



AAPA 2026 **Annual Conference**

Here Comes the Sun:
Illuminating the Future of Pathology

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AAPA NATIONAL MEETING

From Bench to Biomarkers

Practical Clinical, Pathologic, and Molecular Insights into
Mesenchymal Neoplasms Across Age Groups

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Learning Objectives

- Recognize key clinical and pathologic differences between pediatric and adult mesenchymal neoplasms.
- Understand how gross examination and specimen triage influence diagnosis and molecular testing.
- Identify major molecular alterations relevant to selected bone and soft tissue tumors.
- Recognize common diagnostic pitfalls and benign mimics.
- Appreciate the central role of the Pathologists' Assistant in multidisciplinary sarcoma care.

Why This Topic Matters

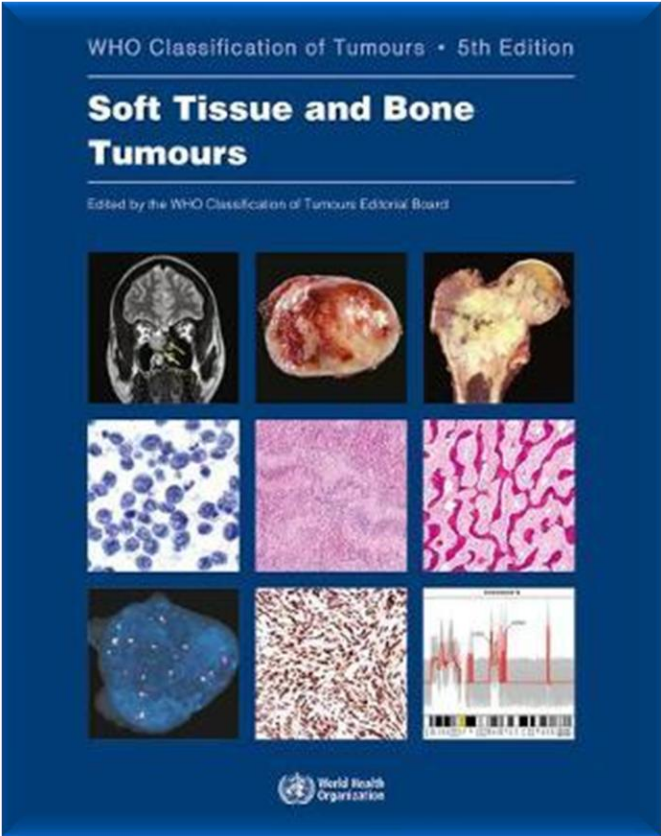
- Mesenchymal neoplasms are uncommon but diagnostically challenging.
- Diagnosis is an integration of clinical, radiologic, gross, microscopic and molecular findings.
- Specimen handling directly affects diagnostic accuracy and patient care.

Challenges (1)

- There is a wide variety of tumor types and subtypes.
- More than 120 soft tissue tumor entities (>50 types of sarcomas).
- About 50 primary bone tumor entities.
- Different subtypes of the same type of tumor can have very different behaviors.
- Most are seen infrequently.
- Nomenclature can be VERY confusing (e.g., Low-grade fibromyxoid sarcoma vs Low-grade myxofibrosarcoma).

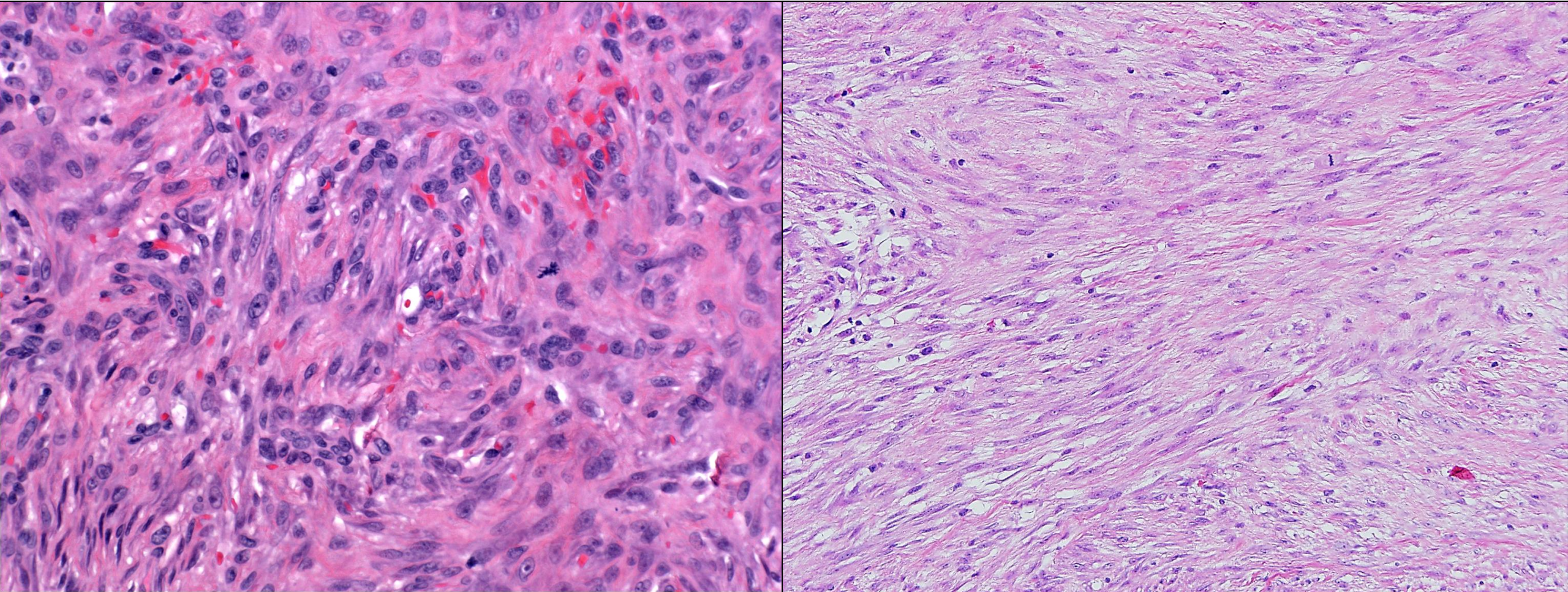
Soft tissue tumours	
Soft tissue tumours: Introduction	
Adipocytic tumours	
Lipoma	
Lipomatosis	
Lipomatosis of nerve	
Lipoblastoma and lipoblastomatosis	
Angiolipoma	
Myolipoma of soft tissue	
Chondroid lipoma	
Spindle cell lipoma and pleomorphic lipoma	
Hibernoma	
Atypical spindle cell / pleomorphic lipomatous tumour	
Atypical lipomatous tumour / well-differentiated liposarcoma	
Dedifferentiated liposarcoma	
Myxoid liposarcoma	
Pleomorphic liposarcoma	
Myxoid pleomorphic liposarcoma	
Fibroblastic and myofibroblastic tumours	
Nodular fasciitis	
Proliferative fasciitis and proliferative myositis	
Myositis ossificans and fibro-osseous pseudotumour of digits	
Ischaemic fasciitis	
Elastofibroma	
Fibrous hamartoma of infancy	
Fibromatosis coli	
Juvenile hyaline fibromatosis	
Inclusion body fibromatosis	
Fibroma of tendon sheath	
Desmoplastic fibroblastoma	
Myofibroblastoma	
Calcifying aponeurotic fibroma	
EWSR1-SMAD3-positive fibroblastic tumour (emerging)	
Angiomyofibroblastoma	
Cellular angiofibroma	
Angiofibroma of soft tissue	
Nuchal-type fibroma	
Acral fibromyxoma	
Gardner fibroma	
Palmar fibromatosis and plantar fibromatosis	
Desmoid fibromatosis	
Lipofibromatosis	
Giant cell fibroblastoma	
Dermatofibrosarcoma protuberans	
Solitary fibrous tumour	
Inflammatory myofibroblastic tumour	
Low-grade myofibroblastic sarcoma	
Superficial CD34-positive fibroblastic tumour	
Myxoinflammatory fibroblastic sarcoma	
Infantile fibrosarcoma	
Adult fibrosarcoma	
Myxofibrosarcoma	
Low-grade fibromyxoid sarcoma	
Sclerosing epithelioid fibrosarcoma	
So-called fibrohistiocytic tumours	
Tenosynovial giant cell tumour	
Deep fibrous histiocytoma	
Plexiform fibrohistiocytic tumour	
Giant cell tumour of soft tissue	
Vascular tumours	
Haemangiomas	
Synovial haemangioma	
Intramuscular angioma	
Arteriovenous malformation/haemangioma	
Venous haemangioma	
Anastomosing haemangioma	
Epithelioid haemangioma	
Lymphangioma and lymphangiomatosis	
Tufted angioma and kaposiform haemangioendothelioma	
Retiform haemangioendothelioma	
Papillary intralymphatic angioendothelioma	
Composite haemangioendothelioma	
Kaposi sarcoma	
Pseudomyogenic haemangioendothelioma	
Epithelioid haemangioendothelioma	
Angiosarcoma	
Pericytic (perivascular) tumours	
Glomus tumour	
Myopericytoma, including myofibroma	
Angioleiomyoma	
Smooth muscle tumours	
Leiomyoma	
EBV-associated smooth muscle tumour	
Inflammatory leiomyosarcoma	
Leiomyosarcoma	
Skeletal muscle tumours	
Rhabdomyoma	
Embryonal rhabdomyosarcoma	
Alveolar rhabdomyosarcoma	
Pleomorphic rhabdomyosarcoma	
Spindle cell / sclerosing rhabdomyosarcoma	
Ectomesenchymoma	
Gastrointestinal stromal tumour	
Gastrointestinal stromal tumour	
Chondro-osseous tumours	
Soft tissue chondroma	
Extraskeletal osteosarcoma	
Peripheral nerve sheath tumours	
Schwannoma	
Neurofibroma	
Perineurioma	
Granular cell tumour	
Dermal nerve sheath myxoma	
Solitary circumscribed neuroma	
Ectopic meningioma and meningotheial hamartoma	
Benign triton tumour / neuromuscular choristoma	
Hybrid nerve sheath tumour	
Malignant peripheral nerve sheath tumour	
Malignant melanotic nerve sheath tumour	
Tumours of uncertain differentiation	
Intramuscular myxoma	
Juxta-articular myxoma	
Deep (aggressive) angliomyxoma	
Atypical fibroxanthoma	
Angiomatoid fibrous histiocytoma	
Ossifying fibromyxoid tumour	
Myoepithelioma, myoepithelial carcinoma, and mixed tumour	
Pleomorphic hyalinizing angiectatic tumour of soft parts	
Haemosiderotic fibrolipomatous tumour	
Phosphatūric mesenchymal tumour	
NTRK-rearranged spindle cell neoplasm (emerging)	
Synovial sarcoma	
Epithelioid sarcoma	
Alveolar soft part sarcoma	
Clear cell sarcoma of soft tissue	
Extraskeletal myxoid chondrosarcoma	
Desmoplastic small round cell tumour	
Extrarenal rhabdoid tumour	
PEComa, including angiolipoma	
Intimal sarcoma	
Undifferentiated sarcoma	
Undifferentiated small round cell sarcomas of bone and soft tissue	
Ewing sarcoma	
Round cell sarcoma with EWSR1-non-ETS fusions	
CIC-rearranged sarcoma	
Sarcoma with BCOR genetic alterations	

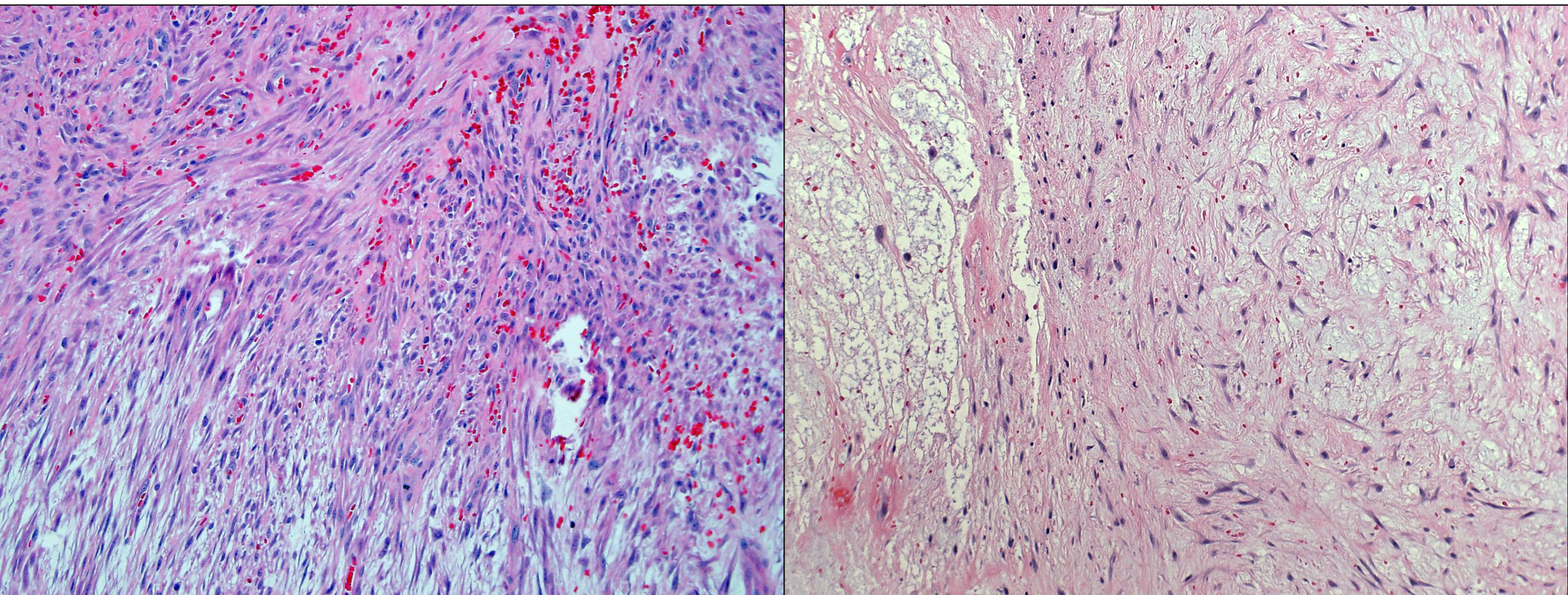
Bone tumours
Bone tumours: Introduction
Chondrogenic tumours
Subungual exostosis
Bizarre parosteal osteochondromatous proliferation
Periosteal chondroma
Enchondroma
Osteochondroma
Chondroblastoma
Chondromyxoid fibroma
Osteochondromyxoma
Synovial chondromatosis
Central atypical cartilaginous tumour / chondrosarcoma, grade 1
Secondary peripheral atypical cartilaginous tumour / chondrosarcoma, grade 1
Central chondrosarcoma, grades 2 and 3
Secondary peripheral chondrosarcoma, grades 2 and 3
Periosteal chondrosarcoma
Clear cell chondrosarcoma
Mesenchymal chondrosarcoma
Dedifferentiated chondrosarcoma
Osteogenic tumours
Osteoma
Osteoid osteoma
Osteoblastoma
Low-grade central osteosarcoma
Osteosarcoma
Parosteal osteosarcoma
Periosteal osteosarcoma
High-grade surface osteosarcoma
Secondary osteosarcoma
Fibrogenic tumours
Desmoplastic fibroma of bone
Fibrosarcoma of bone
Vascular tumours of bone
Haemangioma of bone
Epithelioid haemangioma of bone
Epithelioid haemangioendothelioma of bone
Angiosarcoma of bone
Osteoclastic giant cell-rich tumours
Aneurysmal bone cyst
Giant cell tumour of bone
Non-ossifying fibroma
Notochordal tumours
Benign notochordal cell tumour
Conventional chordoma
Dedifferentiated chordoma
Poorly differentiated chordoma
Other mesenchymal tumours of bone
Chondromesenchymal hamartoma of chest wall
Adamantinoma
Simple bone cyst
Fibrocartilaginous mesenchymoma
Fibrous dysplasia
Osteofibrous dysplasia
Lipoma and hibernoma of bone
Leiomyosarcoma of bone
Undifferentiated pleomorphic sarcoma
Bone metastases
Haematopoietic neoplasms of bone
Solitary plasmacytoma of bone
Primary non-Hodgkin lymphoma of bone
Langerhans cell histiocytosis
Erdheim-Chester disease
Rosal-Dorfman disease



Challenges (2)

- Certain benign tumors can mimic sarcomas.

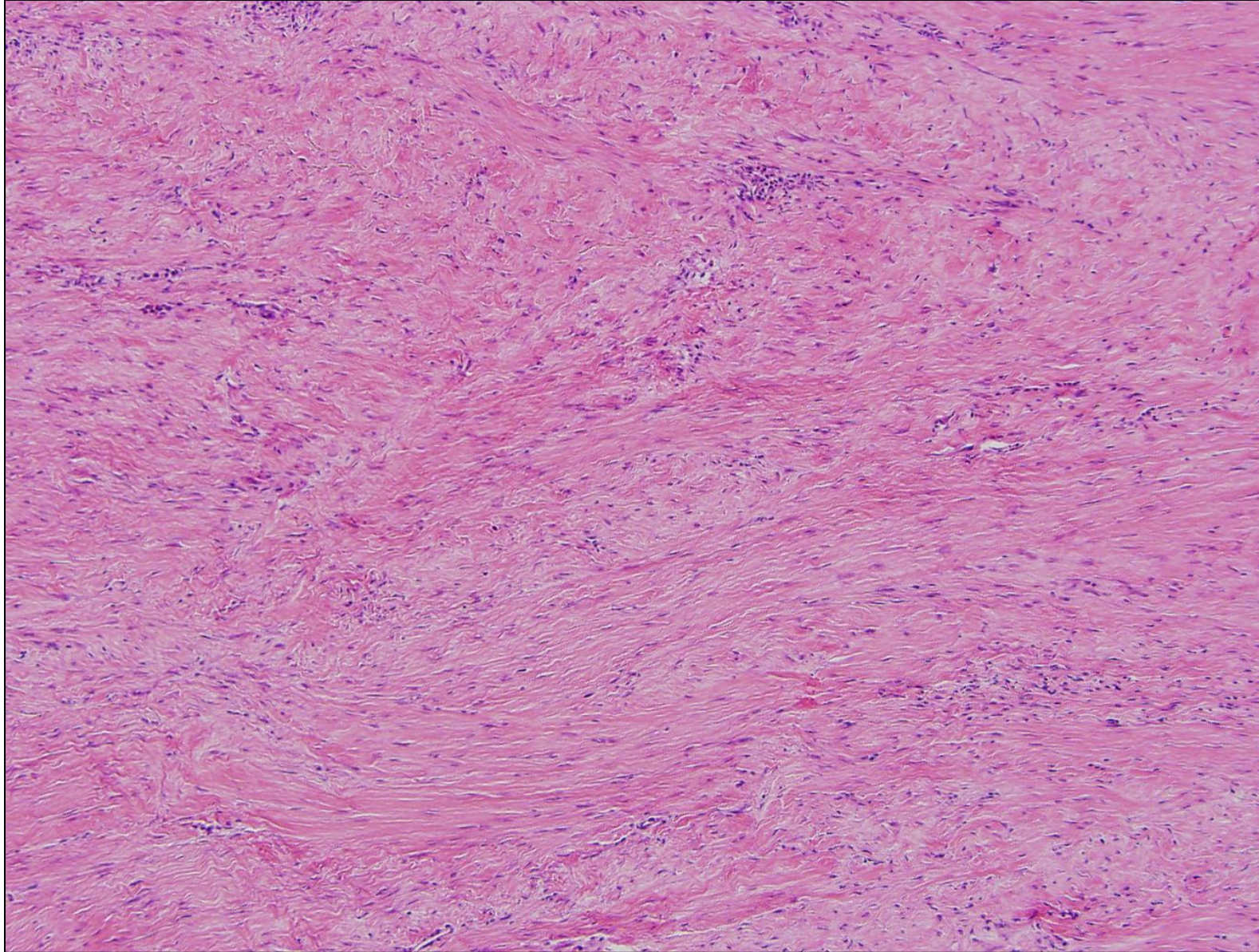




Dx: Nodular fasciitis

Challenges (3)

- Certain sarcomas may have a benign appearance.



