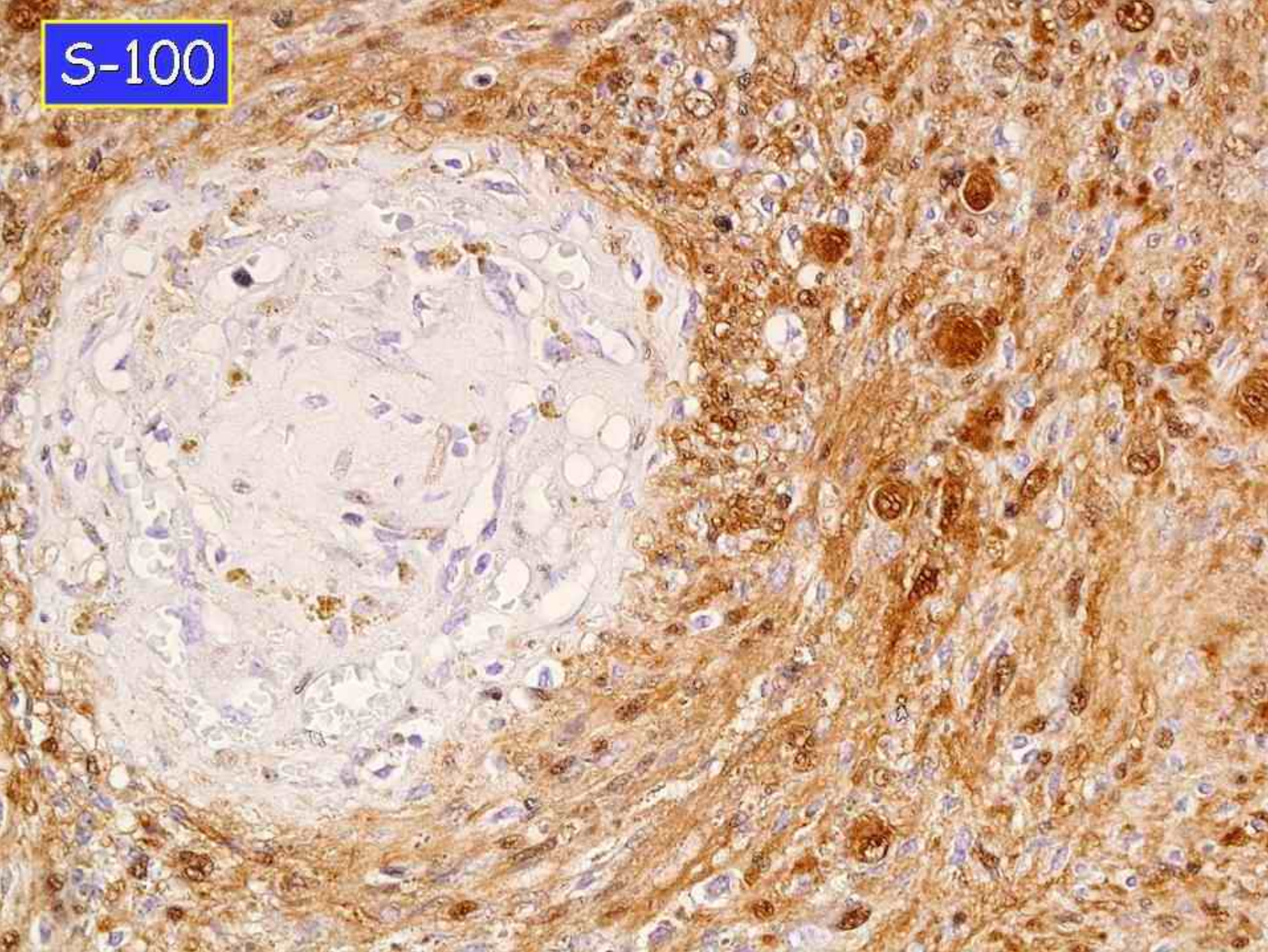
- 46 year old male
- Patient admitted to ER with ematemesis and severe anemia
- 5 cm ulcerated mass in the stomach










S-100

Diagnosis

Cellular Schwannoma

Cellular Schwannoma

- Woodruff, 1981
- Mistaken for sarcoma in 30% of cases
- Retroperitoneum/mediastinum
- Capsulated
- Predominantly Antoni A

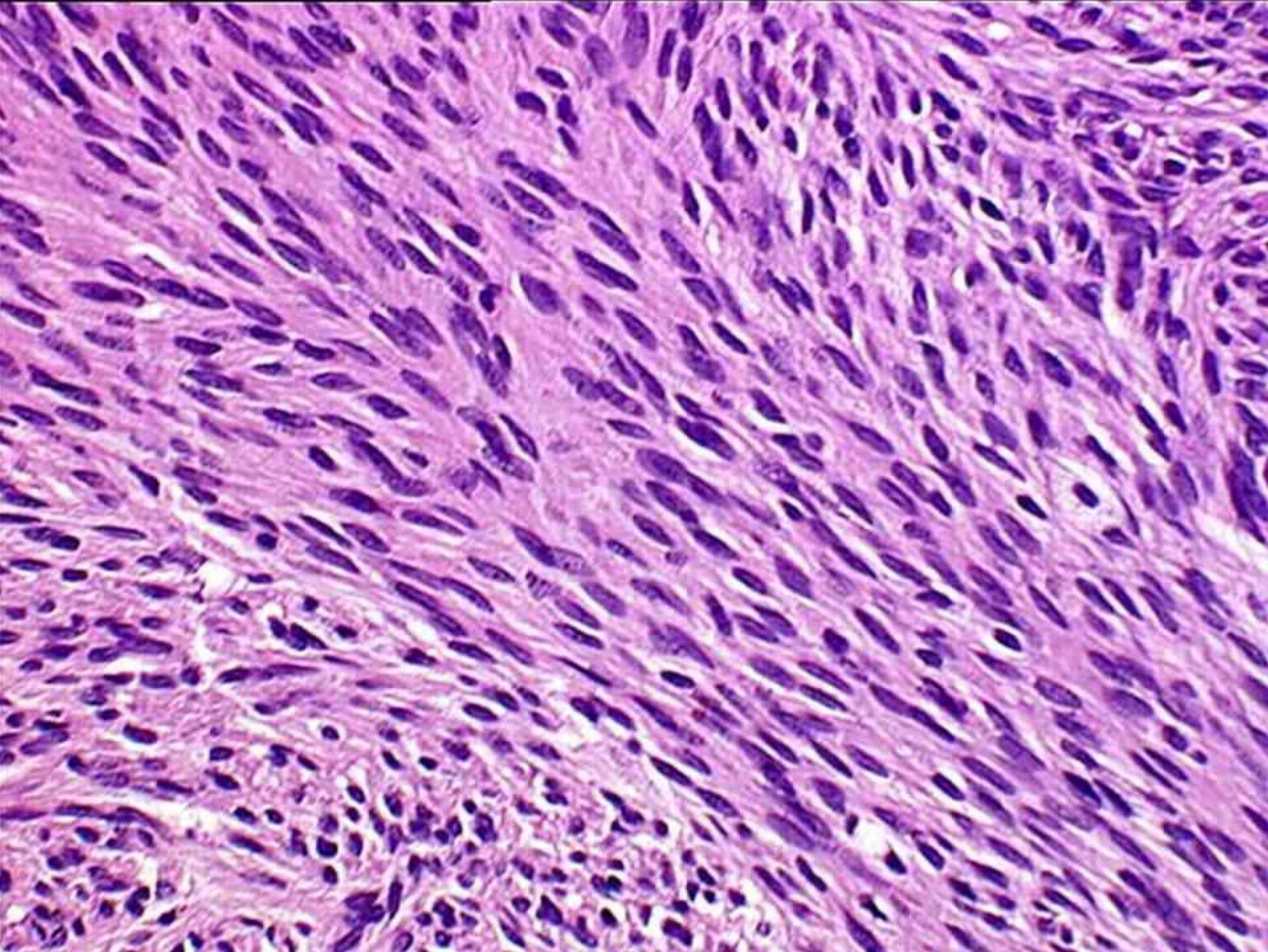
The American Journal of Surgical Pathology
Volume 5 Number 8
December 1981

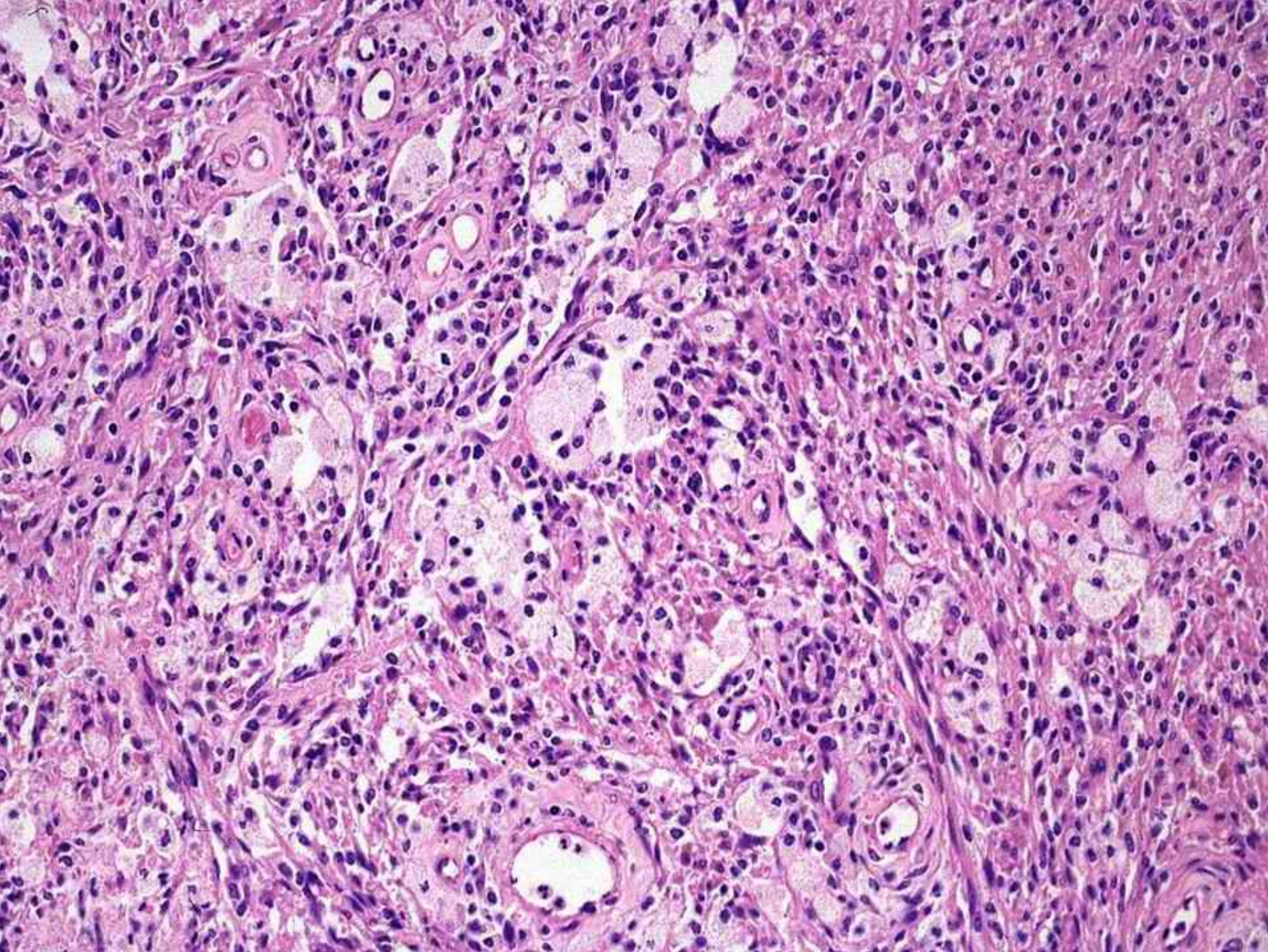
James M. Woodruff, M.D.
Myron Susin, M.D.
Thomas A. Godwin, M.D.
Nael Martini, M.D.
Robert A. Erlandson, Ph.D.

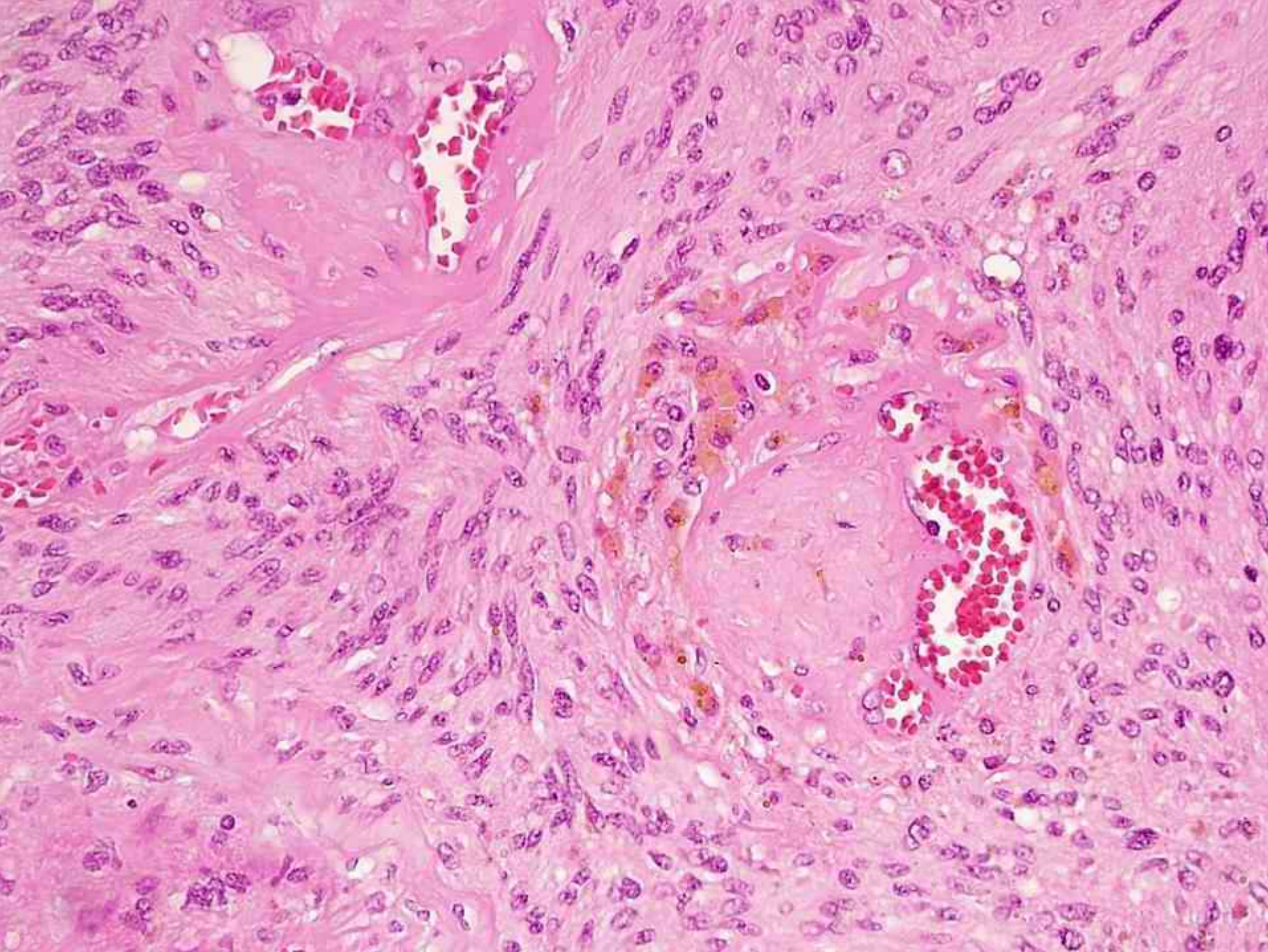
Cellular schwannoma

A variety of schwannoma sometimes mistaken for a malignant tumor


METRIC 1
2

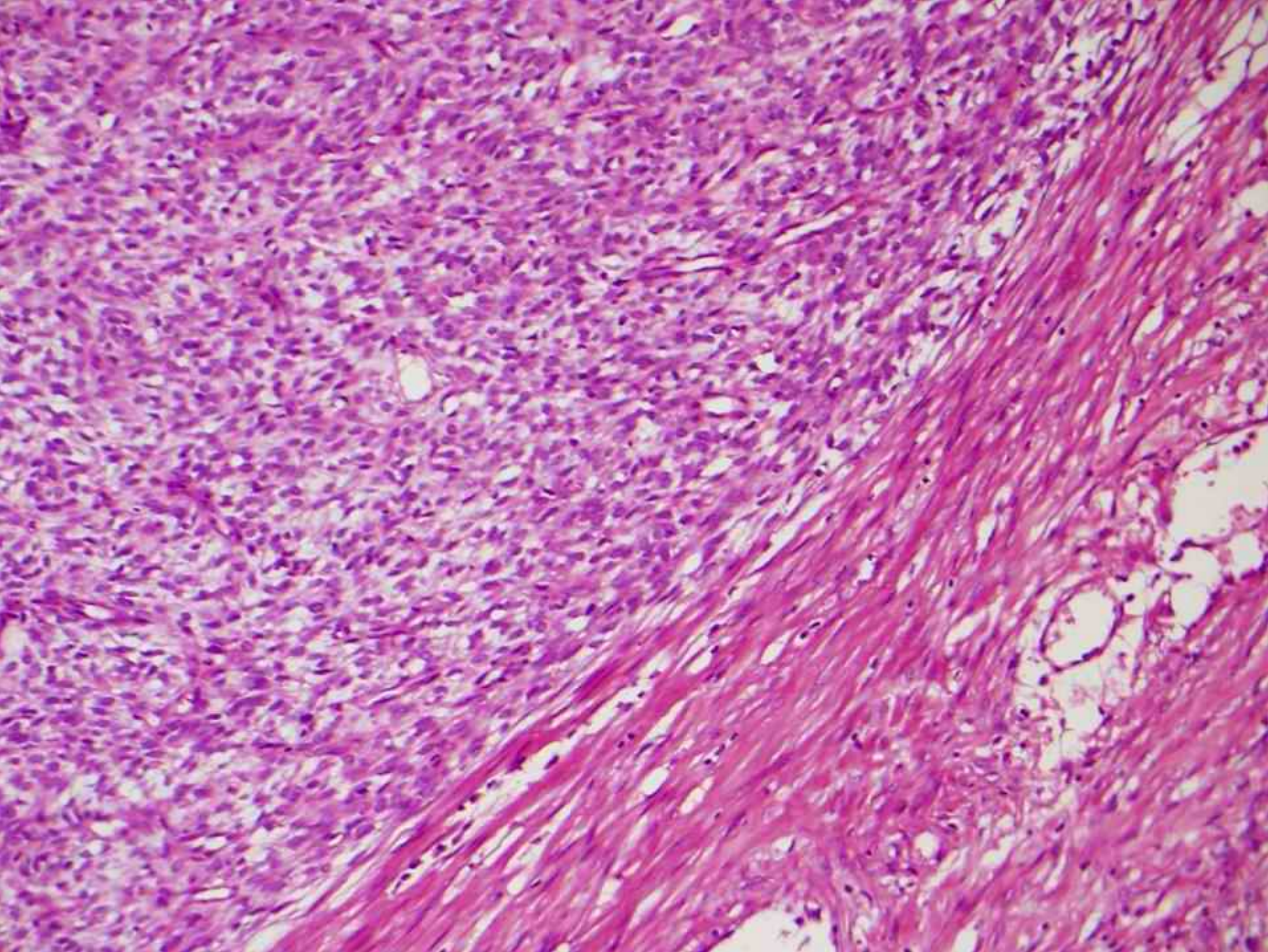


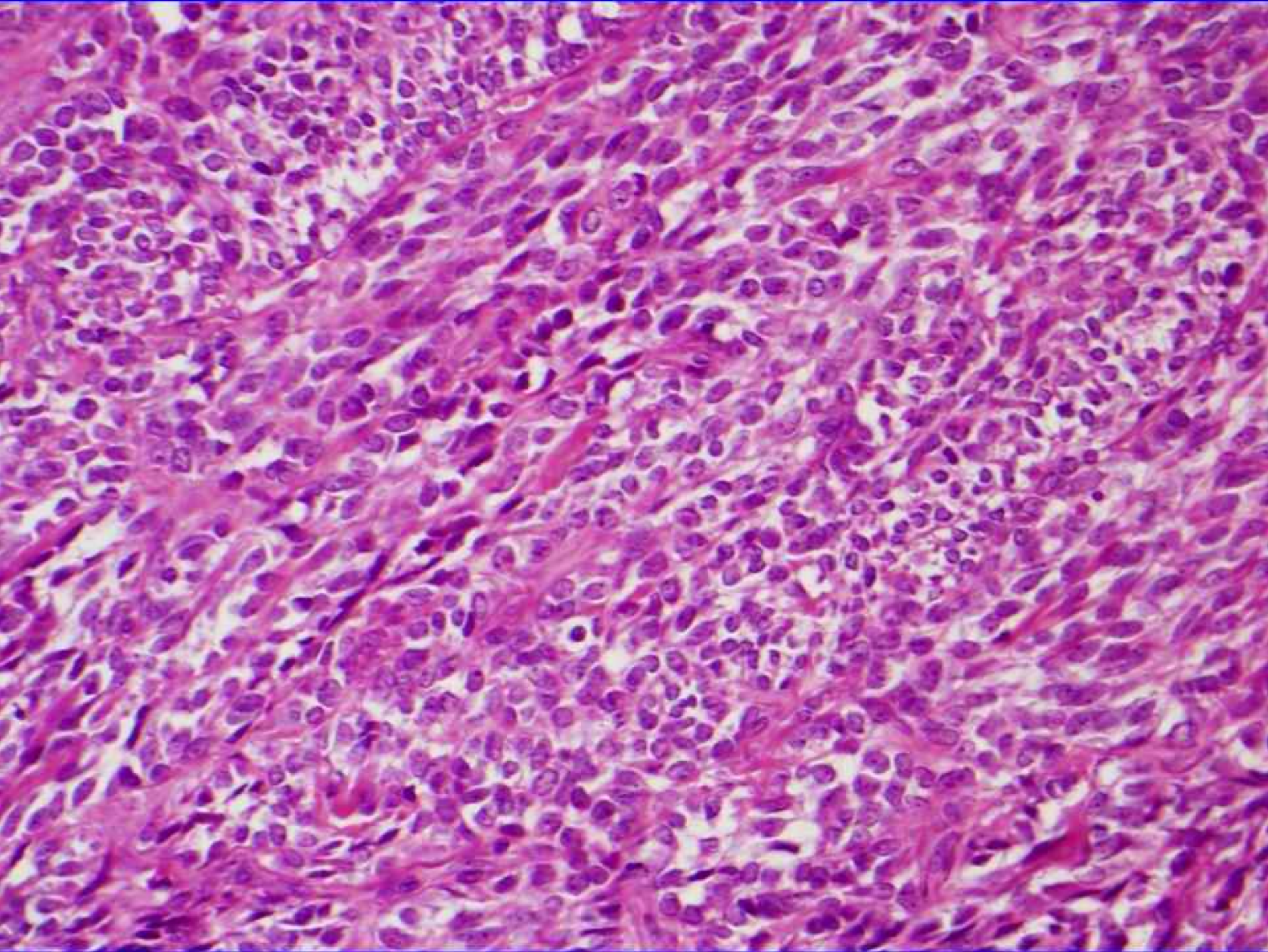


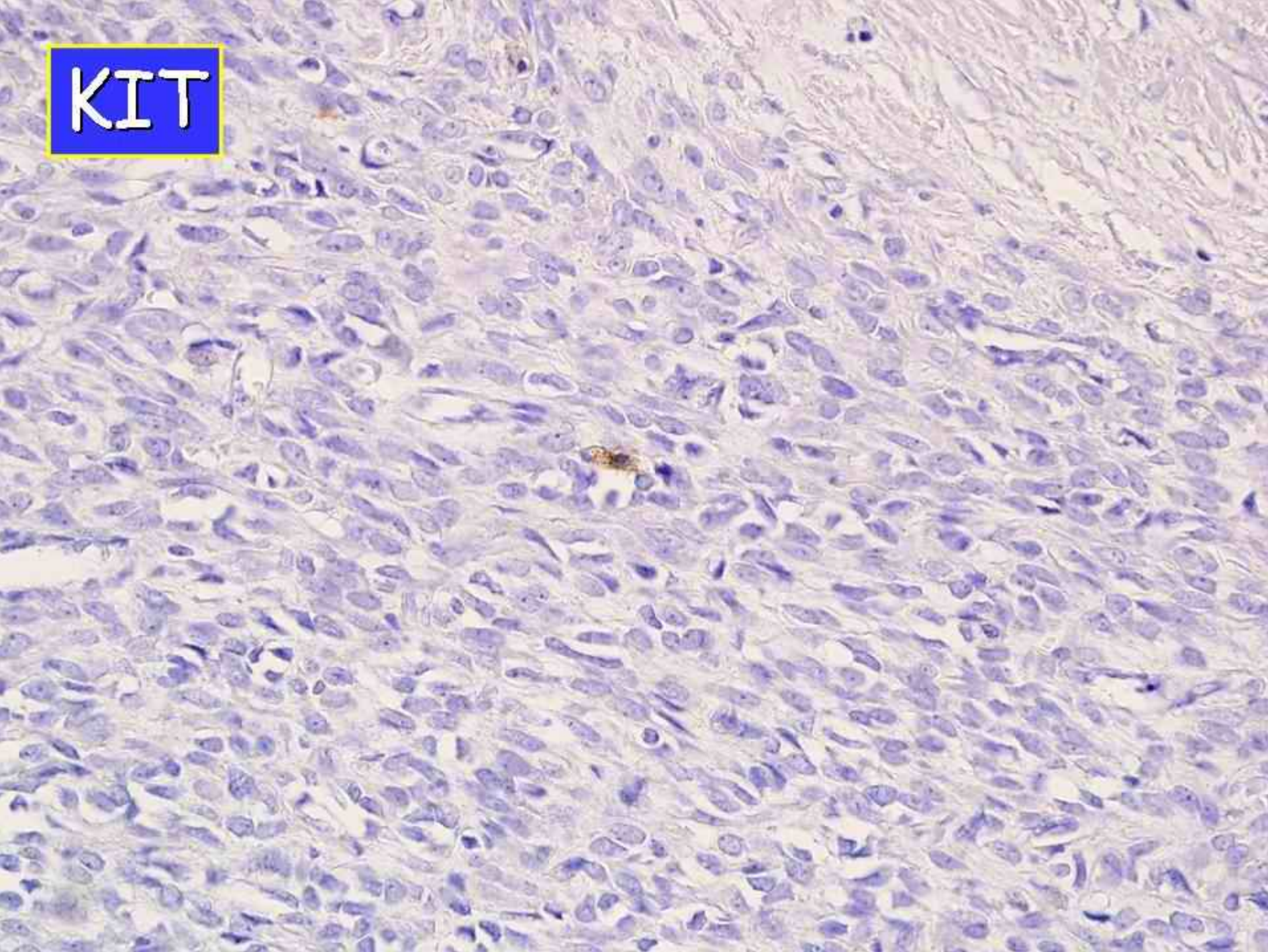


Clinical History

- 51 year old female
- Duodenal mass
- Diagnosed as GIST and put on Imatinib
- Tumor progression
- Dose escalation to 800 mg
- Second opinion required