Challenges (4)

- A significant number of sarcomas are morphologically undifferentiated or of uncertain histogenesis.
- They require extensive immunohistochemical and/or molecular studies for their correct classification.
 - Cytogenetics
 - FISH
 - Fusion panels
 - NGS

Clinical Clues

- Age matters
 - Infant vs child vs adolescent vs adult
- Location matters
 - Bone vs soft tissue
 - Epiphysis/metaphysis/diaphysis
 - Superficial vs deep
- Clinical context
 - Pain, trauma, syndromes, prior radiation



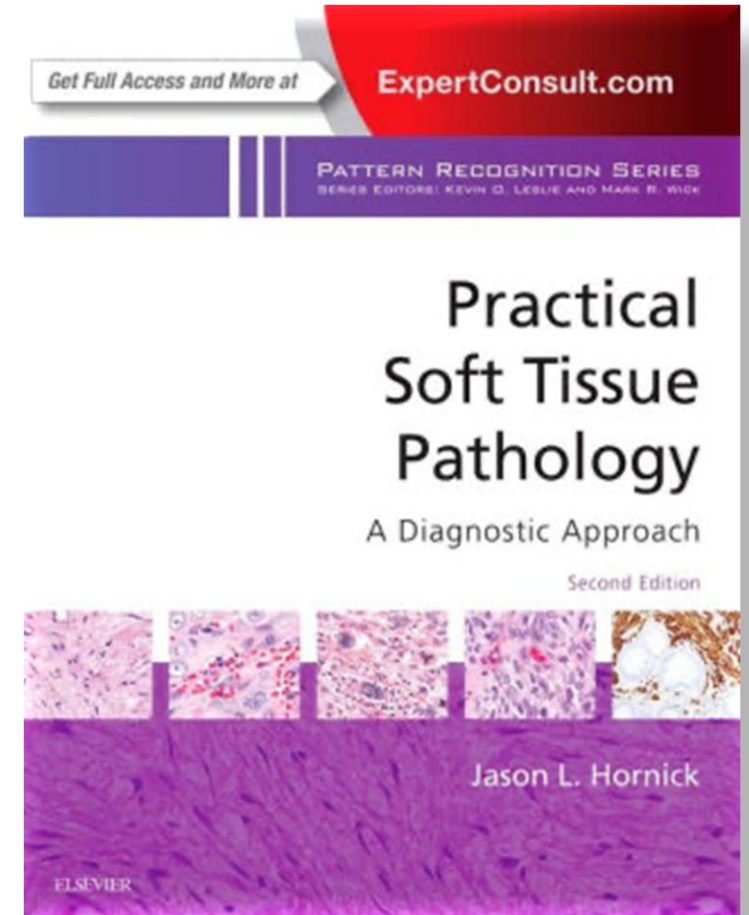
An Integrated Diagnostic Framework

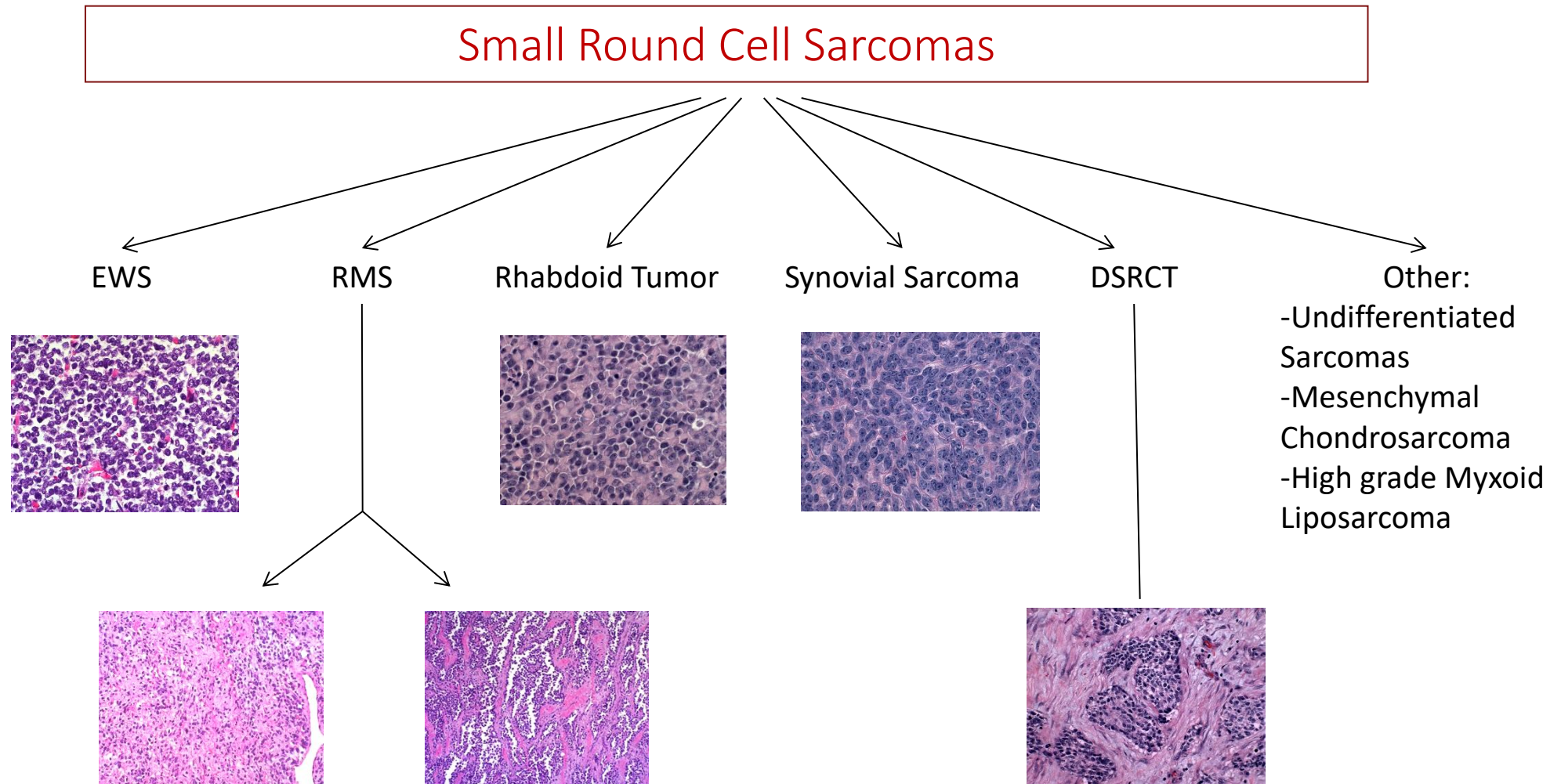
- Every case follows a similar roadmap:
 - Clinical history
 - Imaging
 - Gross examination
 - Histology
 - Immunohistochemistry
 - Molecular pathology
 - Integrated WHO diagnosis

Pattern-Based Approach to Diagnosis

Pattern	Selected Diseases to Be Considered
Spindle cell	Nodular fasciitis Myofibroma/myopericytoma Cellular benign fibrous histiocytoma Dermatofibrosarcoma protuberans Superficial or desmoid fibromatosis Neurofibroma Schwannoma Leiomyoma Leiomyosarcoma Gastrointestinal stromal tumor Solitary fibrous tumor Spindle cell lipoma Atypical spindle cell lipomatous tumor Soft tissue perineurioma Low-grade fibromyxoid sarcoma Monophasic synovial sarcoma Malignant peripheral nerve sheath tumor Biphenotypic sinonasal sarcoma Dedifferentiated liposarcoma Clear cell sarcoma Nodular Kaposi sarcoma Pseudomyogenic hemangioendothelioma
Epithelioid	Epithelioid hemangioma Epithelioid hemangioendothelioma Epithelioid angiosarcoma Glomus tumor Granular cell tumor Cellular neurothekeoma Myoepithelioma/myoepithelial carcinoma Epithelioid schwannoma Epithelioid malignant peripheral nerve sheath tumor Gastrointestinal stromal tumor Perivascular epithelioid cell tumor (PEComa) Epithelioid sarcoma SMARCA4-deficient thoracic sarcoma Malignant rhabdoid tumor Alveolar soft part sarcoma Clear cell sarcoma Sclerosing epithelioid fibrosarcoma
Pleomorphic	Atypical fibrous histiocytoma Atypical fibroxanthoma "Ancient" schwannoma Dedifferentiated liposarcoma

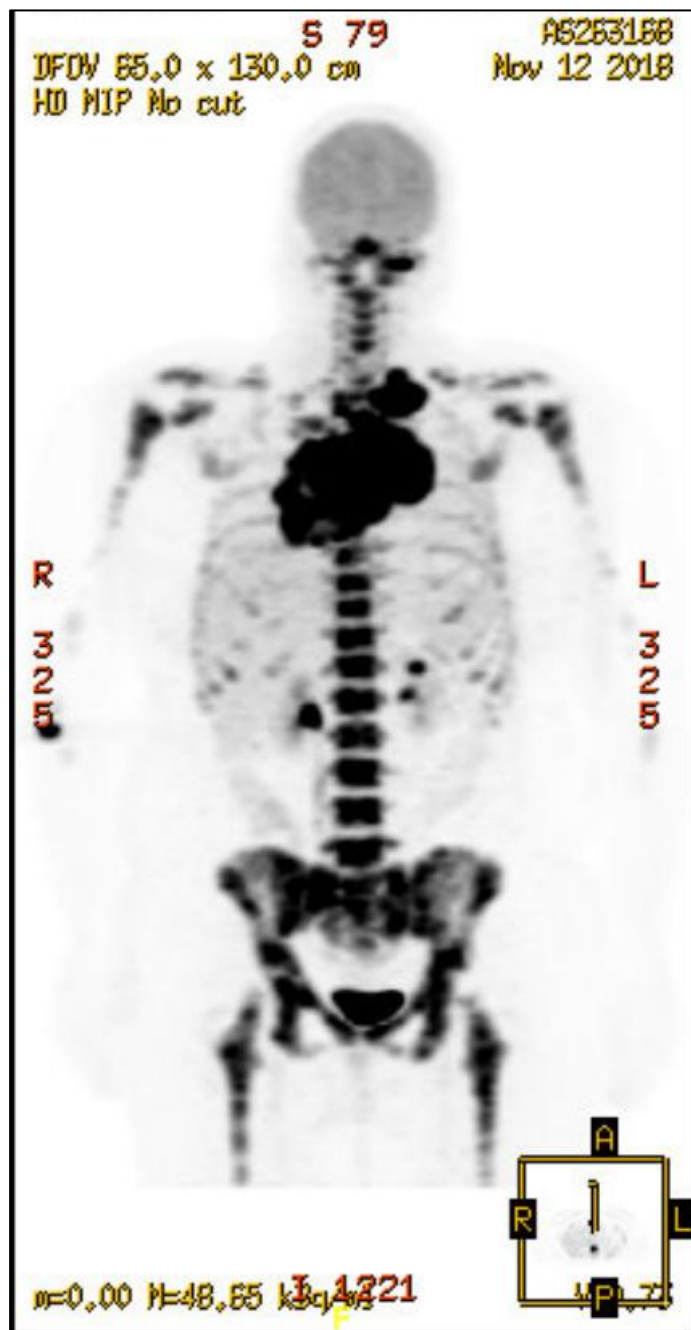
Pattern	Selected Diseases to Be Considered
Pleomorphic— <i>cont'd</i>	Pleomorphic liposarcoma Pleomorphic leiomyosarcoma Pleomorphic rhabdomyosarcoma Myxofibrosarcoma Myxoinflammatory fibroblastic sarcoma Extraskelatal osteosarcoma Undifferentiated pleomorphic sarcoma
Round cell	Ewing sarcoma Embryonal rhabdomyosarcoma Alveolar rhabdomyosarcoma Round cell (high-grade myxoid) liposarcoma Poorly differentiated synovial sarcoma Desmoplastic small round cell tumor Mesenchymal chondrosarcoma CIC-rearranged sarcomas BCOR-rearranged sarcomas
Biphasic or mixed	Biphasic synovial sarcoma Mixed tumor Glandular malignant peripheral nerve sheath tumor Myoepithelioma/myoepithelial carcinoma Gastrointestinal stromal tumor Ectopic hamartomatous thymoma Dedifferentiated liposarcoma
Myxoid	Intramuscular/cellular myxoma Dermal nerve sheath myxoma Superficial acral fibromyxoma Superficial angiomyxoma Deep angiomyxoma Ossifying fibromyxoid tumor Myoepithelioma/myoepithelial carcinoma Myxofibrosarcoma Pleomorphic liposarcoma Myxoid liposarcoma Extraskelatal myxoid chondrosarcoma Low-grade fibromyxoid sarcoma Myxoinflammatory fibroblastic sarcoma Neurofibroma Soft tissue or reticular perineurioma Malignant peripheral nerve sheath tumor Spindle cell lipoma

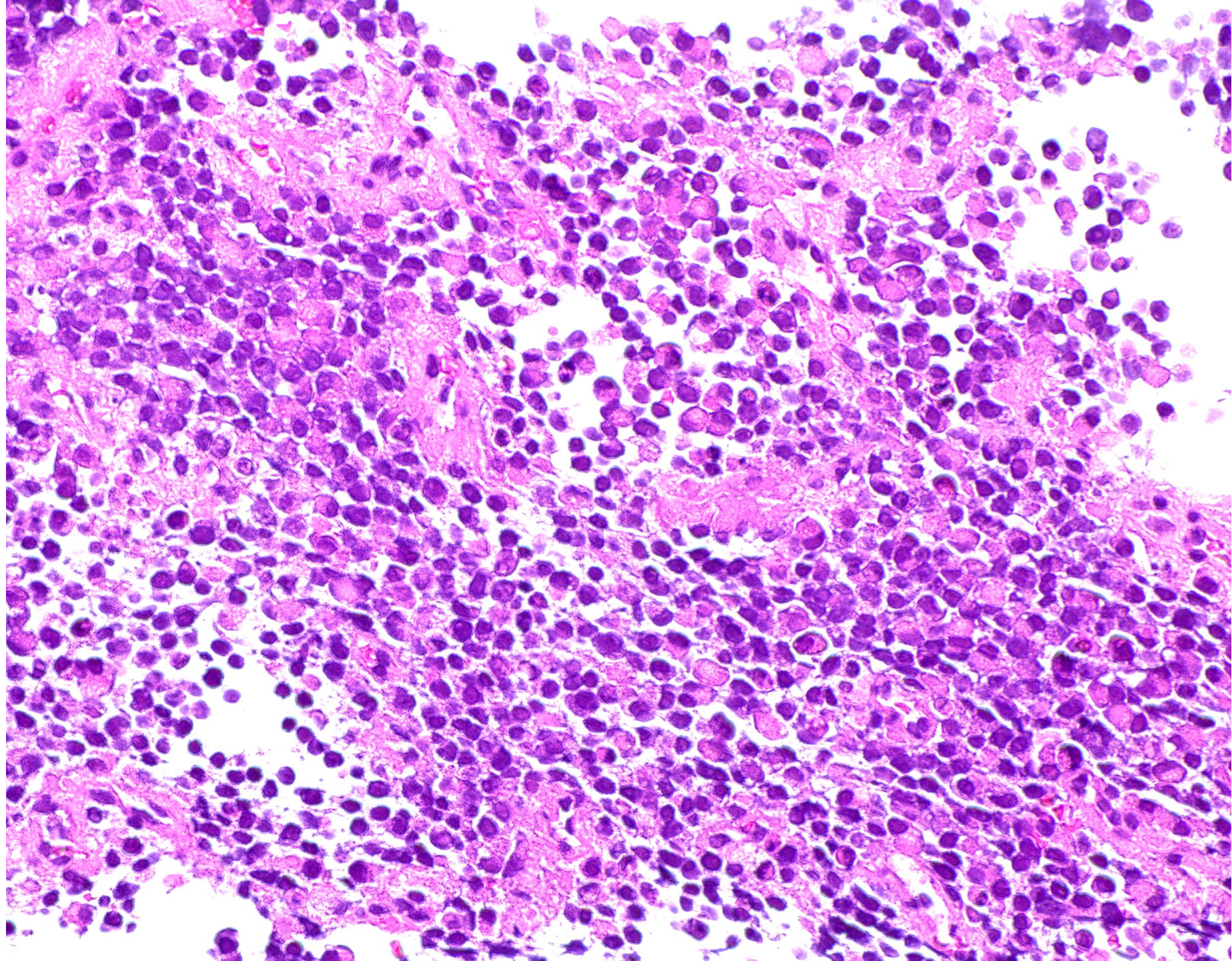


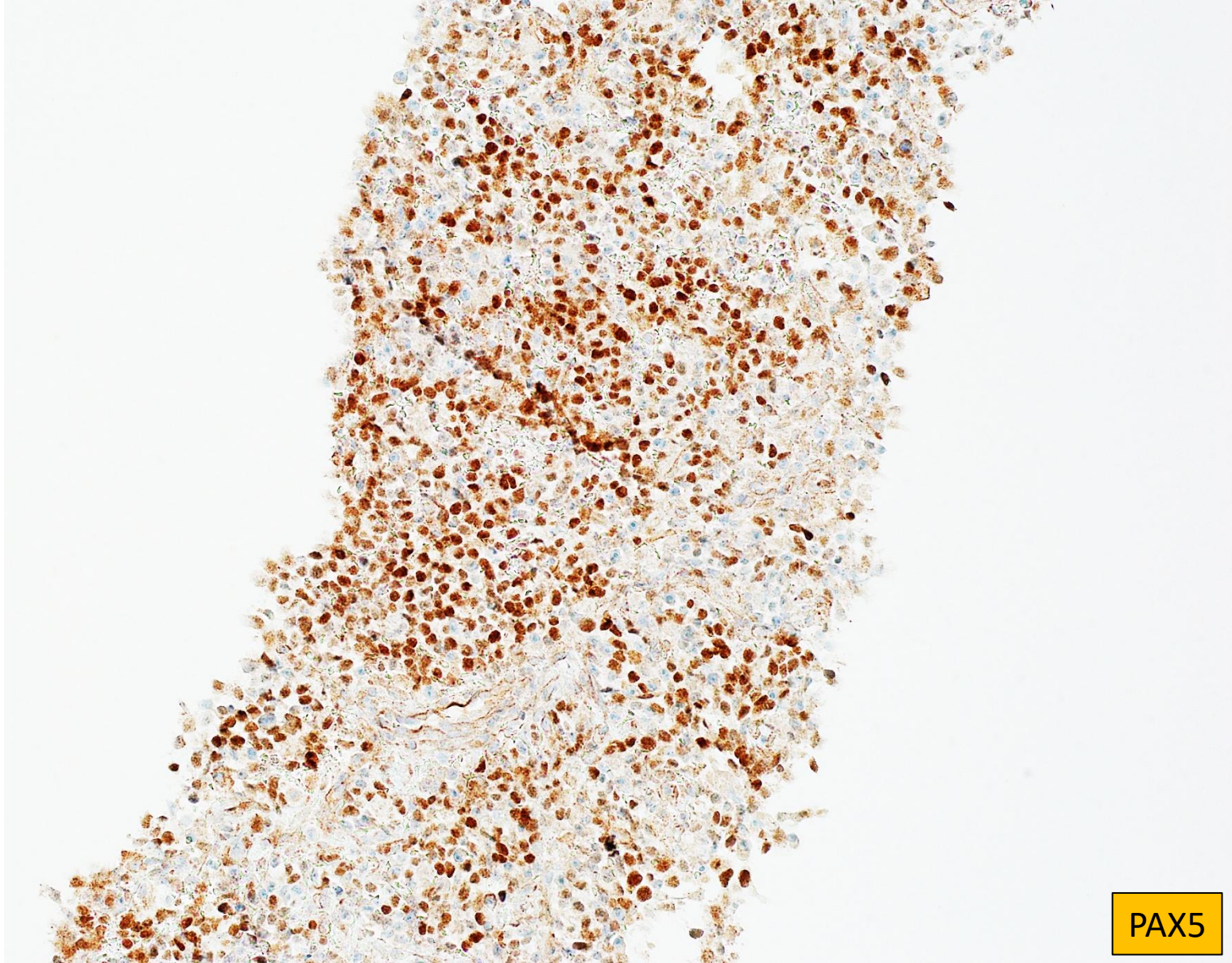


Clinical Case

- 22-year-old female who presented with painful supraclavicular lymphadenopathy (3 cm).
- Weight loss of 30 lbs and lethargy
- Images: multiples lymphadenopathies, diffuse bone abnormalities and mediastinal mass 12 x 10 cm; highly suspicious for lymphoma.







Results

CD19
Negative

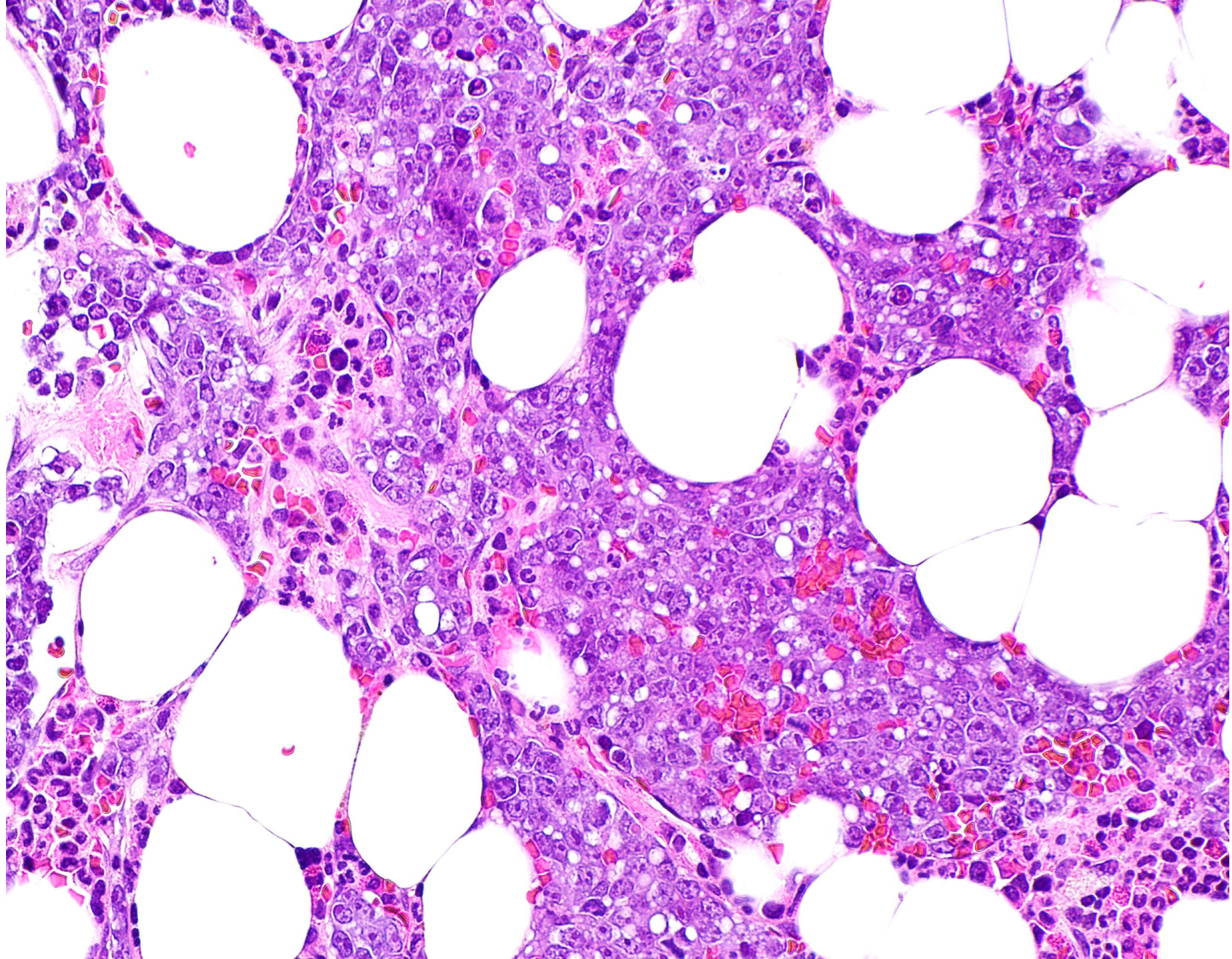
cMyc
Positive

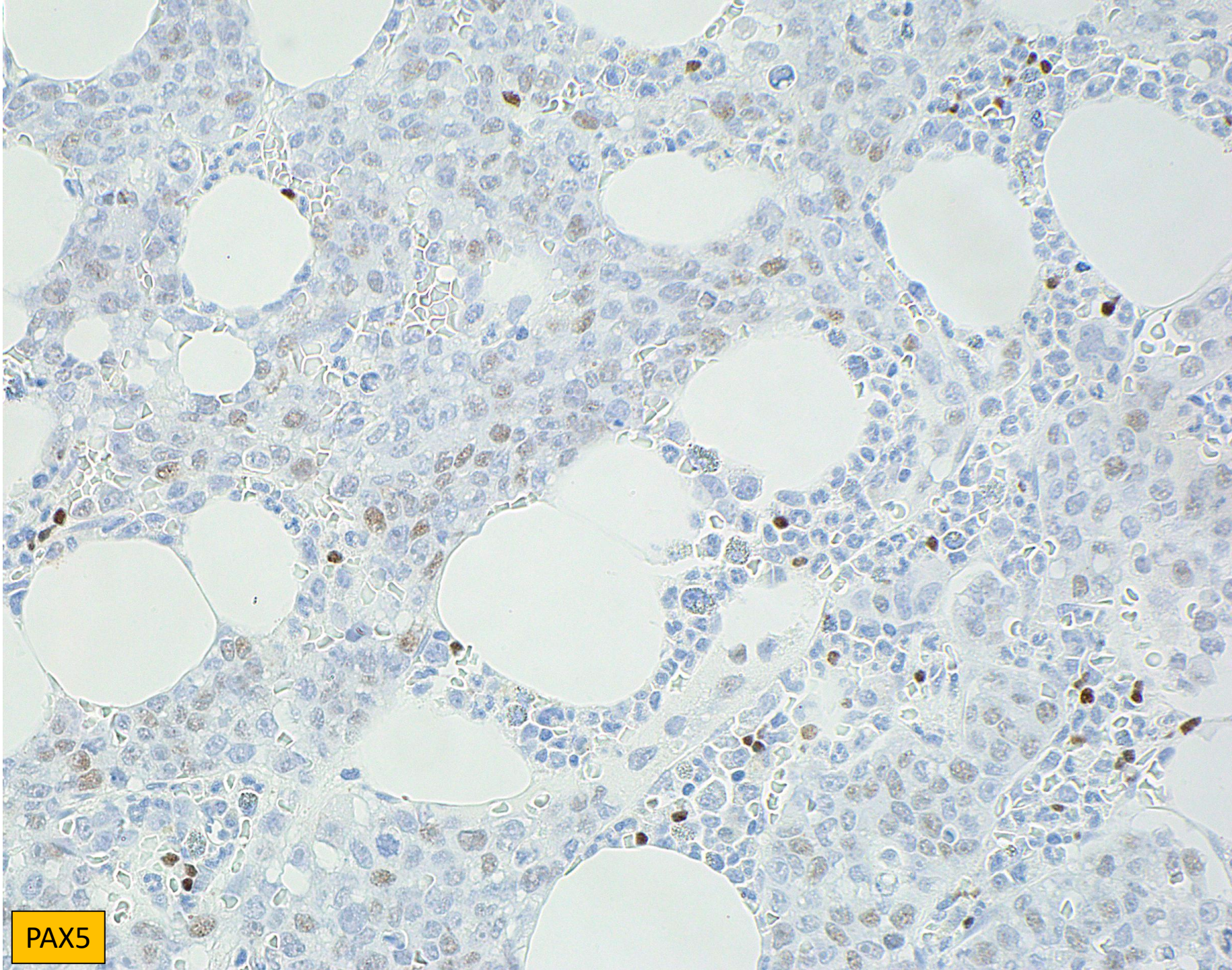
TdT
Negative

Lymph node, left supraclavicular, ultrasound-guided needle core biopsy:

- Poorly differentiated, necrotic malignancy, most suggestive of a B lymphoproliferative neoplasm, see comment.

COMMENT: The findings are highly concerning for a B lymphoblastic lymphoma/leukemia, given the patient's age and mediastinal mass(...) Because of the extensive necrosis, definitive diagnosis may not be attainable with this biopsy(...)





PAX5

Hematologic Masquerade of Rhabdomyosarcoma

Avery A. Sandberg,^{1*} John F. Stone,¹ Lawrence Czarnecki,² and Jesse D. Cohen³

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Eur J Pediatr (2007) 166:505–506

DOI 10.1007/s00431-006-0269-y

SHORT REPORT

Alveolar rhabdomyosarcoma mimicking lymphoma with bone marrow involvement

Christof Andreas Hanke • Jochen Roessler •

Sabine Stegmaier • Eva Koscielniak •

Charlotte Marie Niemeyer • Udo Kontny

Imataki et al. *Diagnostic Pathology* (2017) 12:77

DOI 10.1186/s13000-017-0667-7

Diagnostic Pathology

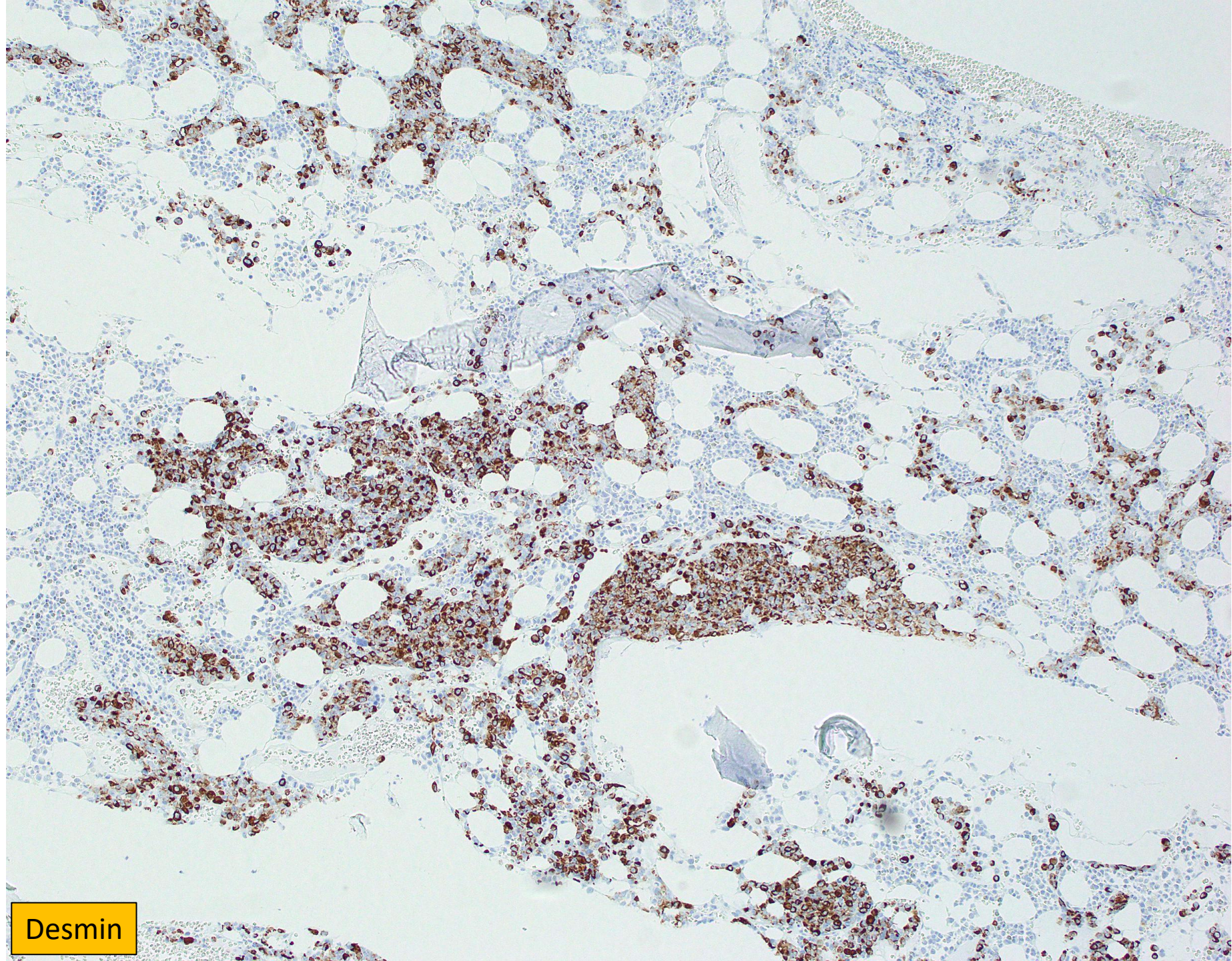
CASE REPORT

Open Access

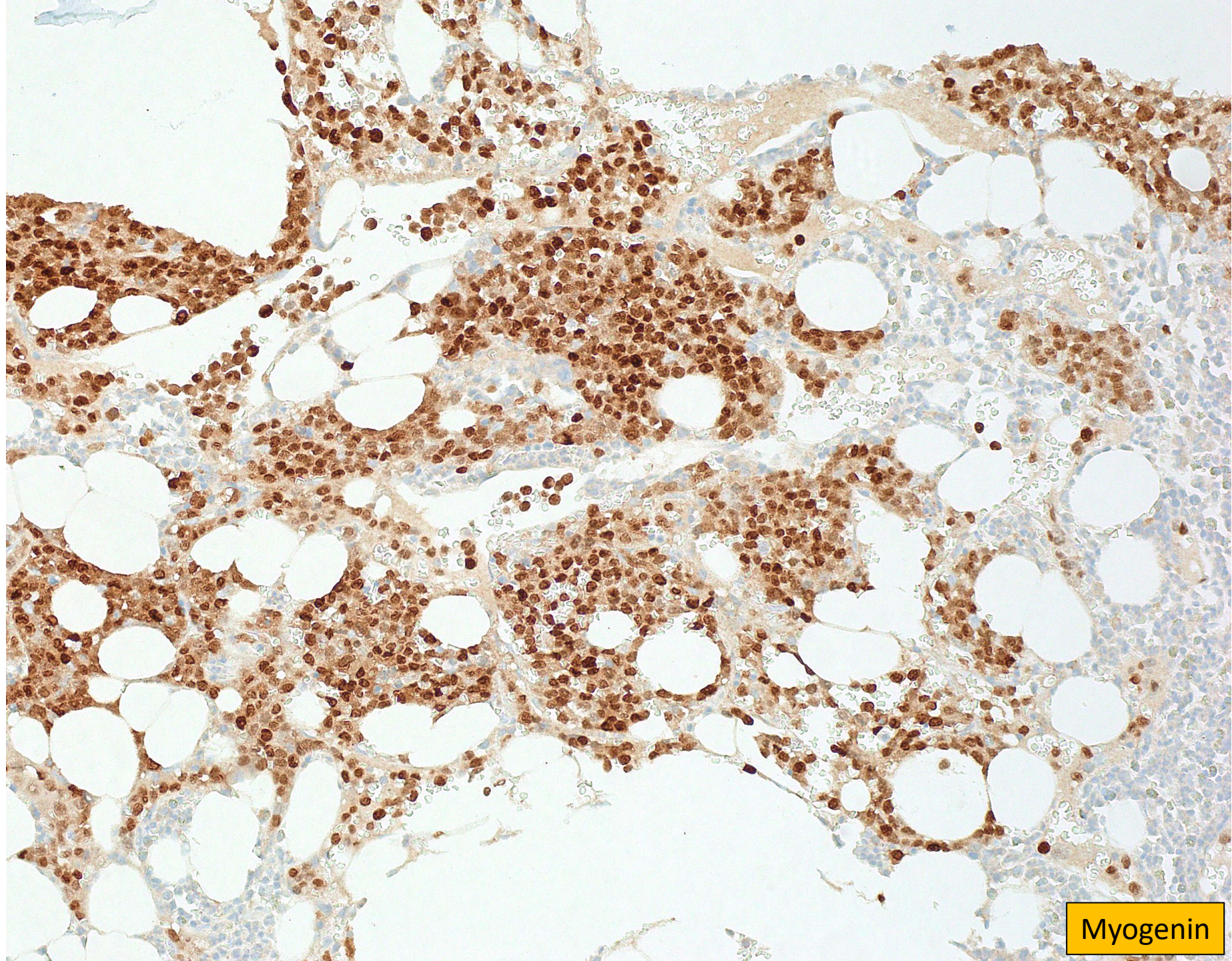


Complete mimicry: a case of alveolar rhabdomyosarcoma masquerading as acute leukemia

Osamu Imataki^{1,4*} , Makiko Uemura¹, Shumpei Uchida¹, Shigeyuki Yokokura¹, Akihiro Takeuchi², Ryo Ishikawa³, Akihiro Kondo², Kayoko Seo² and Norimitsu Kadowaki¹

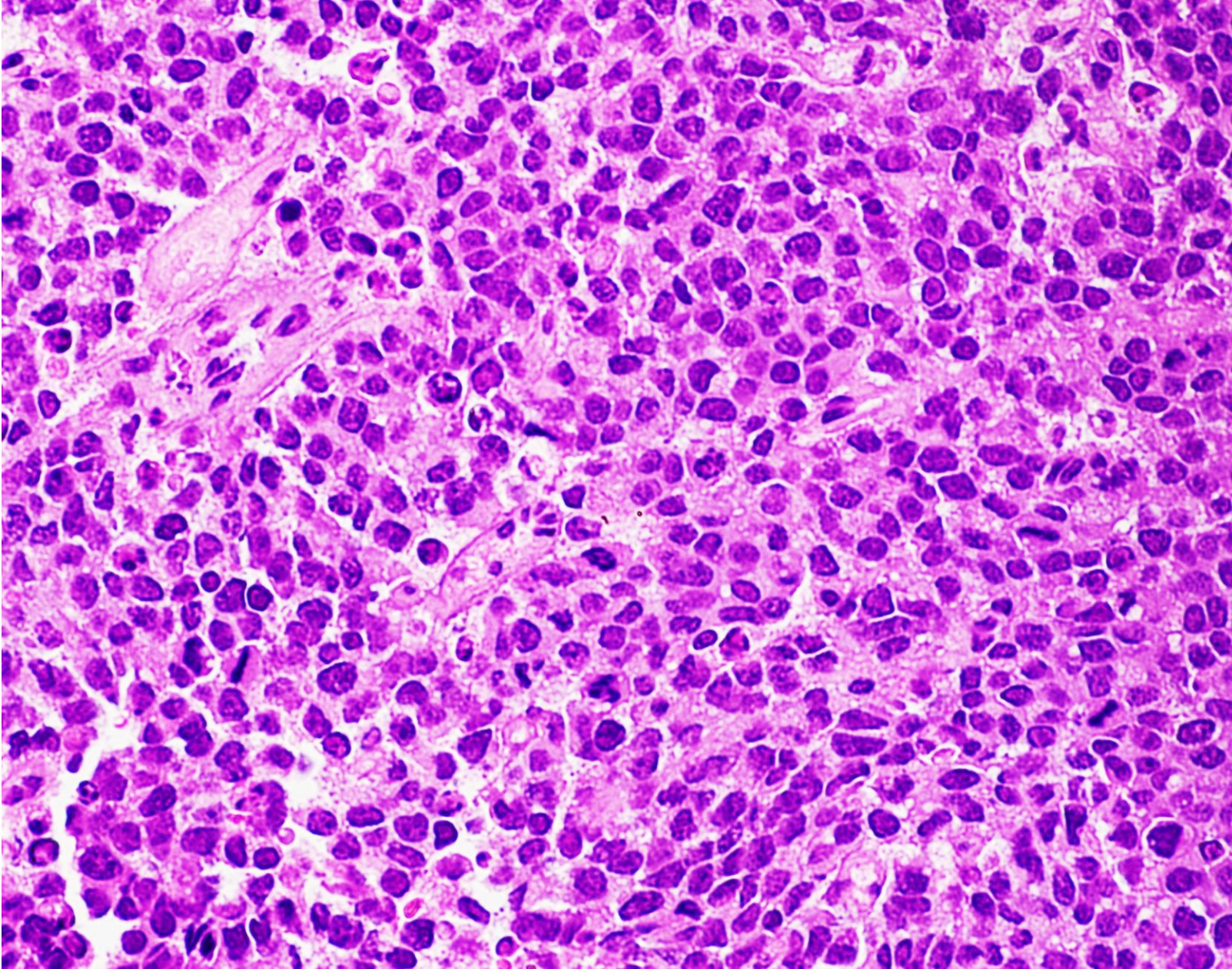


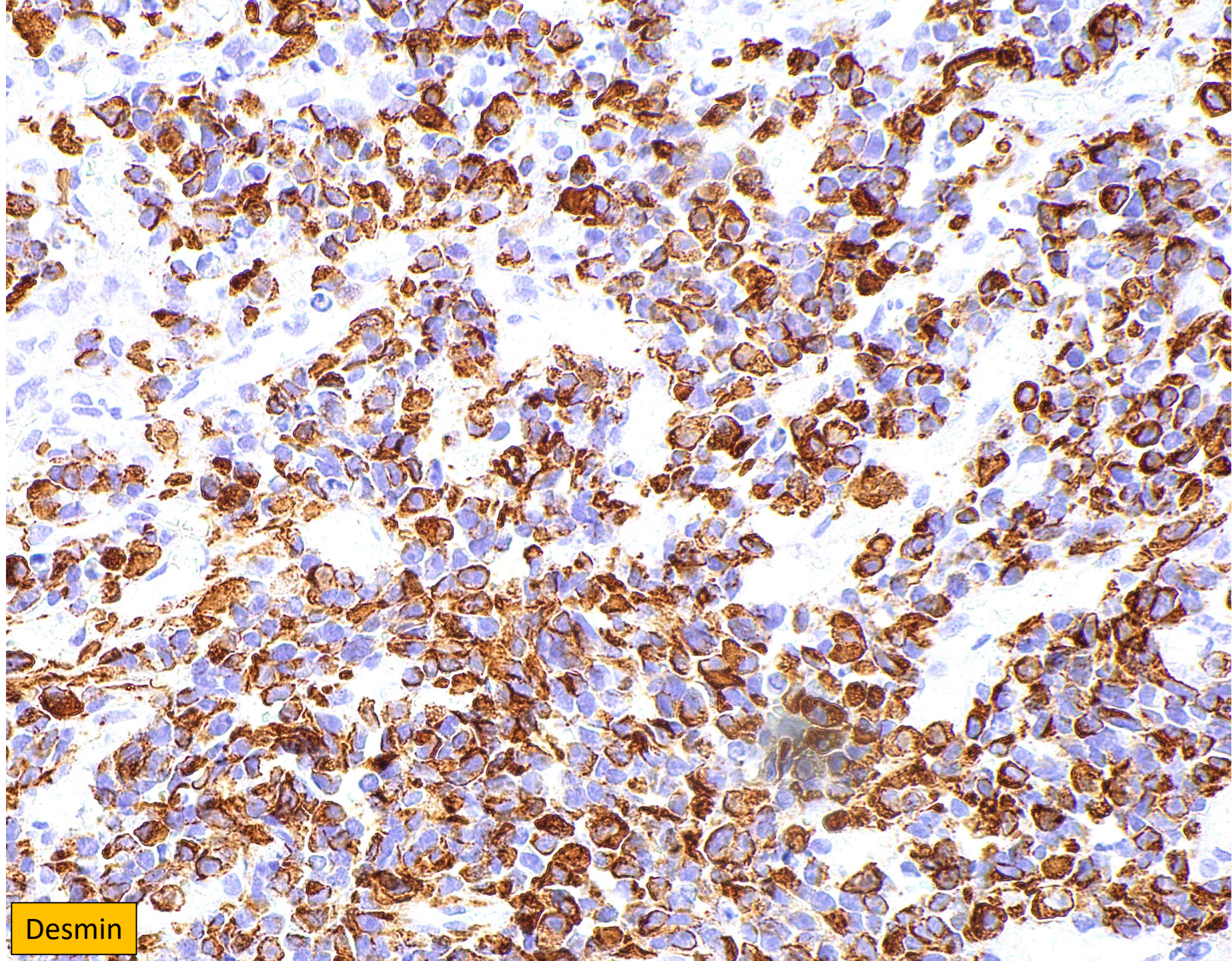
Desmin



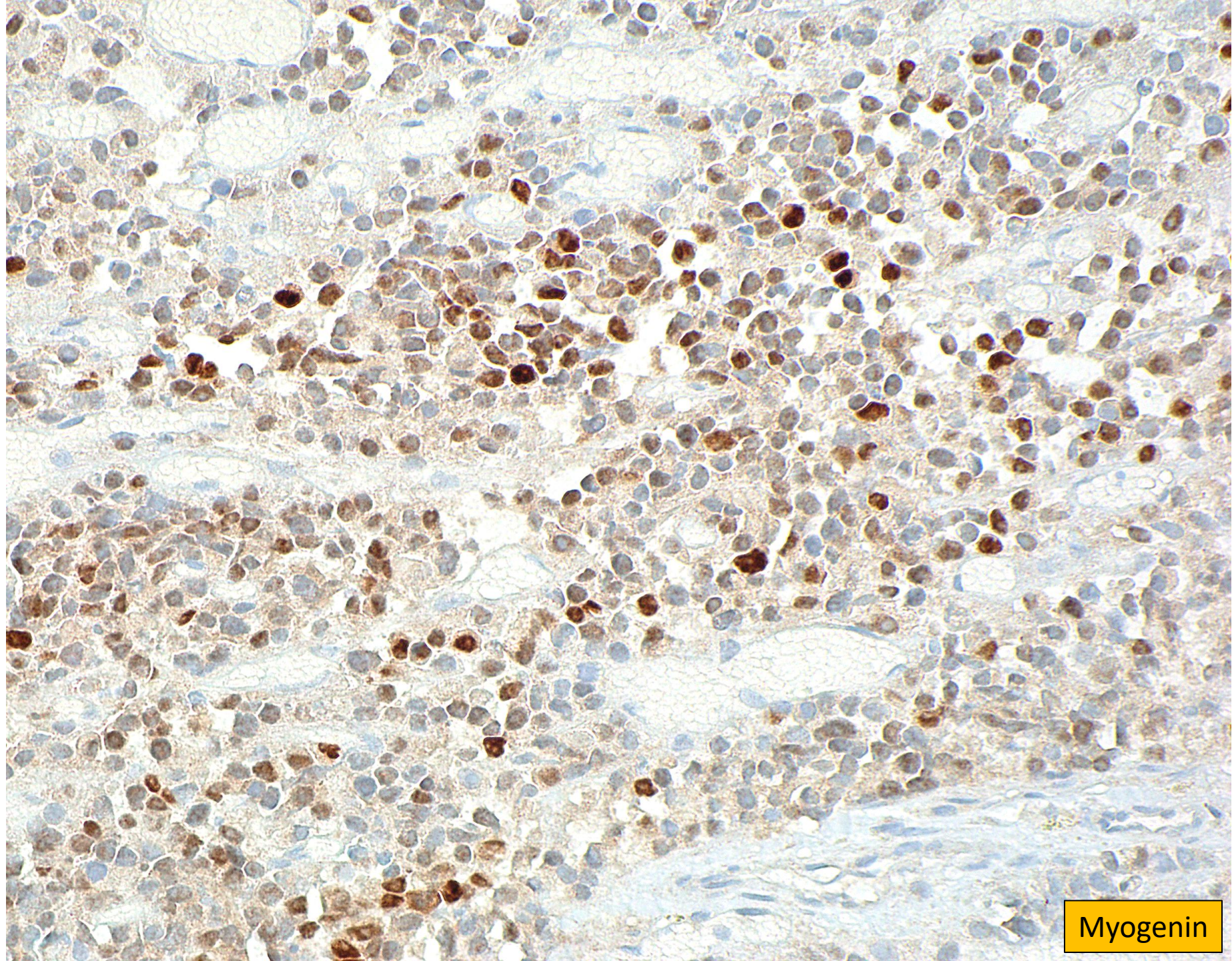
Myogenin

Lymph node, supraclavicular, biopsy:





Desmin



Myogenin

RMS - Classification

- Currently classified in four subtypes
 - Embryonal
 - Alveolar
 - Sclerosing/Spindle cell
 - Pleomorphic

Table 1. International classification of rhabdomyosarcoma^a

Diagnosis	Histology	Incidence (%) ^b	Five-year survival (%)	Prognosis
Embryonal, botryoid	Favorable	6	95	Superior
Embryonal, spindle cell	Favorable	3	88	Superior
Embryonal, not otherwise specified (NOS)	Favorable	49	66	Intermediate
Alveolar, NOS or solid variant	Unfavorable	31	53	Poor
Anaplasia, diffuse	Unfavorable	2	45	Poor
Undifferentiated sarcoma	Unfavorable	3	44	Poor

^aWith the addition of IRSG-defined anaplastic variant.

^bTotal incidence is only 94%; some 6% of accepted cases fall into the sarcoma NOS category because of insufficient or inadequate tissue to make a more specific diagnosis.

Qualman et al., 1998

Pediatric Sclerosing Rhabdomyosarcoma

Eduardo Zambrano, MD, MSc, Antonio R Pérez-Atayde, MD,
William Ahrens, MD, Miguel Reyes-Múgica, MD

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Sclerosing rhabdomyosarcoma, a particular phenotypic variant of rhabdomyosarcoma initially described in the adult population, has emerged as a potential pitfall in the evaluation of pediatric sarcomas. Because of its densely hyalinized collagenous matrix and its occasional expression of a pseudovascular pattern of growth, sclerosing rhabdomyosarcoma has been at times misdiagnosed as chondrosarcoma, osteosarcoma, or angiosarcoma. We describe 3 pediatric patients with sclerosing rhabdomyosarcoma and provide a detailed description of its distinguishing pathologic features. Awareness about this rhabdomyosarcoma variant and

careful immunophenotypical evaluation are necessary to establish the correct diagnosis. Although no specific genetic aberrations have been yet recognized, the cytogenetic findings in 2 tumors of this series suggest a link with embryonal rhabdomyosarcoma. It is likely that further genotyping will result in better nosologic delineation of sclerosing rhabdomyosarcoma and that it will uncover pathogenetically and prognostically relevant genes.