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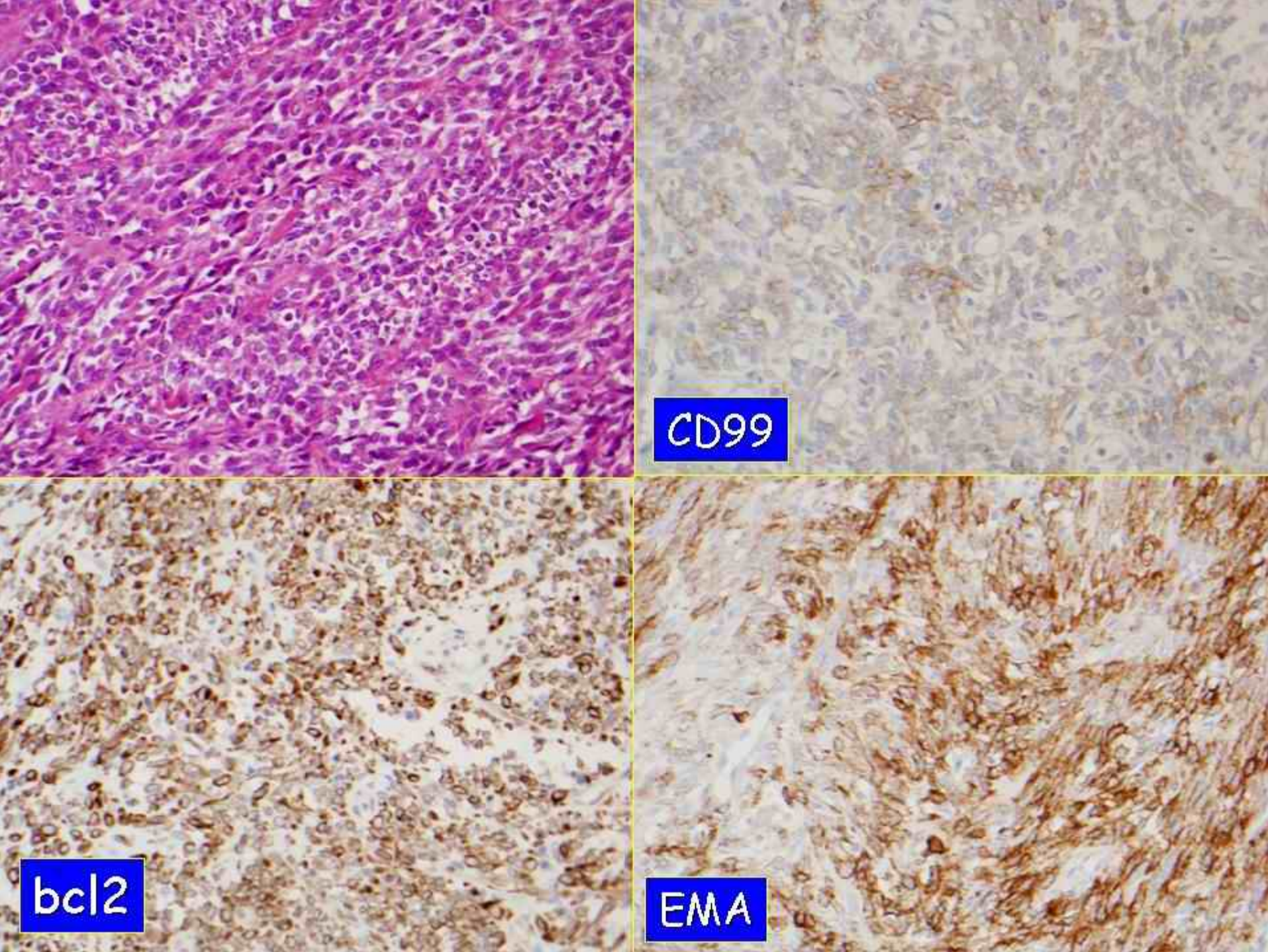
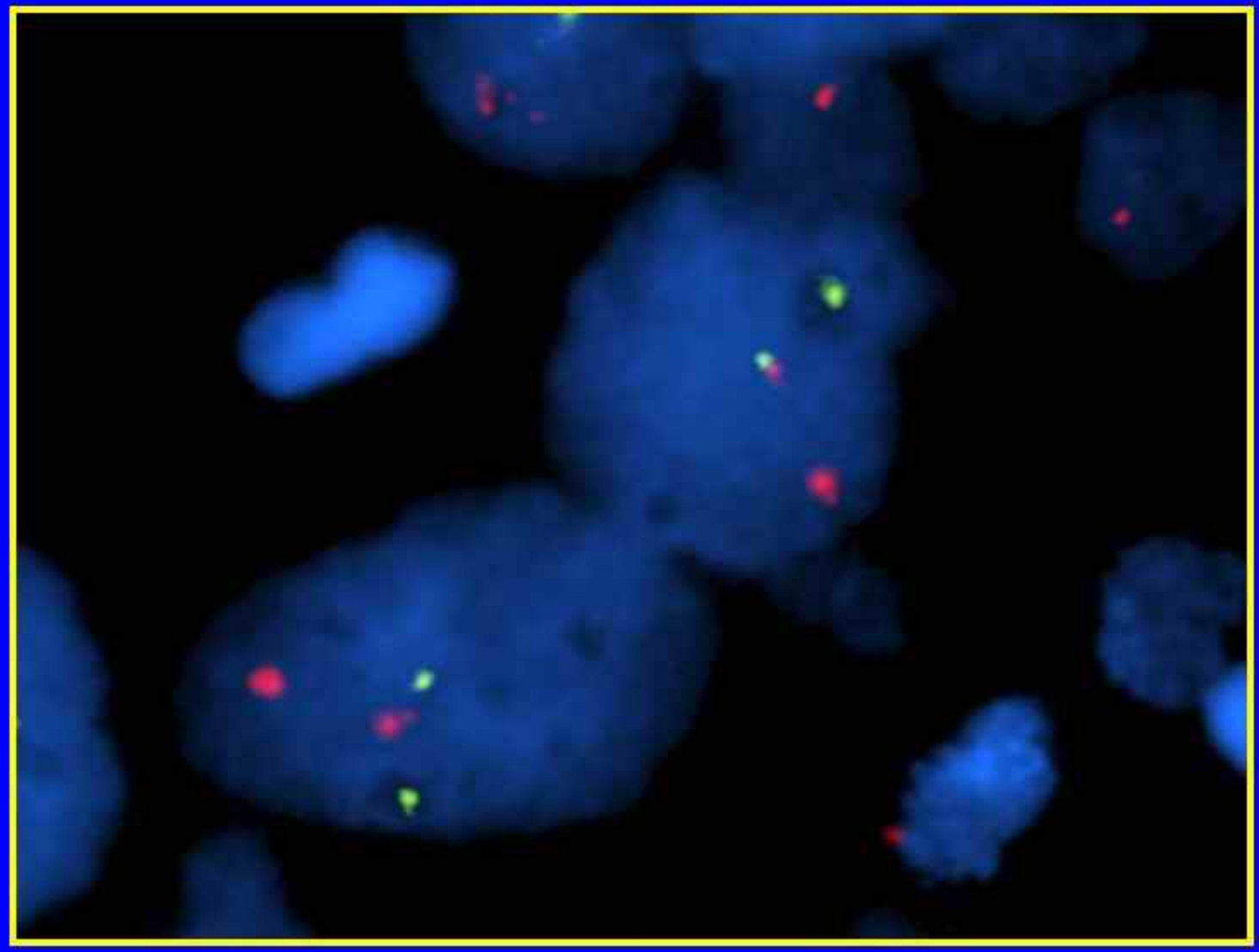

CD99
bcl2
EMA

Interphase FISH: SYT rearrangement



Diagnosis

Synovial Sarcoma

Synovial Sarcoma

- 10% of ST sarcomas
- Young adults
- Lower Limbs/head & neck/mediastinum
- Males > females
- Monophasic spindle cell/epithelial
- Biphasic

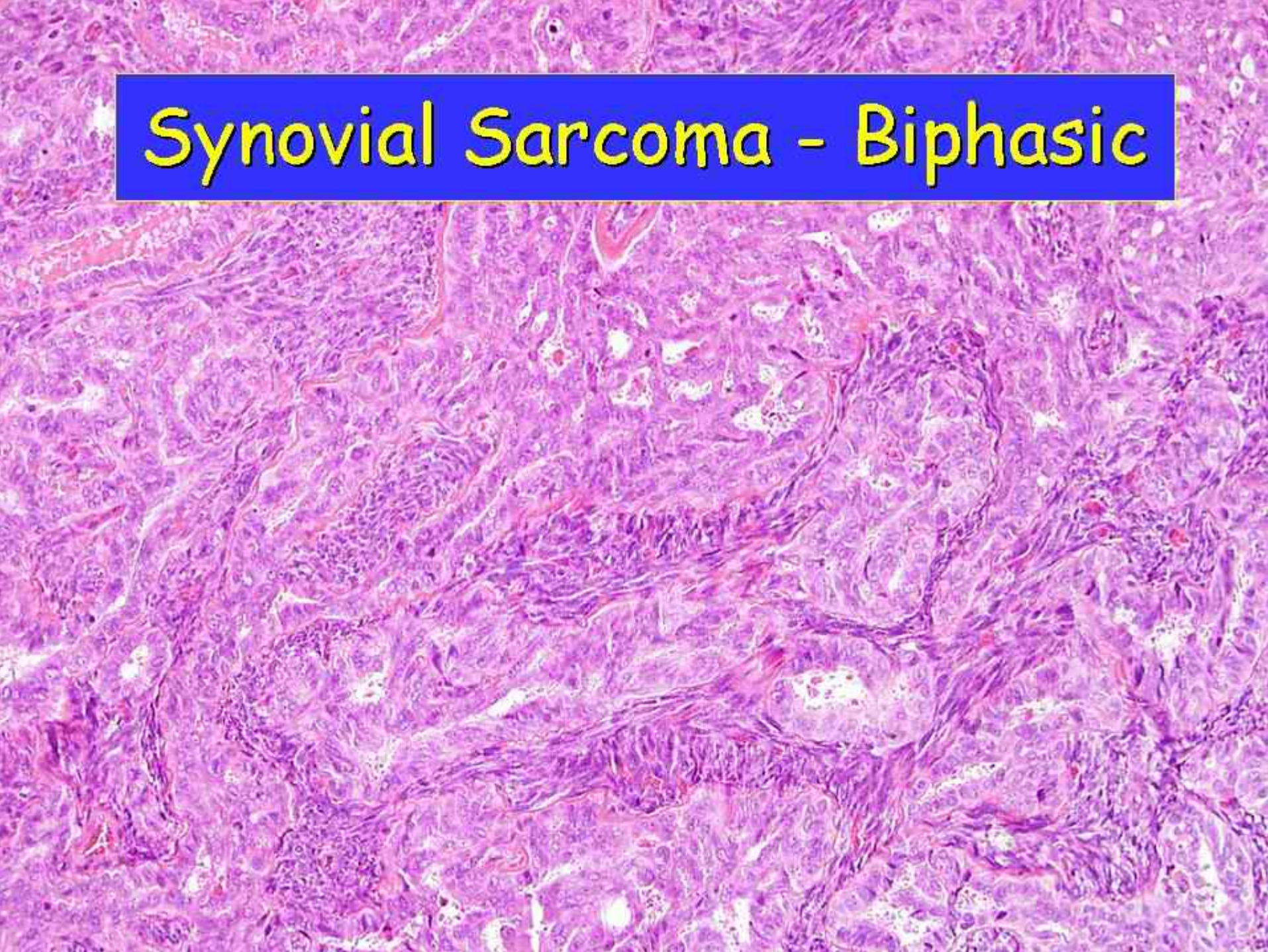
Synovial Sarcoma: classic types

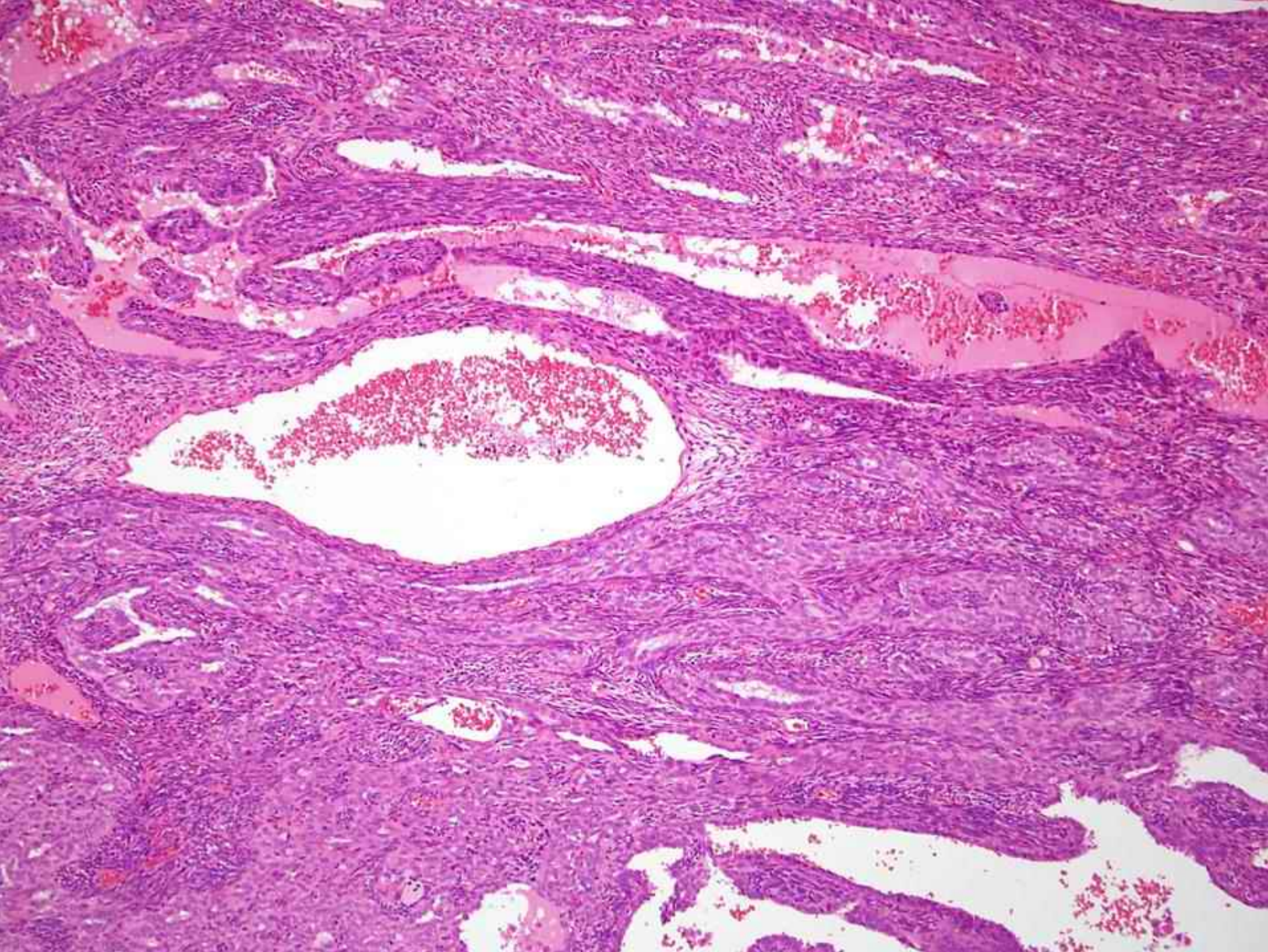
- Monophasic spindle cell and biphasic
- Spindle cells/collagenous background
- HPC-like vascular pattern
- Gland-like structures

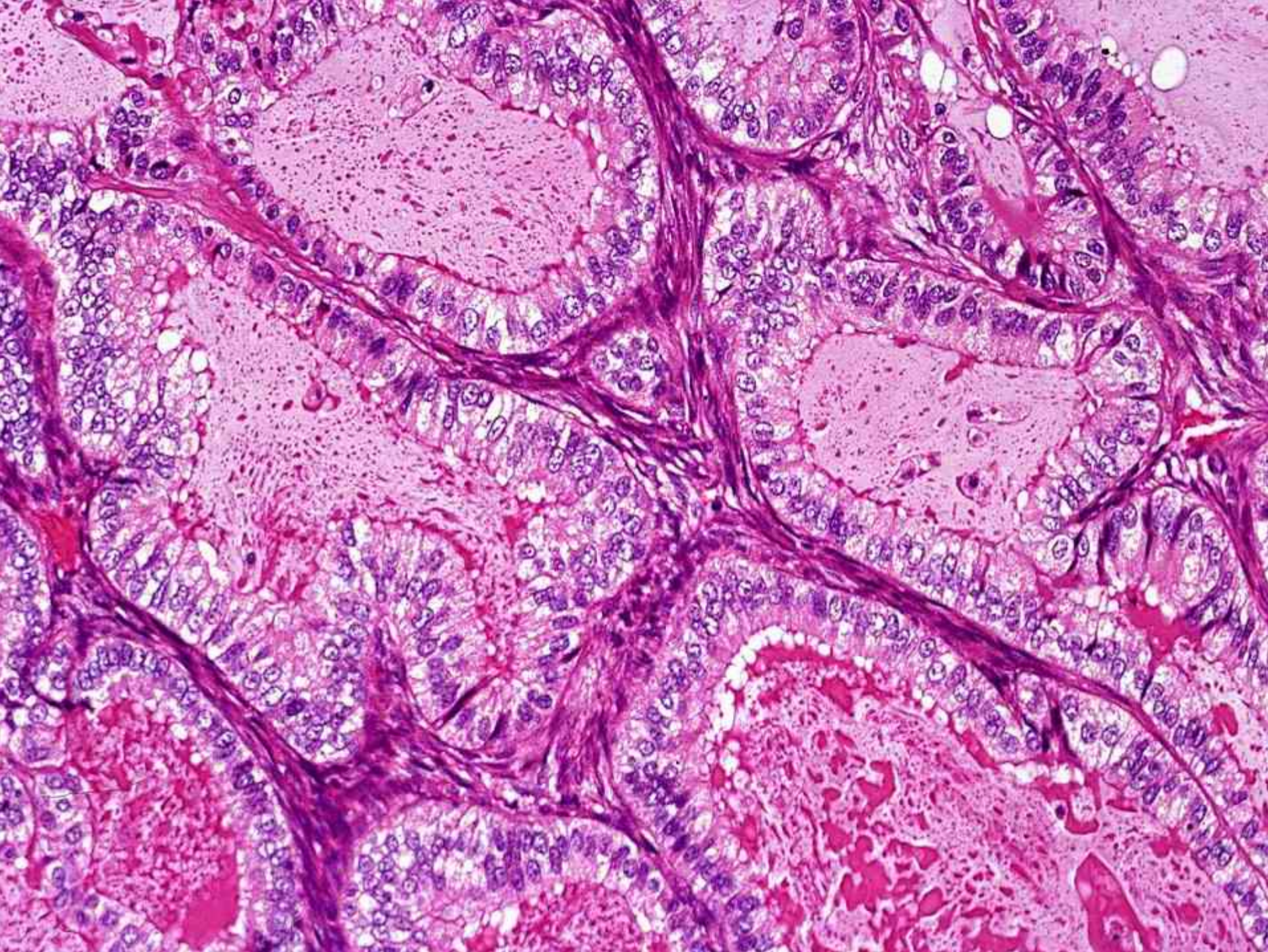
Synovial Sarcoma

Synovial Sarcoma

Synovial Sarcoma - Biphasic





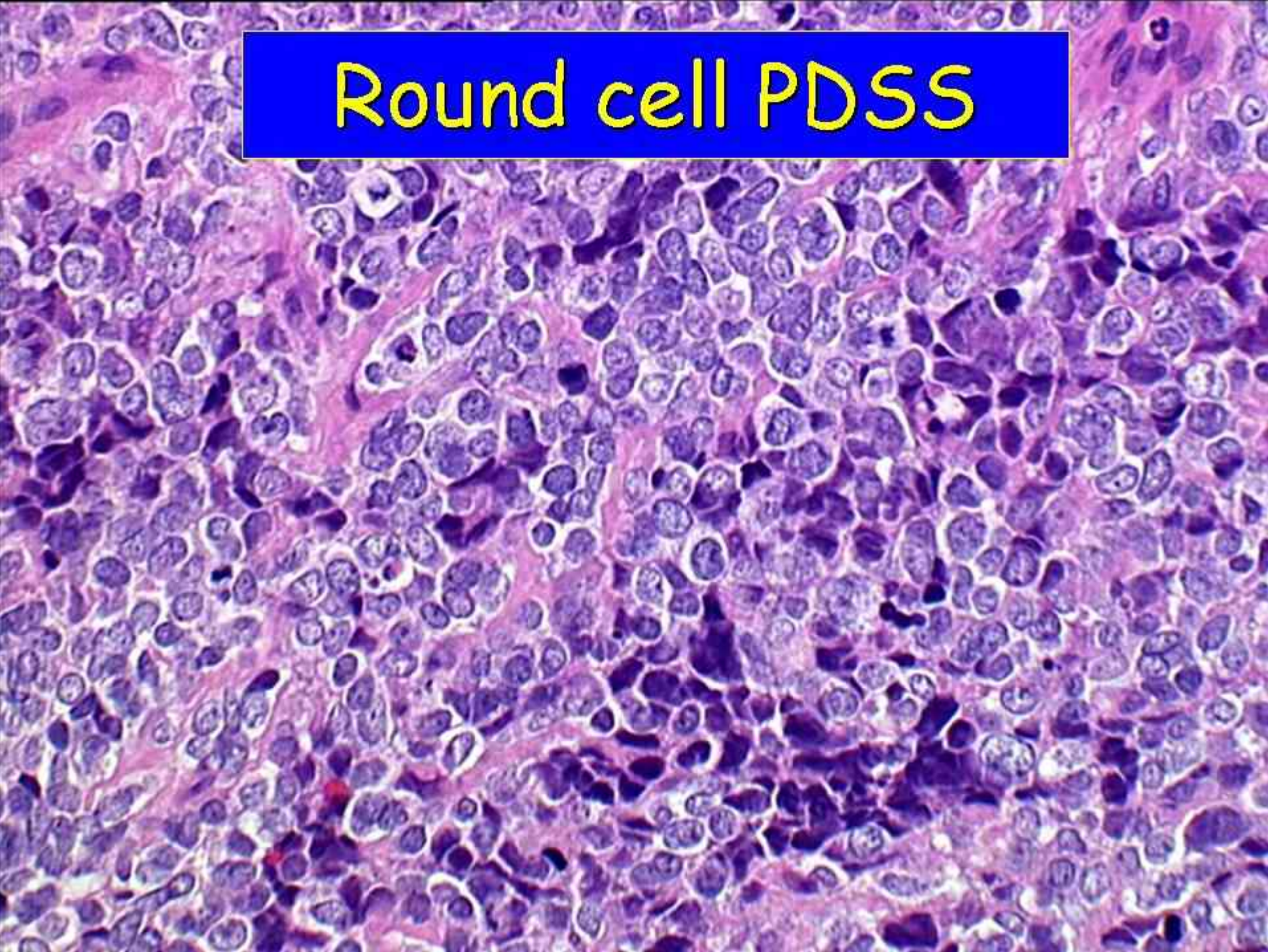



Synovial Sarcoma - monophasic

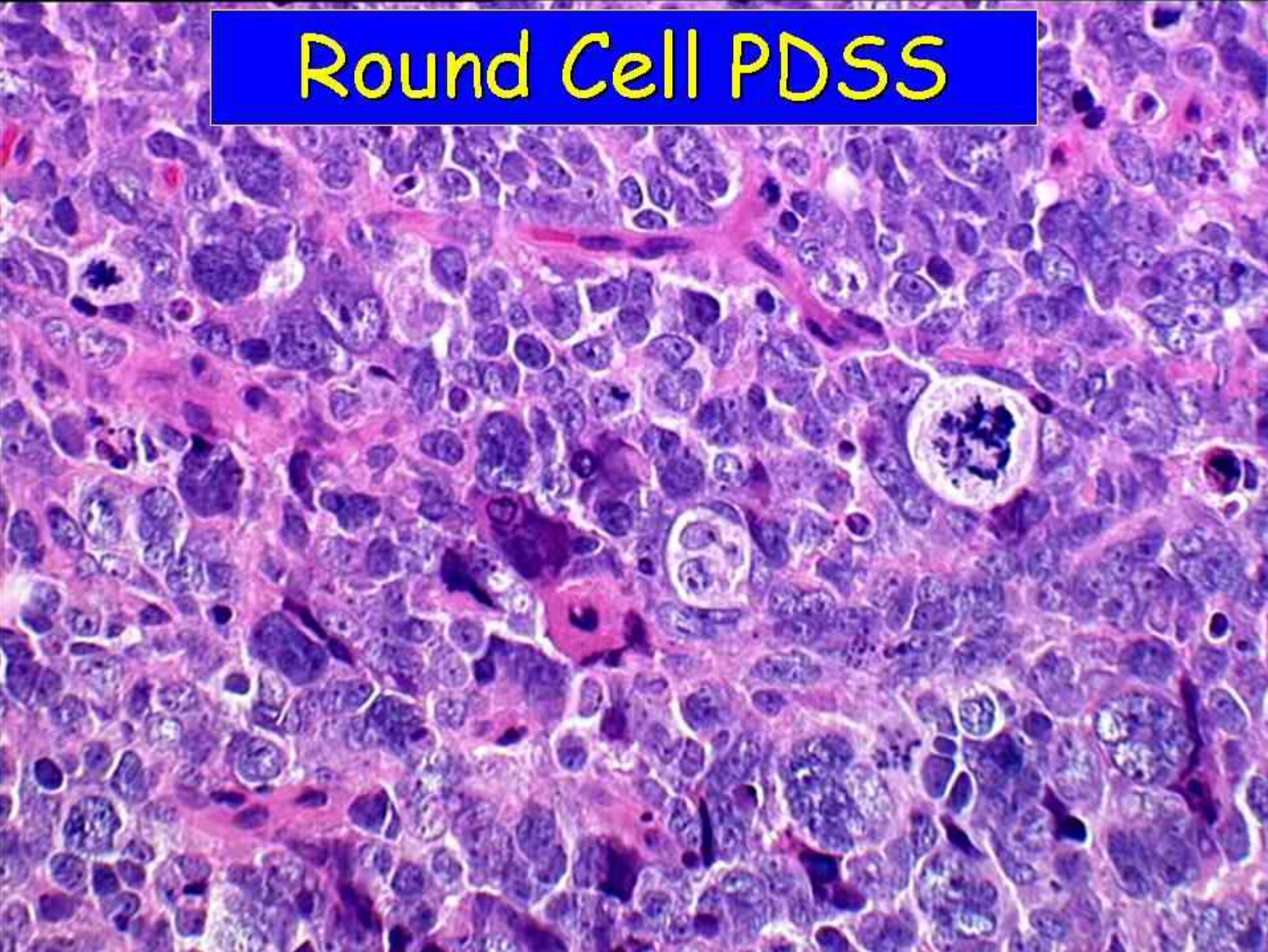
Poorly Differentiated Synovial Sarcoma

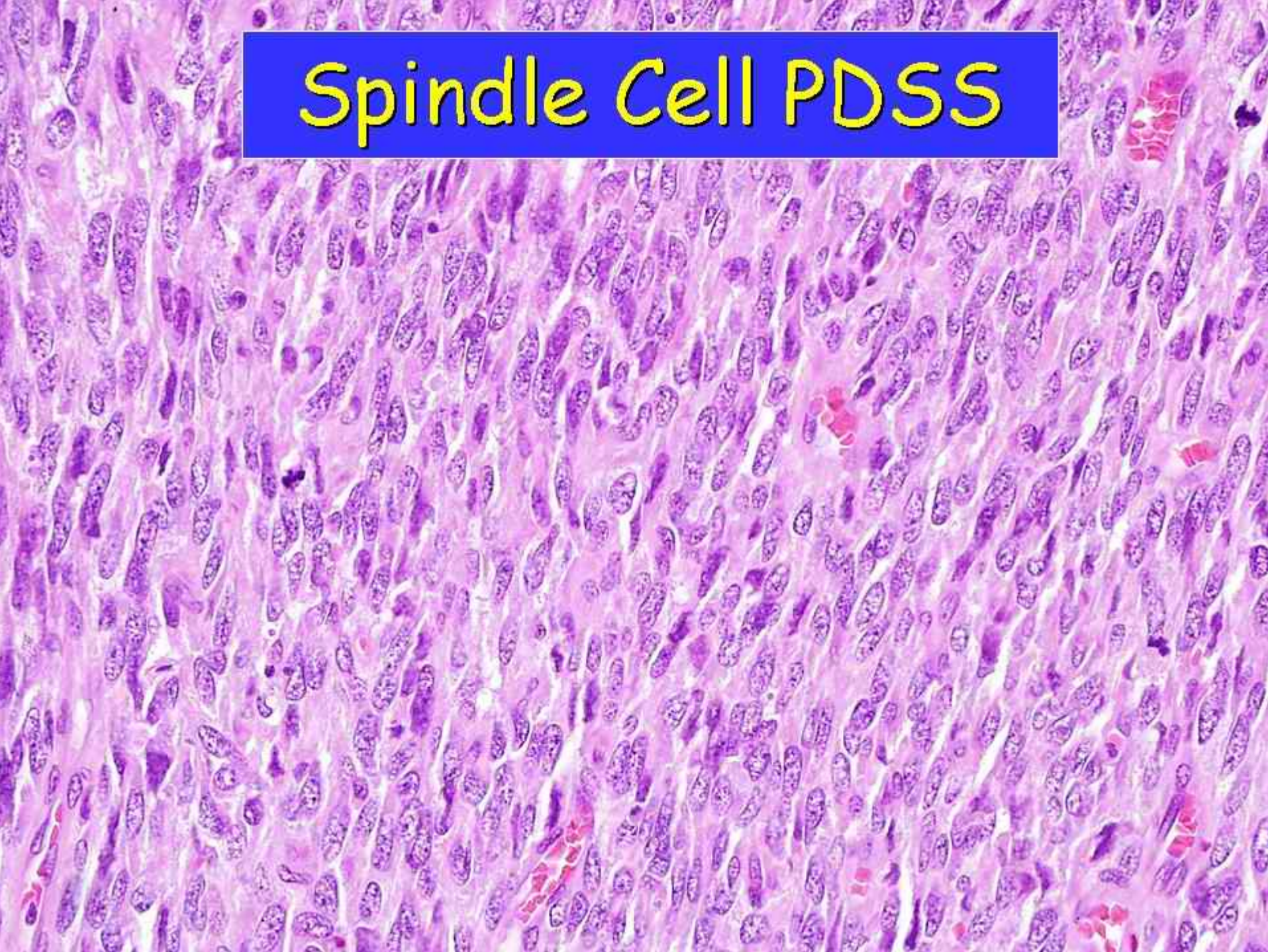
- 20% of cases of synovial sarcoma
- Round cell
  - DD: ES/PNET, DSRCT, ARMS and MCC
- Large cell
  - DD: Epithelioid sarcoma, ERT, PD carcinoma
- Spindle cell
  - MPNST and fibrosarcoma