Keywords: sclerosing rhabdomyosarcoma, sarcomas in children; hyalinized collagenous matrix

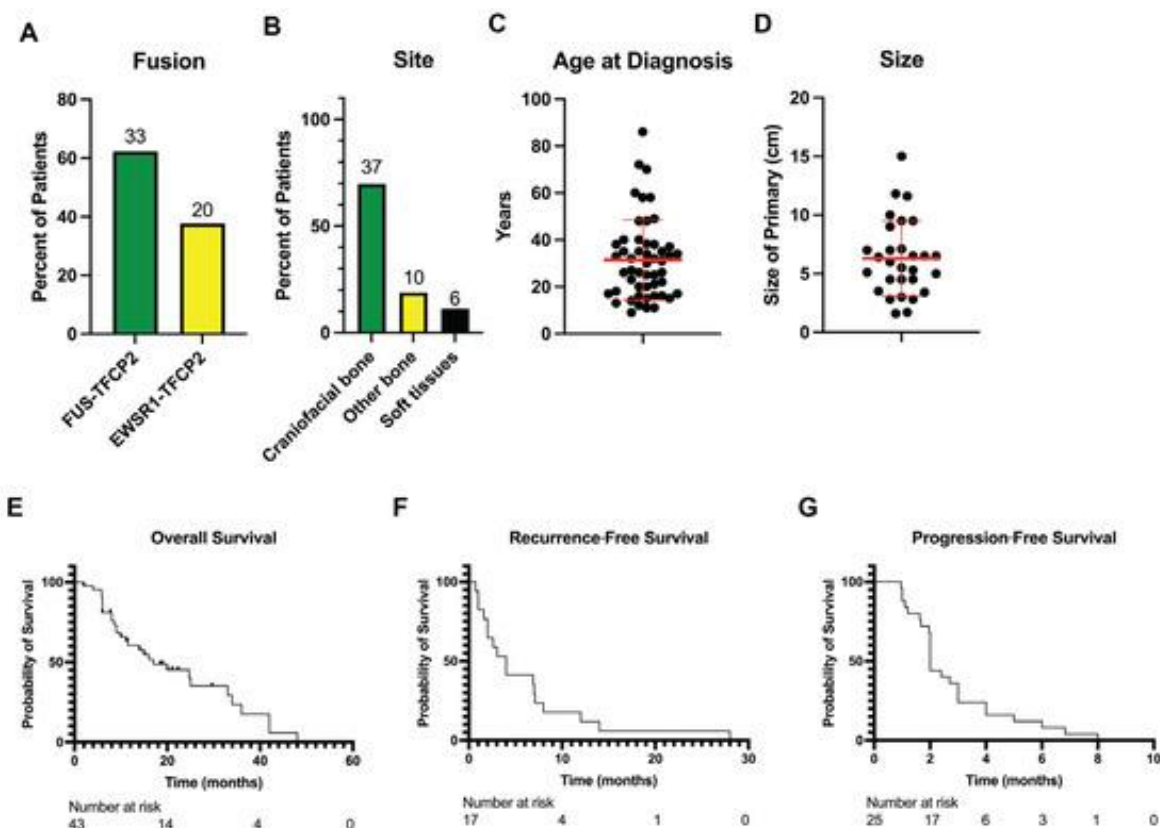
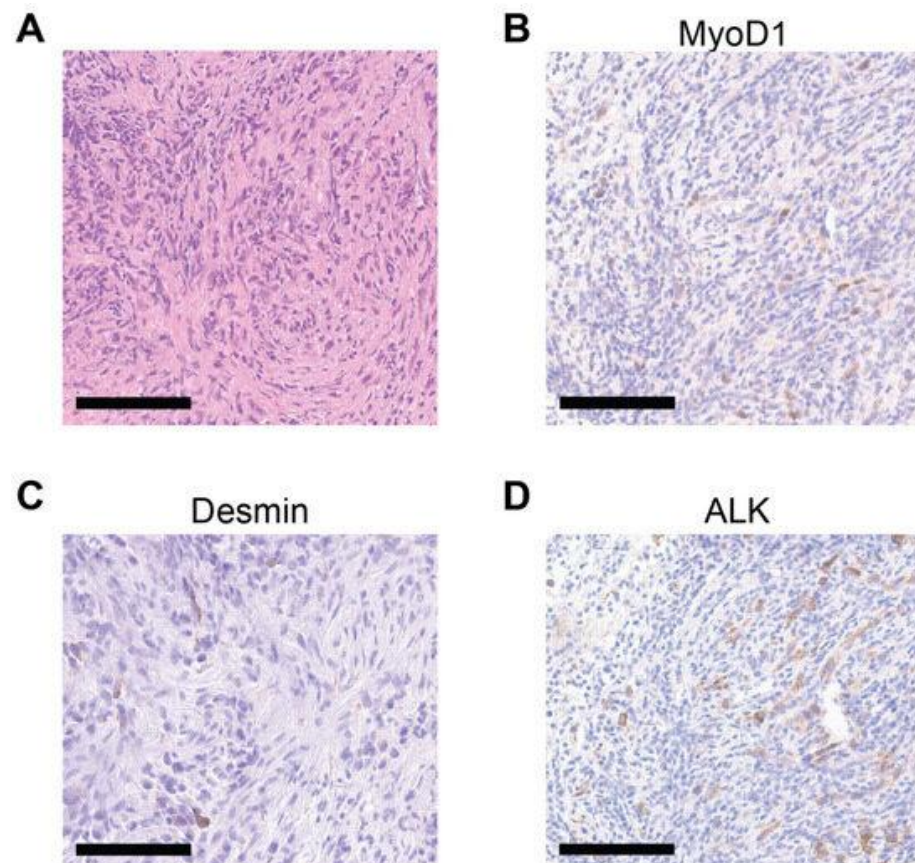
TABLE 1. Clinicopathologic and Molecular Features of Pediatric SRMS/ScRMS

RMS#	Age/Sex	Site	Diagnosis	Molecular Results	FU (y)	IRS	Status
1*	0.7/M	Post-neck	SRMS	SRF-NCOA2†	3	I	NED, CR2
2*	4W/M	Chest wall	SRMS	TEAD1-NCOA2	3	IIa	NED
3*,‡	0.3/F	Chest wall	SRMS	VGLL2-NCOA2	13	III	NED, CR4
4	0/M	Calf	SRMS	TEAD1-NCOA2	NA	NA	NA
5	0.2/F	Back	SRMS	VGLL2-NCOA2	NA	NA	NA
6	0/F	Back	SRMS	VGLL2-CITED2†	9	III	NED, CR
7	0/F	Back	SRMS	VGLL2-CITED2†	6	III	NED, CR
8	0.7/F	Back	SRMS	VGLL2-CITED2	8	II	NED, CR
9	0/F	Lower neck/back	SRMS	VGLL2-CITED2	Recent case	I	In therapy
10	0.8/M	Chest wall	SRMS	VGLL2	NA	NA	NA
11	0.4/M	Paravertebral	SRMS	—	NA	NA	NA
12§	10/F	Paraspinal	SRMS	MyoD1 (L122R)‖	3	III	DOD
13§	2/F	Buttock	SRMS	MyoD1 (L122R)	1	IIa	DOD
14	17/M	Paravertebral	ScRMS	MyoD1 (L122R)‖	2	III	DOD
15§	15/F	Infratemporal	ScRMS	MyoD1 (L122R)‖,¶	1	III	DOD
16§	13/F	Back	ScRMS	MyoD1 (L122R)‖,¶	2	III	DOD
17	10/F	Buttock	ScRMS	MyoD1 (L122R) ¶,‡ FGFR4 (V548M)	0.5	III	DOD
18	8/M	Thigh	ScRMS	MyoD1 (L122R)‖	1	III	NED, CR1
19	11/F	H&N	ScRMS	MyoD1 (L122R)‖,¶	Recent case	I	In therapy
20	9/M	H&N	SRMS	MyoD1 (L122R)‖	3	III	AWD (2 nd LR)
21	9/F	H&N	SRMS	MyoD1 (L122R)‖	1	III	DOD
22	3/M	Intra-abd	SRMS	—	13	I	NED, CR2
23	16/M	Paratesticular	SRMS	—	1	I	NED, CR
24	5/F	Intra-abd	SRMS	FGFR4 (V550L)	NA	NA	NA
25	2.8/F	Ovary/salpinx	SRMS	—	2	III	DOD
26	11/M	Paratesticular	ScRMS	—	1	II	NED, CR

Article

TFCP2 Fusion-Positive Rhabdomyosarcomas: A Report of 10 Cases and a Review of the Literature

Madison P. Ginn ¹, Ryan A. Denu ², Davis R. Ingram ³, Khalida M. Wani ³, Alexander J. Lazar ^{3,4}, Douglas J. Harrison ⁵, Michael S. Nakazawa ⁶, Anthony P. Conley ⁶, Shreyaskumar Patel ⁶ and John Andrew Livingston ^{5,6,*}



RMS Subtyping

Alveolar RMS

- Age
- Strong diffuse myogenin staining on BM Bx
- Round cell morphology
- Aggressive, hematological malignancy-like clinical presentation



Embryonal RMS

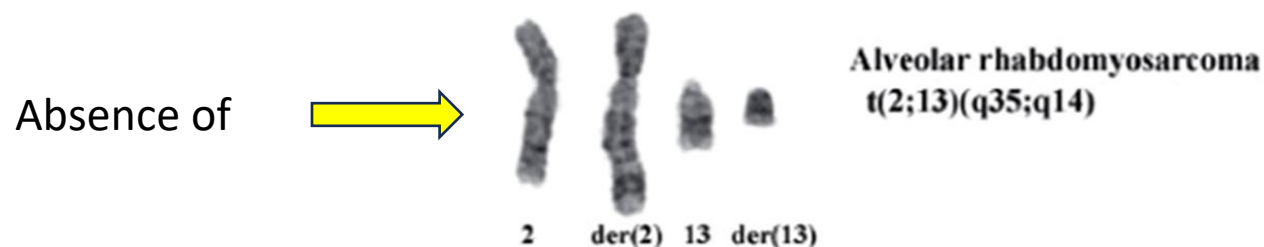
- Patchy myogenin staining on supraclavicular Bx
- No alveolar architecture

KARYOTYPE:

47,XX,+X,8~91dmin[13]/49,sl,+4,+17,80~100dmin[2]/48,XX,+6,+17,4~51dmin[3]/46,XX[3]

INTERPRETATION:

Cytogenetic studies of a bone marrow aspirate specimen revealed three related abnormal clones in eighteen of twenty one metaphase spreads examined, as described in the karyotype result. Notable abnormalities include a hyperdiploid (>46) chromosome count with gain of chromosomes X, 4, 6, 8, 17 and the presence of multiple copies of double minute (dmin) or small chromosome fragments. Three cells with a normal karyotype were observed.



5'FOX01/3'FOX01 (FKHR,
13q14)

Negative rearrangement

100.0

200

Next Generation Sequencing

1719 E. 19th Avenue Denver, CO 80218 Phone: (720) 754-6851 Fax: (303) 839-6907  	Specimen Type: Paraffin Tissue Body Site: Lymph Node Biopsy Specimen ID: IS-5395 (30433343-A1) MRN: 30433343 Reason for Referral: Mediastinal Mass	Collection Date: 11/08/2018 Received Date: 11/16/2018 02:27:00 AM PST Report Date: 12/04/2018 03:33:49 PM EST
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Results:

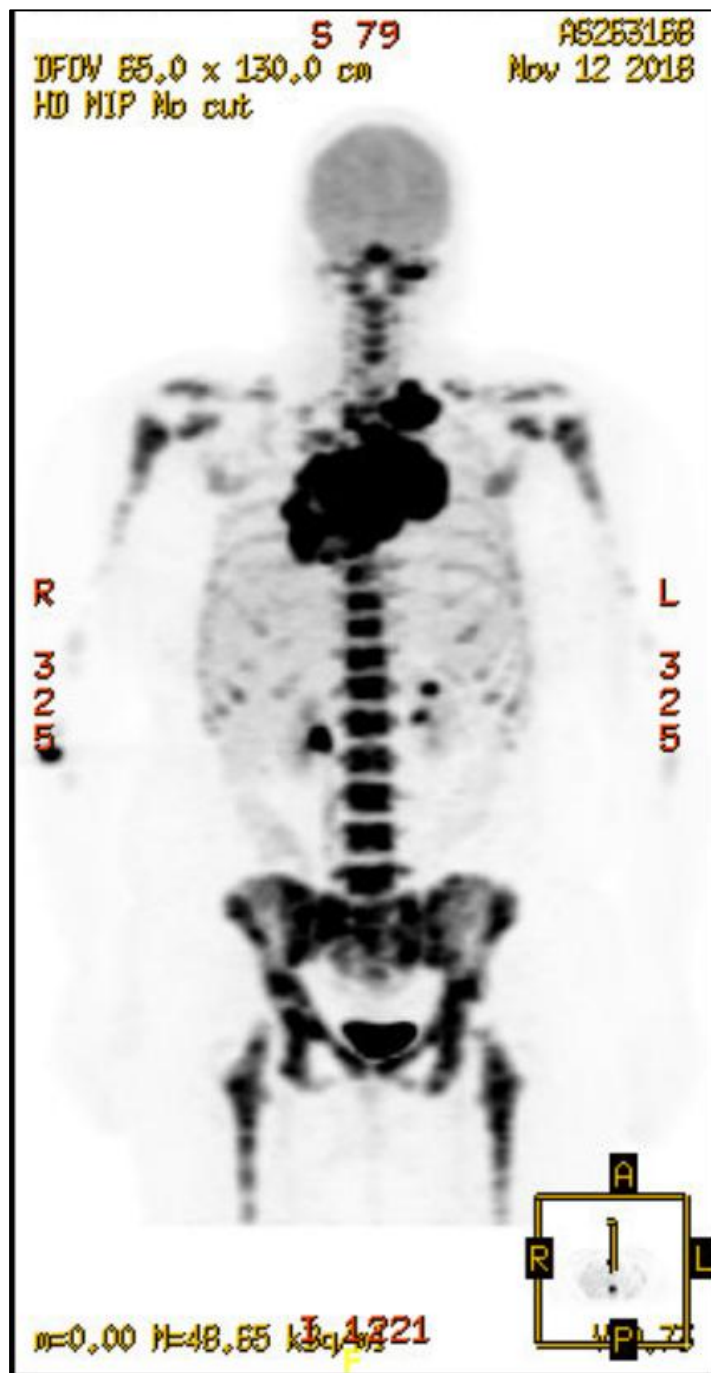
Fusion	Results	Fusion Partner	Fusion Read (%)	Mutation in Fused genes
FOXO1	Not Detected	Not Detected	Not Detected	Not Detected
NCOA2	Not Detected	Not Detected	Not Detected	Not Detected
TFE3	Not Detected	Not Detected	Not Detected	Not Detected

Interpretation:
 THERE IS NO EVIDENCE OF EXPRESSION OF FUSION RNA OR MUTATION INVOLVING FOXO1, NCOA2 AND TFE3 GENES BY NEXT GENERATION SEQUENCING.

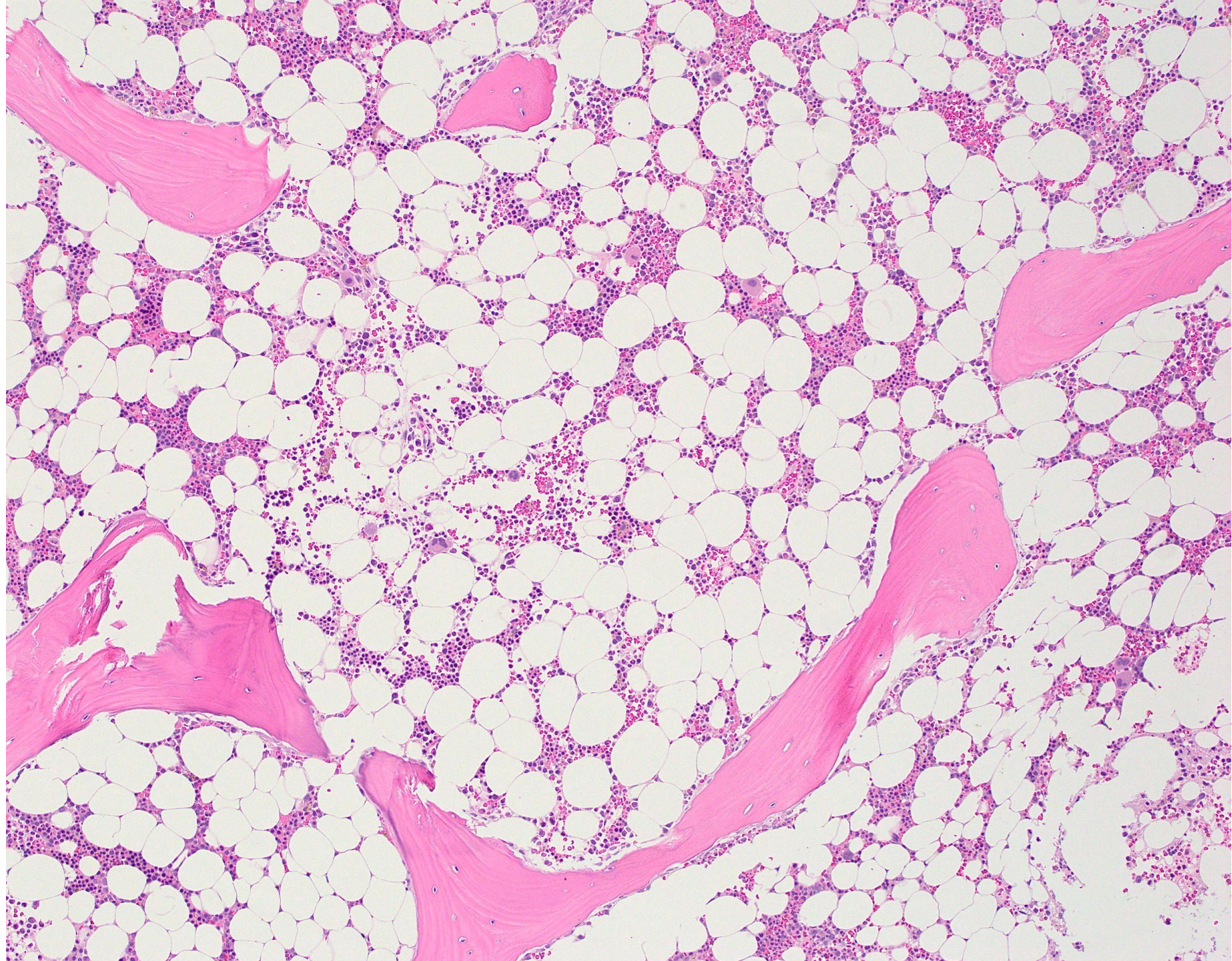
GENOMIC FINDINGS: PIK3CA-H1047R	THERAPIES WITH CLINICAL BENEFIT (IN PT. TUMOR TYPE) None	THERAPIES WITH CLINICAL BENEFIT (IN OTHER TUMOR TYPE) Everolimus Temsirolimus
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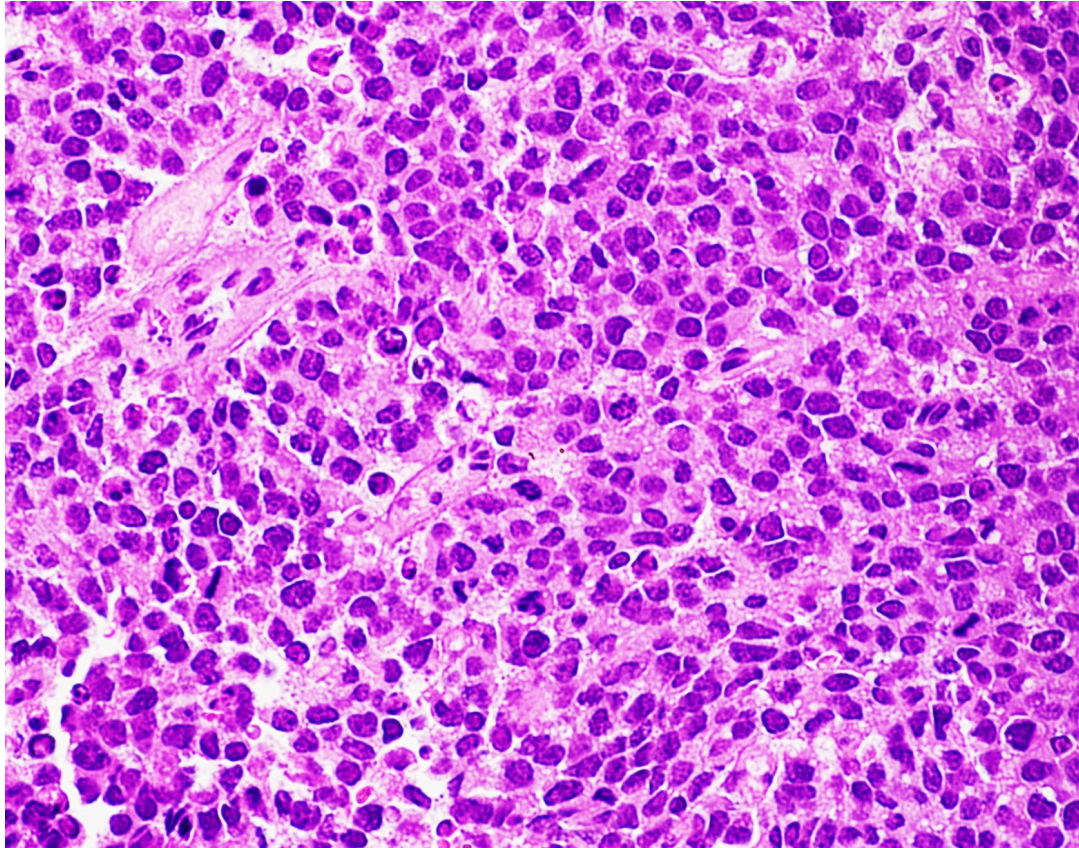
Diagnosis:

- Fusion-negative Rhabdomyosarcoma.
- Embryonal, dense pattern histologic subtype.









KARYOTYPE:

47,XX,+X,8~91dmin[13]/49,s1,+4,+17,80~100dmin[2]/48,XX,+6,+17,4~51dmin[3]/46,XX[3]

INTERPRETATION:

Cytogenetic studies of a bone marrow aspirate specimen revealed three related abnormal clones in eighteen of twenty one metaphase spreads examined, as described in the karyotype result. Notable abnormalities include a hyperdiploid (>46) chromosome count with gain of chromosomes X, 4, 6, 8, 17 and the presence of multiple copies of double minute (dmin) or small chromosome fragments. Three cells with a normal karyotype were observed.

Absence of



Alveolar rhabdomyosarcoma
t(2;13)(q35;q14)

Triaging matters!

When Should Fresh Tissue Be Saved?

- Need for cytogenetics (RPMI)
 - Suspected translocation-associated sarcoma
 - Unusual round cell and spindle cell tumors
 - Suspicion of lymphoma (flow cytometry)
 - * May be held until next day and submitted for histology if necessary
- Snap freeze for biobanking and/or additional special studies
- Avoid unnecessary decalcification when possible (strong acids degrade nucleic acids)
 - Save EDTA-decalcified tissue whenever possible
 - Document decalcification types and times for the pathology report

Clinical Case

- 4-year-old girl with pelvic mass.

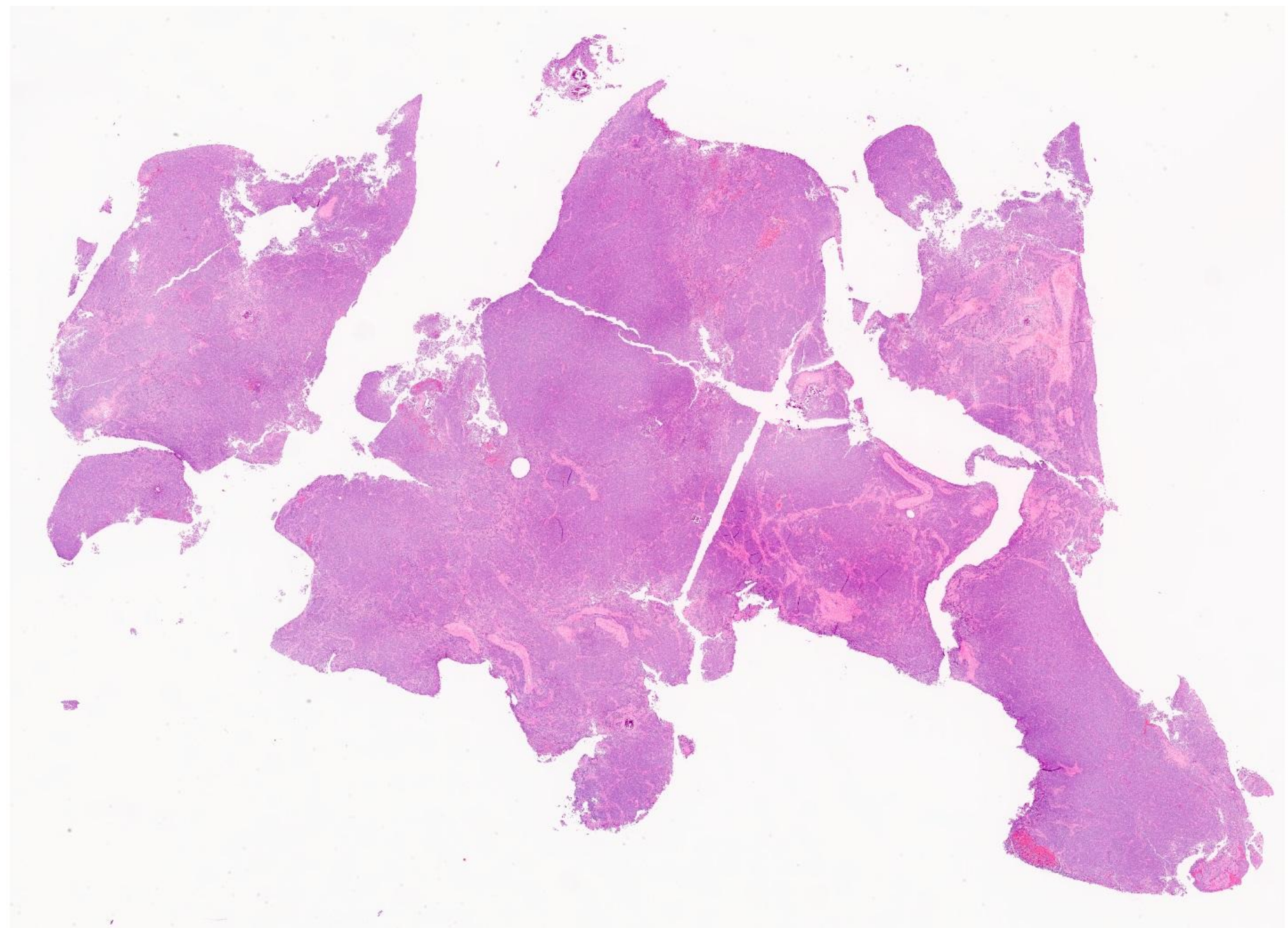
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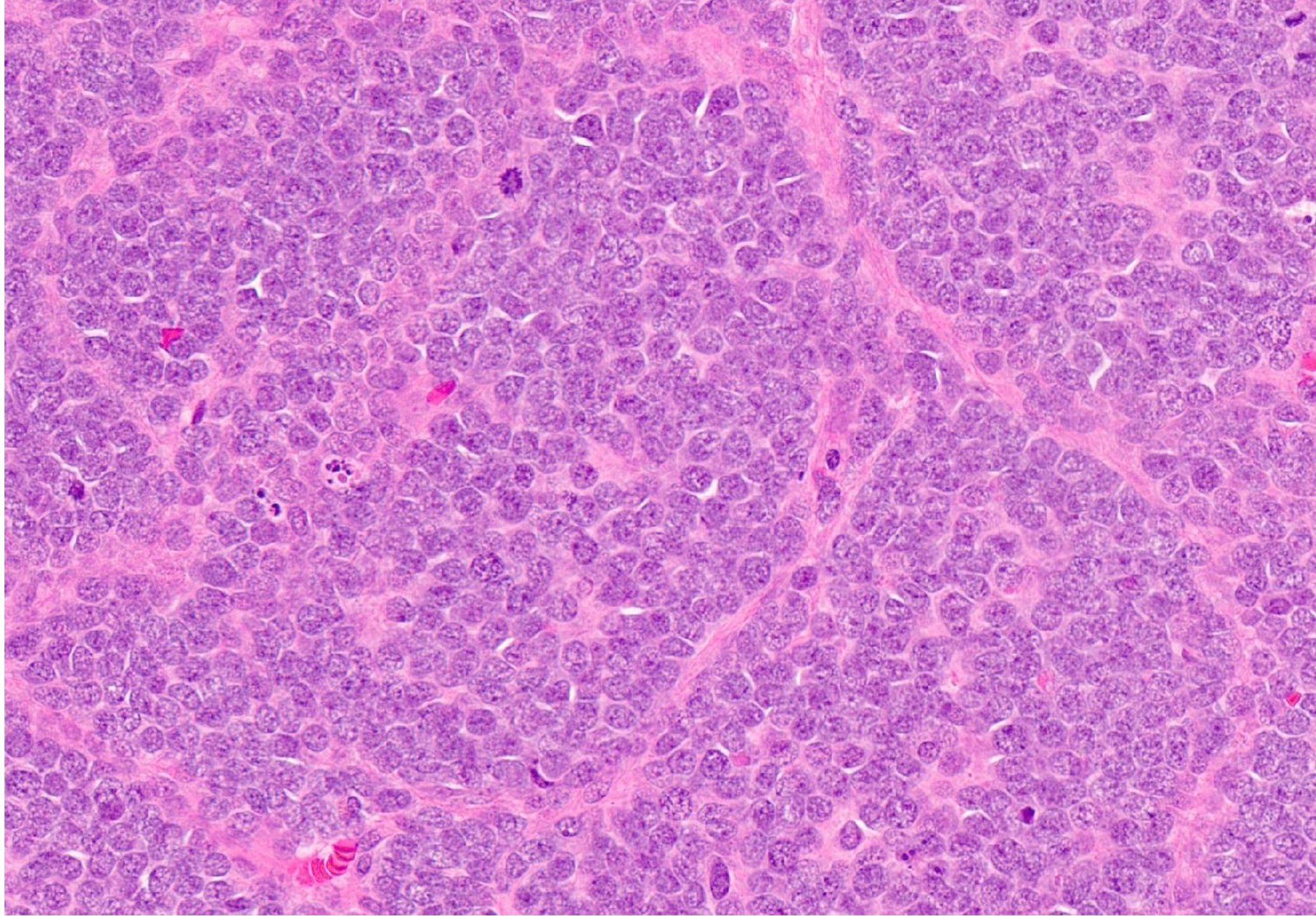


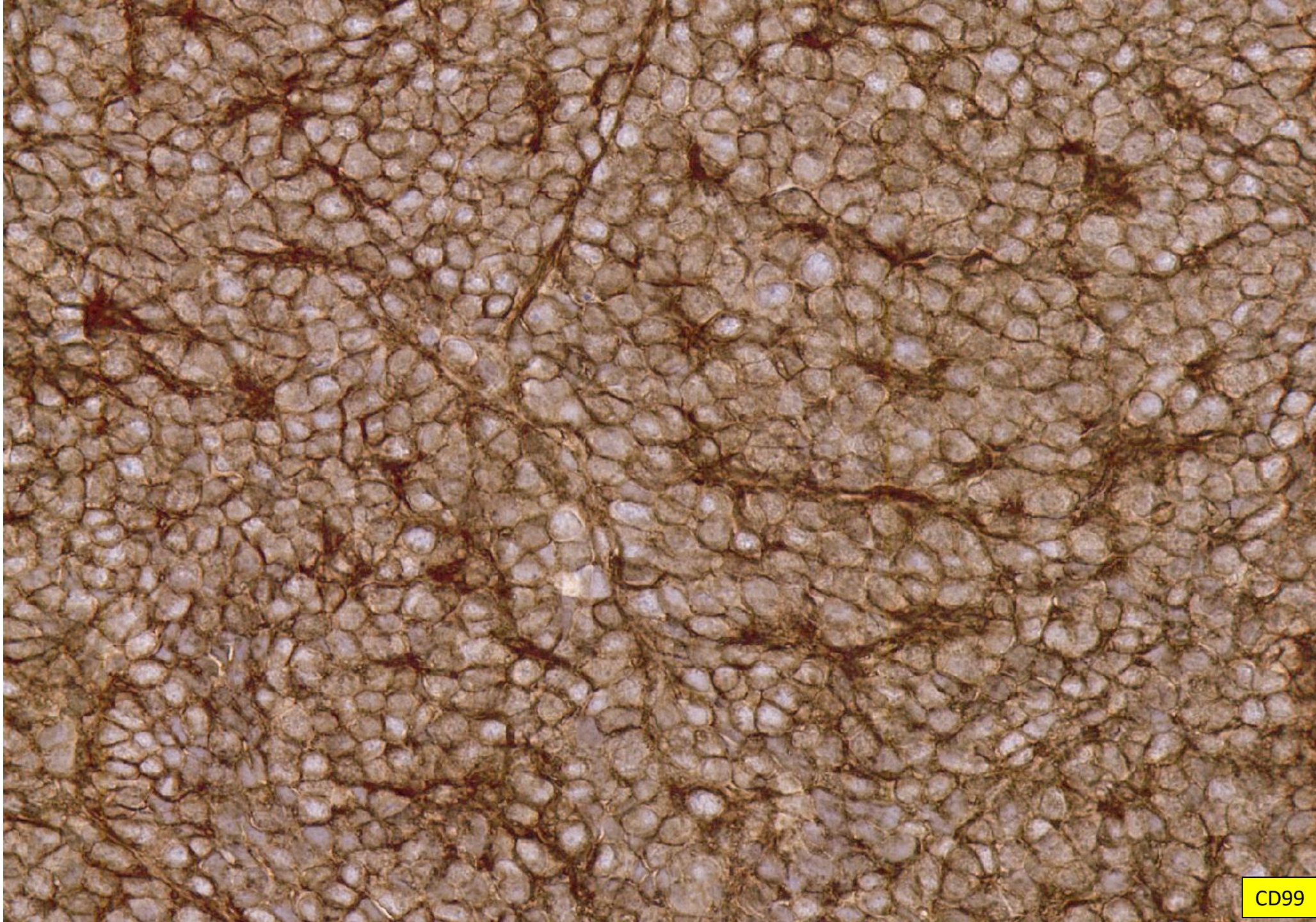
KVP 100
mA 70
3.00 mm
Tilt: +0.0
350ms HELICAL CT

Key Image
Technologist: JKP

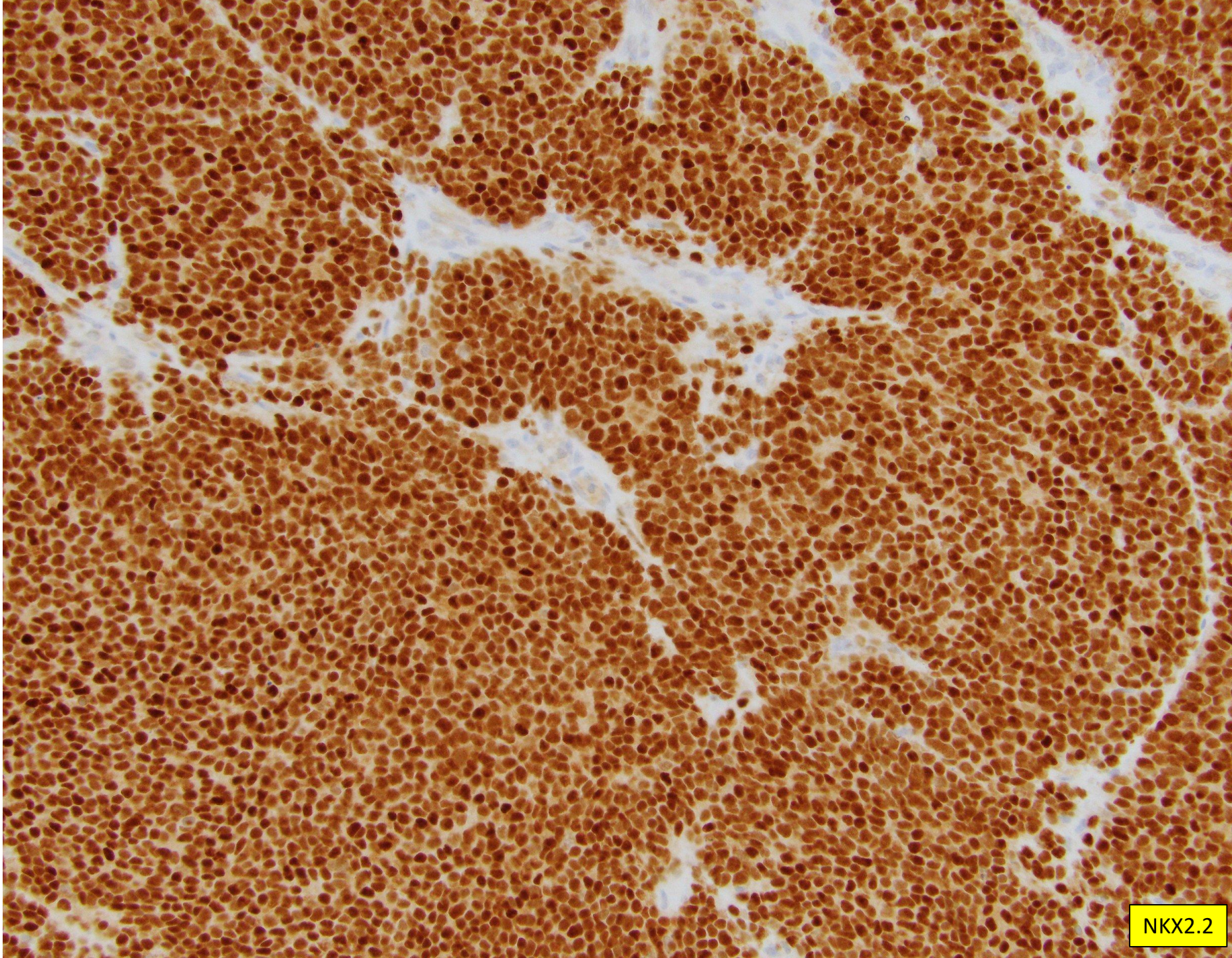




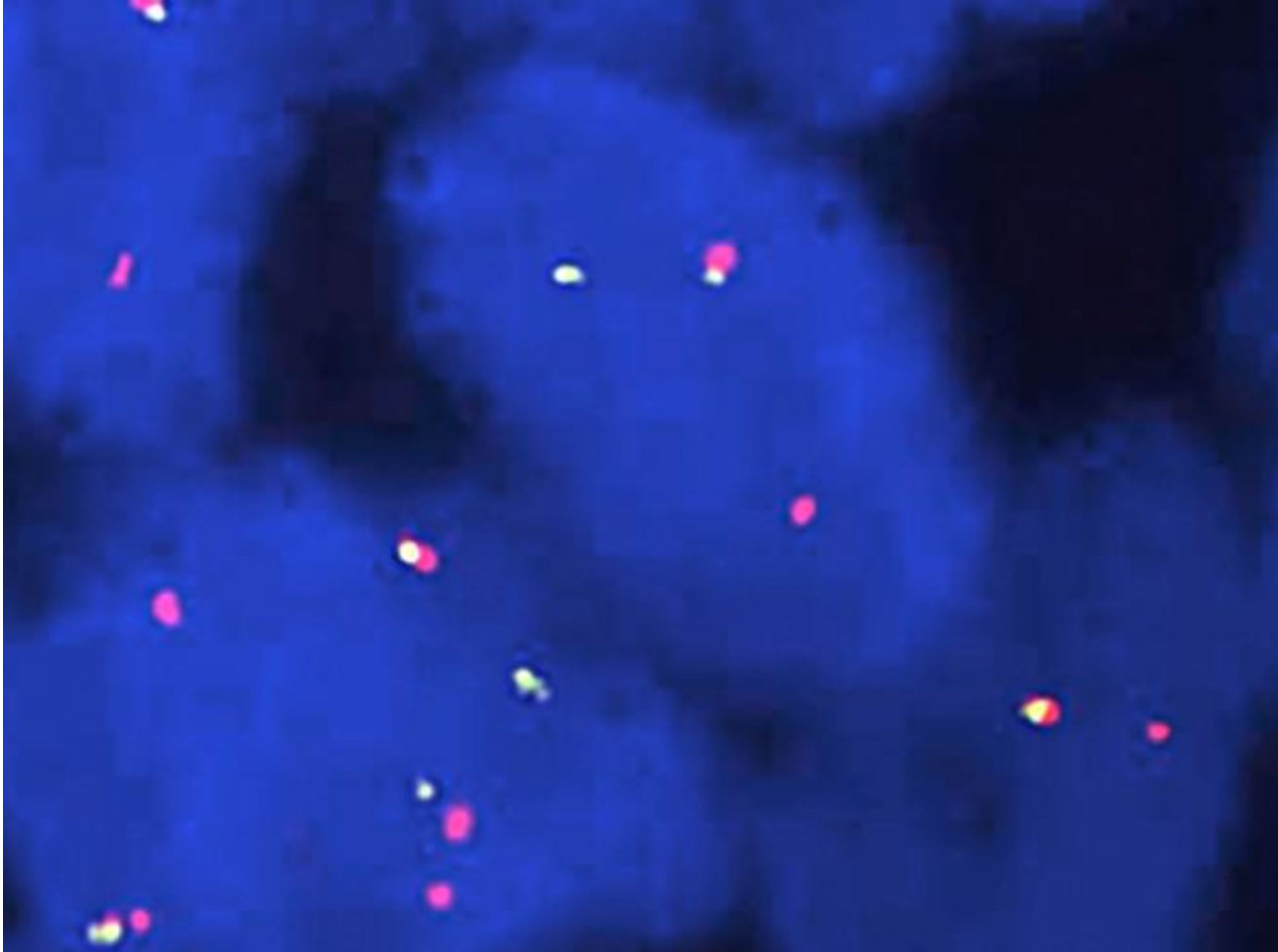




CD99



NKX2.2



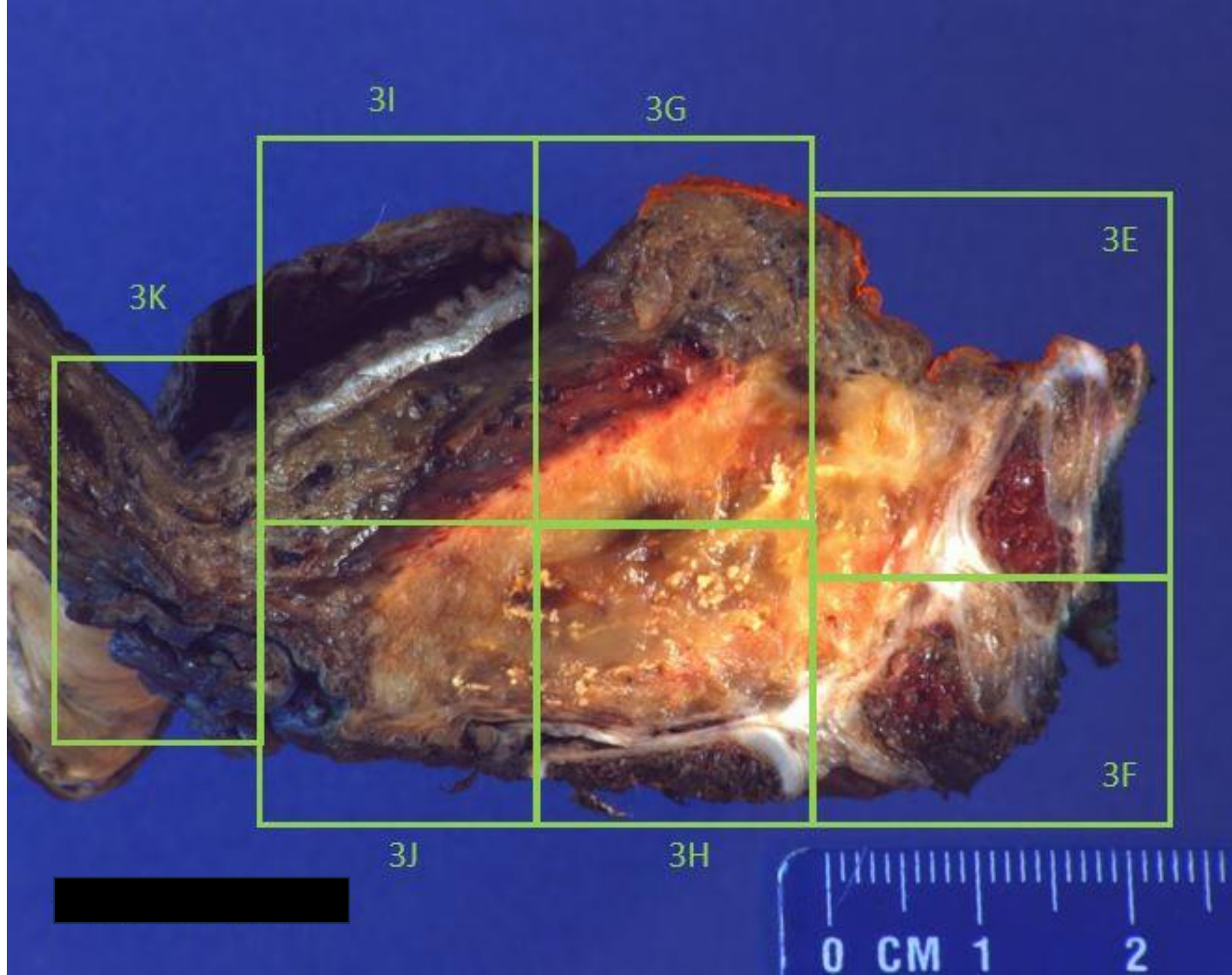
Karyotype: 46,XX,t(11;22)(q24;q12)[11]

Final diagnosis:

Soft tissue mass, pelvis, biopsy:

- EWING SARCOMA

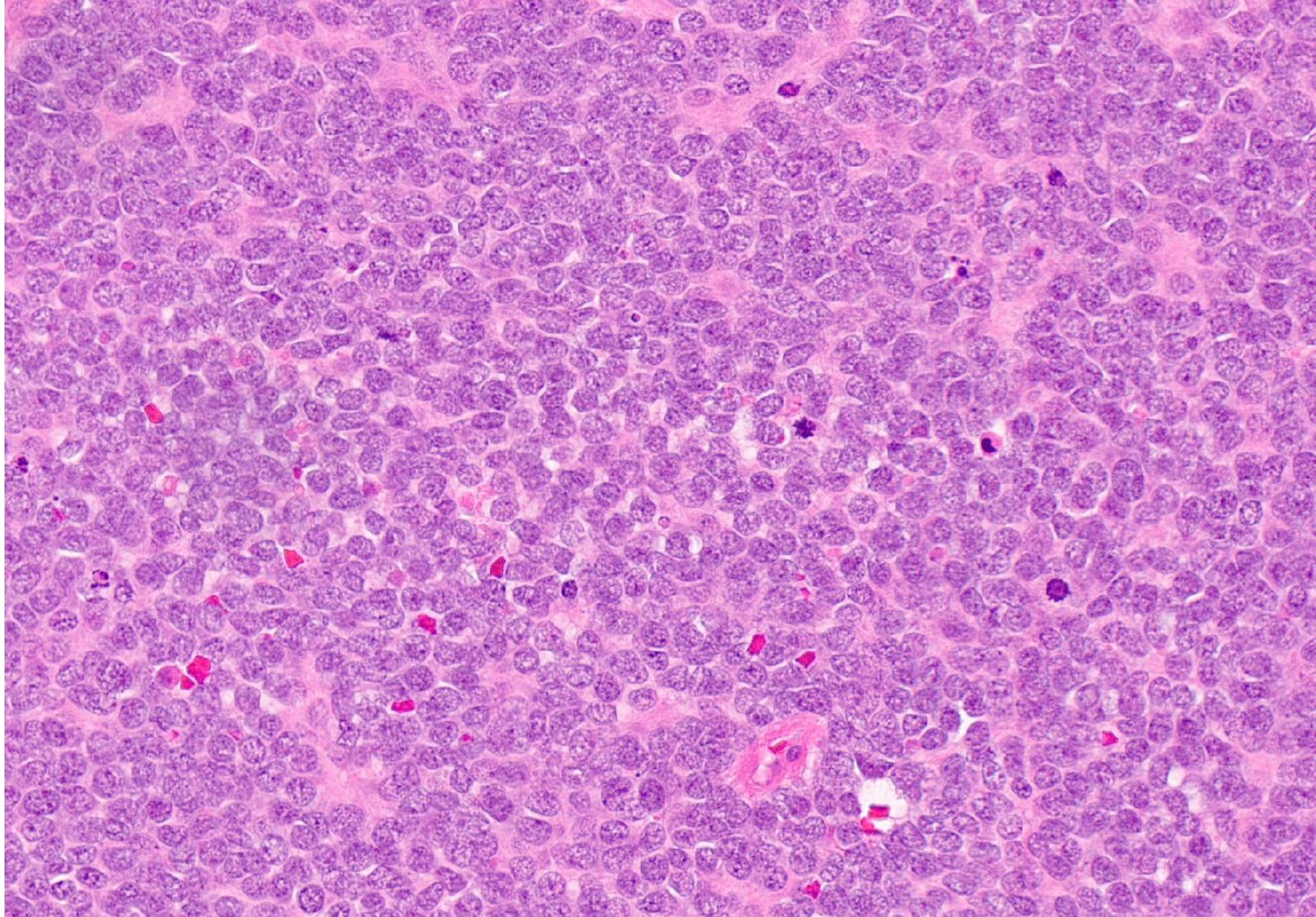


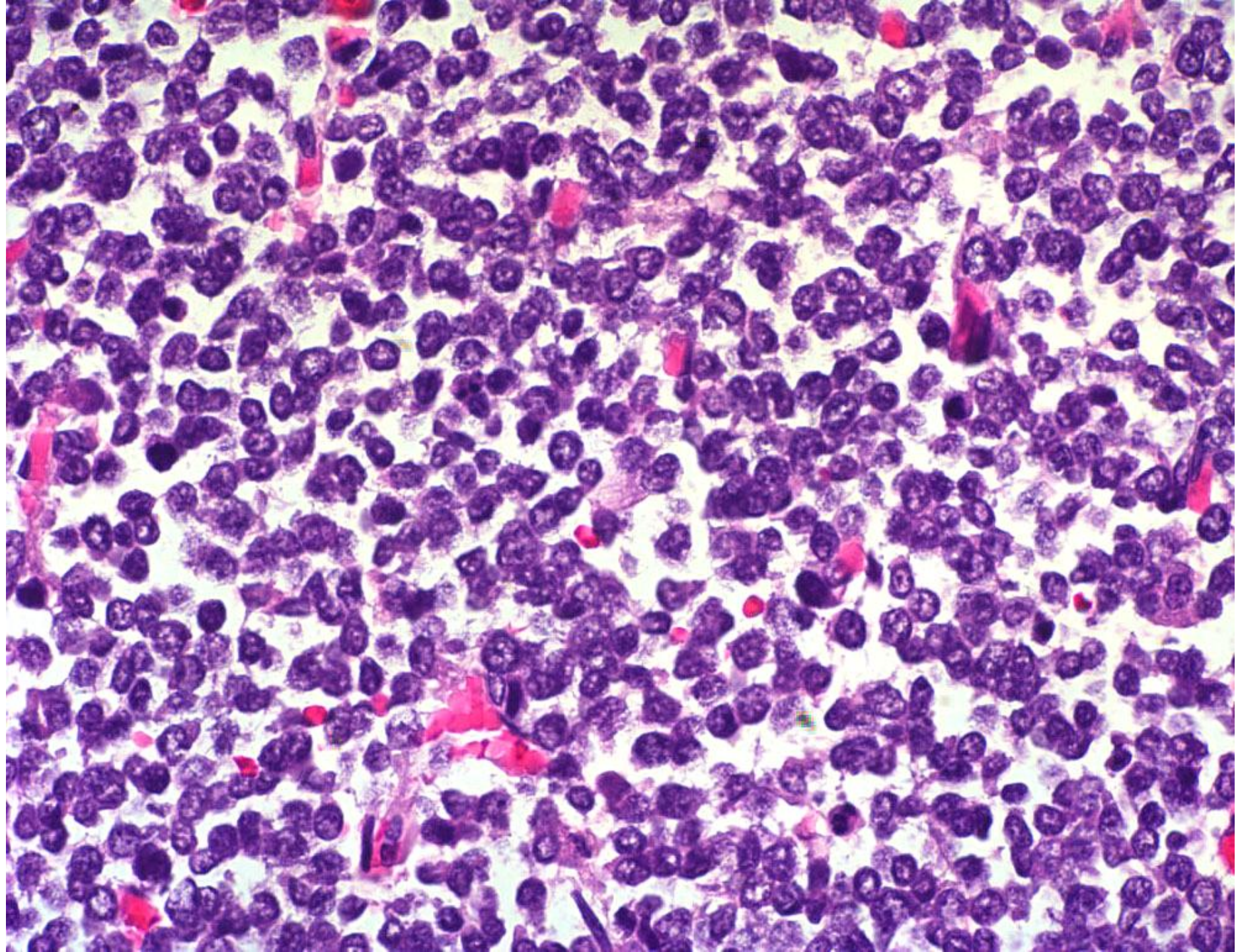


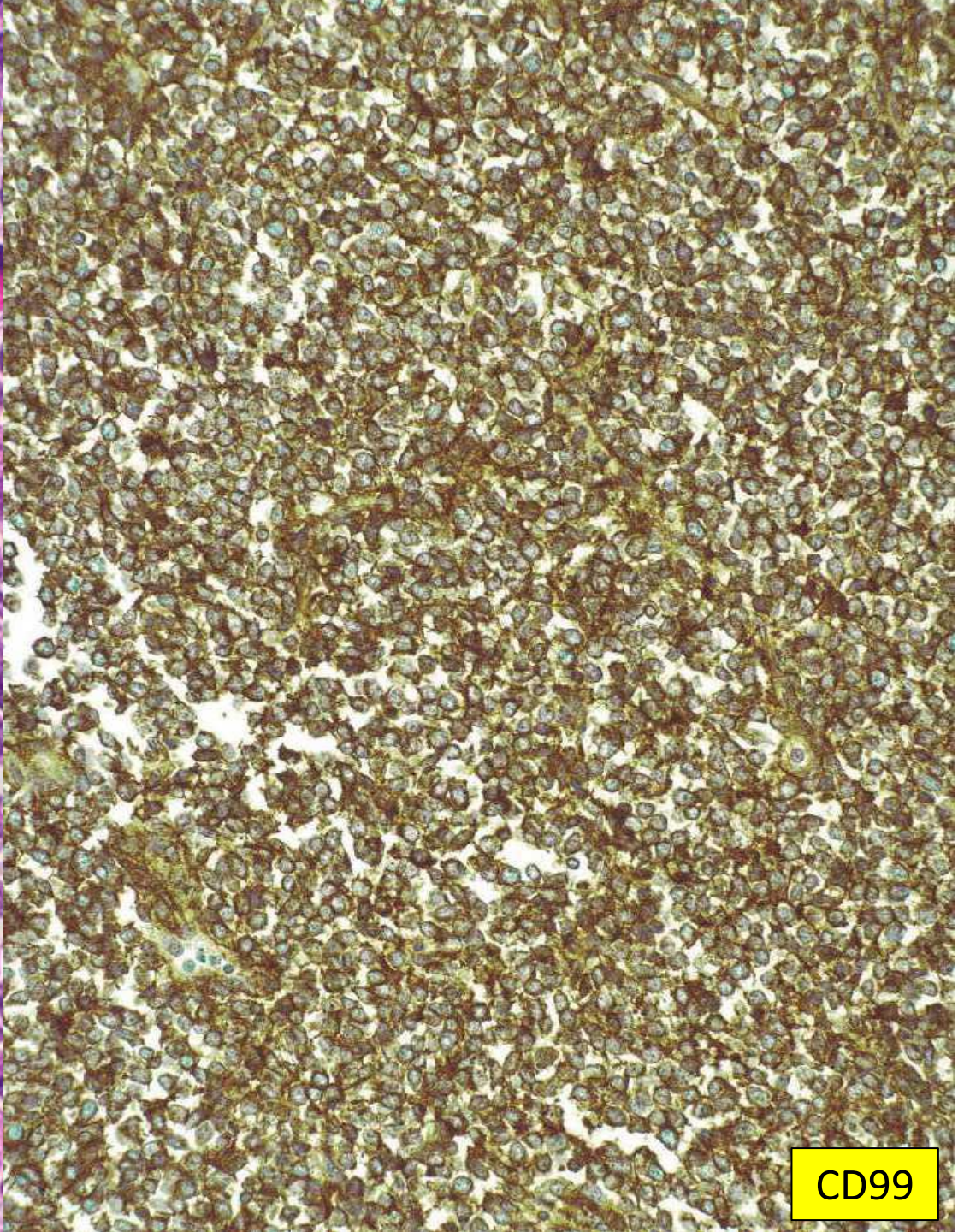
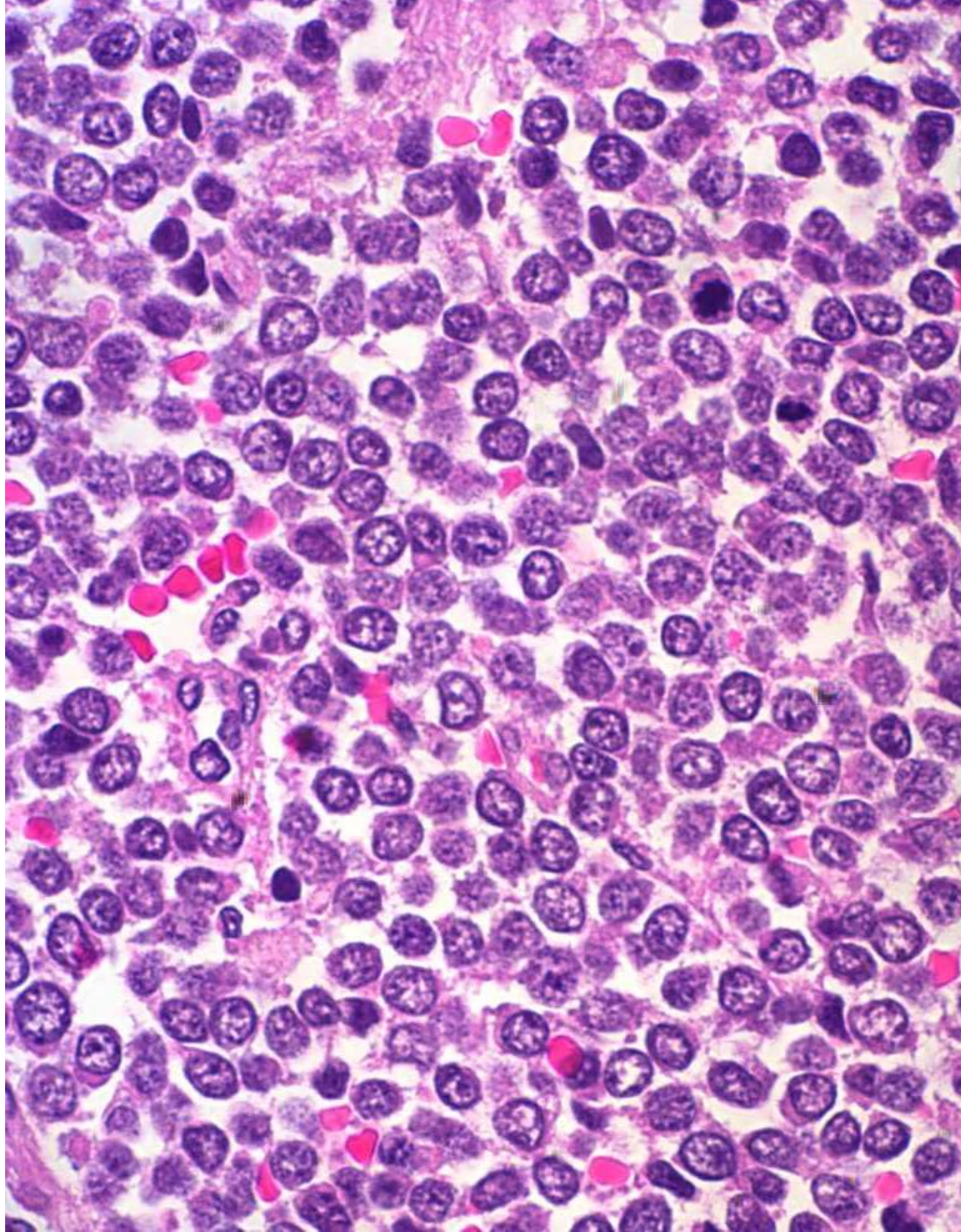
Ewing Sarcoma

- Second pediatric sarcoma in frequency
- 80% in children under 20 years of age
- Mainly bone (long bones shaft)
- Soft tissues (12%)
 - Limbs
 - Paravertebral
 - Retroperitoneum
 - Thoracopulmonary
 - Visceral organs (e.g. kidney)