Round cell PDSS



Round Cell PDSS

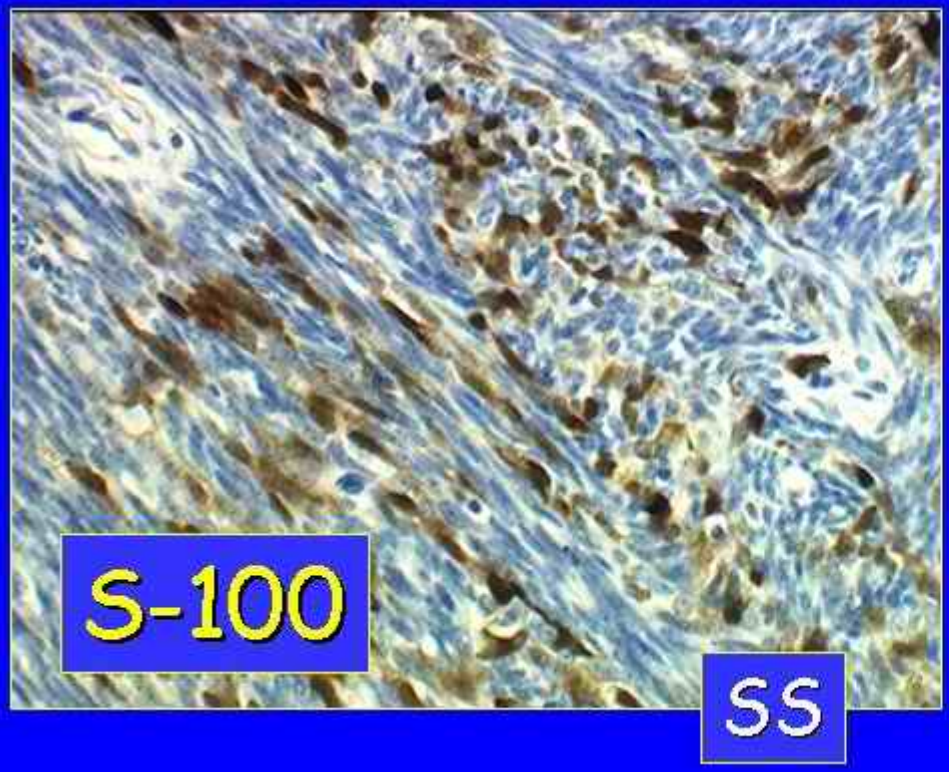


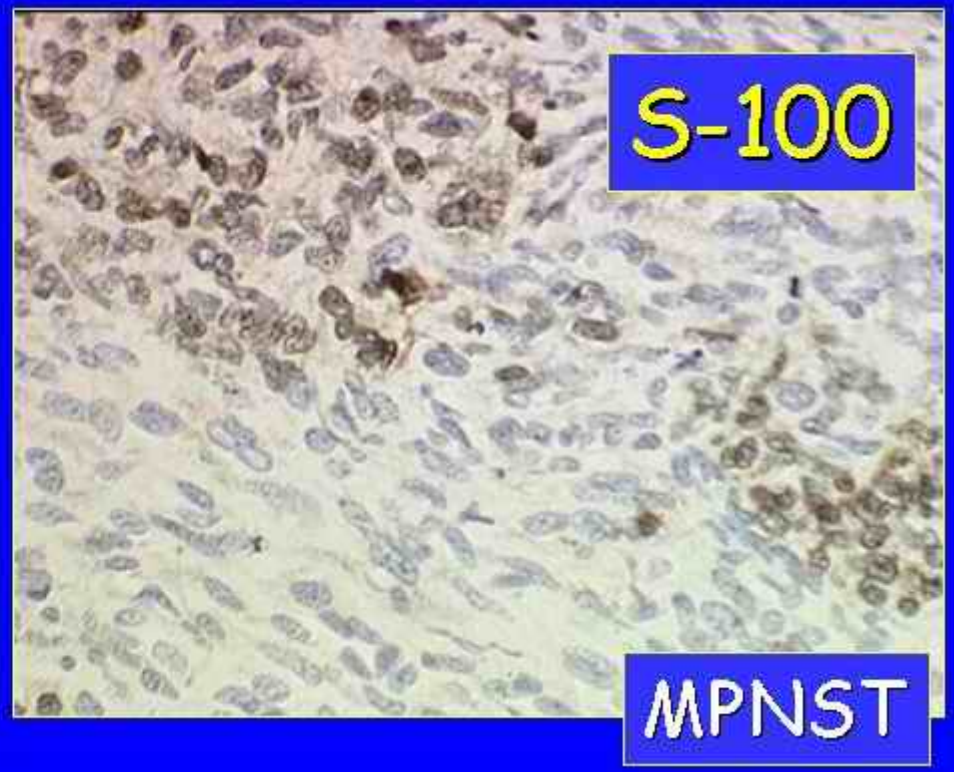

Spindle Cell PDSS

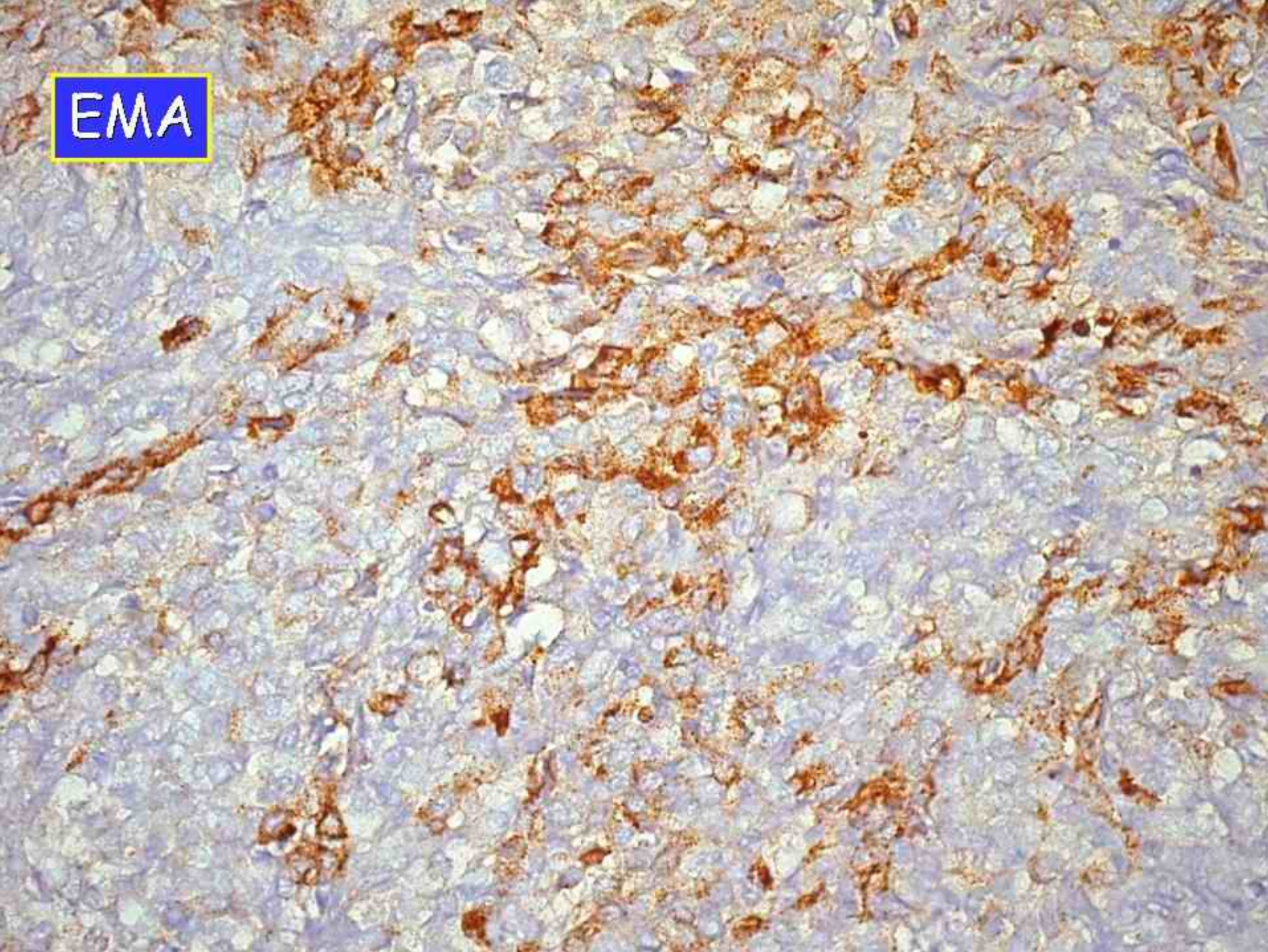
Synovial Sarcoma: immunohistochemistry

- Expression of epithelial markers
  - EMA > cytokeratins
- CD99 (MIC2) positive
- 30% S-100 positive

Synovial Sarcoma: immunohistochemistry



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Synovial Sarcoma: cytogenetics

- t(X;18)(p11.2;q11.2)
- SYT (Synovial sarcoma Translocation) on chromosome 18
- SSX1 (Synovial Sarcoma X breakpoint), SSX2 and SSX4 on chromosome X
- SYT-SSX2 correlates with the monophasic phenotype
- Associated with better metastasis-free survival (?)

MPNST and t(X;18)

- t(X;18) detected in 15/20 MPNSTs
- RT-PCR technique
- 1/4 adult fibrosarcomas
- 1/10 pleomorphic sarcomas
- 1/7 congenital fibrosarcomas
- 2/3 neurofibromas

O'Sullivan MJ et al, Mod Pathol 2000; 13:1336

MPNST and t(X;18)

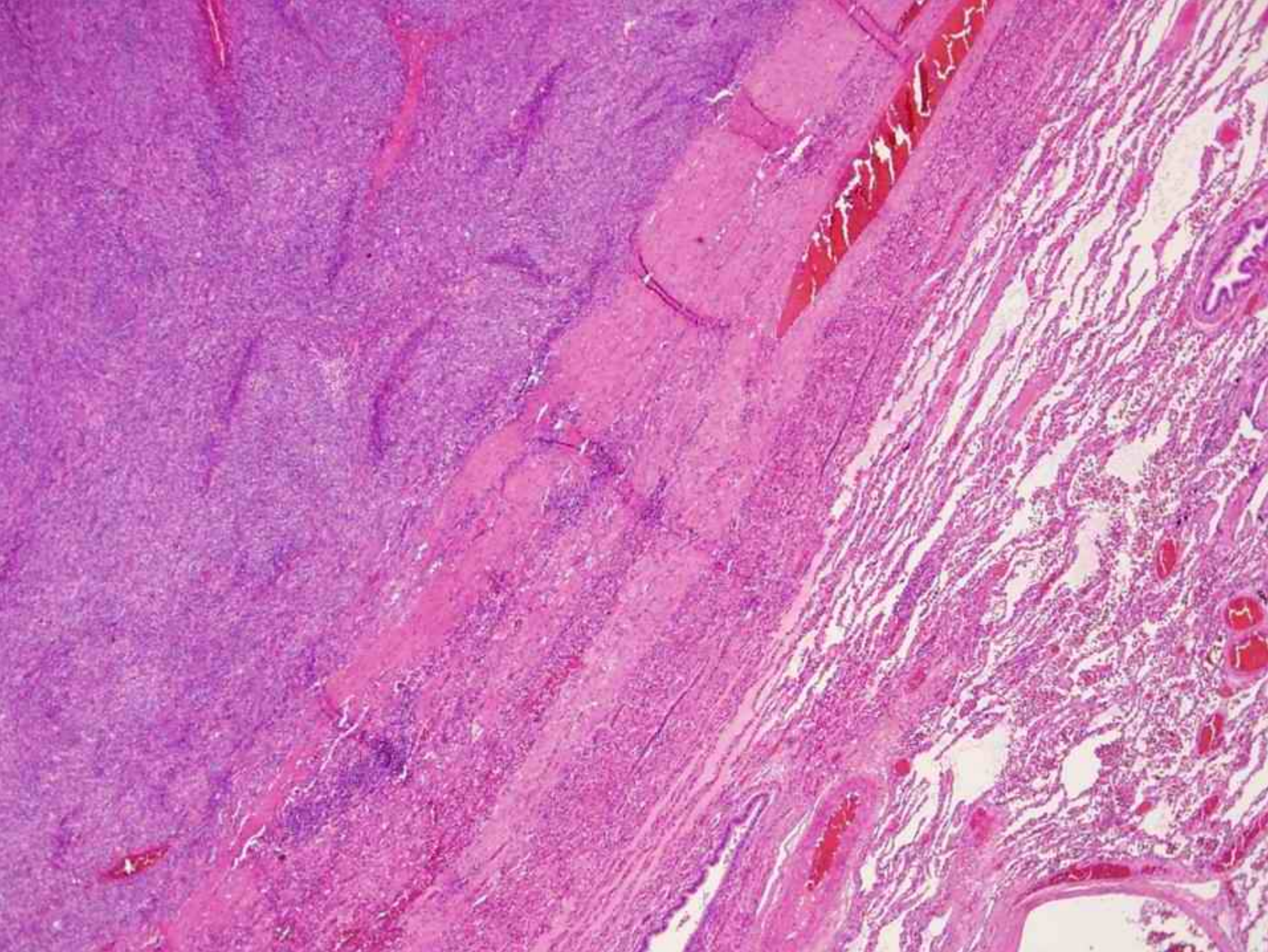
- 53 MPNSTs from 19 papers
  - no t(X;18) reported
- 145 additional unreported cases
  - Memorial Sloan-Kettering Cancer Center, Universities of Nebraska and Pennsylvania; Brigham & Women's Hospital, University of Leuven

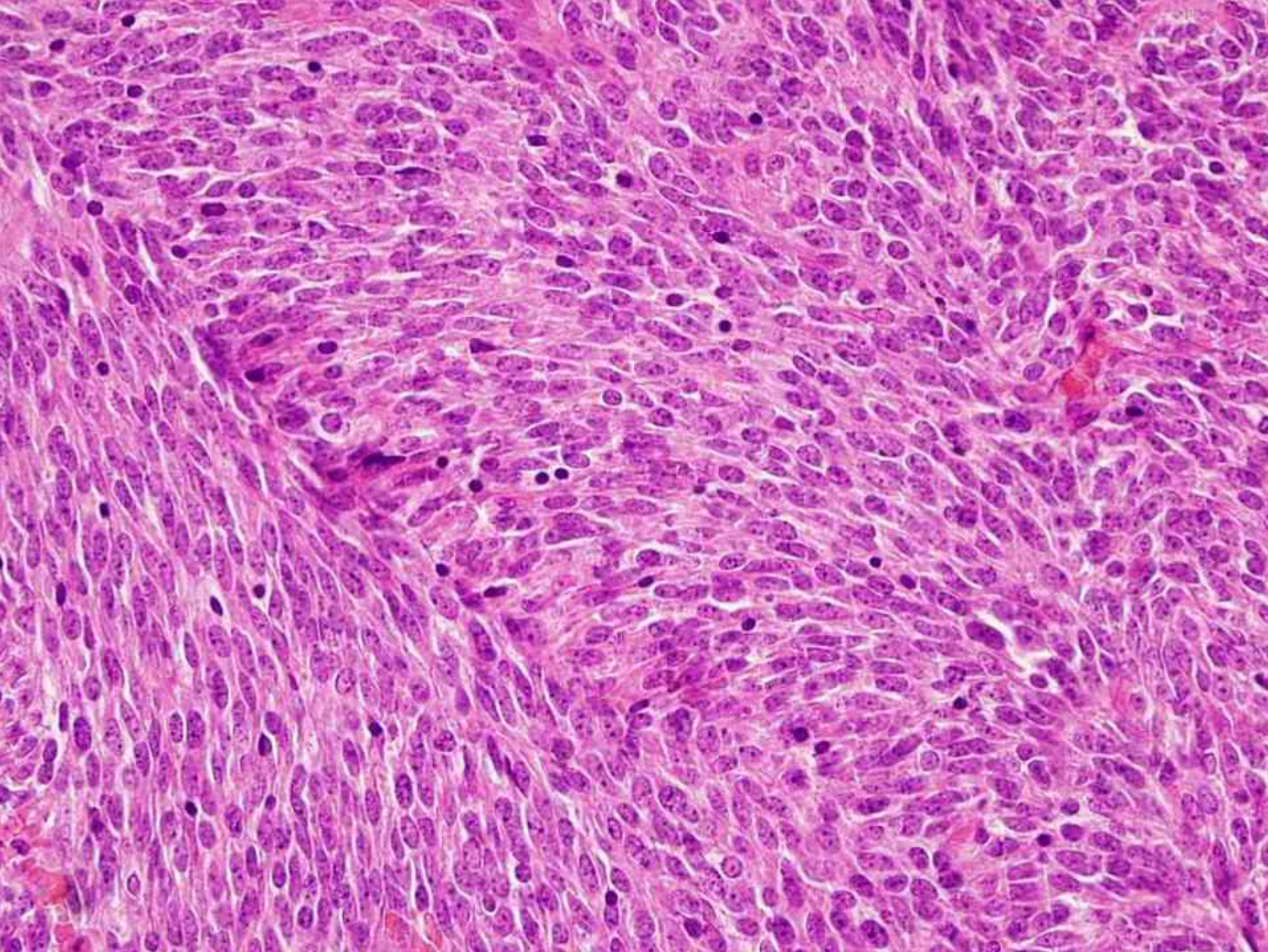
Ladany M et al, Mod Pathol 2001; 14:733

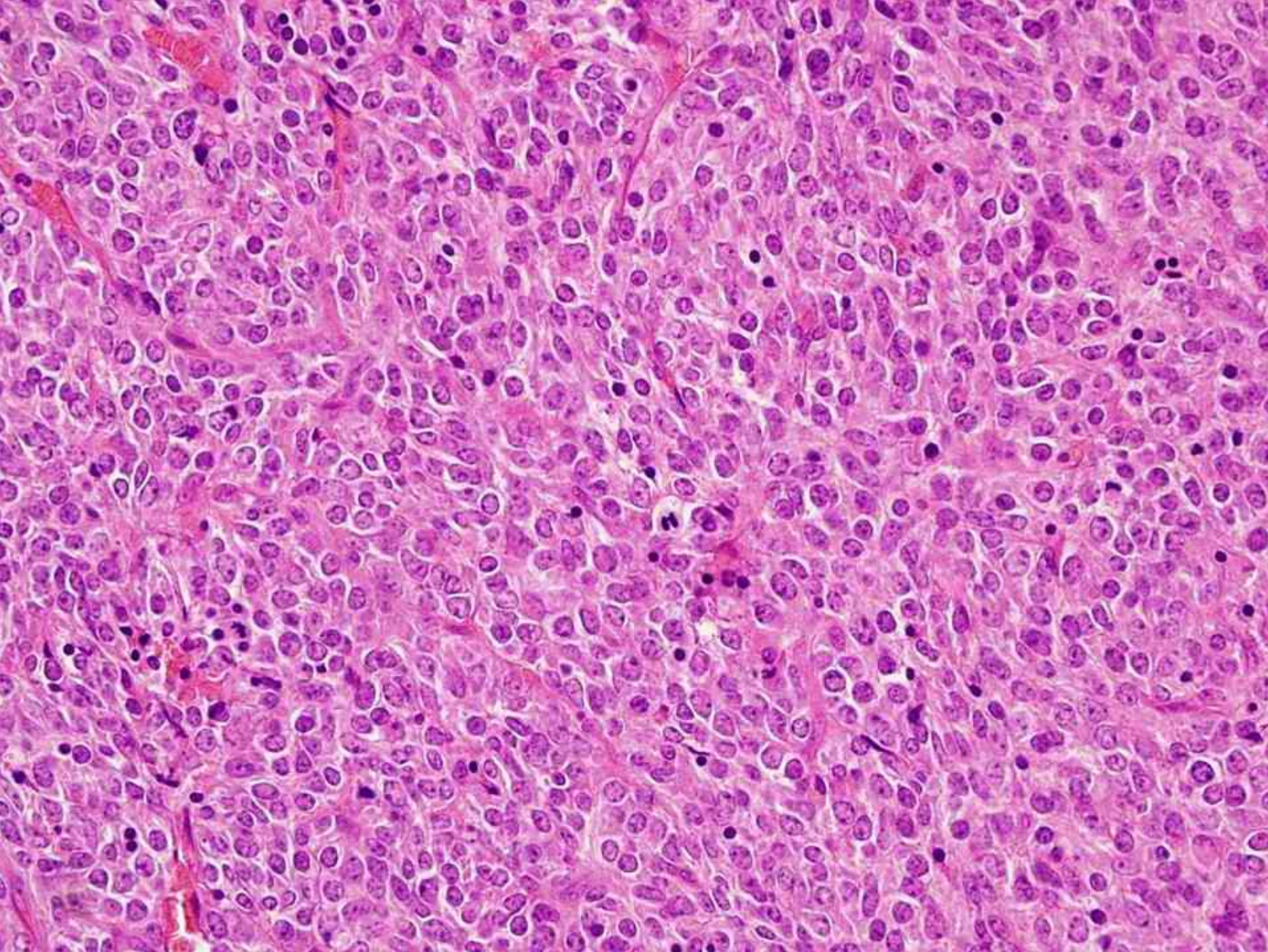
MPNST and t(X;18)

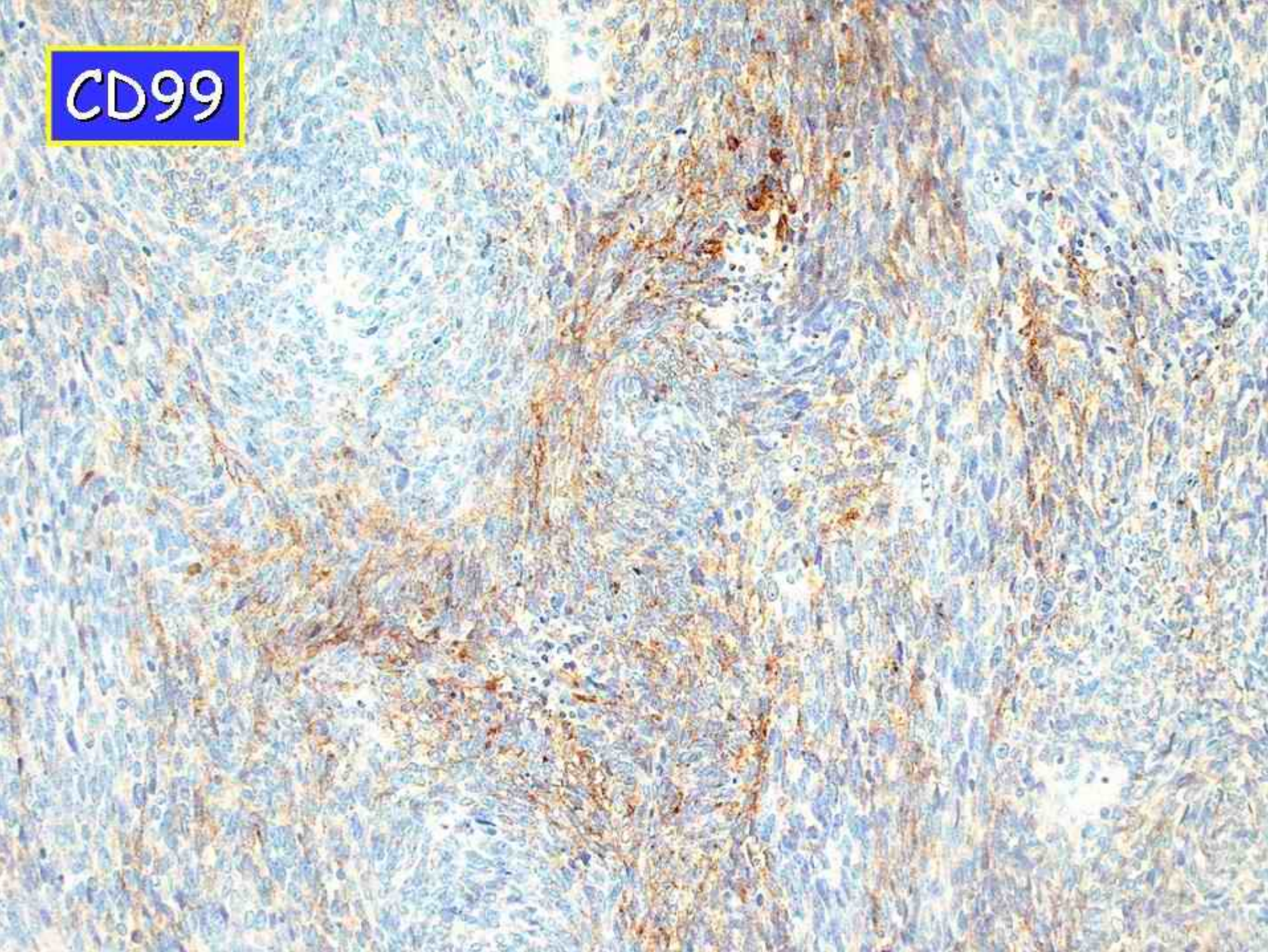
- No other techniques (FISH)
  - applicable to routinely processed material
- Contamination
  - Validation
  - appropriate controls