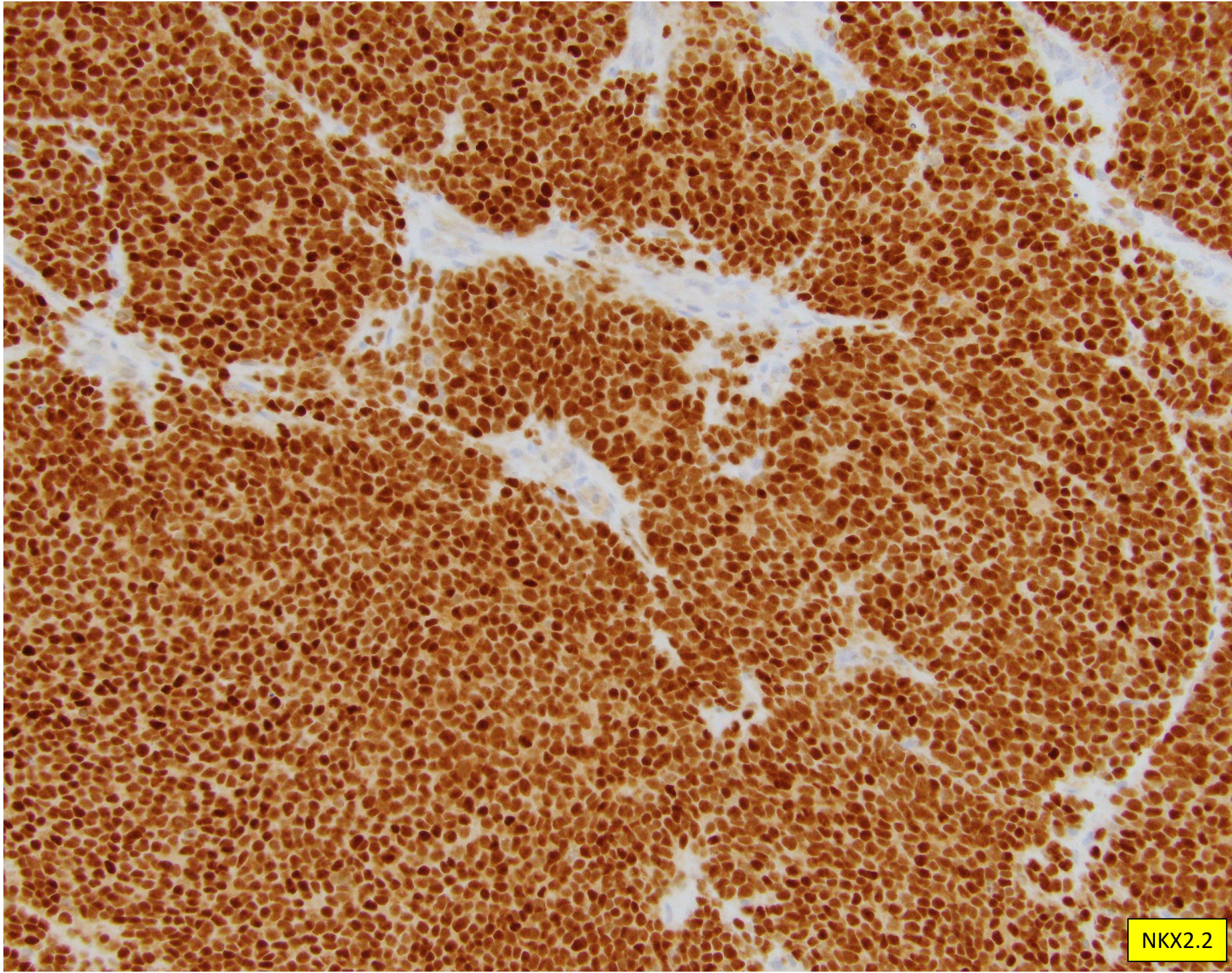




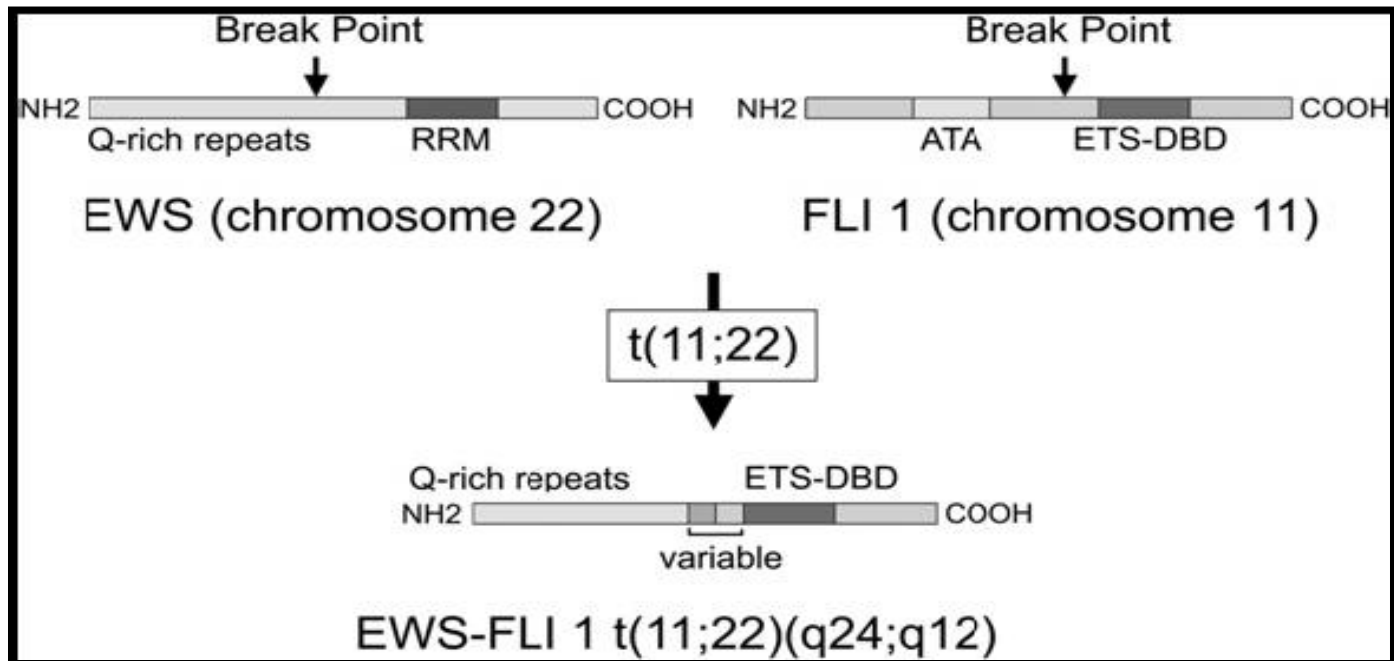




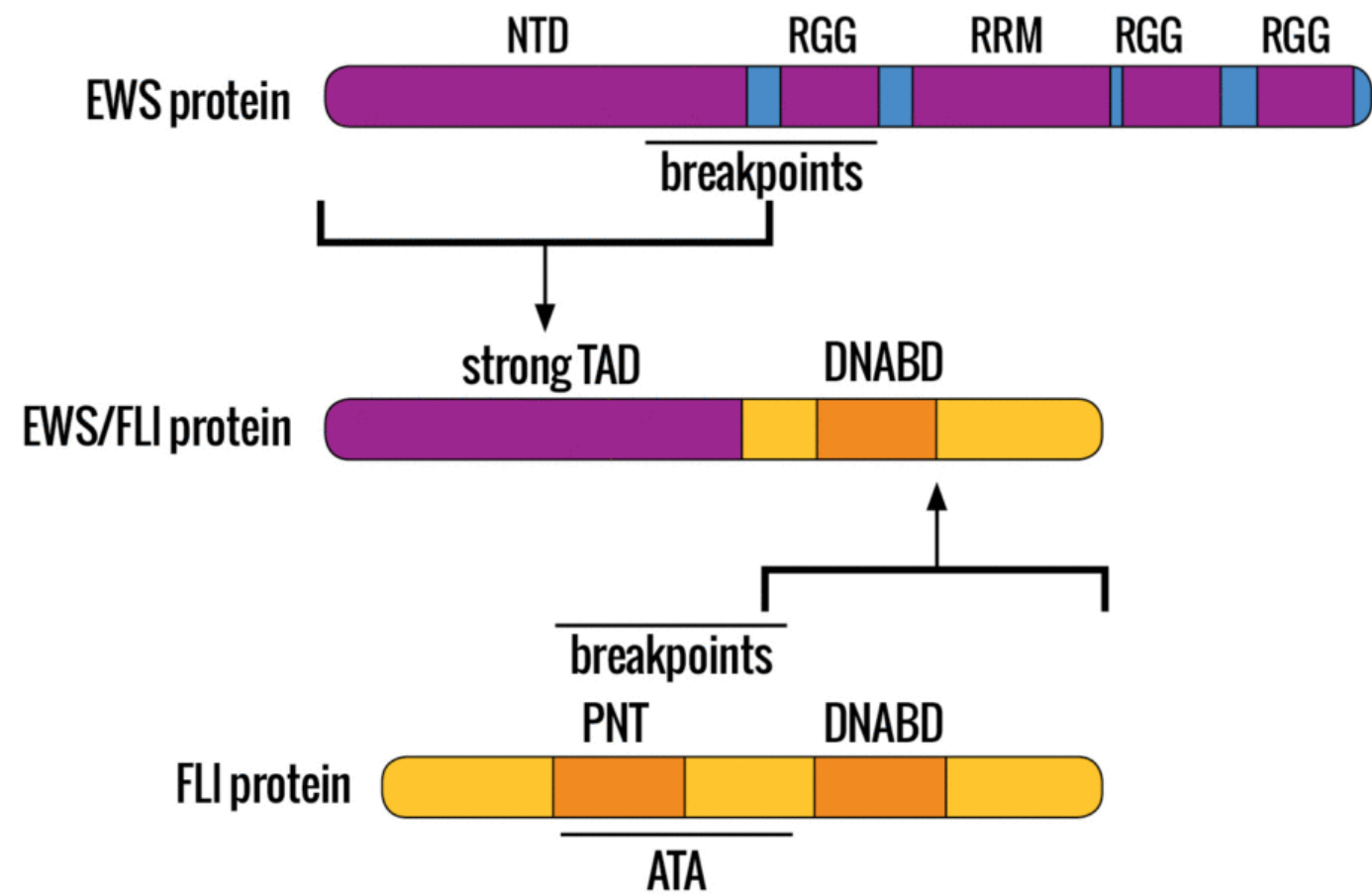
CD99

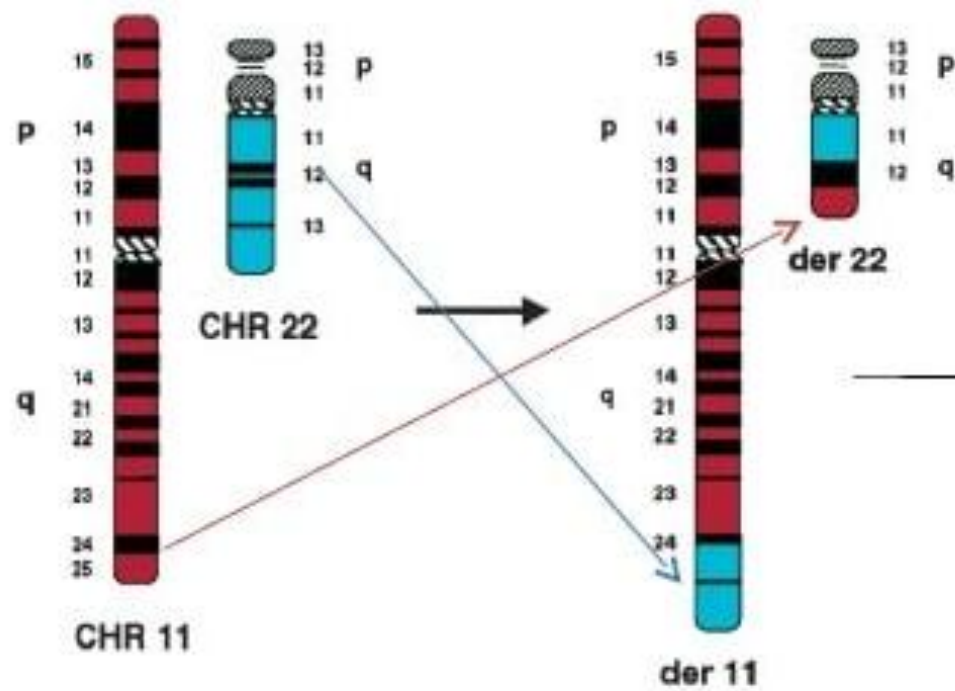


NKX2.2

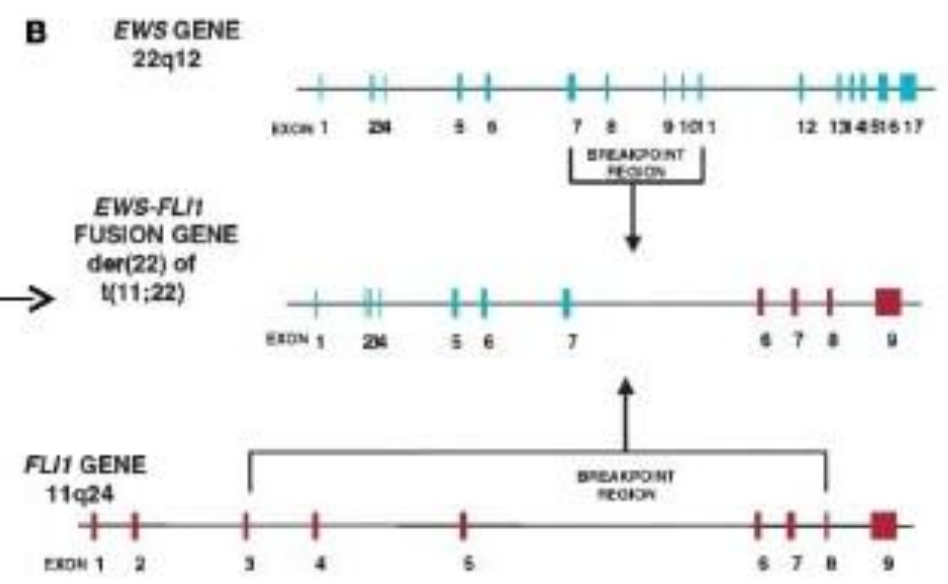


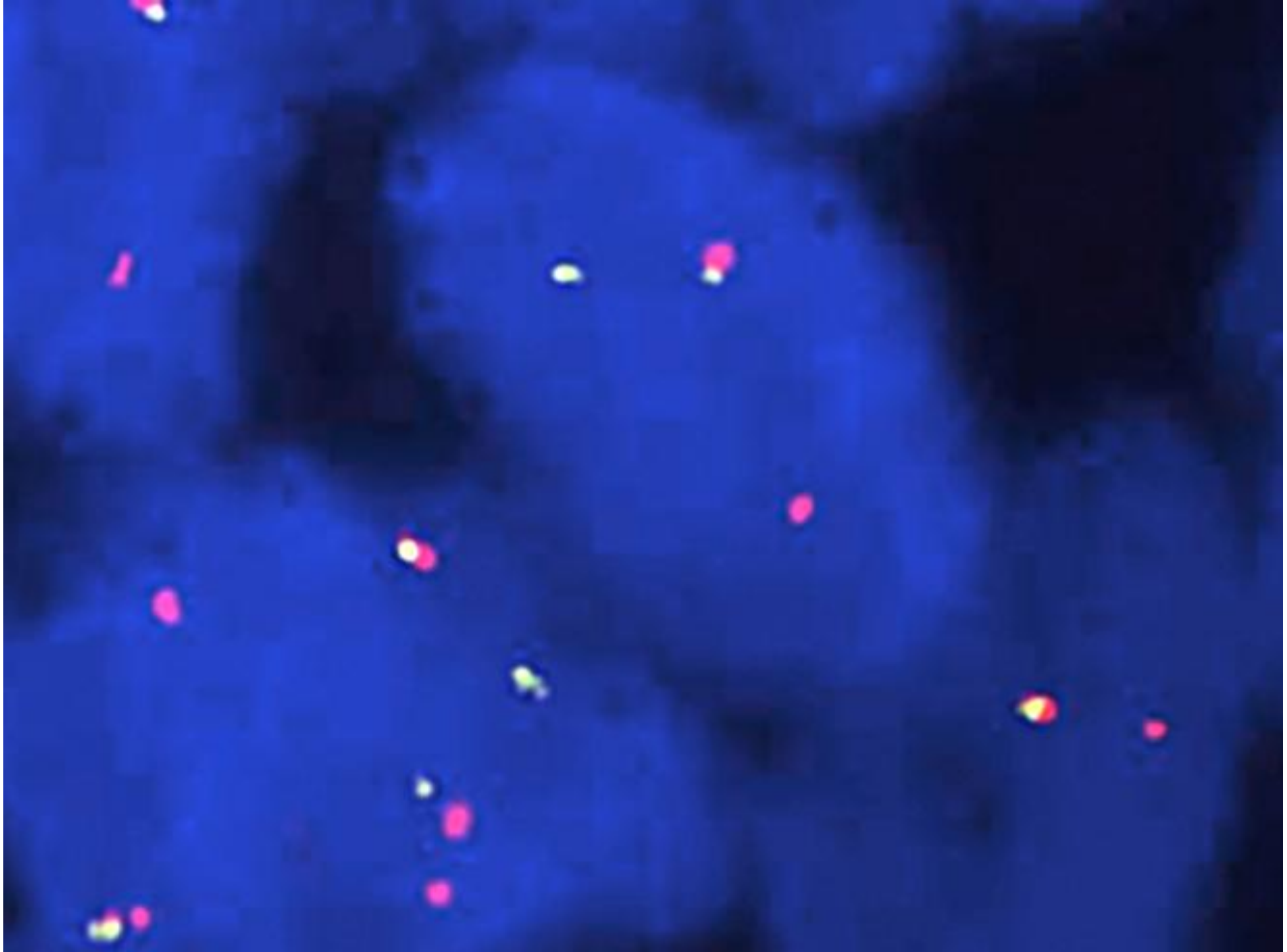
FET	ETS	Frecuency (%)
<i>EWSR1</i>	<i>FLI1</i>	85
<i>EWSR1</i>	<i>ERG</i>	10
<i>EWSR1</i>	<i>ETV1</i>	<1
<i>EWSR1</i>	<i>ETV4</i>	<1
<i>EWSR1</i>	<i>FEV</i>	<1
<i>FUS</i>	ETS	<1





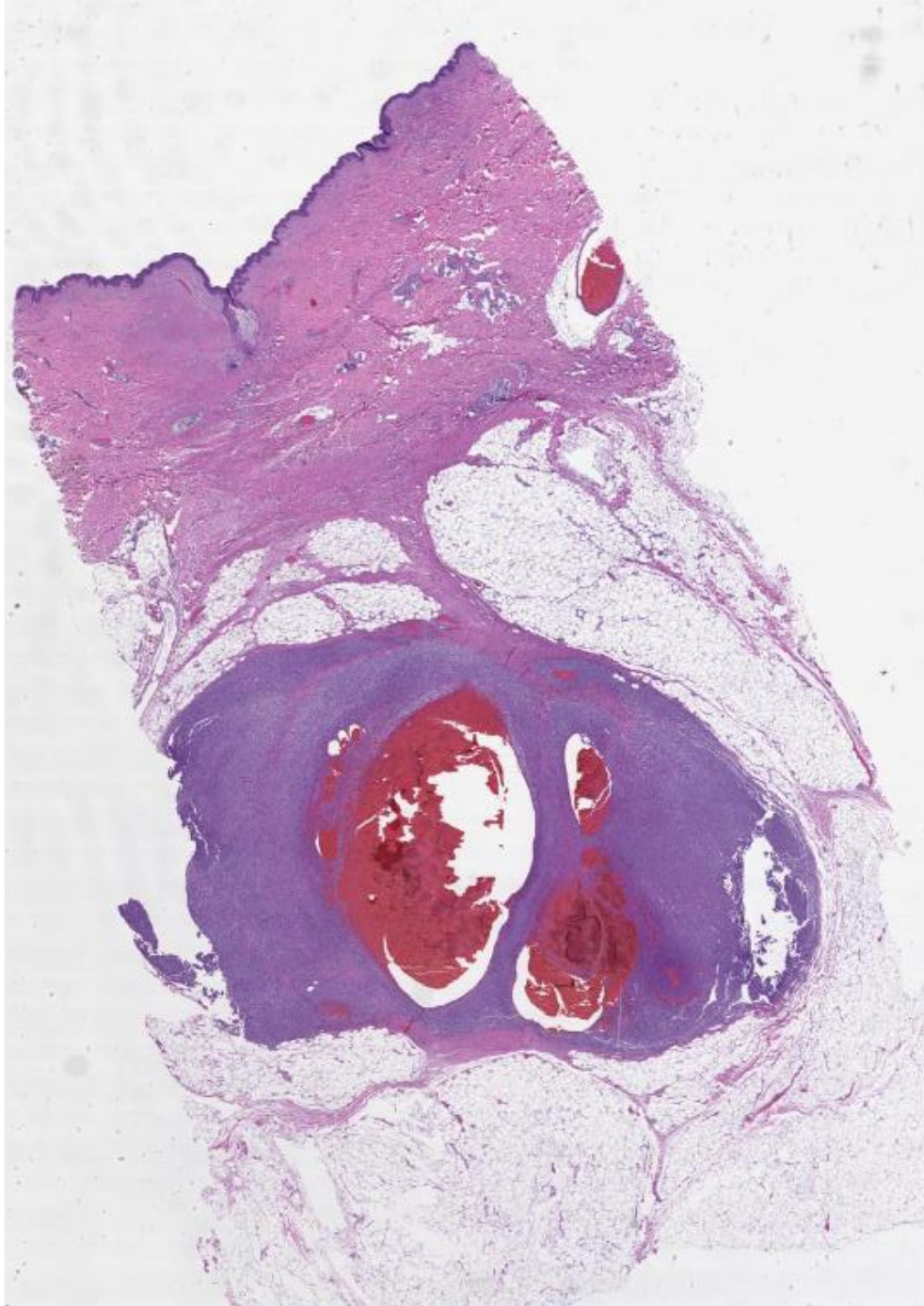
t(11;22)(q24;q12)