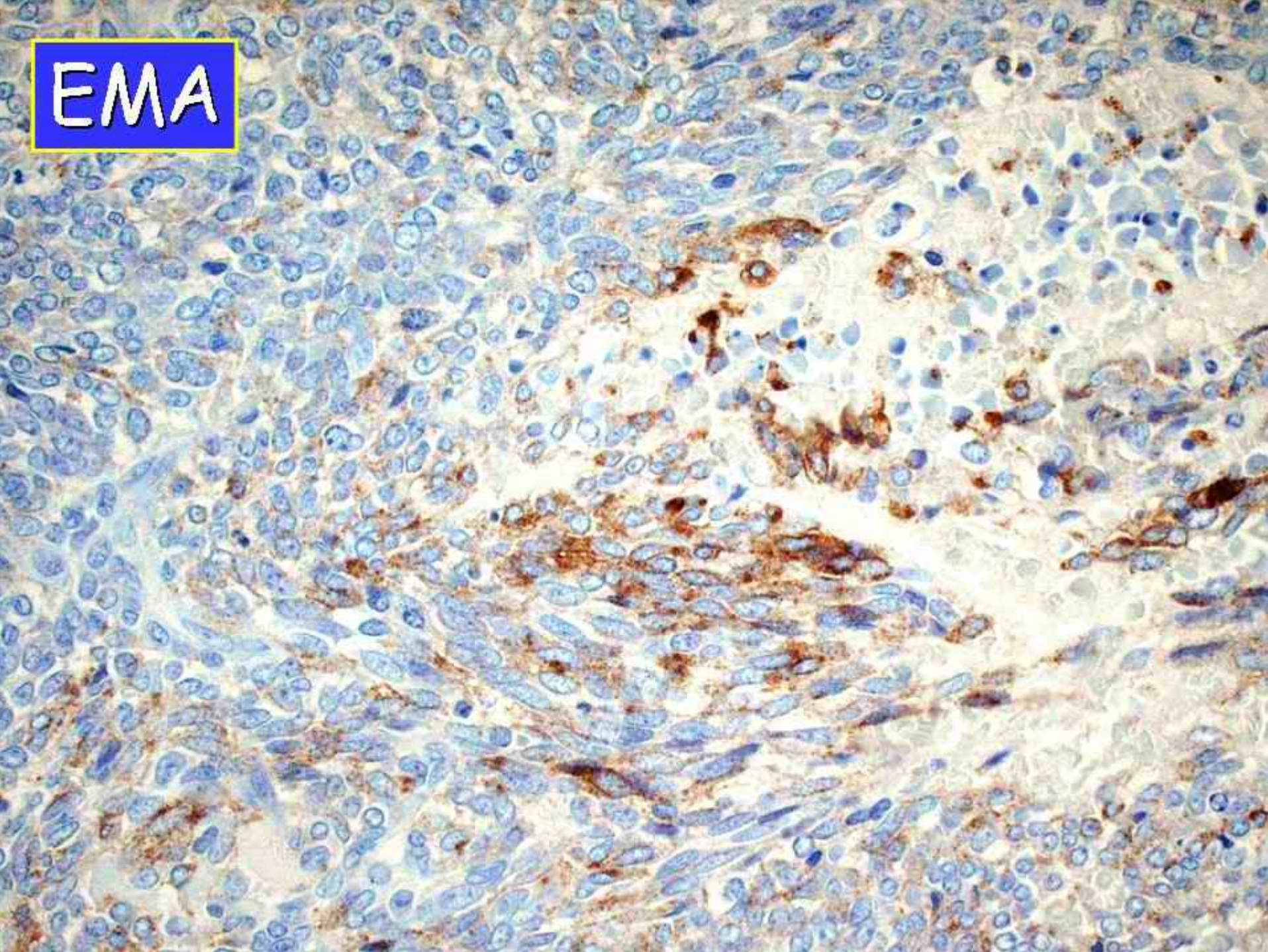

METRIC 1
2





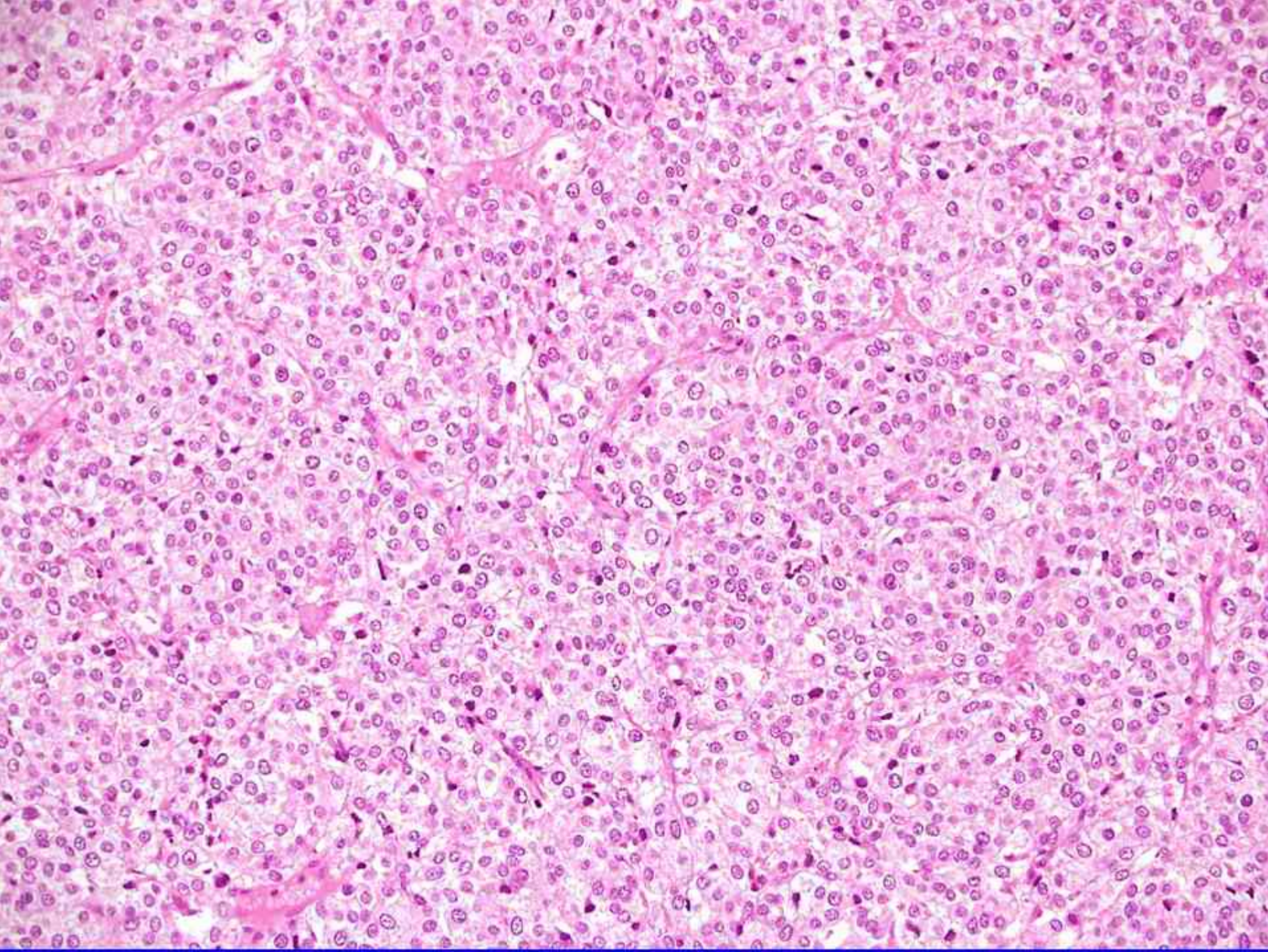


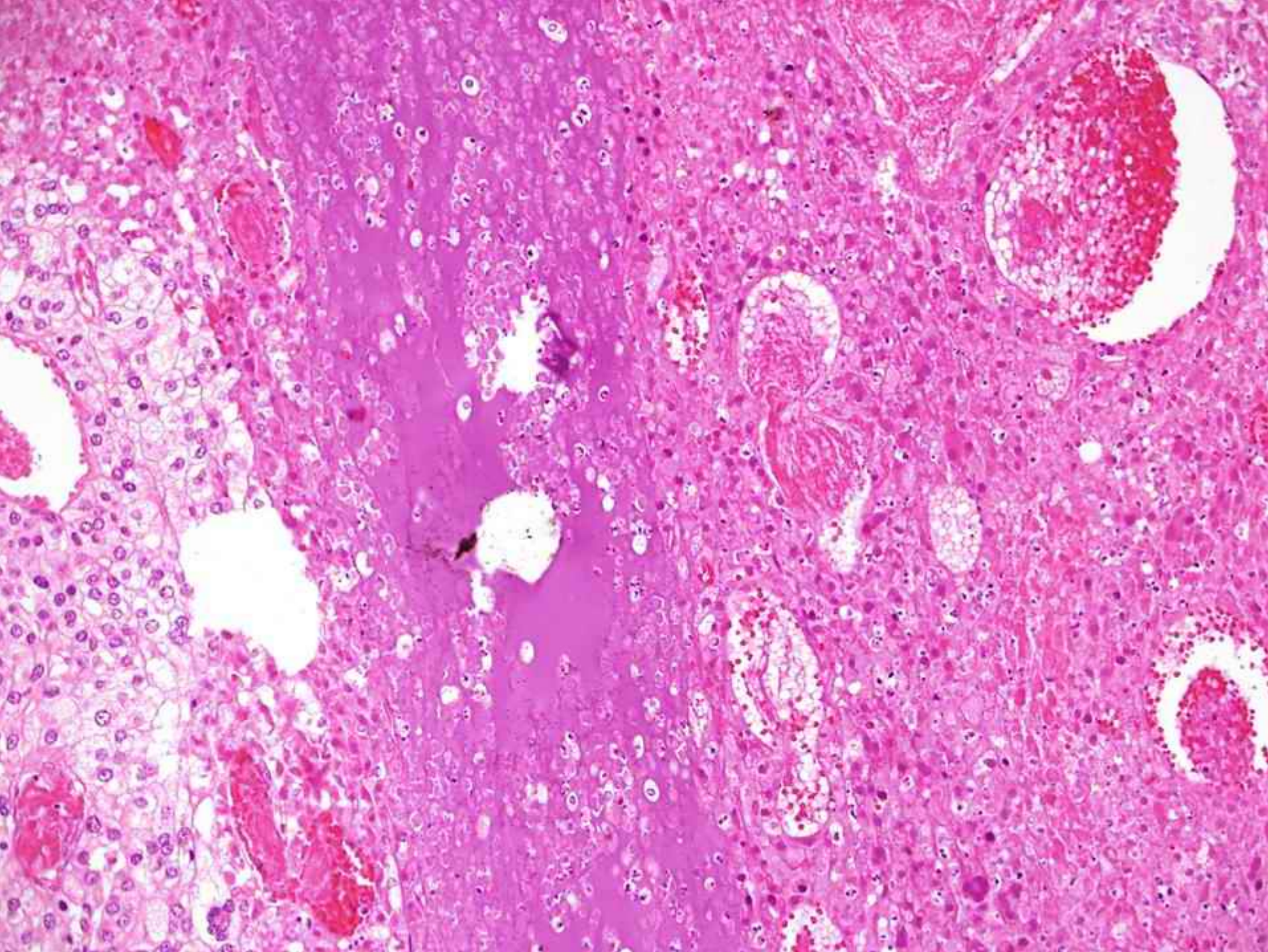

CD99

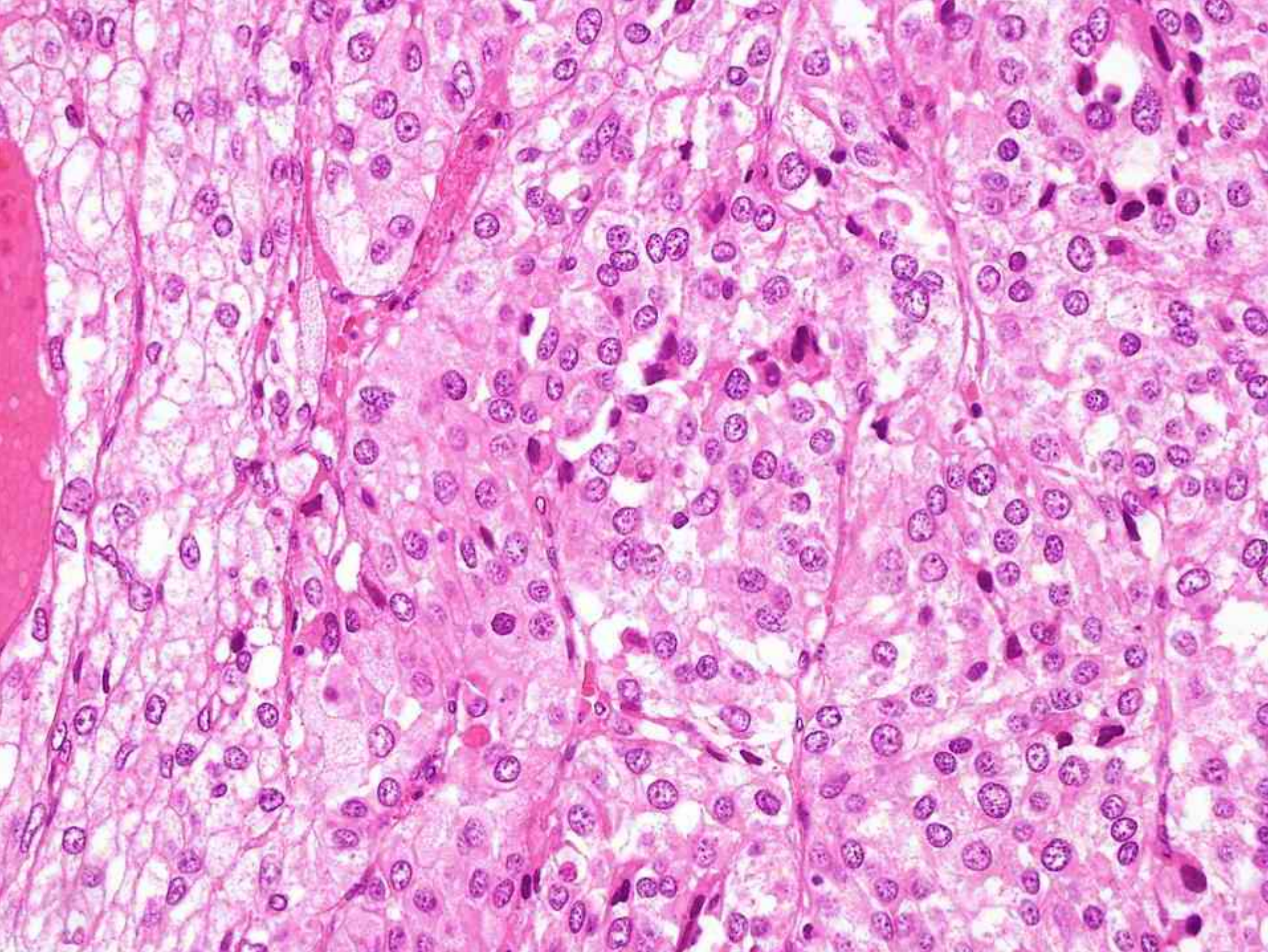

EMA

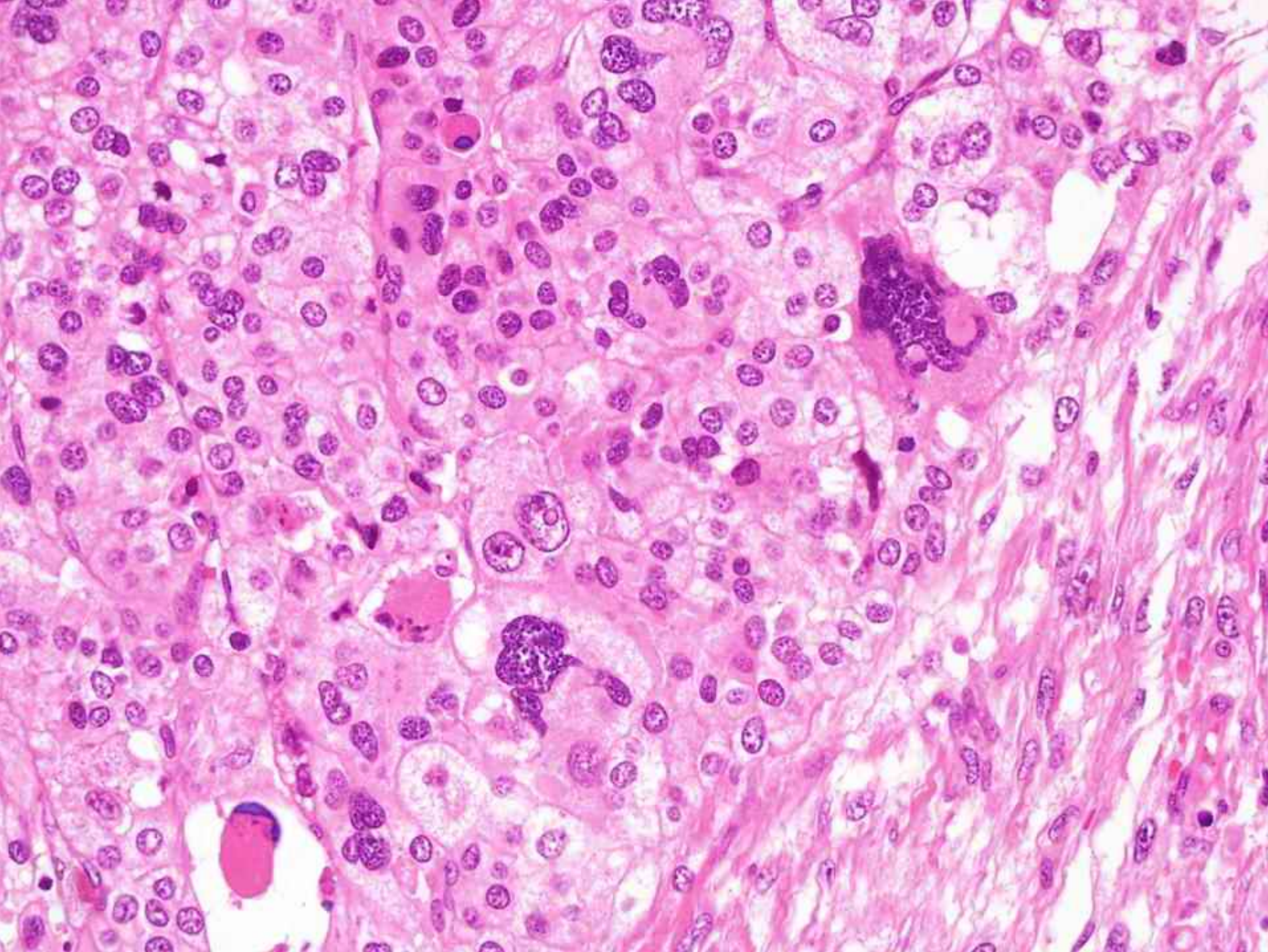
Clinical History

- 41 year old female
- Abdominal pain
- 12 cm intrabdominal mass attached o the right side of colon



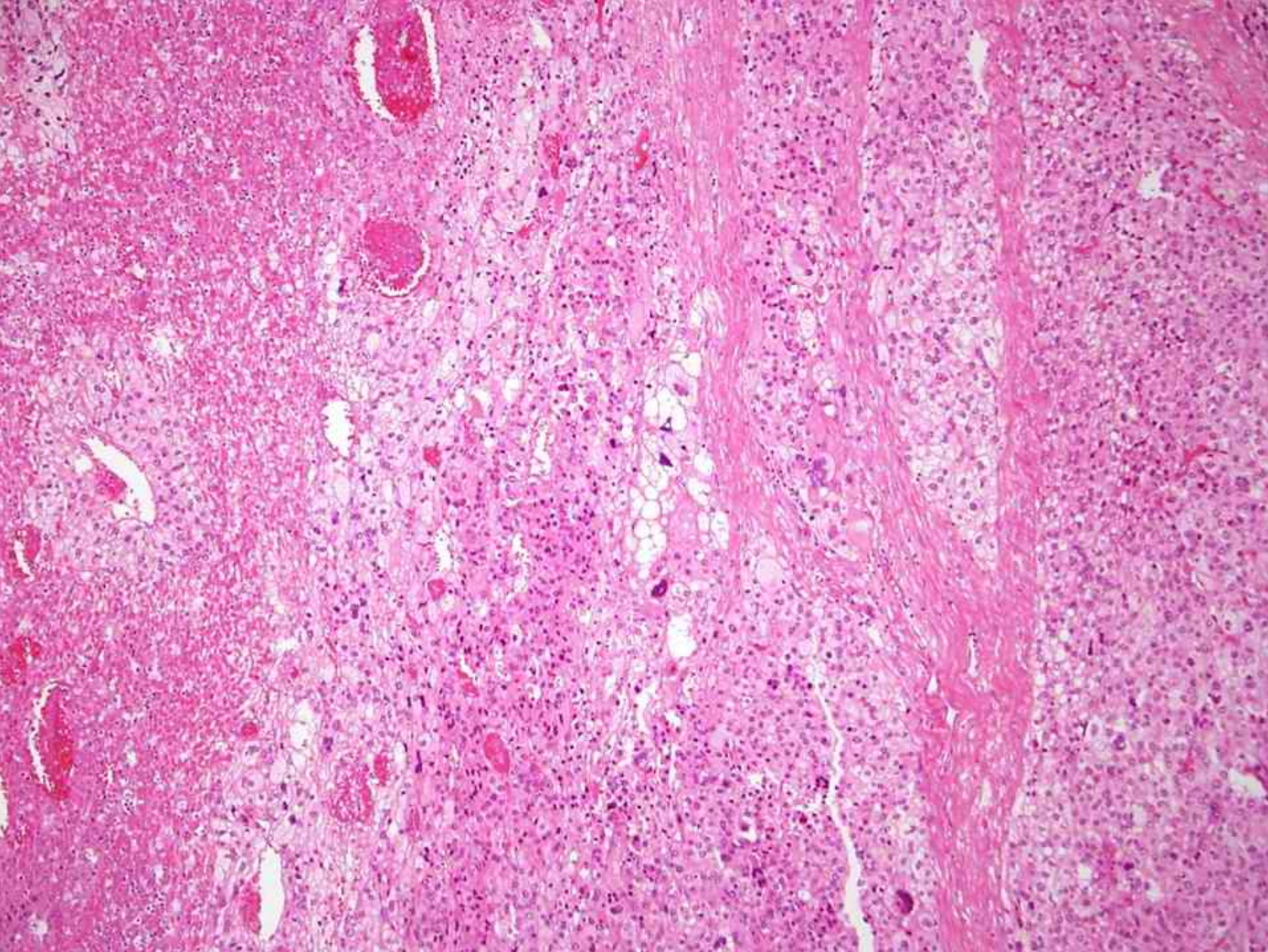


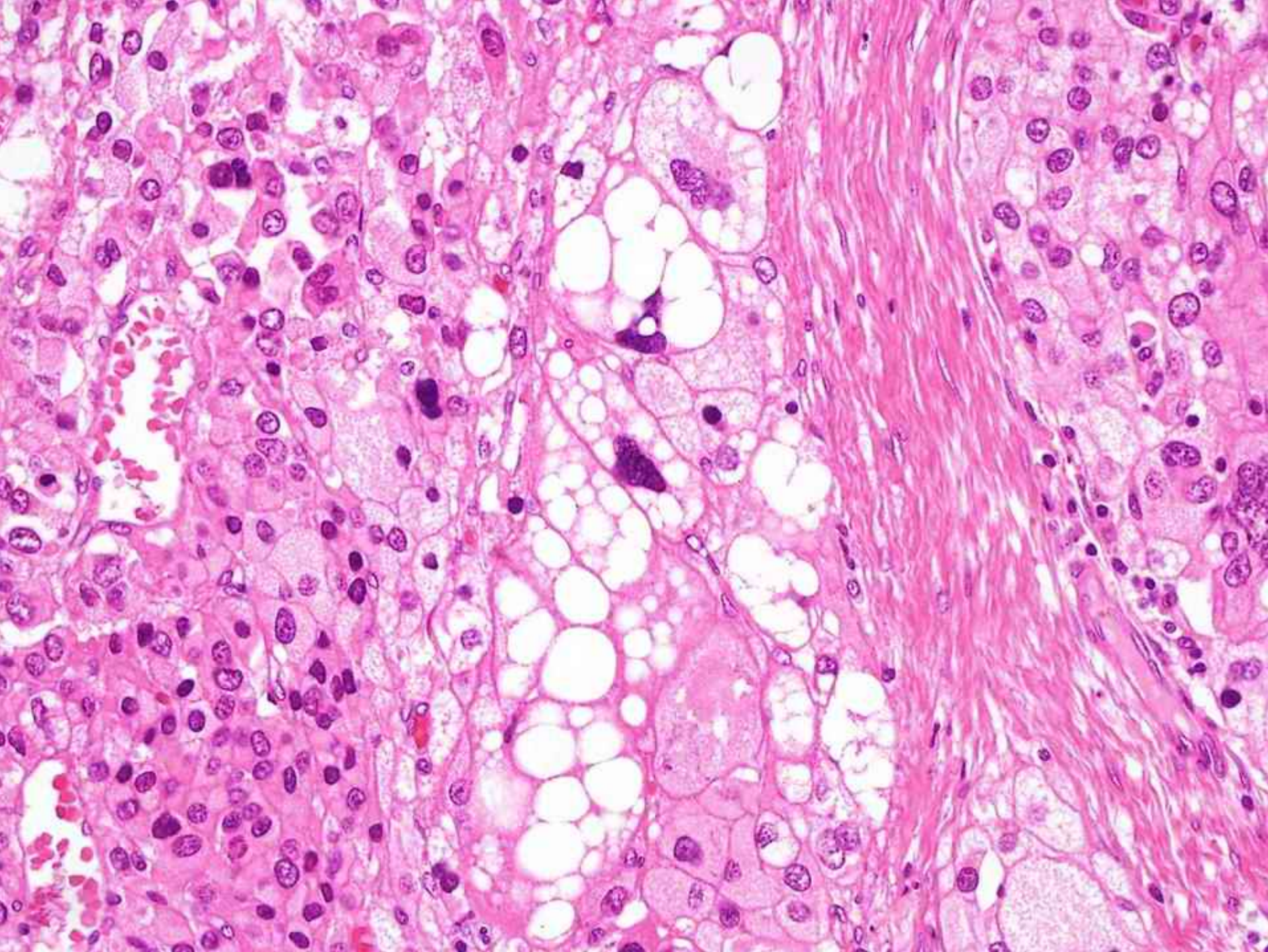




IHC

- Only vimentin + phenotype





Diagnosis

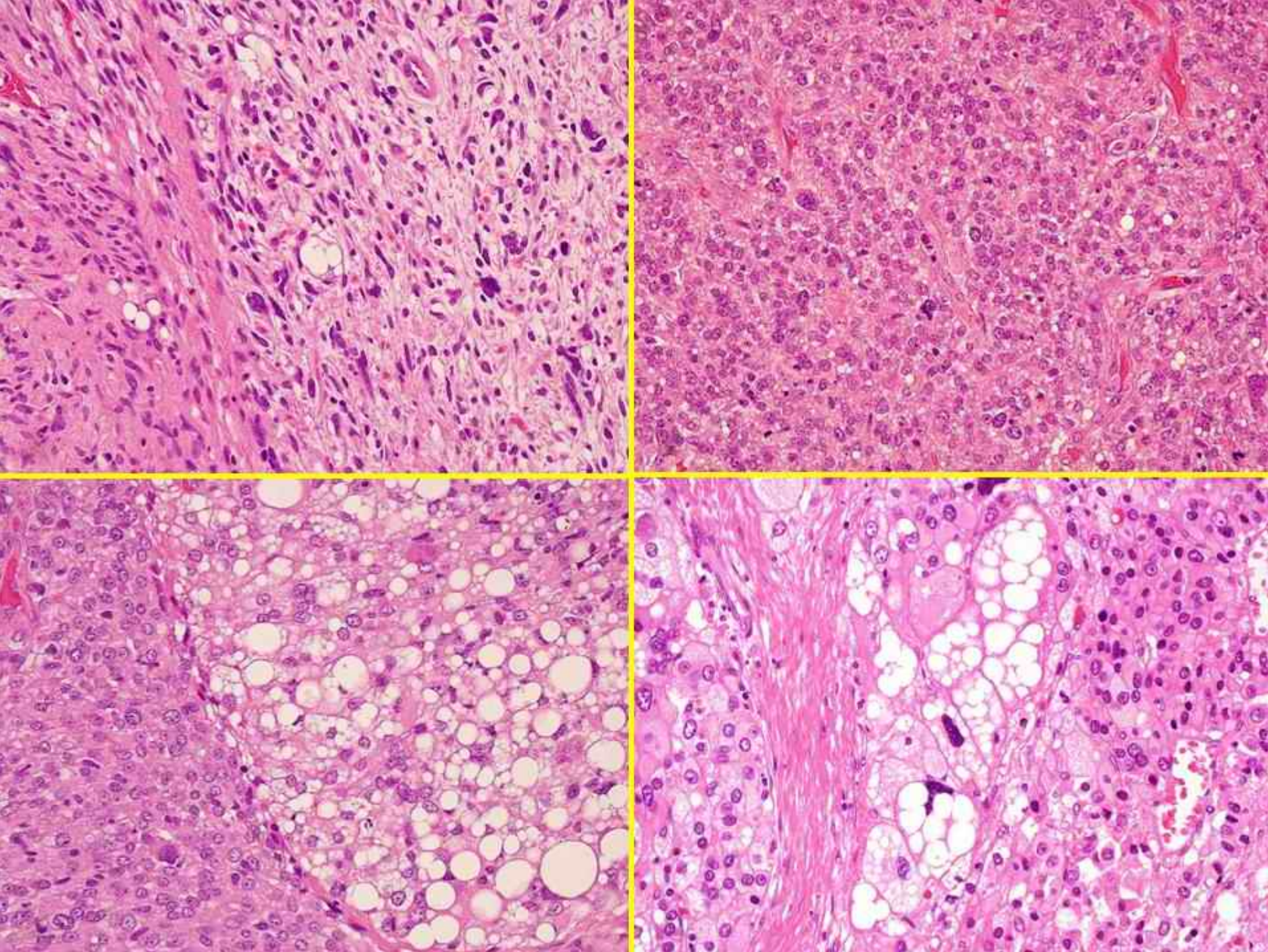
Epithelioid Pleomorphic Liposarcoma

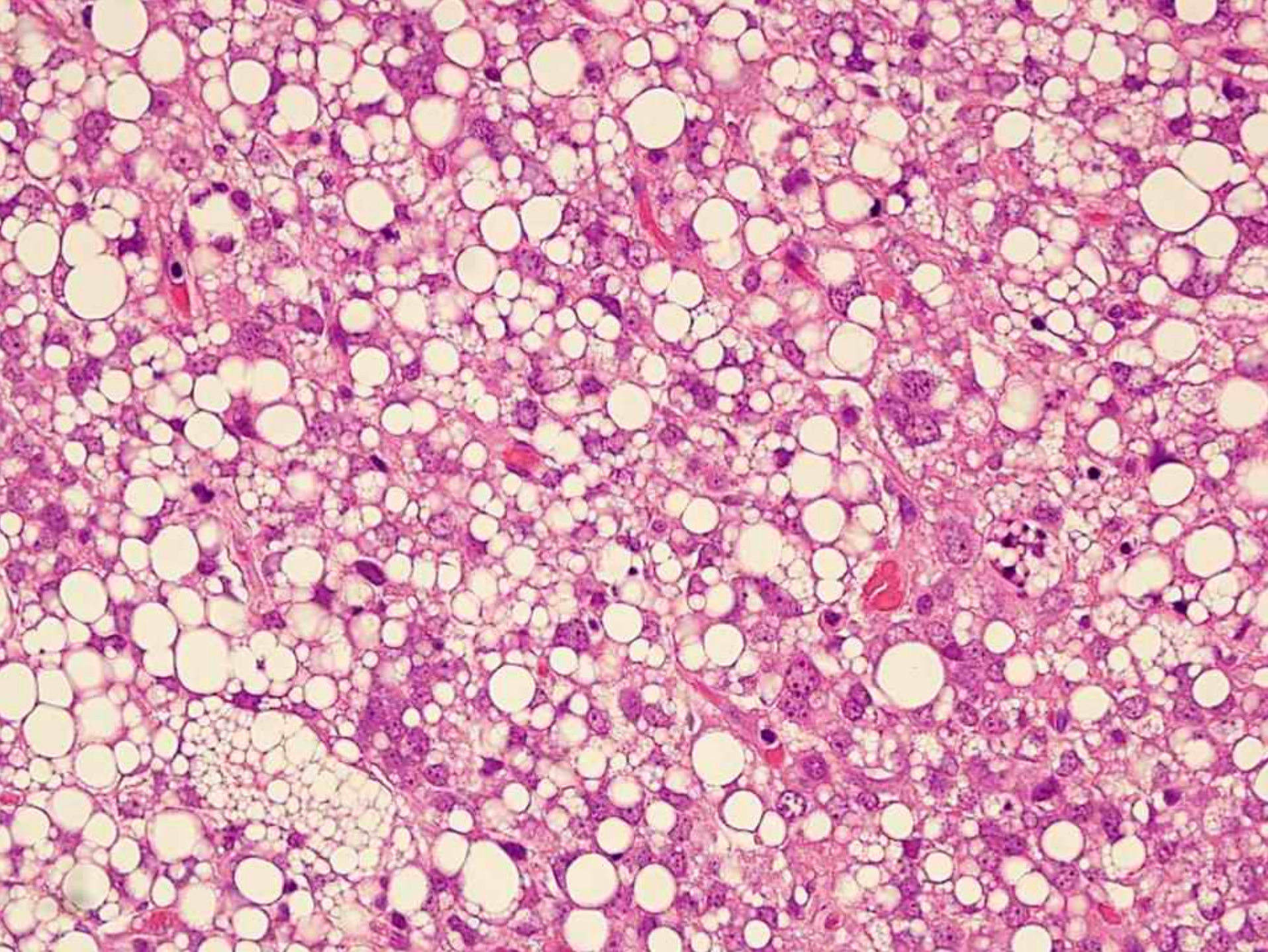
Pleomorphic liposarcoma

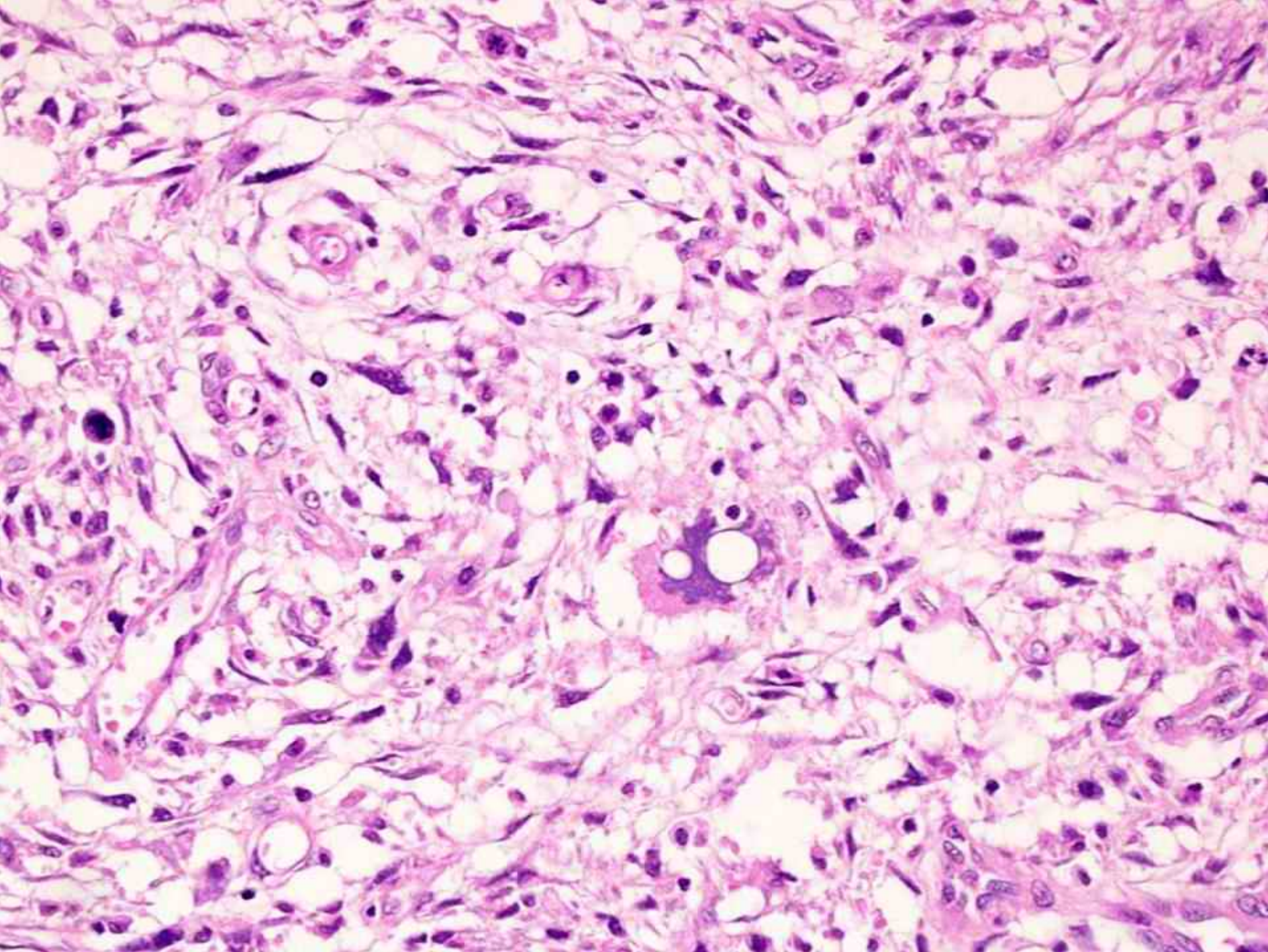
- 5% of all liposarcomas
- M > F, 6th decade
- Lower limbs, upper limbs, retroperitoneum
- Metastatic rate: 30-50%
- 5 yr survival rate = 57%
- Complex Karyotypic aberrations
- TP53 alterations in 50% of cases

Pleomorphic liposarcoma

- Non-distinctive high-grade pleomorphic/spindle cell sarcoma with scattered lipoblasts
- High-grade pleomorphic sarcoma with epithelioid areas and scattered lipoblasts
- Intermediate/high-grade myxofibrosarcoma-like tumor with lipoblasts
- Uniform sheets of pleomorphic lipoblasts

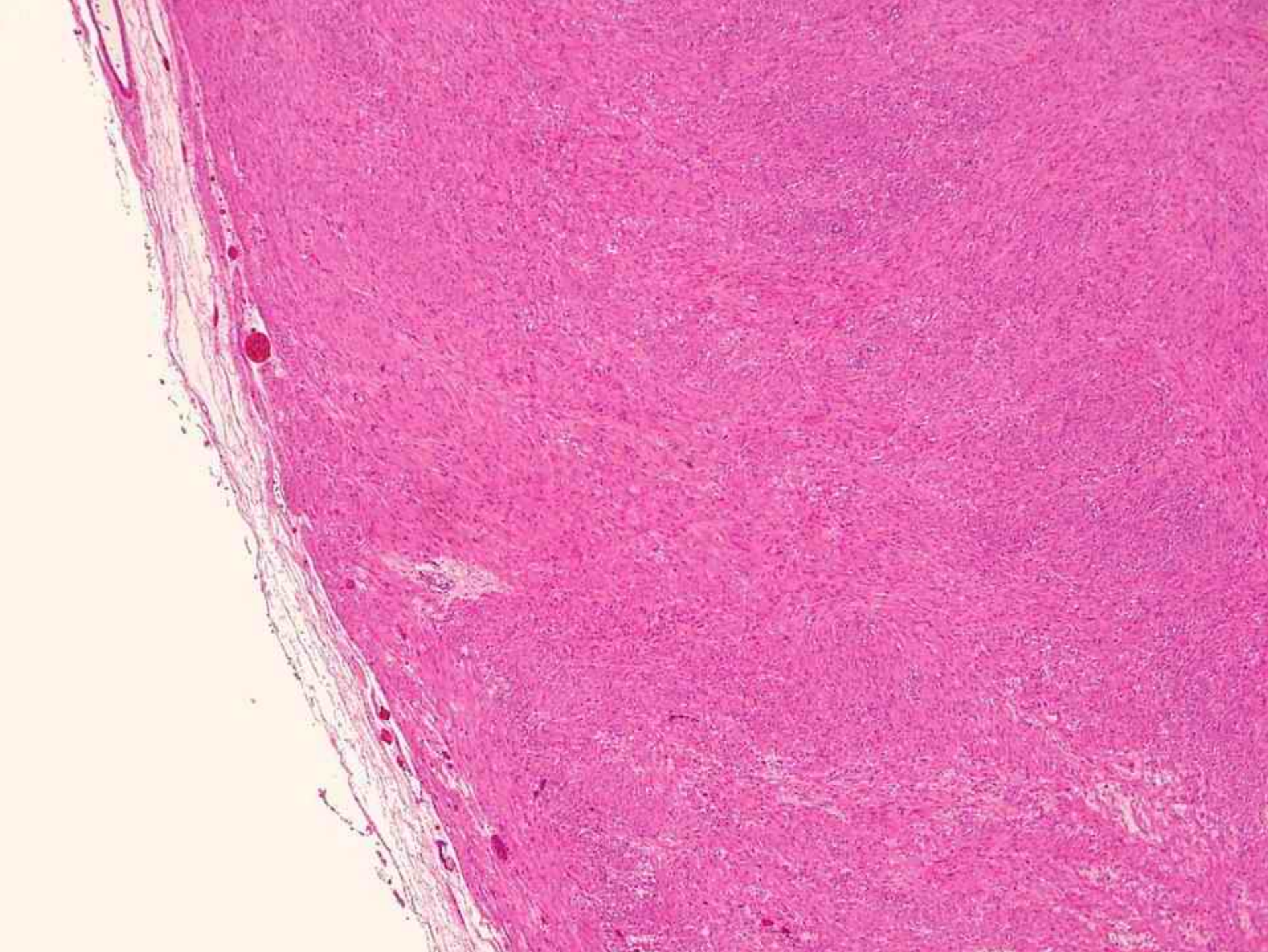


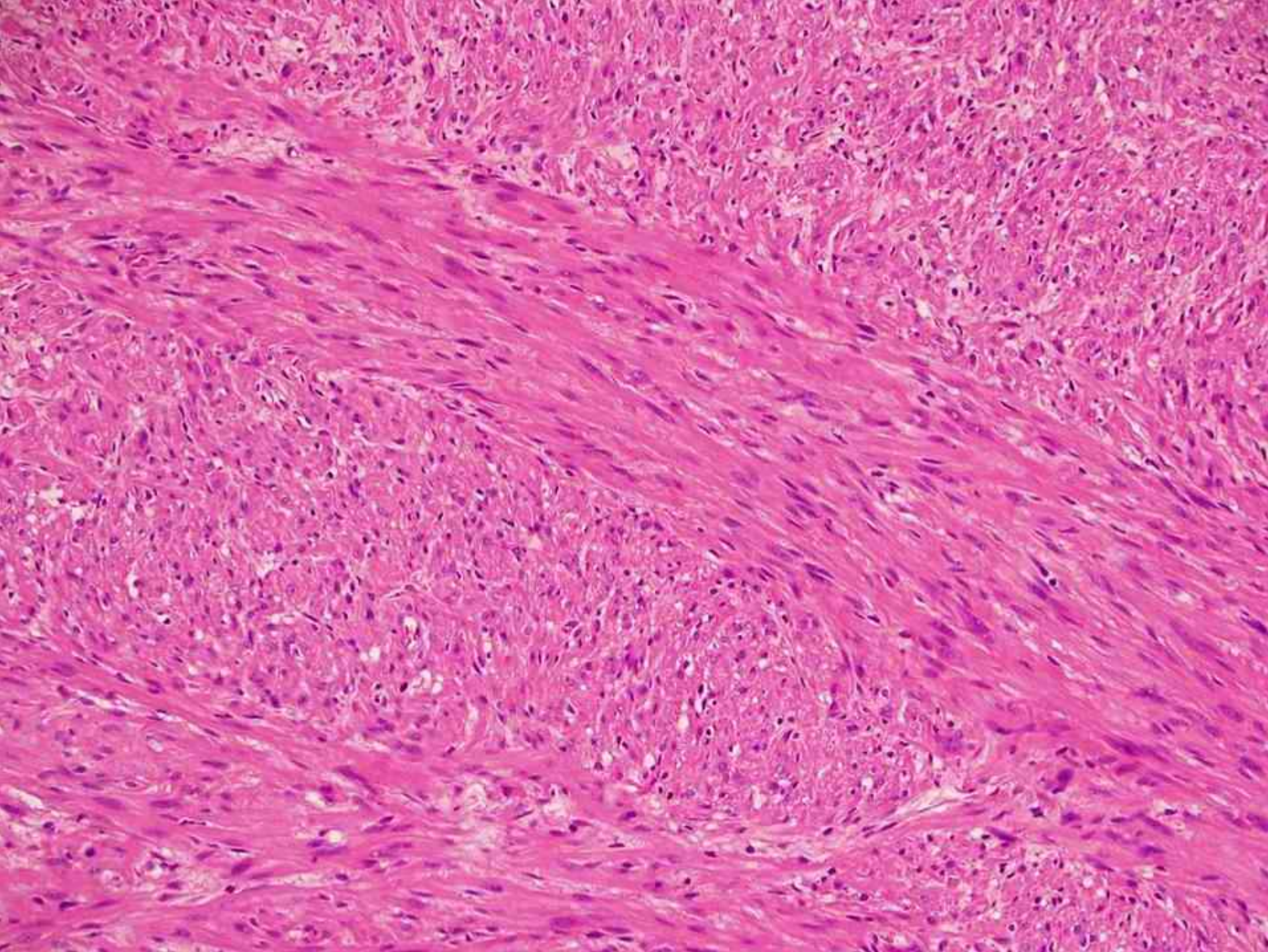


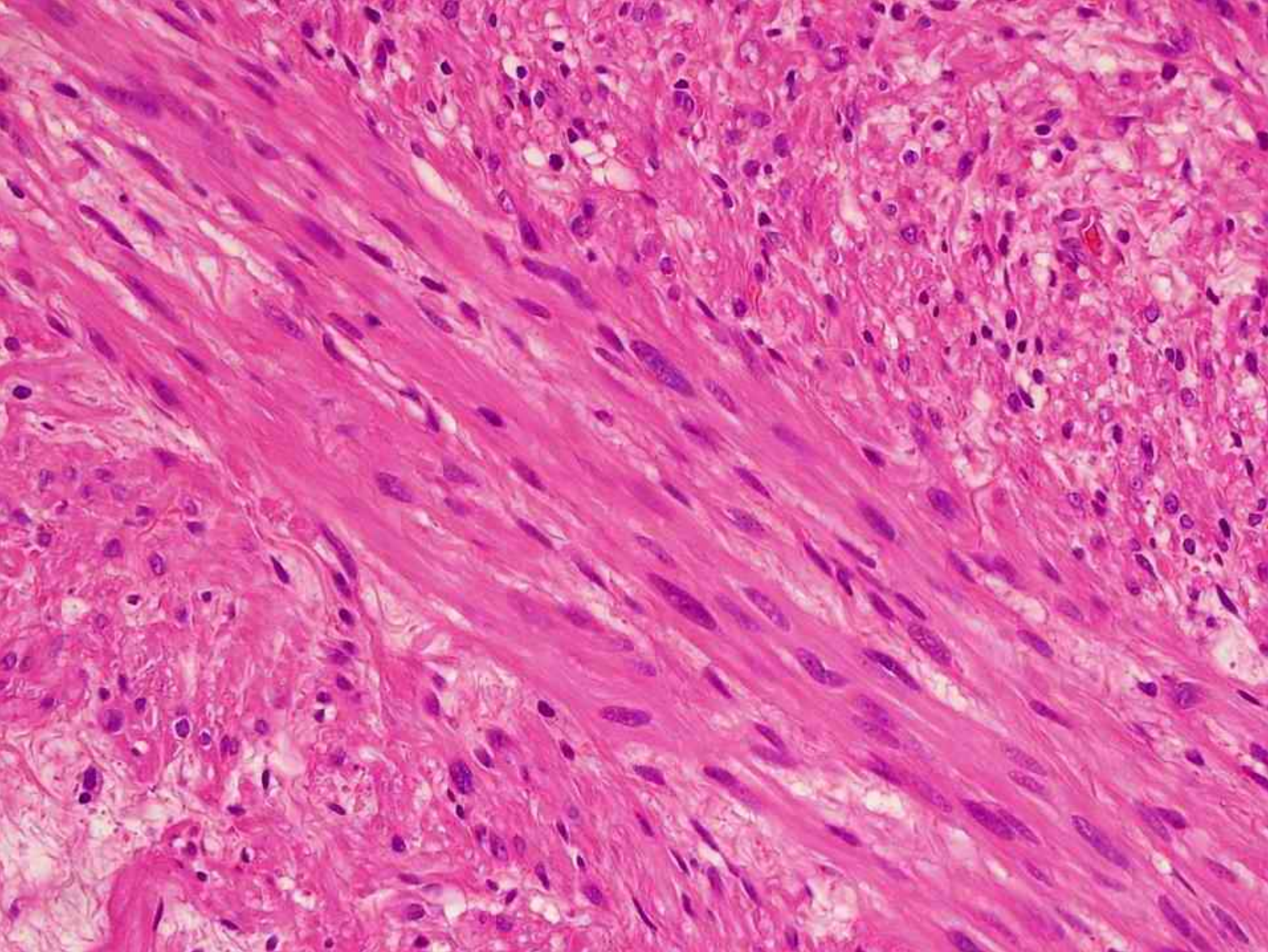


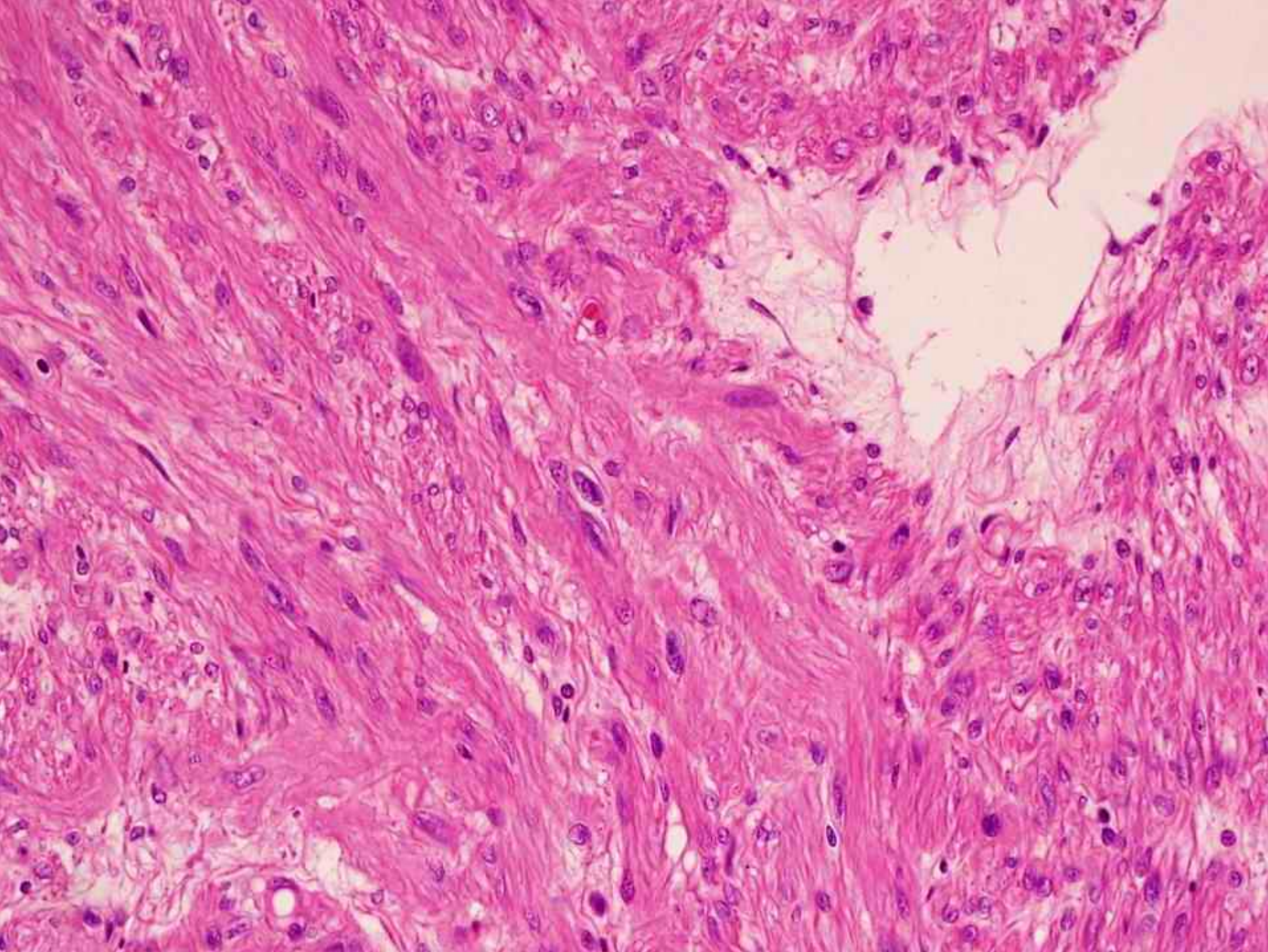
Clinical History

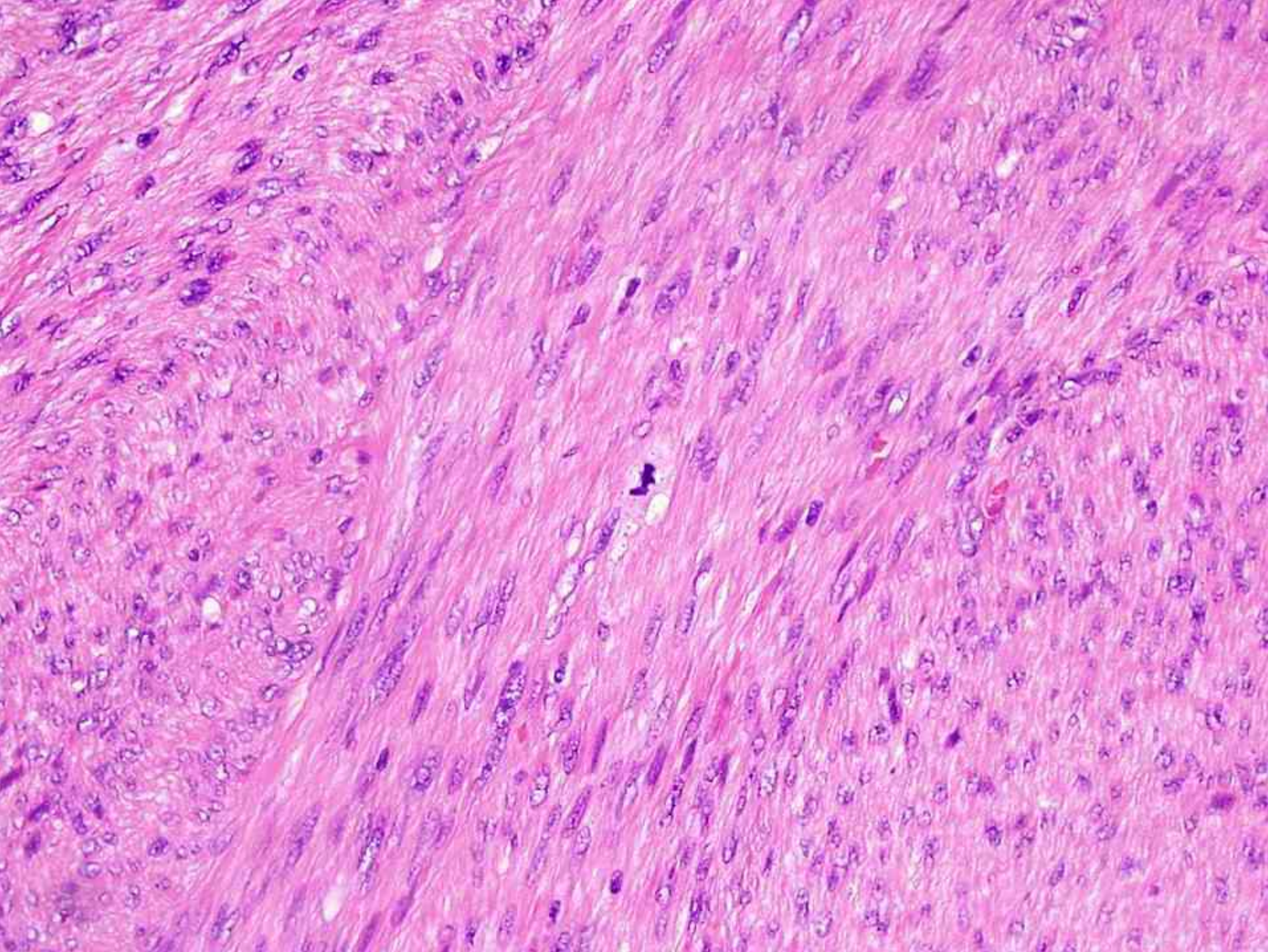
- 44 year old male
- 4 cm lump in the rectum

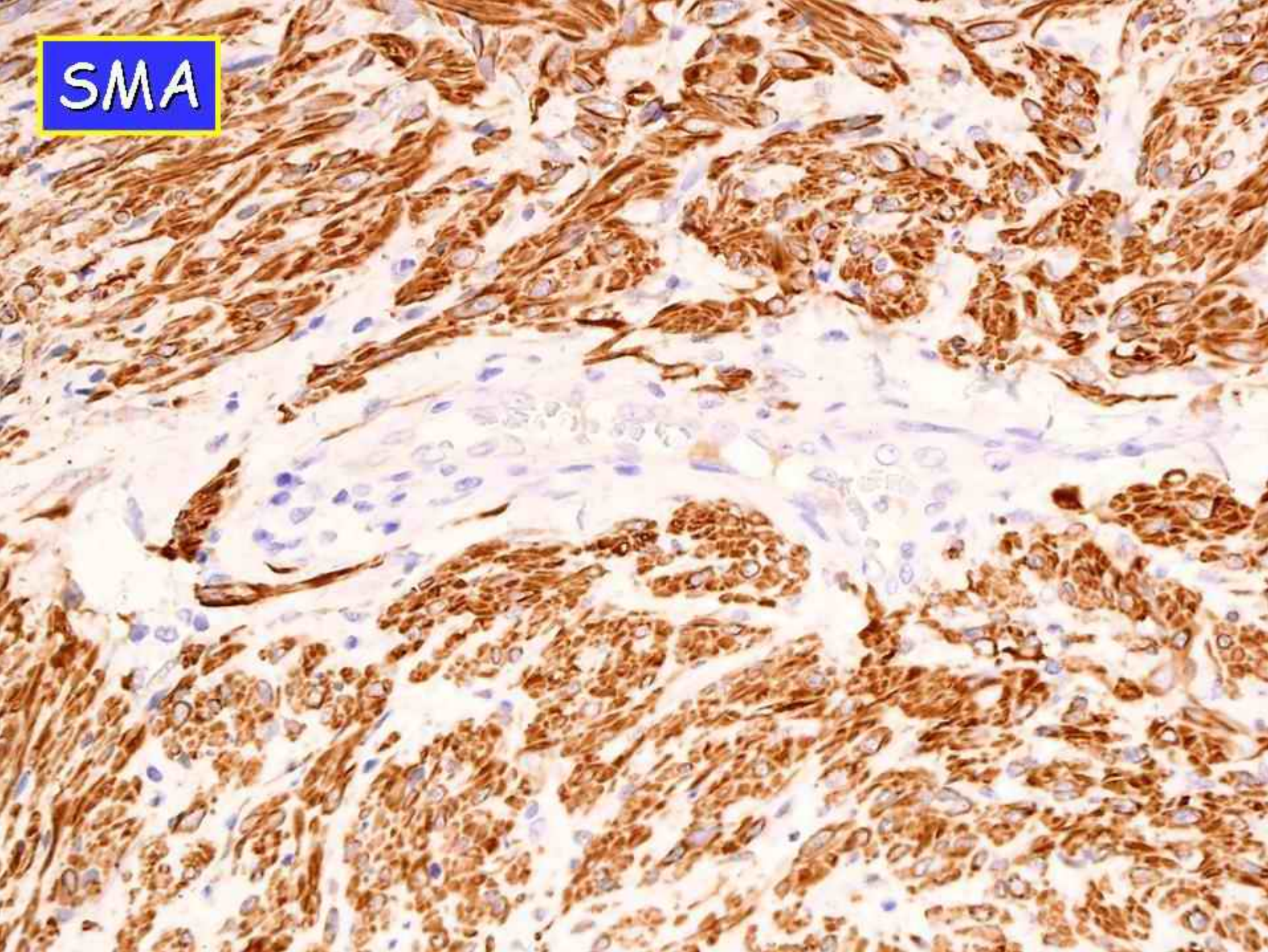


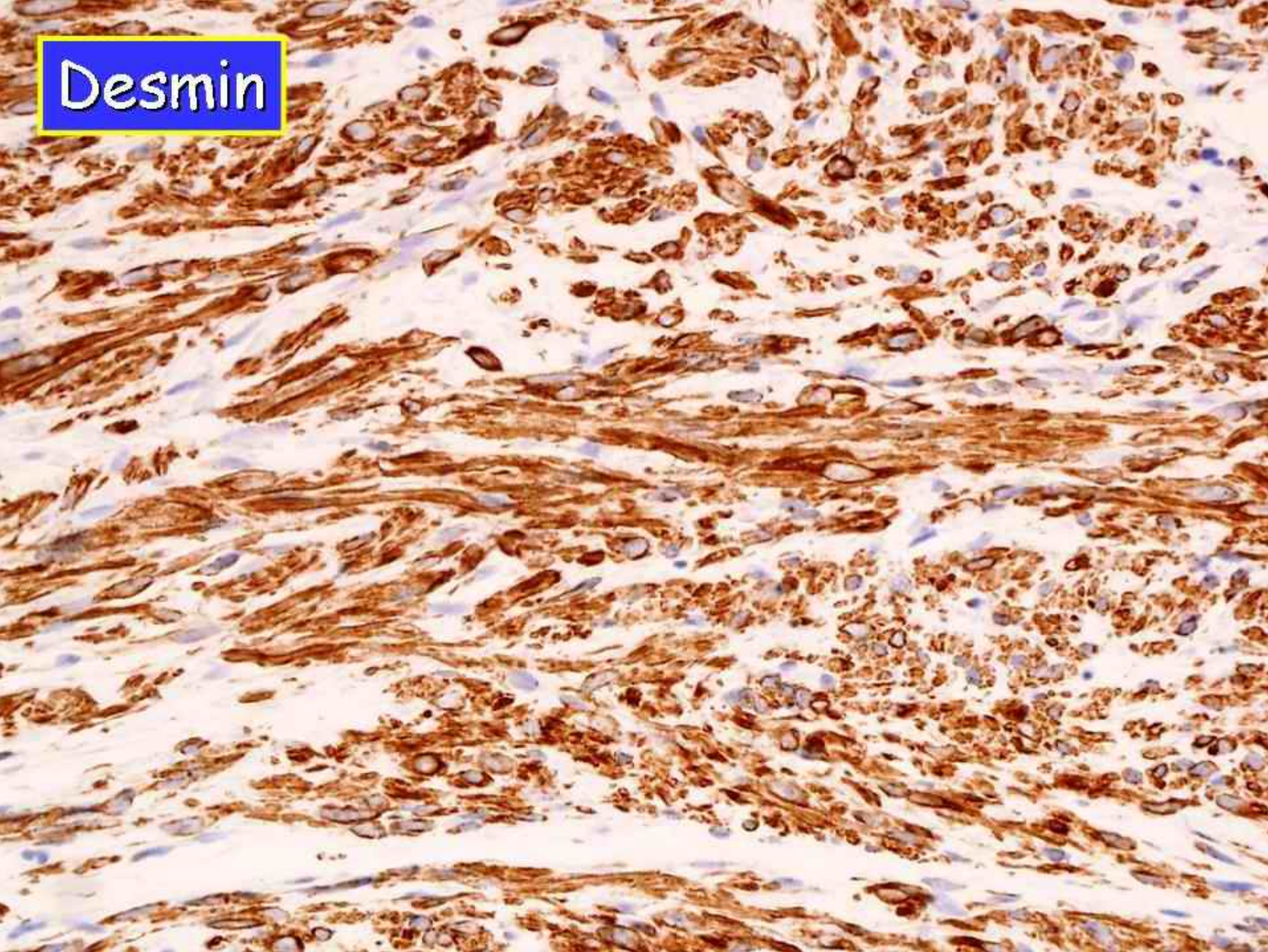









SMA

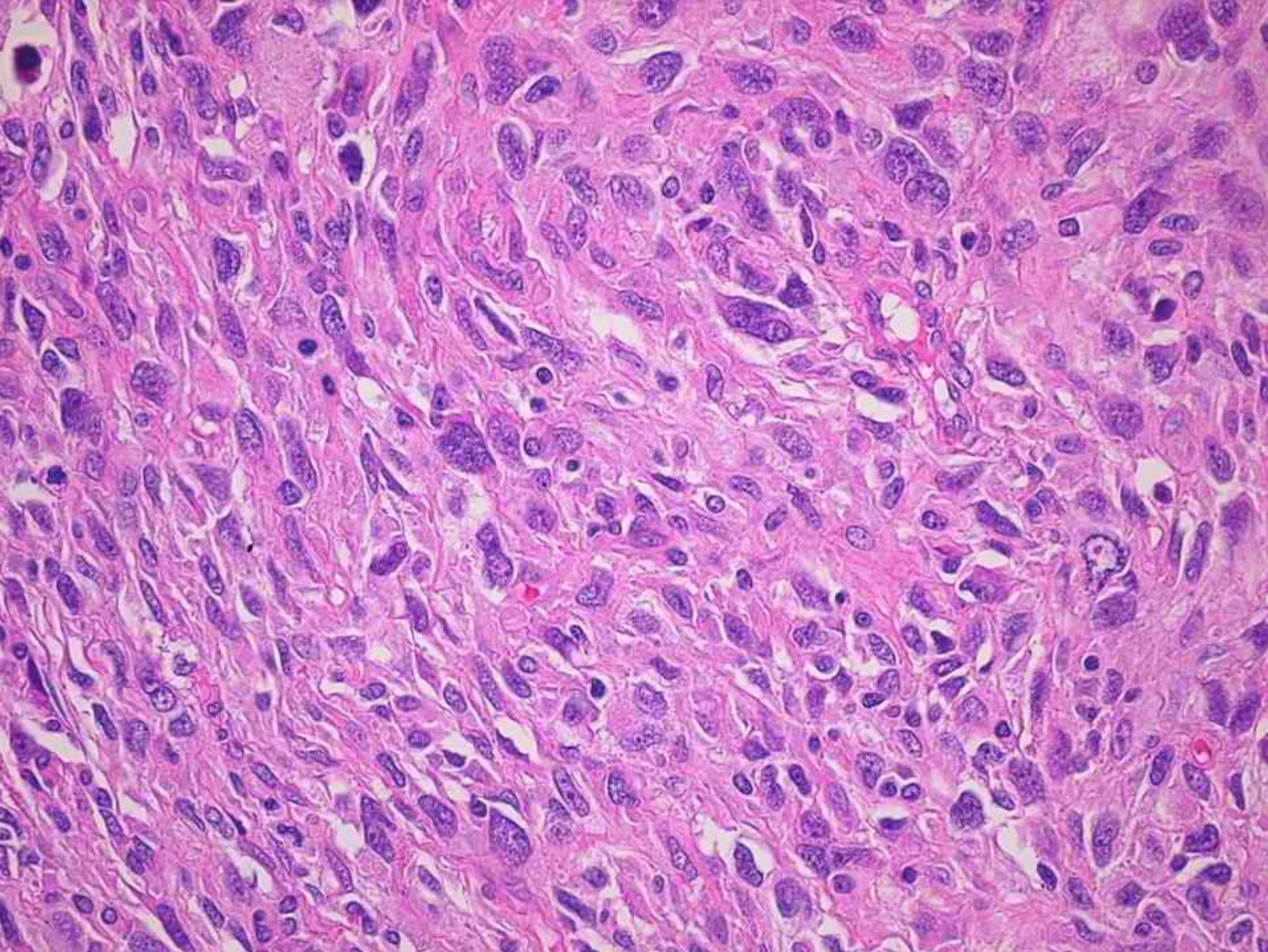

Desmin

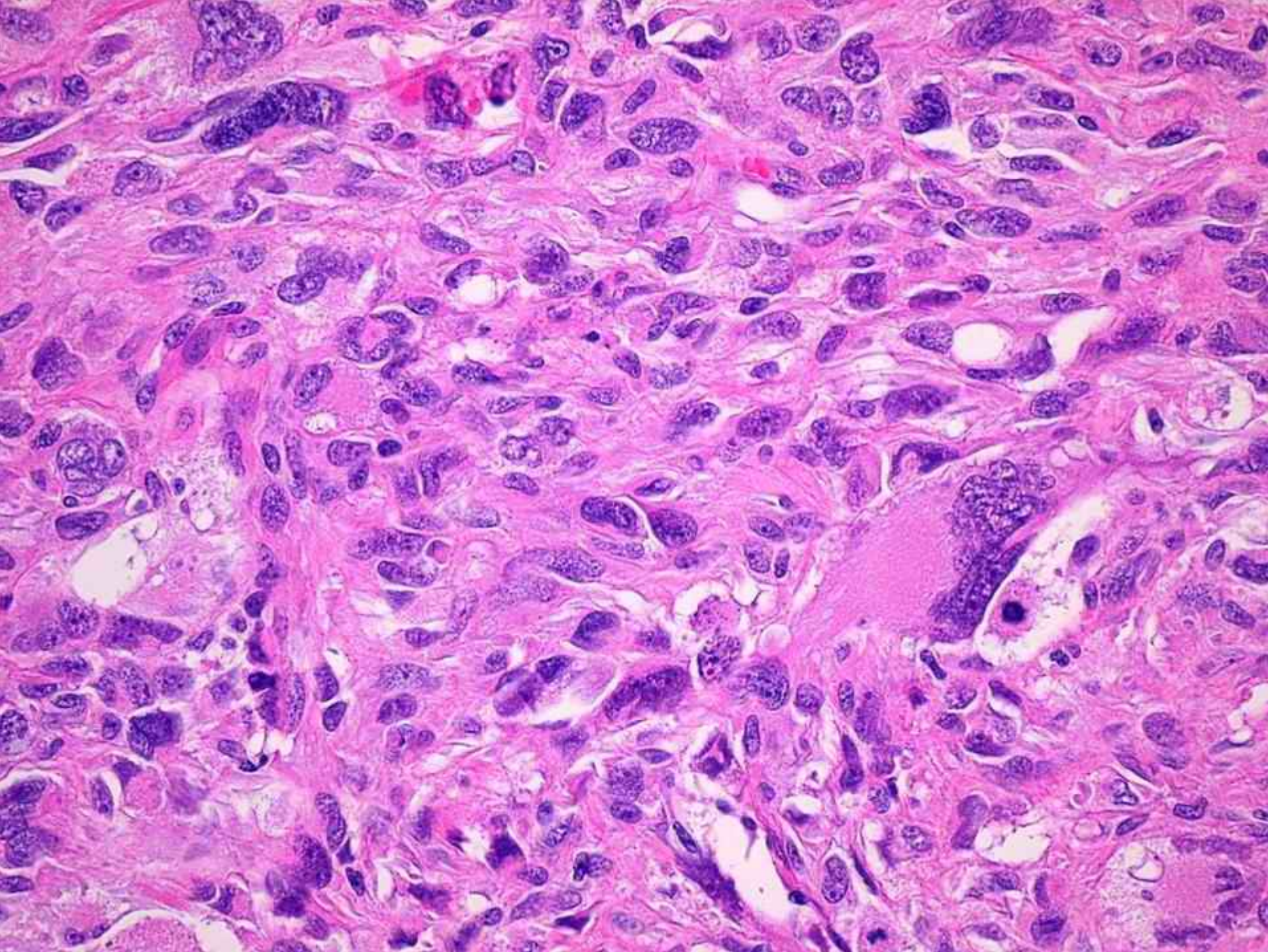
Diagnosis

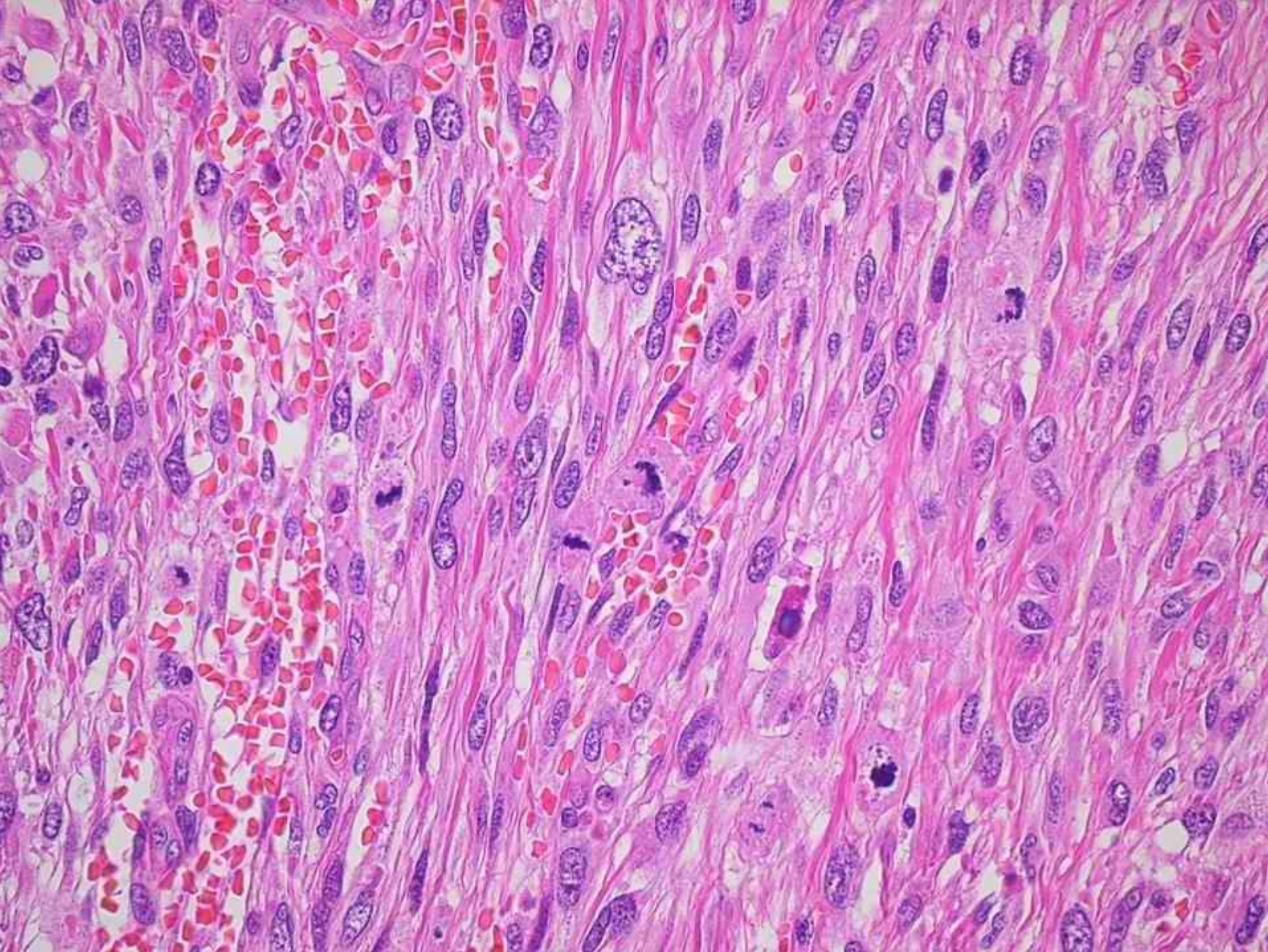
Well Differentiated
Leiomyosarcoma

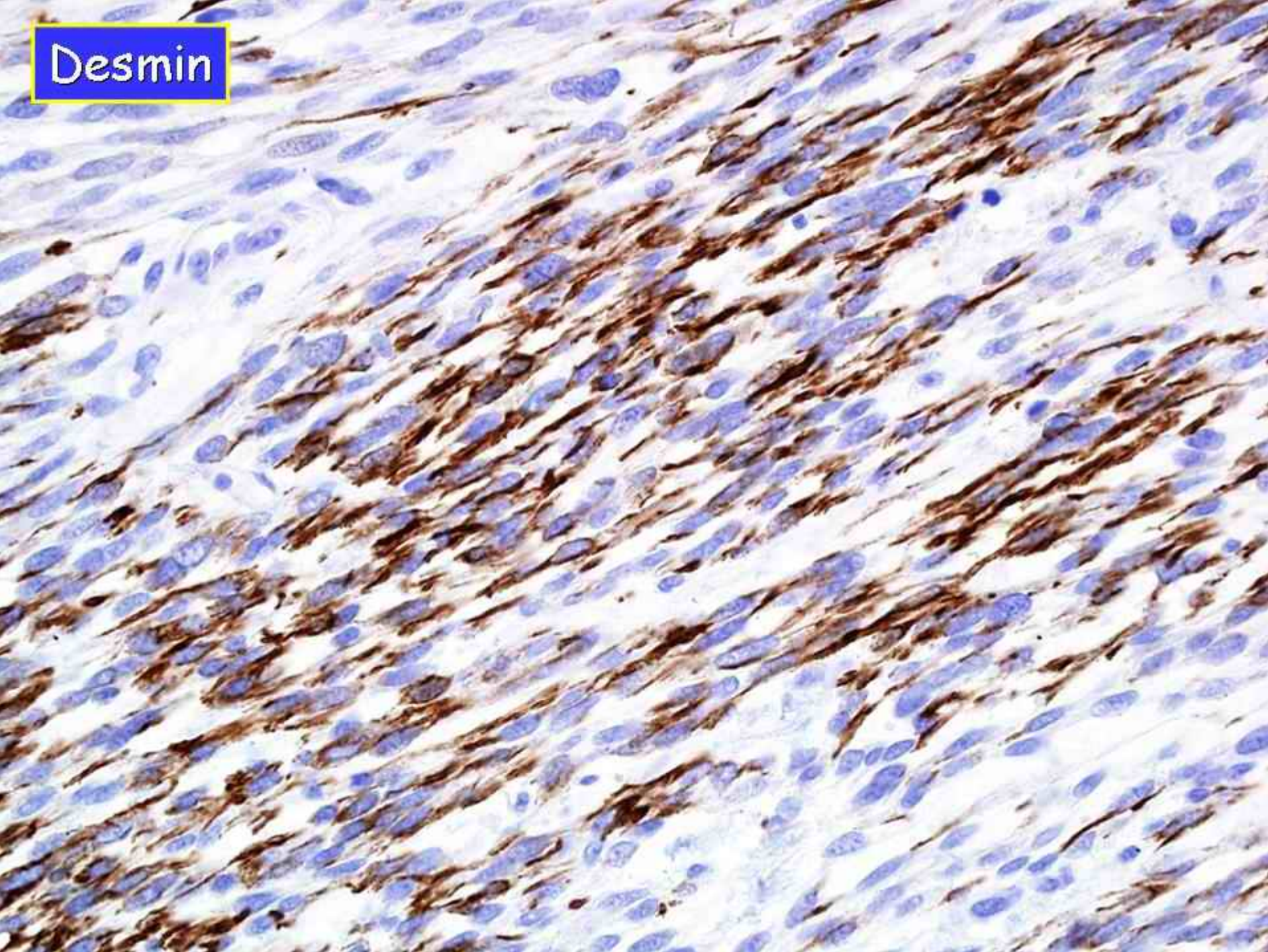
Leiomyosarcoma

- Intra-abdominal LMS
  - retroperitoneum, mesentery, omentum
  - 5th-7th decade
  - 5-year survival = 25% (mets to lungs & liver)
- Subcutaneous and deep ST LMS
  - thigh
  - 5-year survival = 65% (50% mets)
- Cutaneous LMS
  - limbs/head & neck
  - Young adults, M > F
  - no mets





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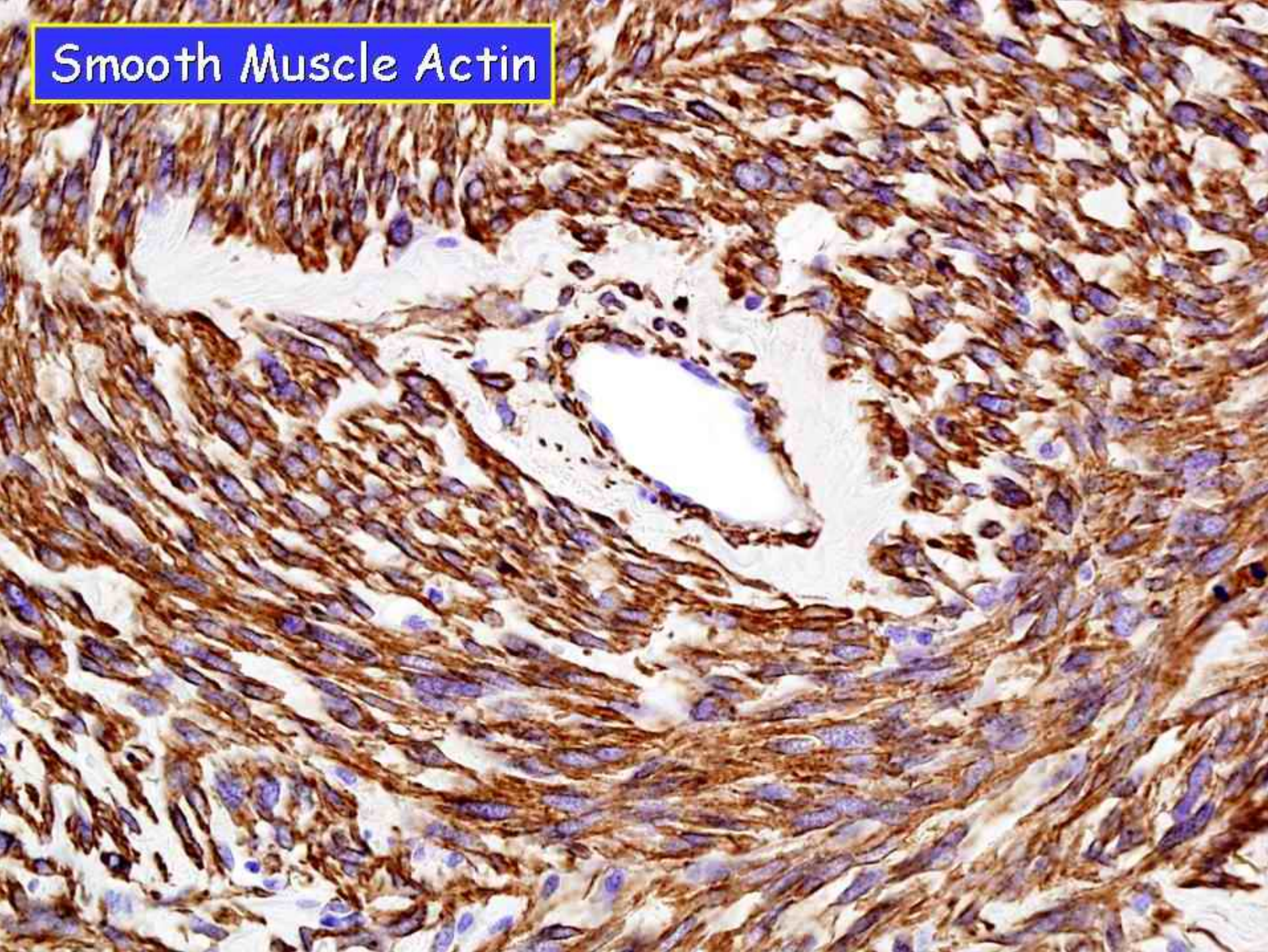
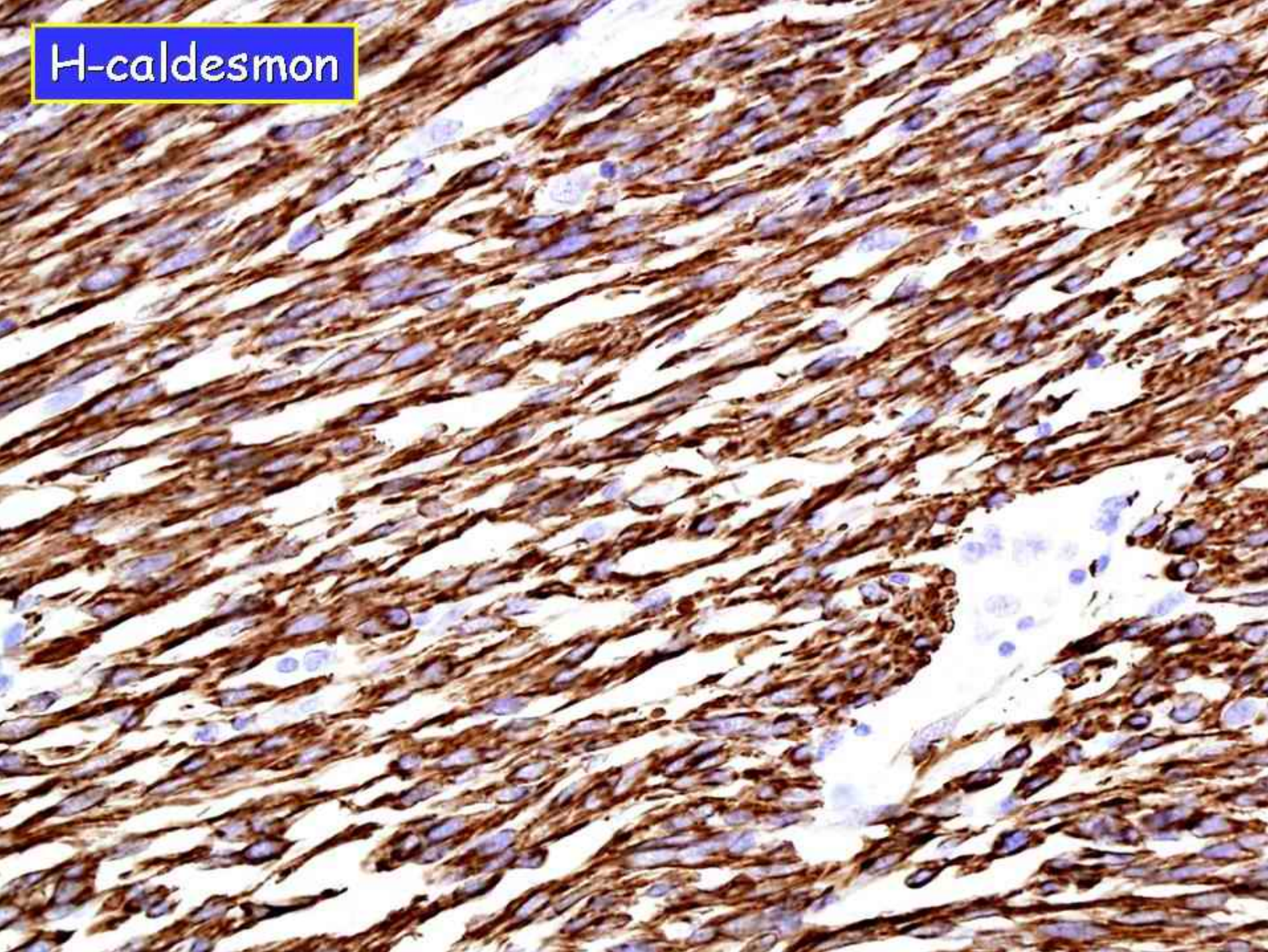

Smooth Muscle Actin


H-caldesmon

Cutaneus leiomyosarcoma

- Limbs/head & neck
- Young adults, M > F
- Multiple local recurrences
- No mets
- Irrespective of morphology

Cutaneus leiomyosarcoma

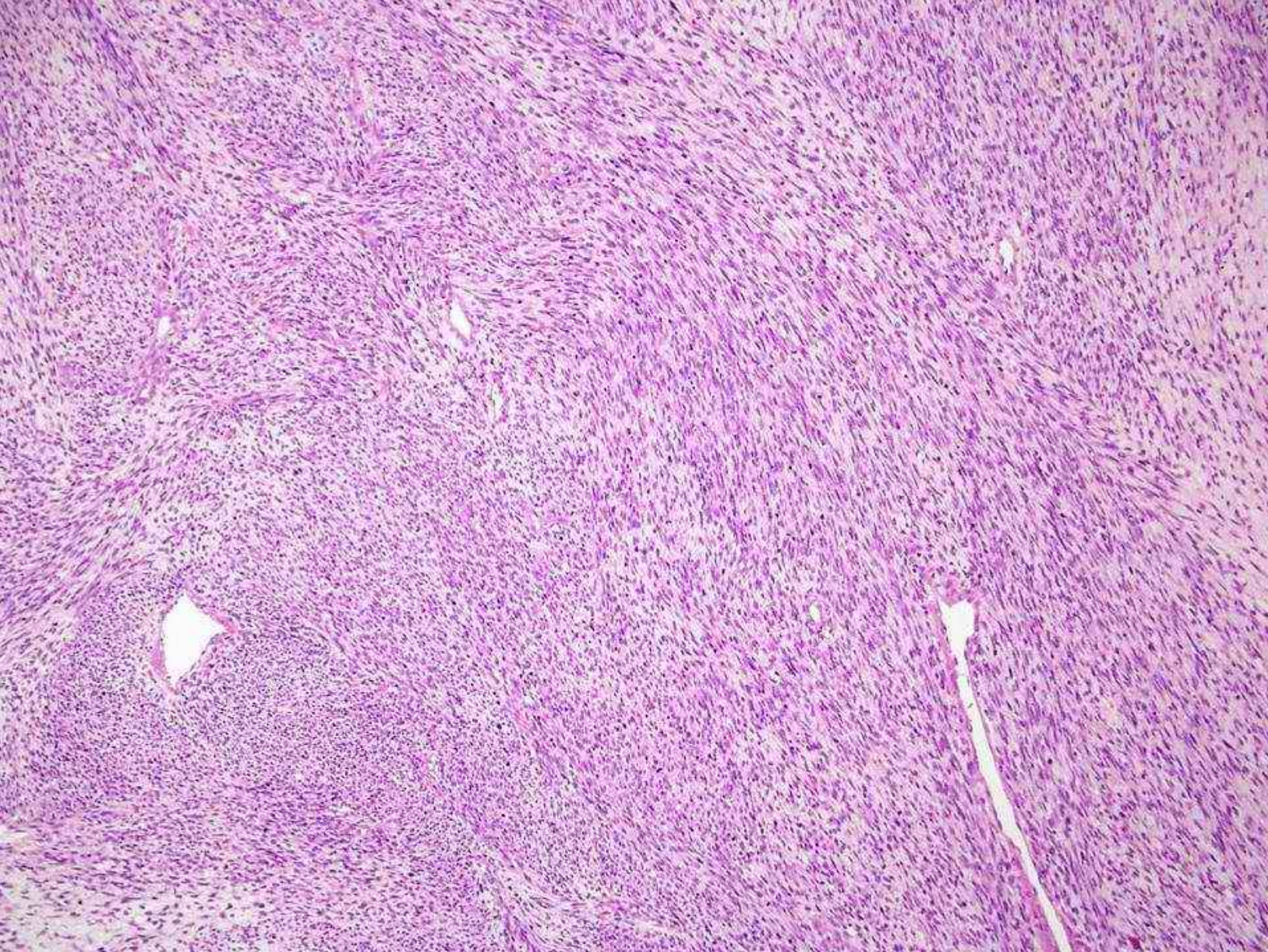
- Indolent clinical behavior
- Always exclude metastatic LMS
- Tropism for the skin of the scalp

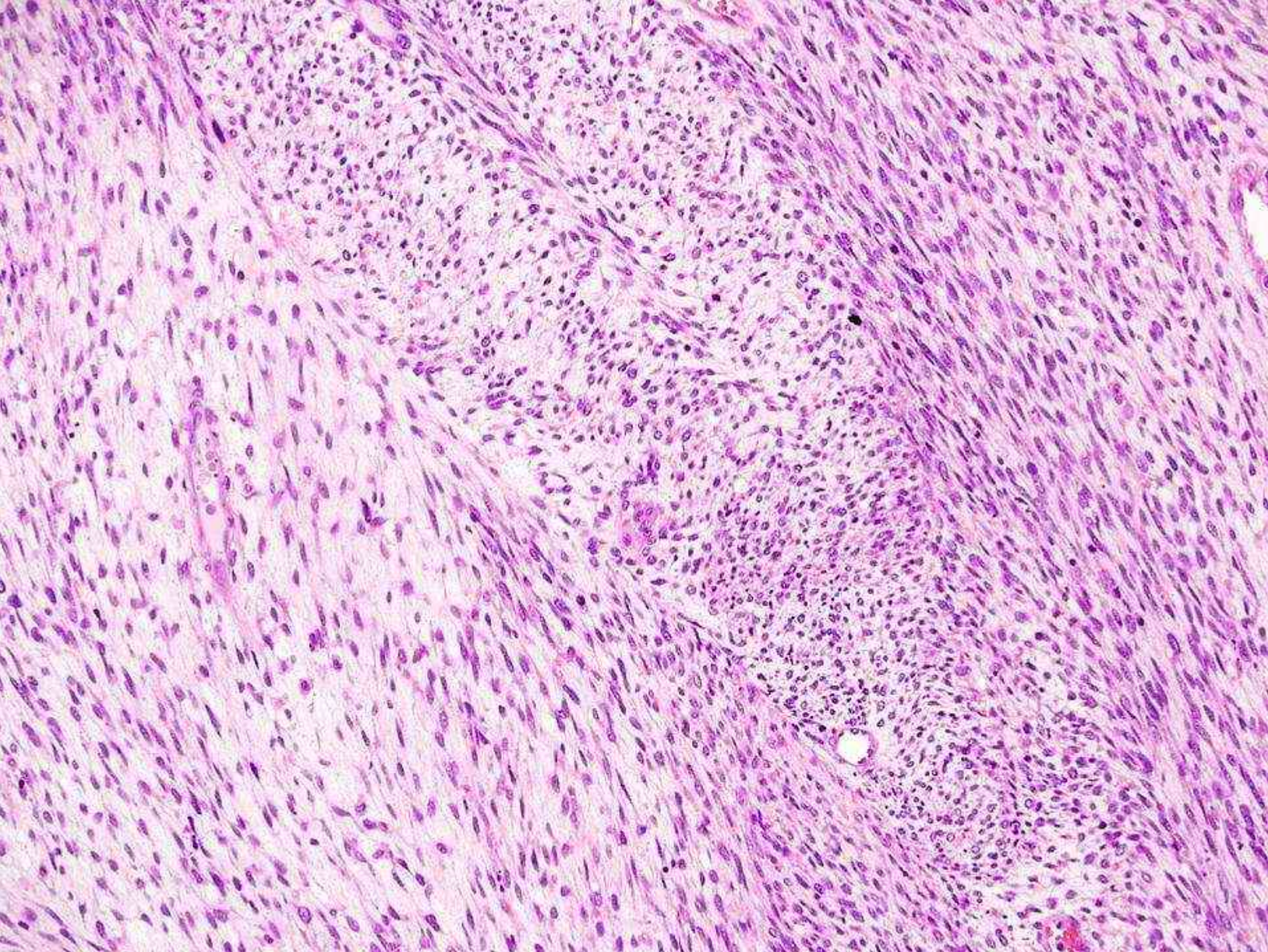
Prognostication in Smooth Muscle Tumors

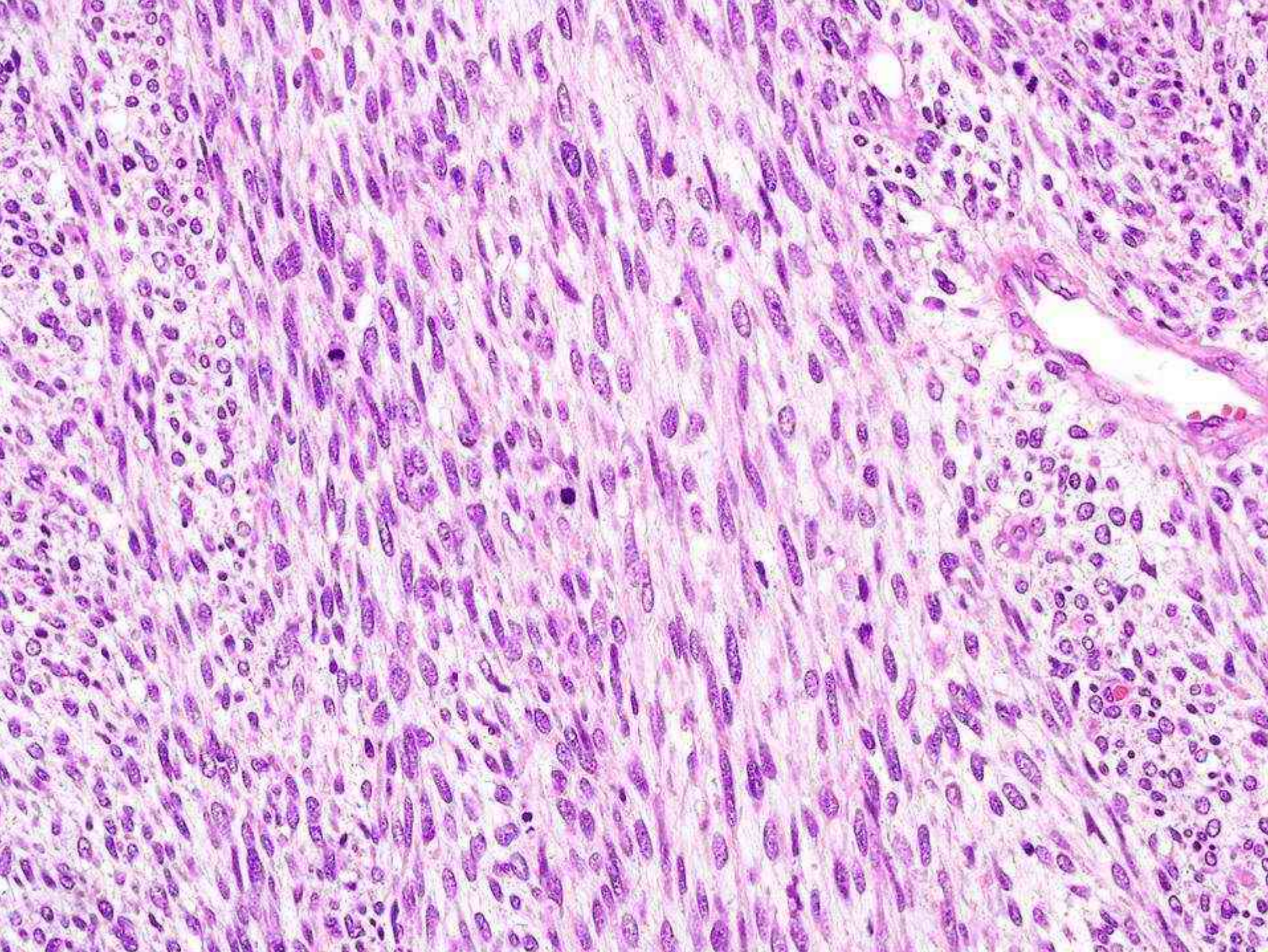
- Anatomic site important
  - Depth
  - Visceral vs. Non viscerale
- Mitotic activity depending upo anatomic site and gender
  - ER + retroperitoneal smooth muscle tumors in females accept mitotic activity

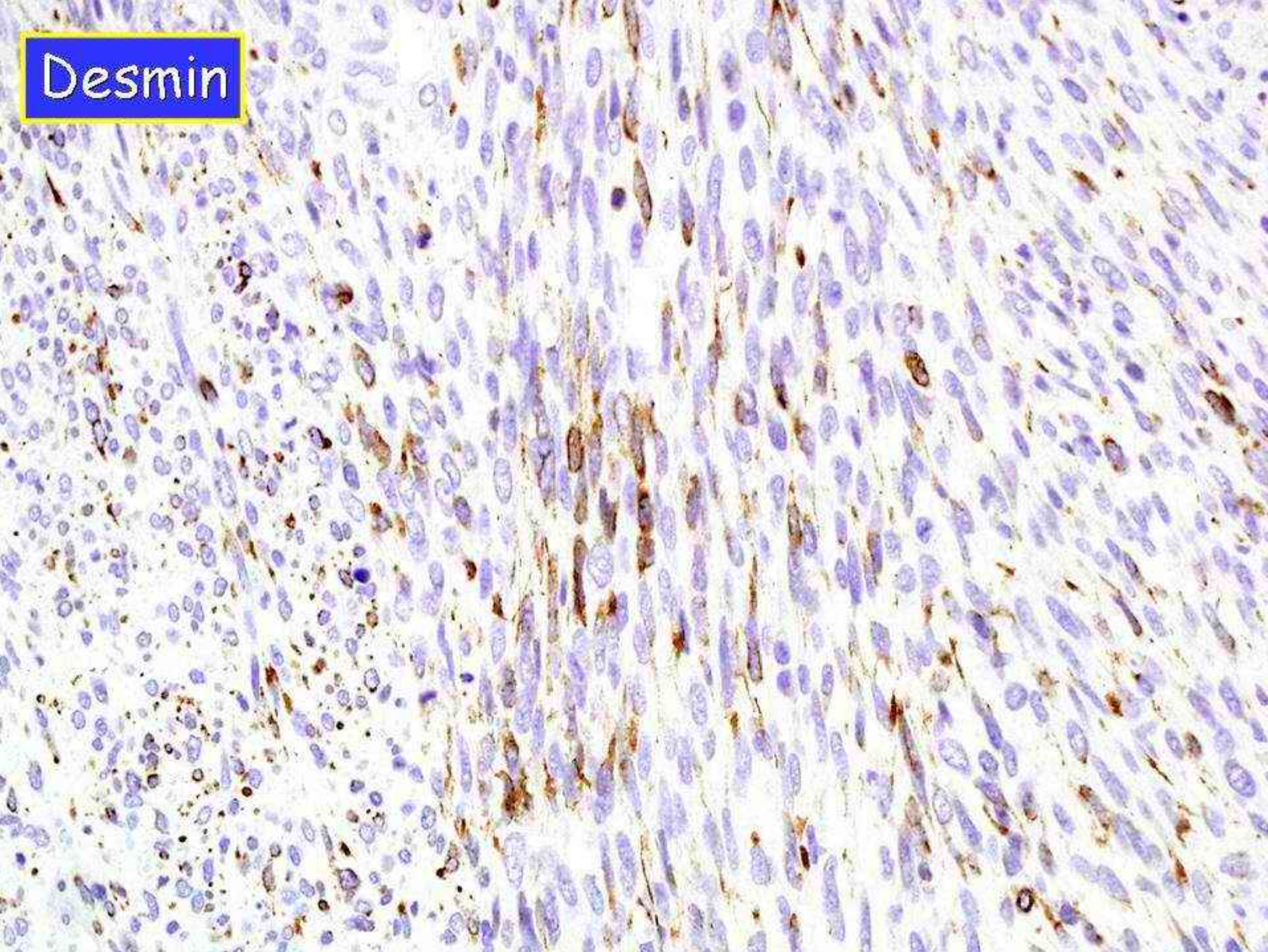
Clinical History

- 4 year old female
- 8 cm intra-abdominal mass attached the large bowel





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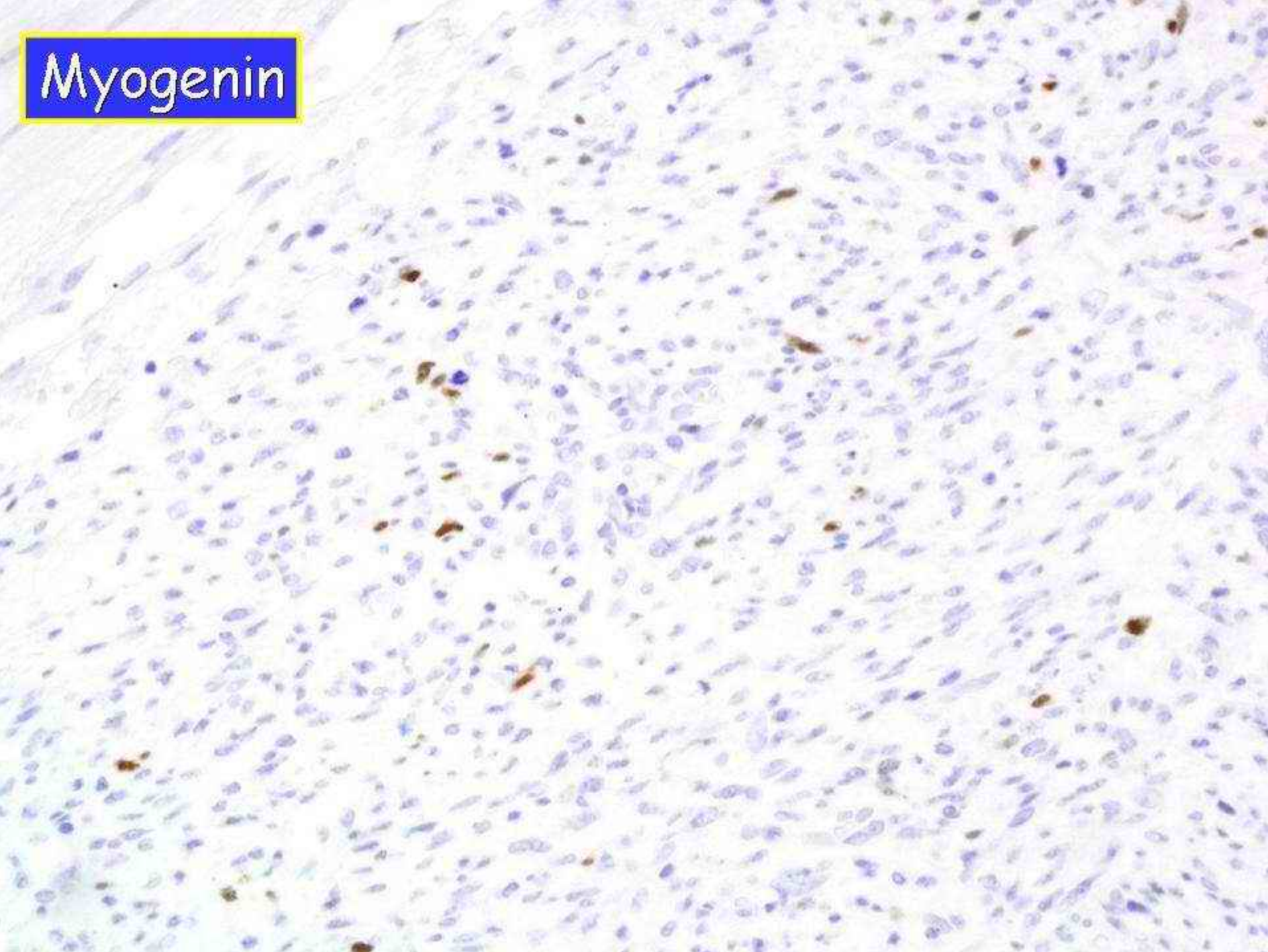
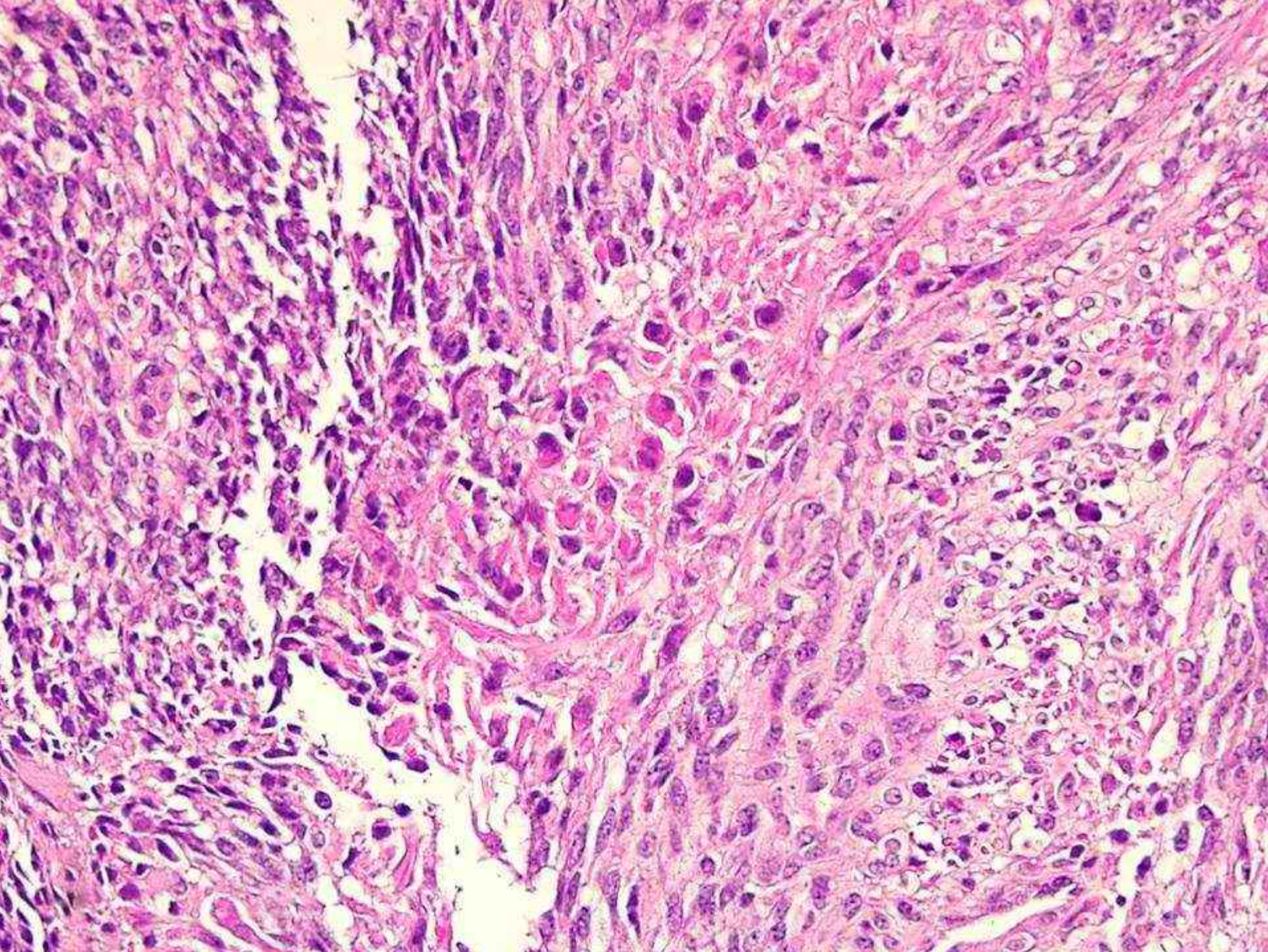

Myogenin

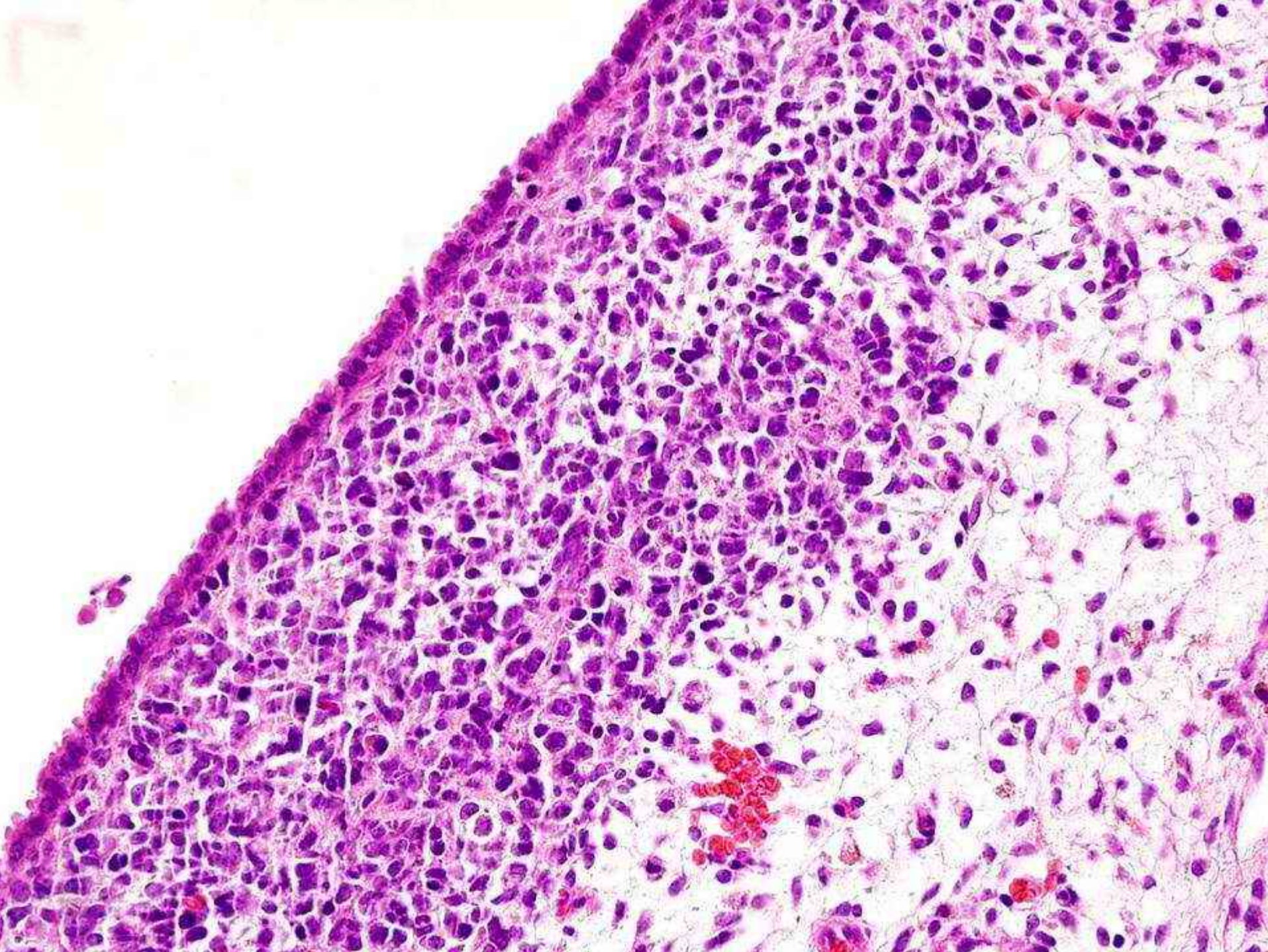
Diagnosis

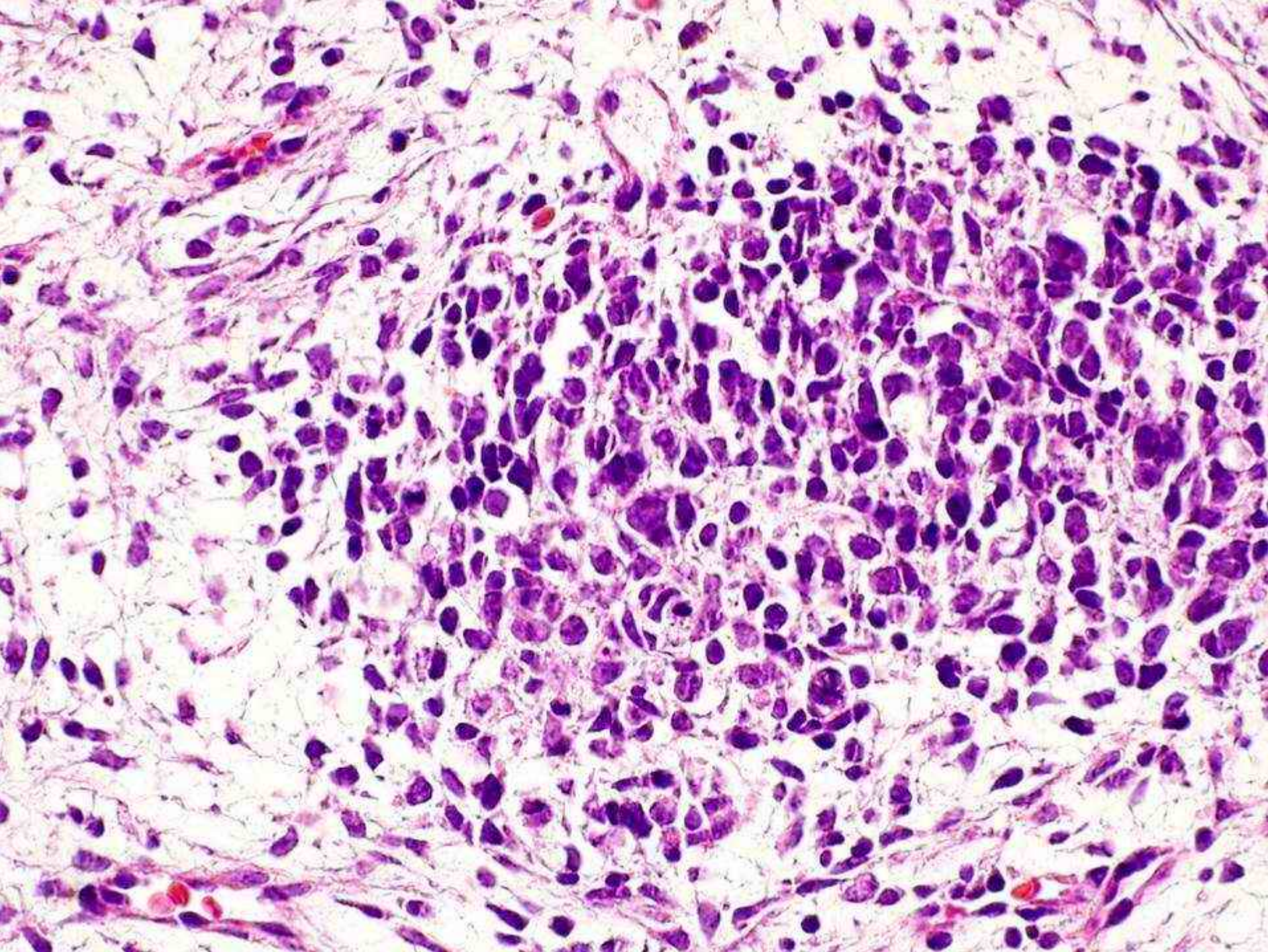
Spindle cell rhabdomyosarcoma

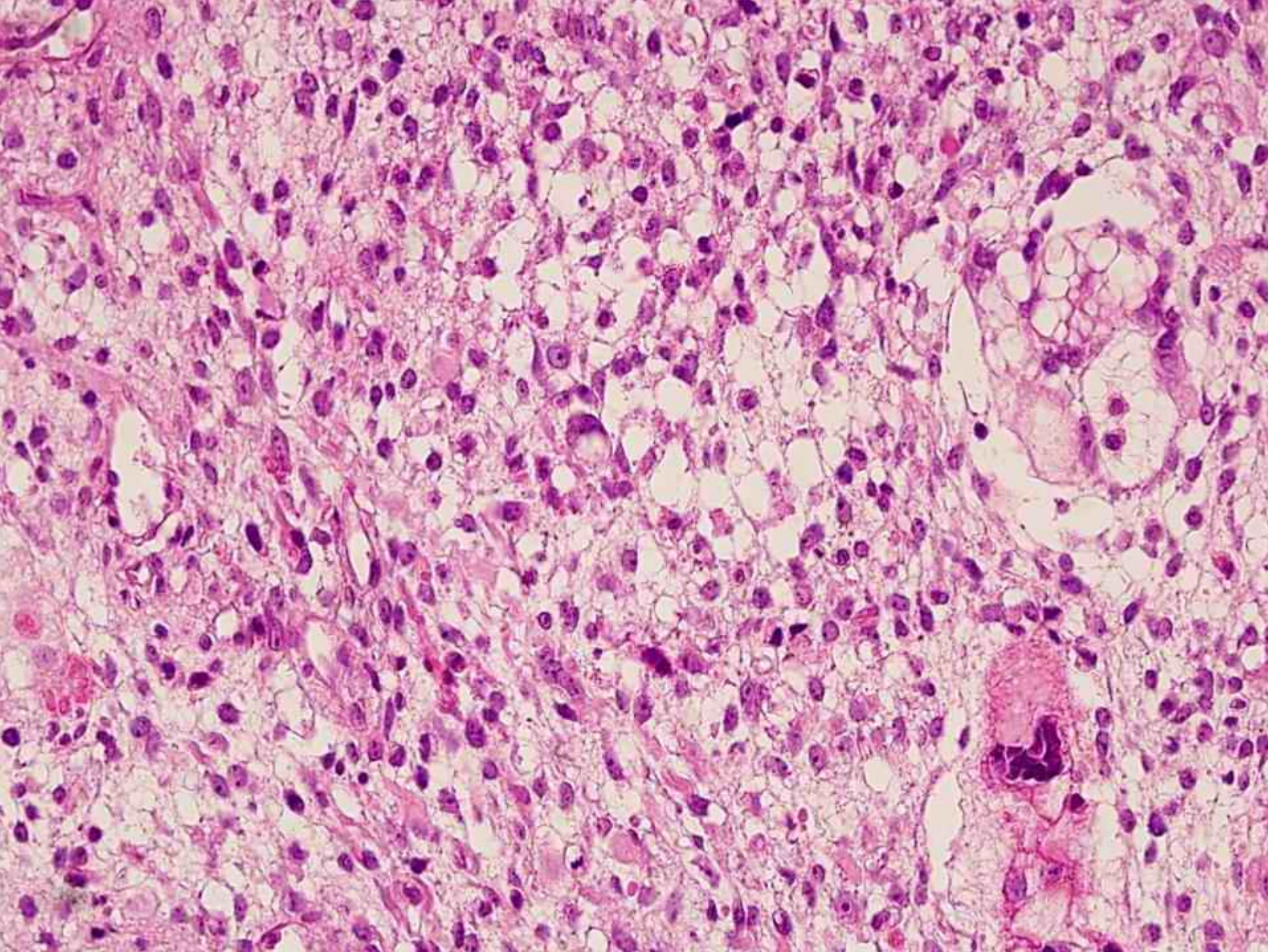
Rhabdomyosarcoma

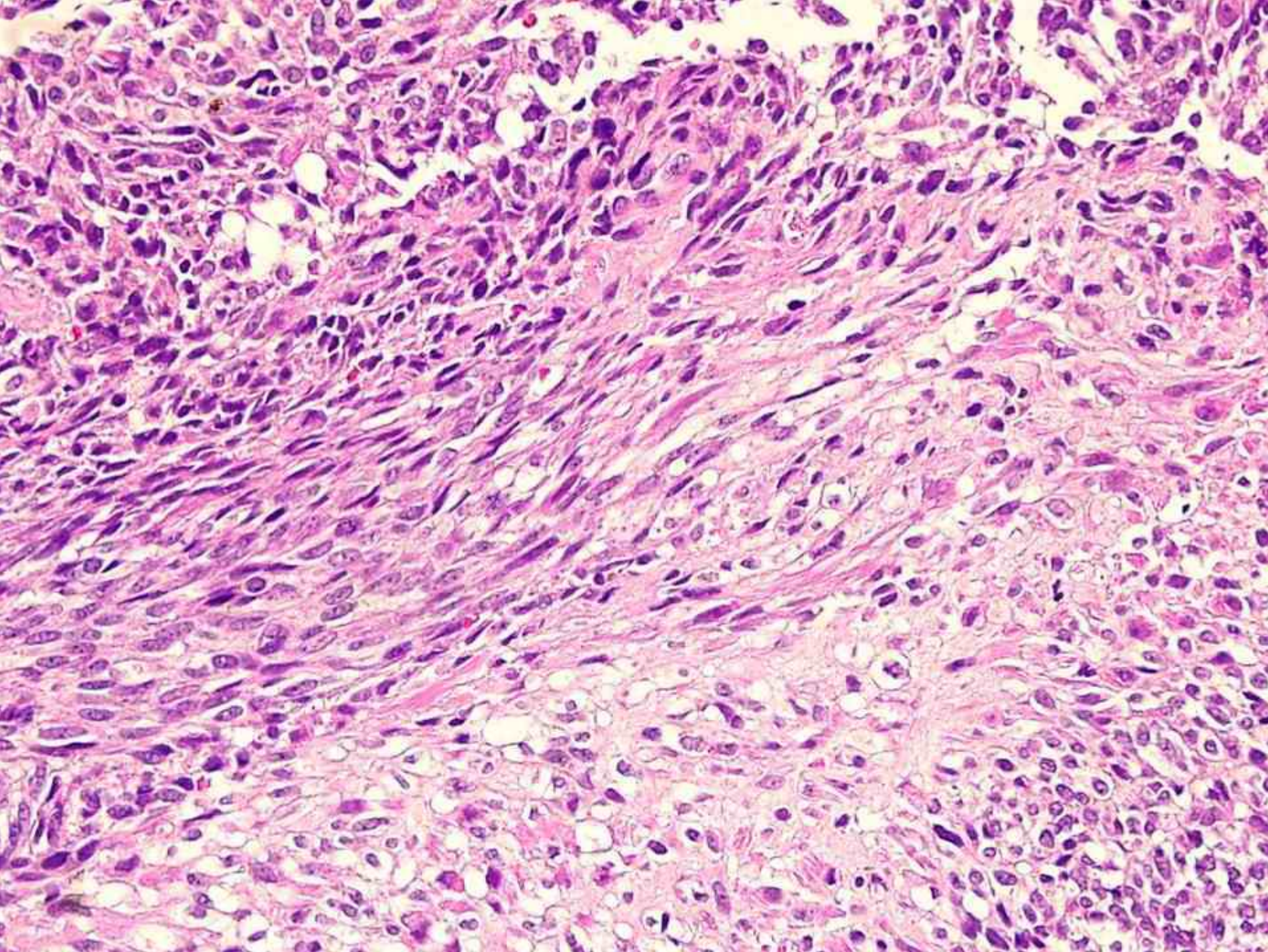
- Embryional
  - Botryoid, spindle cell, anaplastic
- Alveolar
  - Classic, solid, mixed E/A
- Pleomorphic

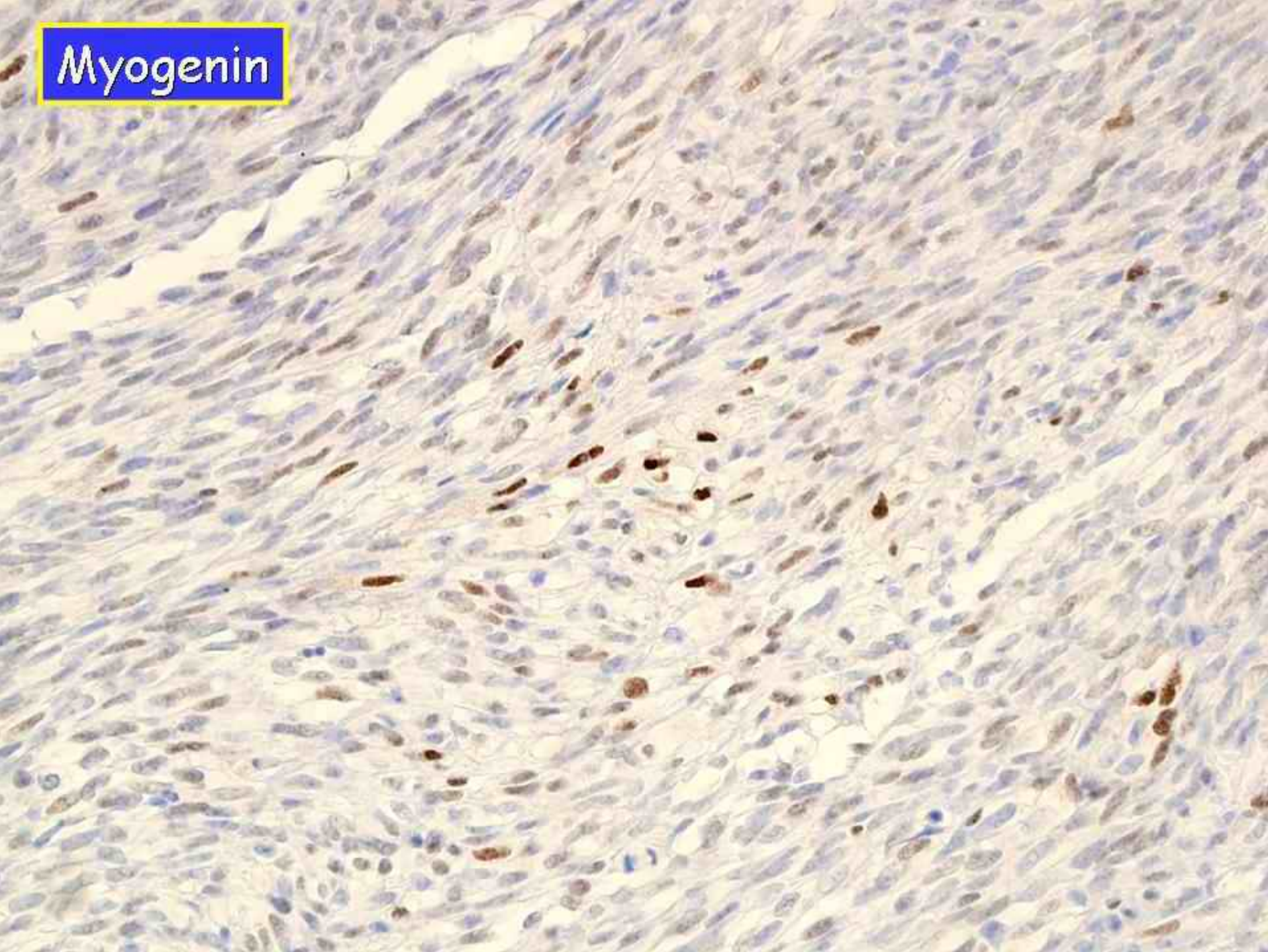










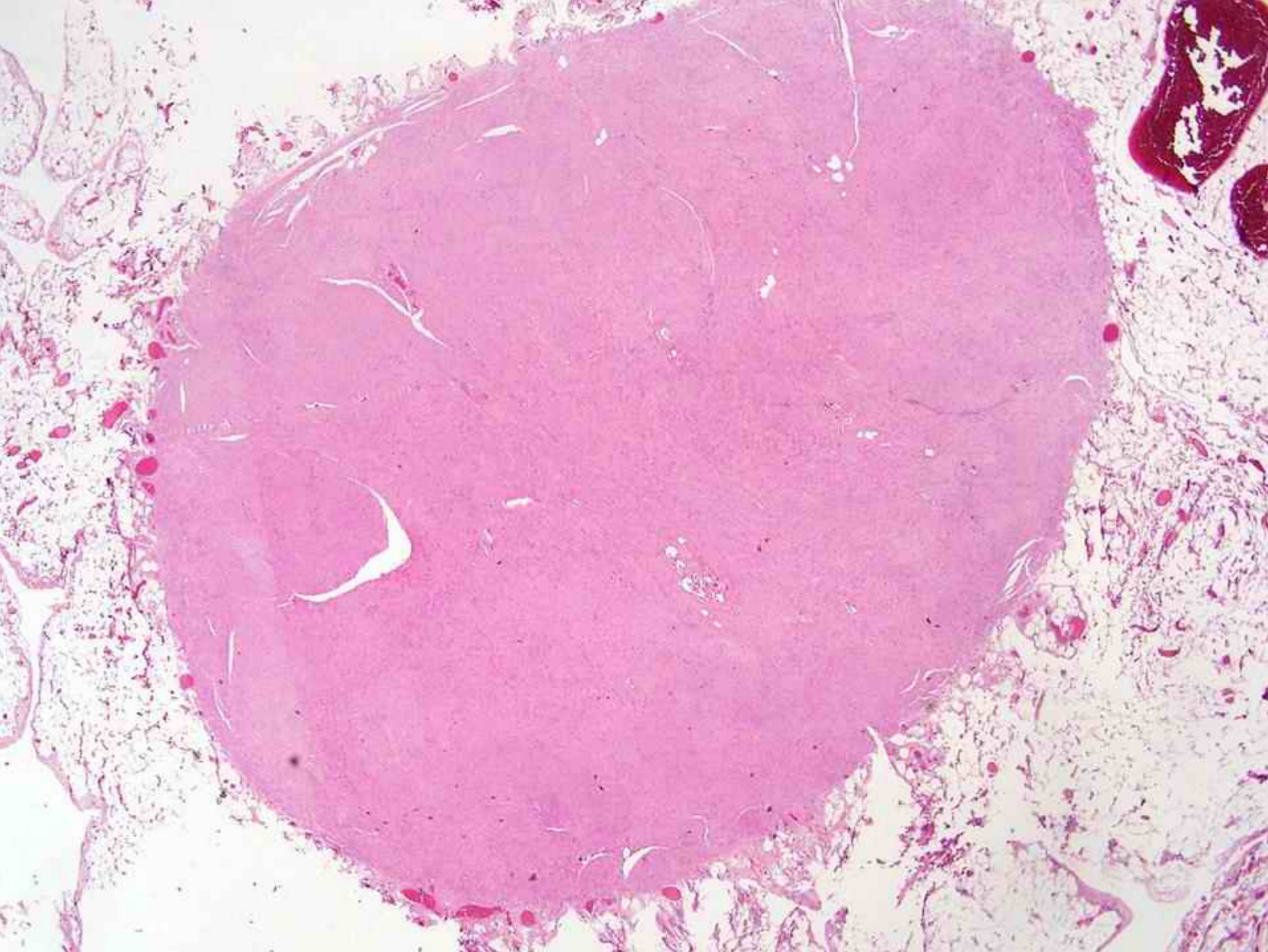

Myogenin

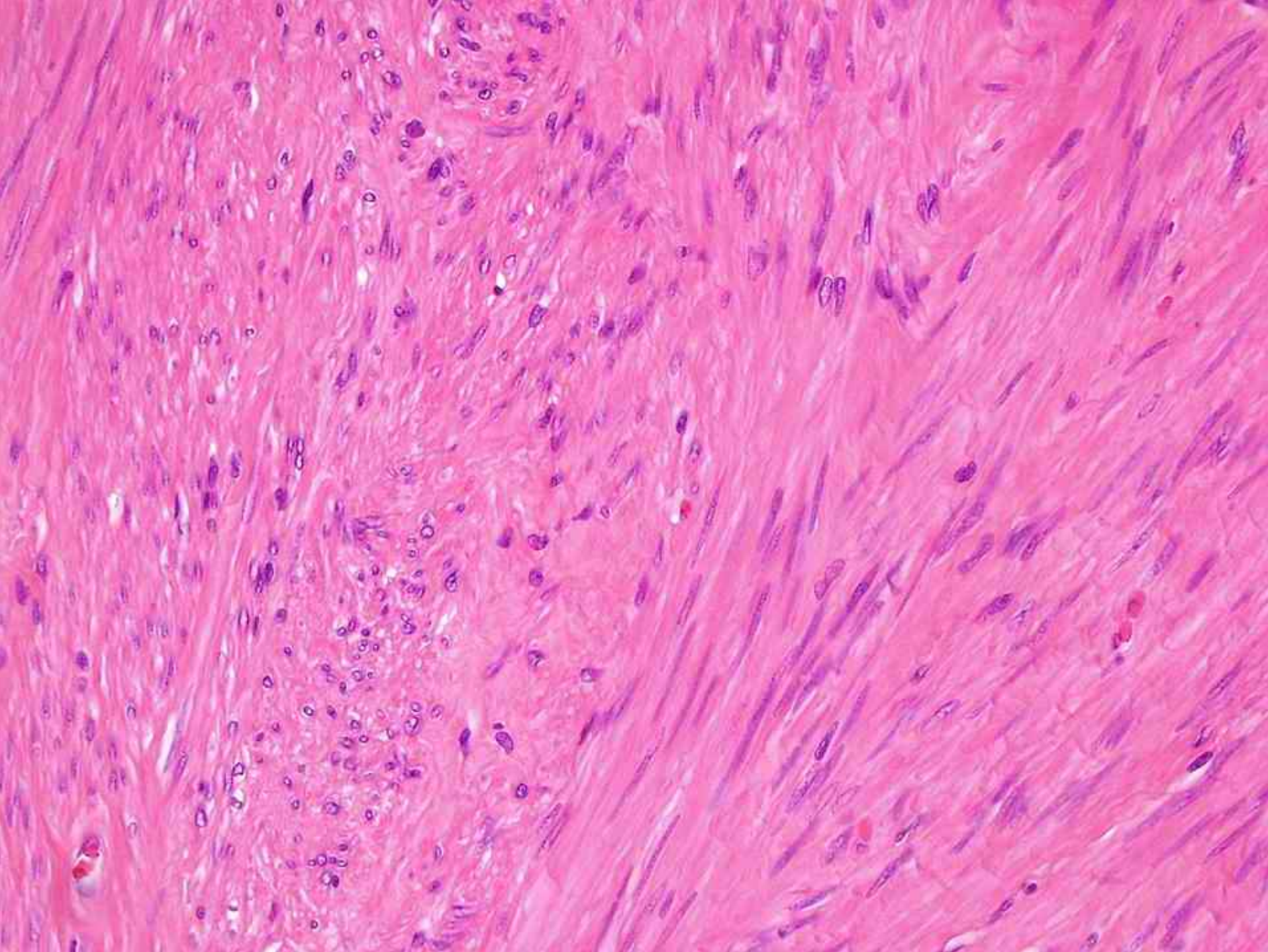
Embryonal Rhabdomyosarcoma

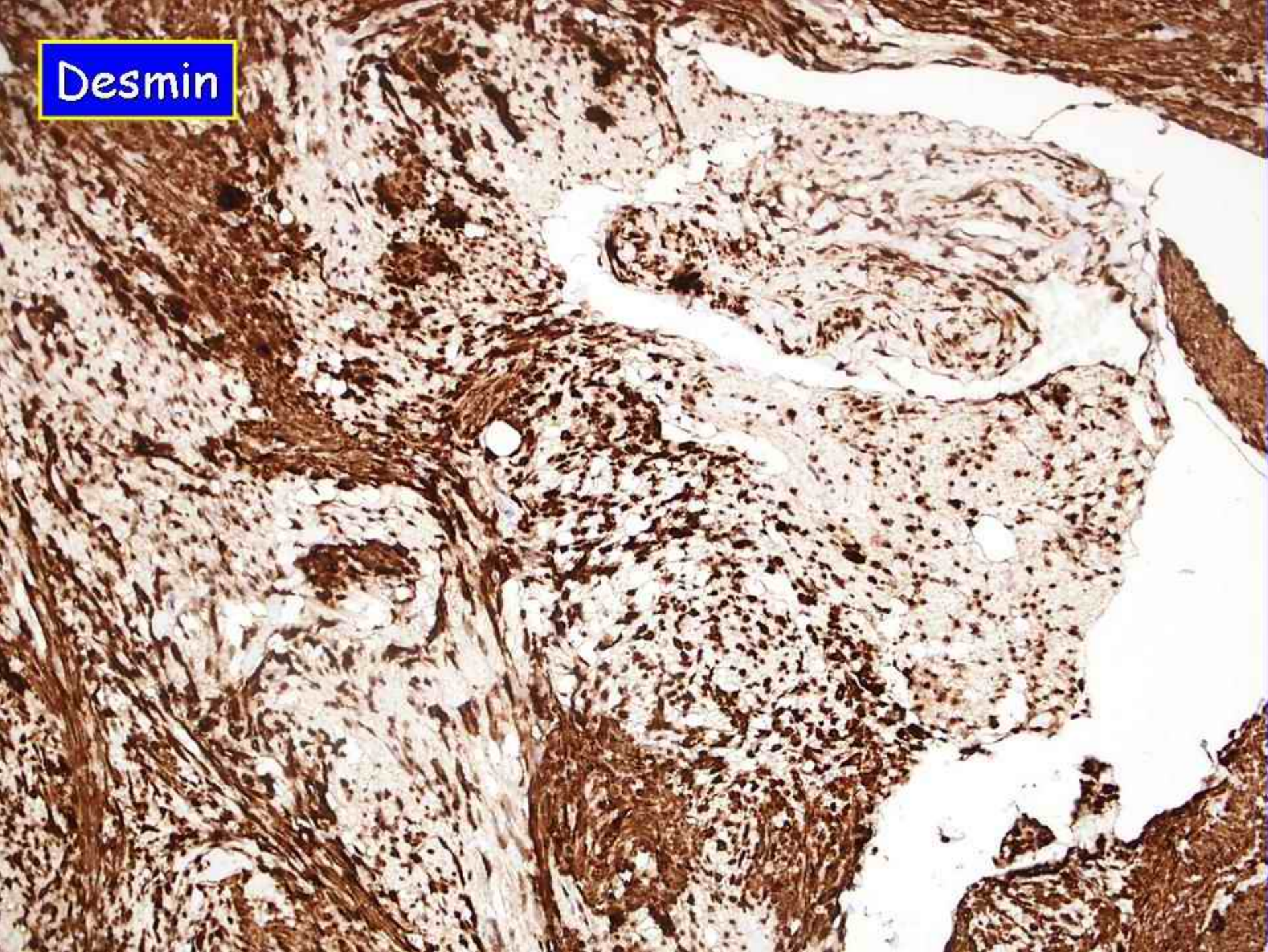
- 60% of childhood RMS
- Peak incidence: 1st decade
- Head & Neck/genital area/limbs and trunk/Visceral
- Botryoid and spindle cell
  - better prognosis
- Overall survival: 60-70% @ five years

Clinical History

- Male, 59
- Laparatomy for colonic CA
- Multiple nodules in mesentery



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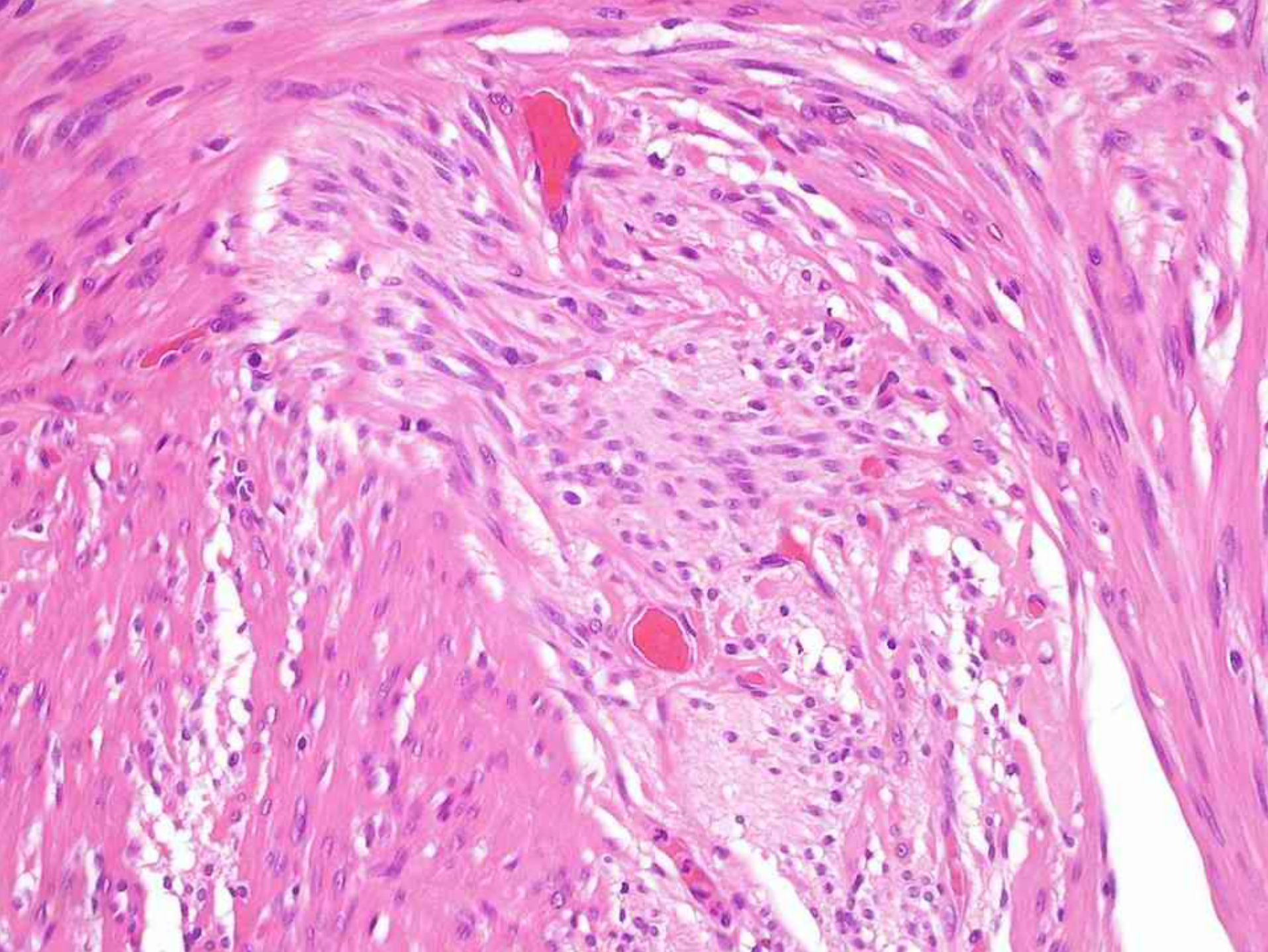

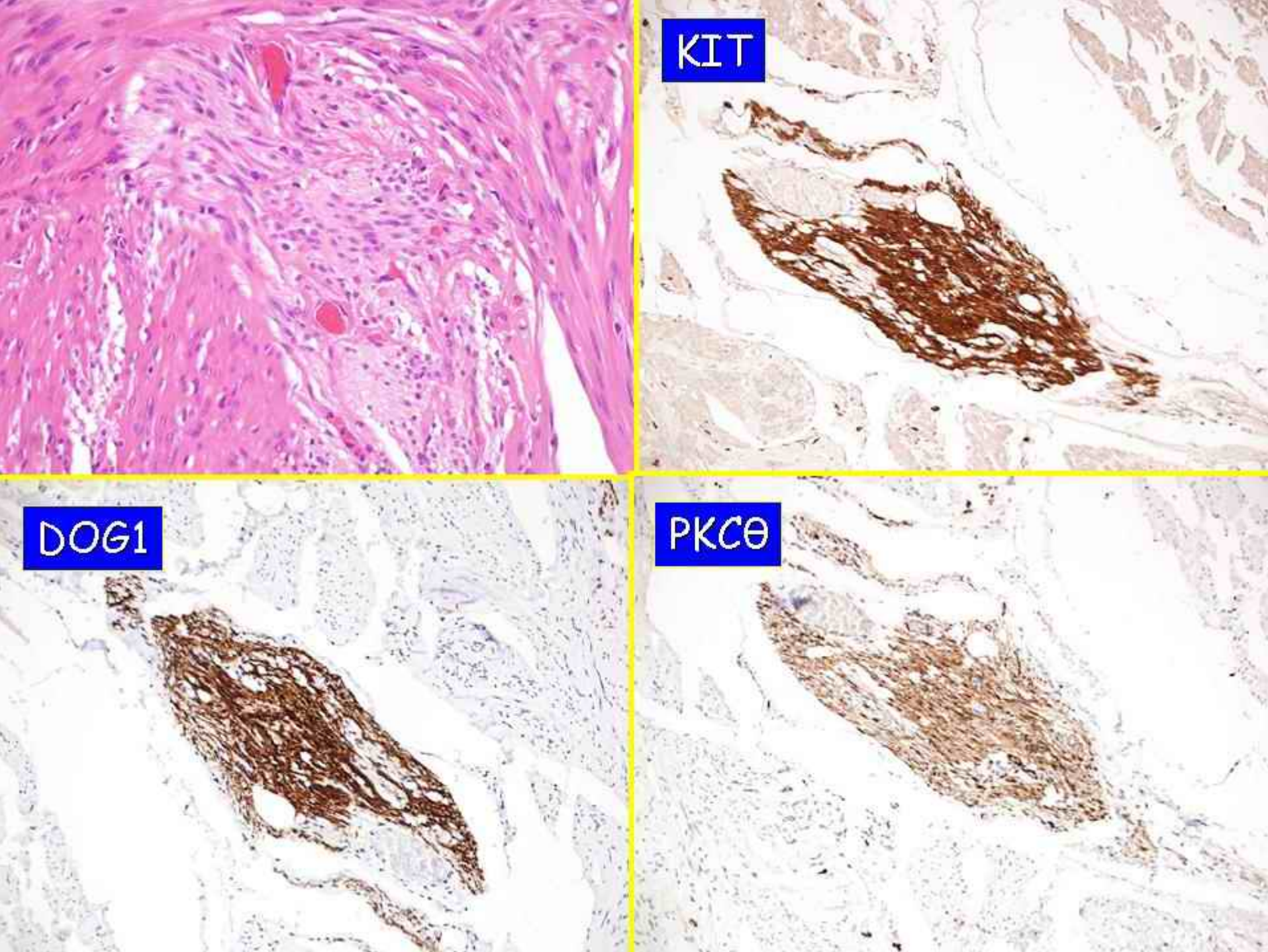
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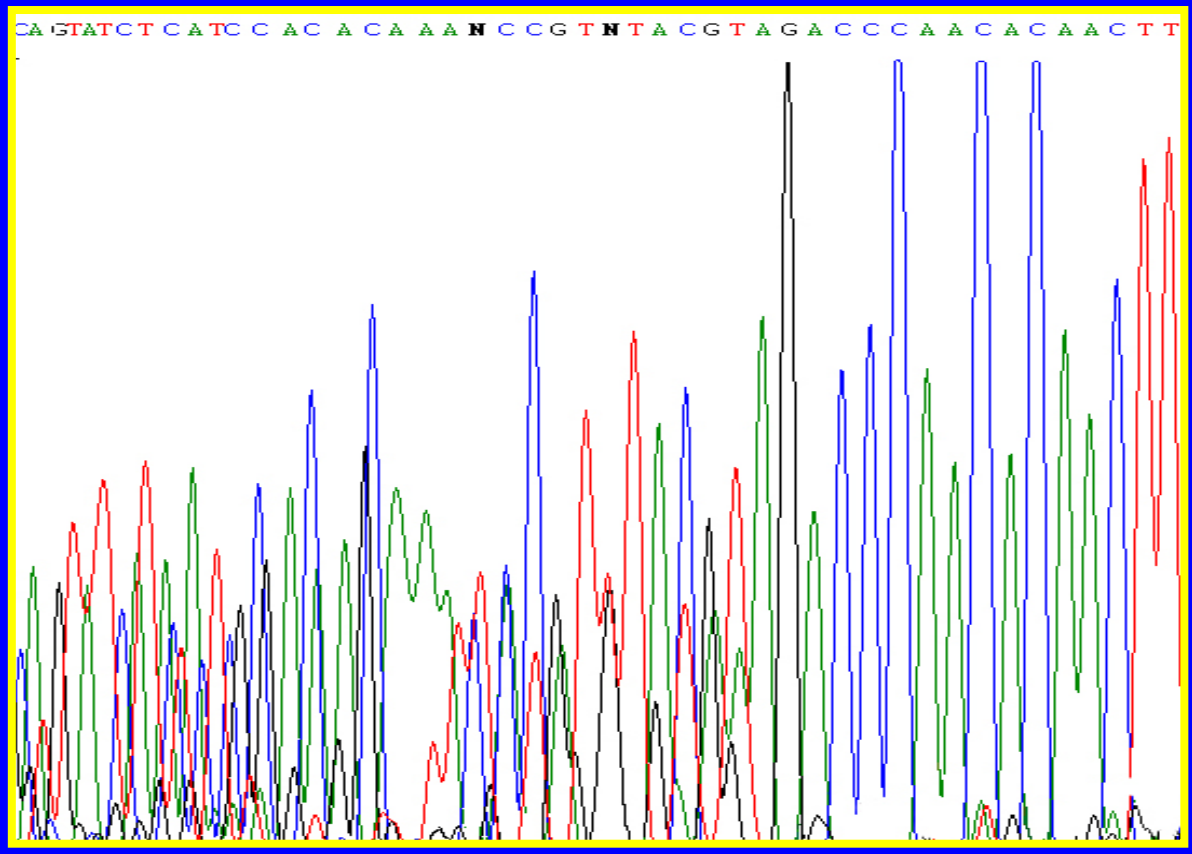

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(seq. rev primer)

Diagnosis

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