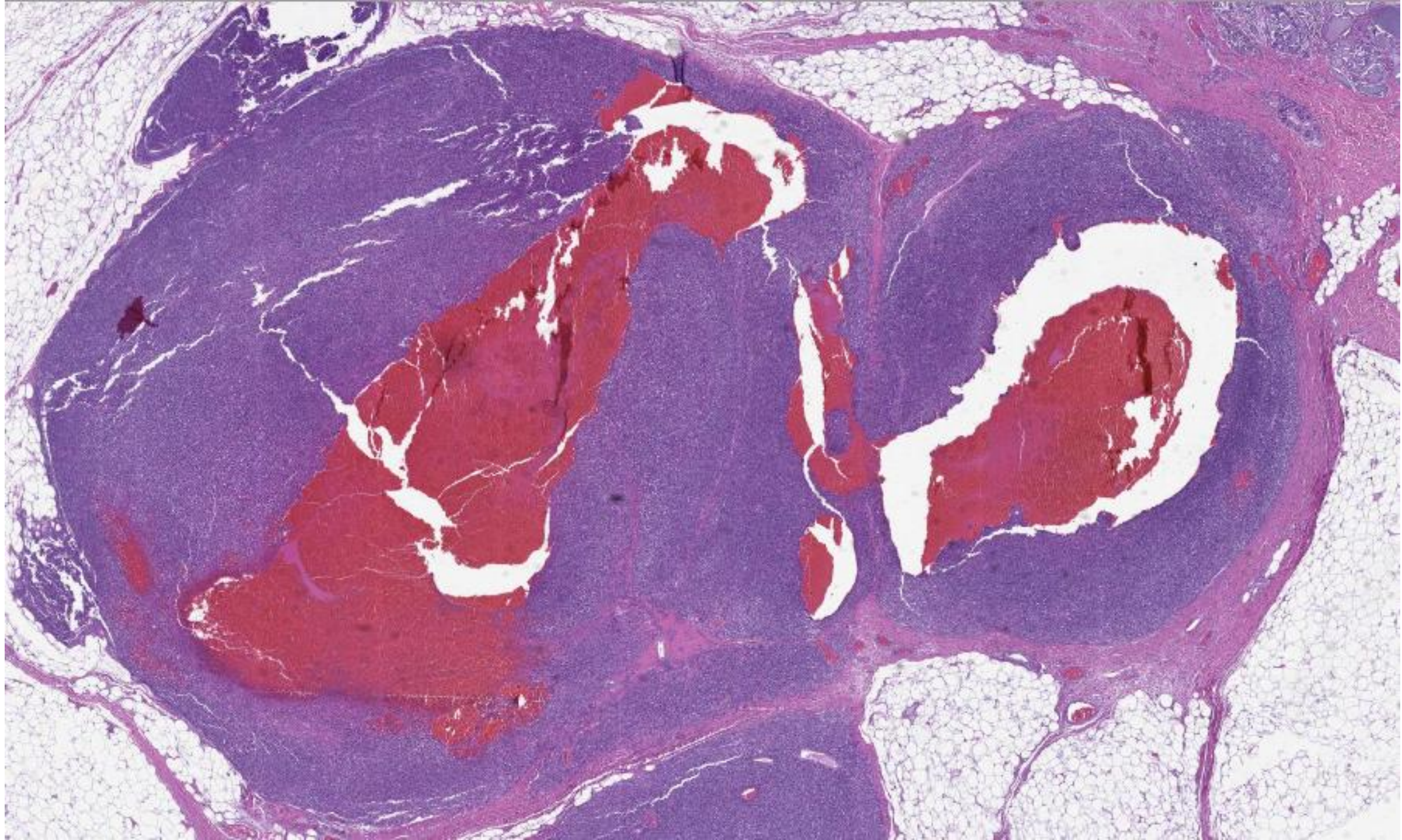


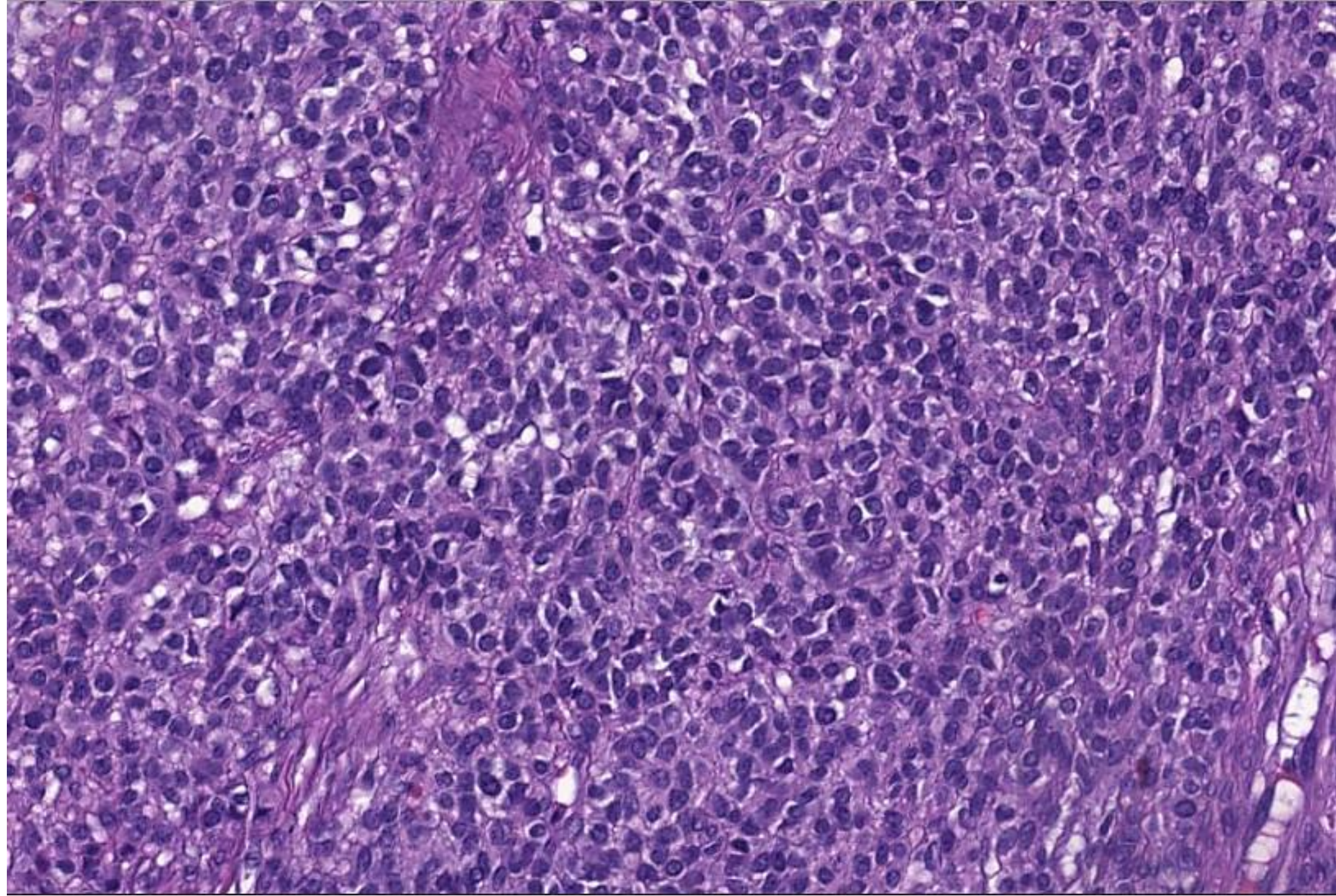


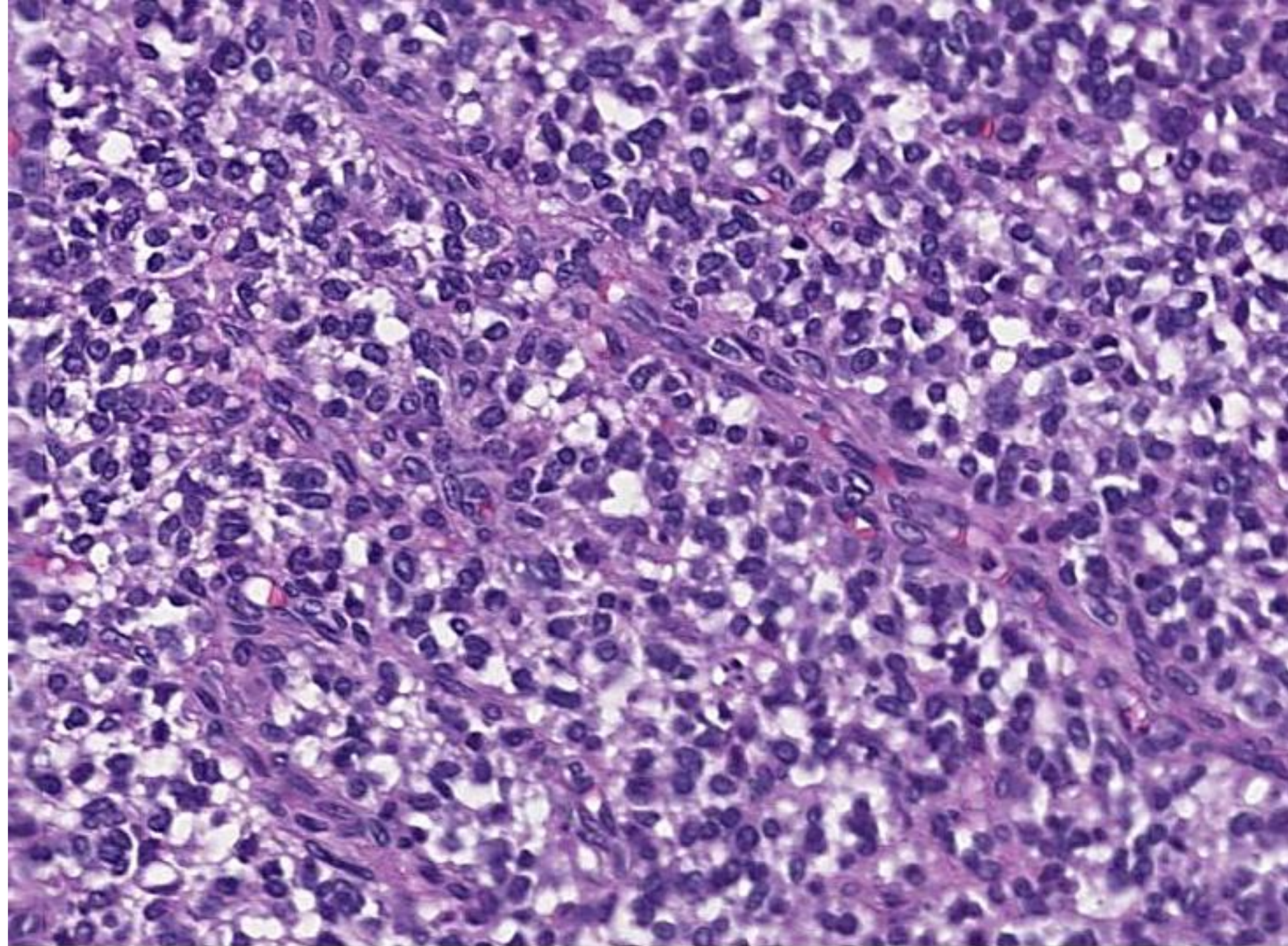
Clinical Case

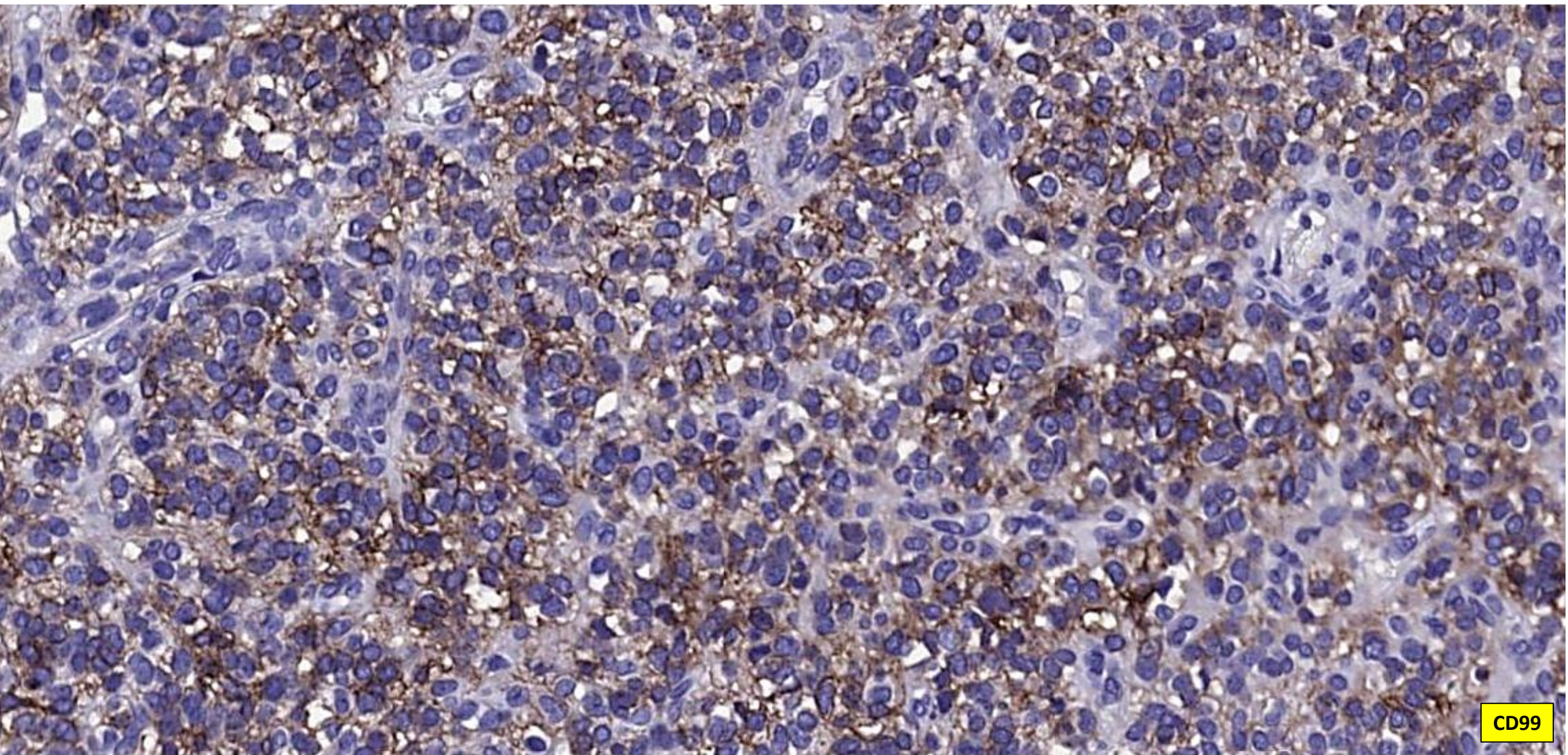
- 56-year-old female patient with superficial/subcutaneous soft tissue tumor in the lower back.



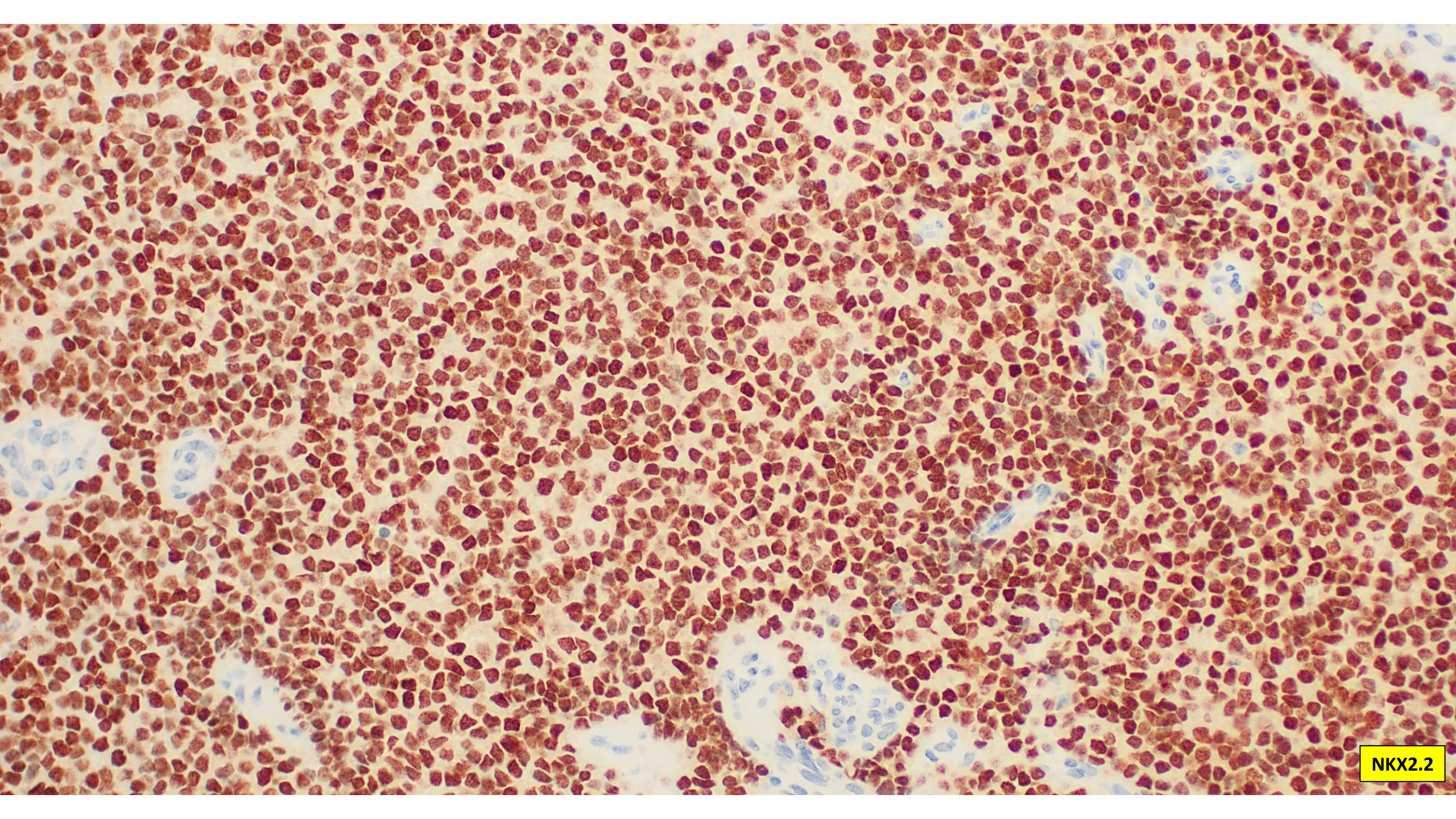


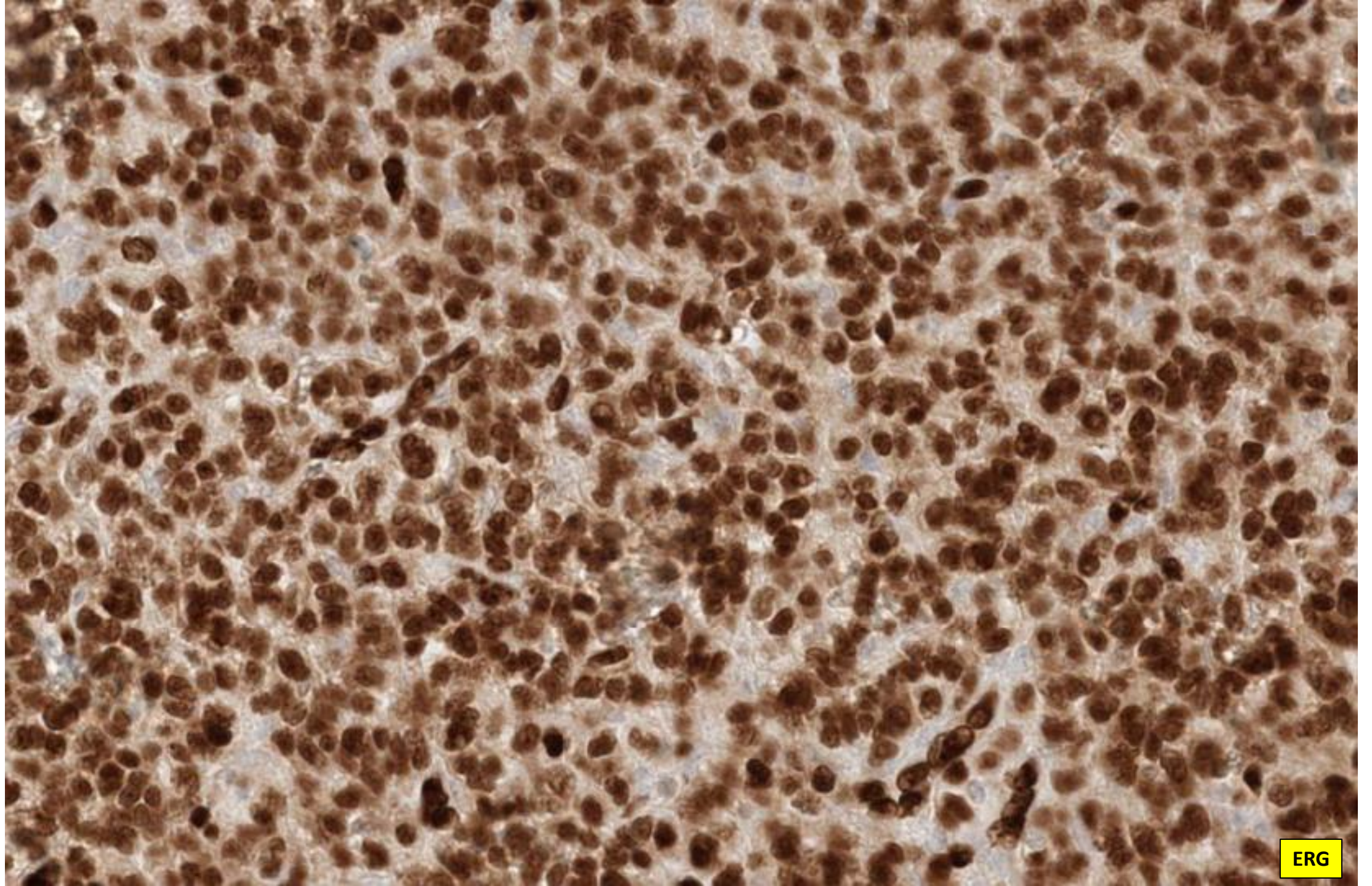




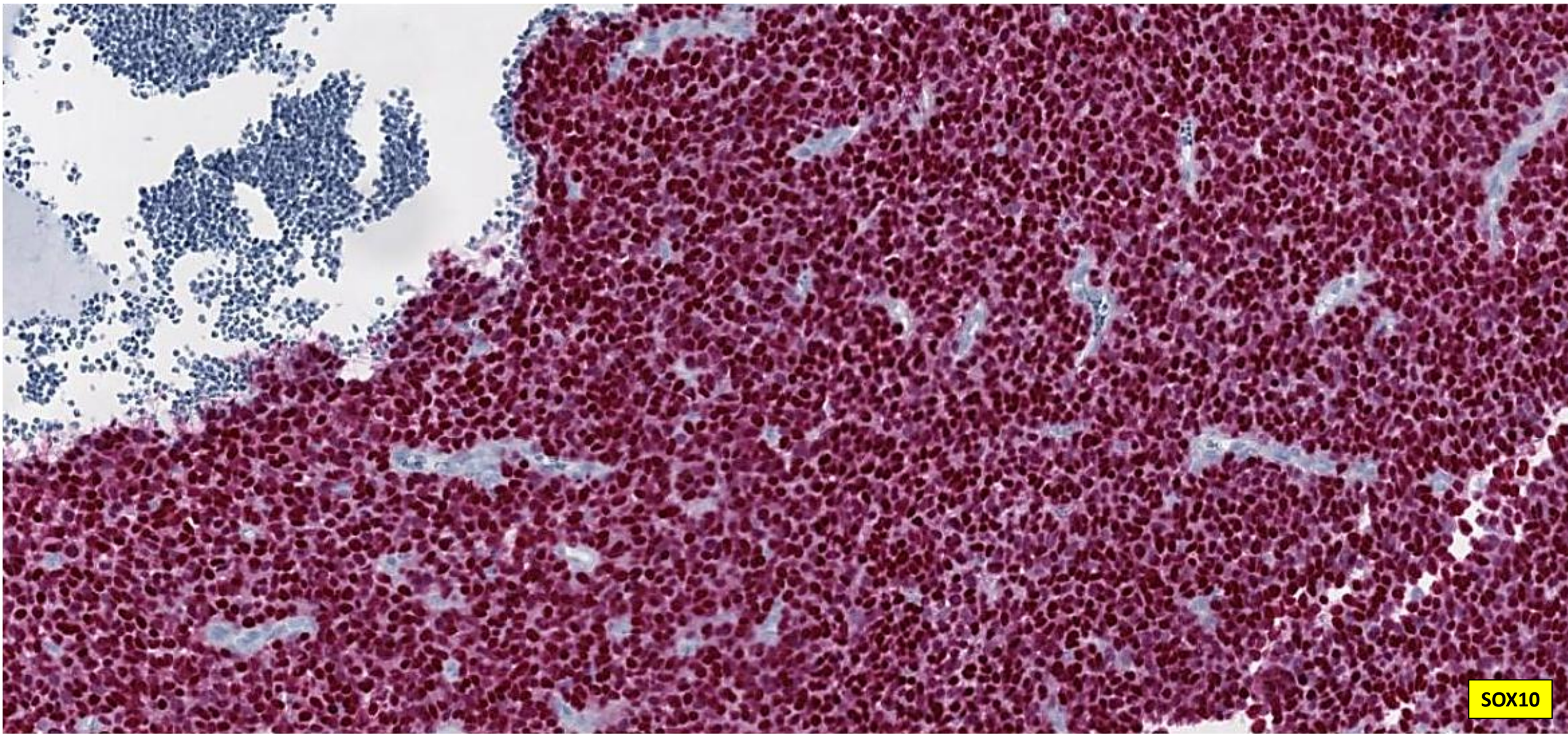


CD99





ERG



SOX10

Molecular studies (NGS)

- Genetic fusion *FUS::ERG*

FET	ETS	Frequency (%)
<i>EWSR1</i>	<i>FLI1</i>	85
<i>EWSR1</i>	<i>ERG</i>	10
<i>EWSR1</i>	<i>ETV1</i>	<1
<i>EWSR1</i>	<i>ETV4</i>	<1
<i>EWSR1</i>	<i>FEV</i>	<1
<i>FUS</i>	ETS	<1

- Ewing sarcoma?

MODERN PATHOLOGY



Journal homepage: <https://modernpathology.org/>

Research Article

Superficial Neurocristic *EWSR1::FLI1* Fusion Tumor: A Distinctive, Clinically Indolent, S100 Protein/SOX10-Positive Neoplasm

Andrew L. Folpe^{a,*}, Michael T. Tetzlaff^b, Steven D. Billings^c, Jorge Torres-Mora^a, Alexander David Borowsky^d, Teresa C. Santiago^e, Baptiste Ameline^f, Daniel Baumhoer^{f,g}

MODERN PATHOLOGY



Journal homepage: <https://modernpathology.org/>

Research Article

Superficial Neurocristic FET::ETS Fusion Tumor: Expanding the Clinicopathological and Molecular Genetic Spectrum of a Recently Described Entity

Carina A. Dehner^{a,*}, Laura M. Warmke^a, Brandon Umphress^a, Faizan Malik^b, Jeffrey M. Cloutier^c, Josephine K. Dermawan^d, Mike Fritz^e, Syril Keena T. Que^e, Baptiste Ameline^f, Karen J. Fritchie^d, Darcy A. Kerr^c, Konstantinos Linos^g, Daniel Baumhoer^{f,h}, Steven D. Billings^d, Andrew L. Folpeⁱ

Table

All cases of superficial neurocristic tumors with FET::ETS fusions reported to date

Case	Age/sex	Tumor site/size in centimeter	Mitotic figures in 10 hpf/necrosis	Immunohistochemistry	Molecular genetics	Treatment	Outcome
1 (current study)	18/M	Left superior medial midback/2.0	4/No	Positive: S100 protein, SOX10, CD99, NKX2.2, CD56 Negative: keratins, caldesmon, CD45, CK7, CD20, WT1, MelanA, HMB45, SALL4, synaptophysin, FLI1, MyoD1, desmin, Myogenin, p63	FUS exon 7:: ETV5 exon 9	Wide excision (Mohs surgery)	ANED at 18 mo
2 (current study)	8/M	Right shoulder/ Unknown	4/No	Positive: S100 protein, SOX10, CD99, CD34 (focal), p16 (focal), CD56 (focal) Negative: Keratin, CD45, SMA, EMA, CK8/18, CD1a, CD21, CD23, CD68, MITF	FUS exon 8:: FLI1 exon 5	Too recent for follow-up	Too recent for follow-up
3 (current study)	10/F	Dorsal foot/	10/No	Positive: S100 protein, SOX10, CD56, NKX2.2, FLI1, synaptophysin (focal); Negative: CD99, keratin Oscar, keratin AE1/AE3, CK7, CK20, CD45, EMA, chromogranin, CD34, desmin, MART1, WT1	FUS exon 7:: ERG exon 5; VUS in MyoD1	Wide excision	Too recent for follow-up
4 (current study; previously published ¹⁴)	9/F	Thigh/1.8	5-9/Yes (Infarct-type)	Positive: S100 protein, CD99 (diffuse), SOX10, CD56, synaptophysin (patchy, focal), PAX7, FLI1 (weak) Negative: MelanA, HMB45, chromogranin, keratin AE1/AE3, desmin, myogenin, MyoD1, vascular markers, CD45; INI1 retained	EWSR1 exon 6:: FLI1 exon 9; EWSR1 rearrangement by FISH	Wide local excision with negative margins; Adjuvant chemotherapy with vincristine, cyclophosphamide, and doxorubicin	ANED at 31 mo
5 (current study; previously published ¹⁵)	58/F	Right distal thigh above knee/1.0	1/No	Positive: S100 protein, SOX10, CD99 (partial), GFAP (focal), EMA (weak), and CEA, NKX2.2 Negative: INSM1, CKAE1/AE3, CK5, Melan-A, calponin, p63, actin, MITF, PAX7	EWSR1 exon 7:: ERG exon 9; EWSR1 rearrangement by FISH	Wide local excision with negative margins	ANED at 24 mo
6 (Arnold et al ²⁵)	16/F	Left lower leg/3.2	Unknown/ Unknown	Positive: S100 protein, CD99 Negative: SMA, MART1, HMB45, desmin, EMA, keratin AE1/AE3,	EWSR1 exon 10:: FLI1 exon 6	Wide excision, followed by chemotherapy and radiation	ANED at 12 mo
7 (Folpe et al ⁶)	50/F	Left thigh/11.0	Unknown/No	Positive: S100 protein, SOX10, CD56, GFAP (focal) Negative: CD99, FLI1, ERG, HMB45, MelanA, keratins, desmin, actins, CD34	EWSR1 exon 7:: FLI1 exon 8	Wide excision	ANED at 17 mo
8 (Folpe et al ⁶)	24/M	Left back/Unknown	Unknown/No	Positive: S100 protein, SOX10 Negative: CD99, FLI1, HMB45, MelanA, keratins, Neurofilament	EWSR1 exon 11::FLI1 exon 5	Wide excision	ANED at 11 mo
9 (Folpe et al ⁶)	19/M	Right buttock/3.0	Unknown/No	Positive: S100 protein, SOX10 Negative: CD99, HMB45, MelanA, keratins, desmins, actins, CD34, CD56; INI-1 retained	EWSR1 exon 11::FLI1 exon 6	Wide excision	ANED at 33 mo
10 (Folpe et al ⁶)	19/M	Left chest wall/1.7 cm	Unknown/No	Positive: S100 protein, SOX10, CD56 (variable), synaptophysin Negative: CD99, FLI1, ERG, HMB45, MelanA, keratins, chromogranin-A, ALK; INI-1 retained	EWSR1 exon 7::FLI1 exon 6	Wide excision	ANED at 62 mo
11 (Folpe et al ⁶)	69/M	Central back/1.0 cm	Unknown/No	Positive: S100 protein, SOX10, CD99 (focal), p16 (focal), p63 (focal) Negative: ERG, MelanA, keratins, actins; INI-1 retained	EWSR1 exon 10::FLI1 exon 6	Wide excision; 1 cycle of Ewing sarcoma-directed chemotherapy	ANED at 12 mo

ANED: alive with no evidence of disease; F: female; M: male

Soft tissue mass, lower back, resection:

**SUPERFICIAL NEUROCRISTIC *FET::ETS* FUSION TUMOR (see comment).
PREVIOUS BIOPSY SITE IDENTIFIED.
MARGINS ARE UNINVOLVED.**

Comment

Thank you for sharing with us this highly unusual and challenging case which, on further review, in our opinion represents an example of superficial neurocristic tumor, a recently described rare entity characterized by superficial dermal/ subcutaneous location frequently involving the trunk, that characteristically harbors *FET::ETS* fusions including *EWSR1::FLI1* and, rarely, *FUS::ERG* rearrangements as reported in this case. Similar to this case, these tumors typically have predominant round to oval cytomorphologies, low mitotic rate and frequent aneurysmal/ angiomatous appearance, with strong and diffuse coexpression of S100 and SOX10, as well as frequent NKX2.2 nuclear expression and membranous CD99 staining (both stains repeated at PCH). Of note, some published cases initially classified as superficial Ewing sarcoma and myoepithelioma were more recently reclassified as this entity. In addition, according to published series, these tumors typically have indolent clinical behavior.

References:

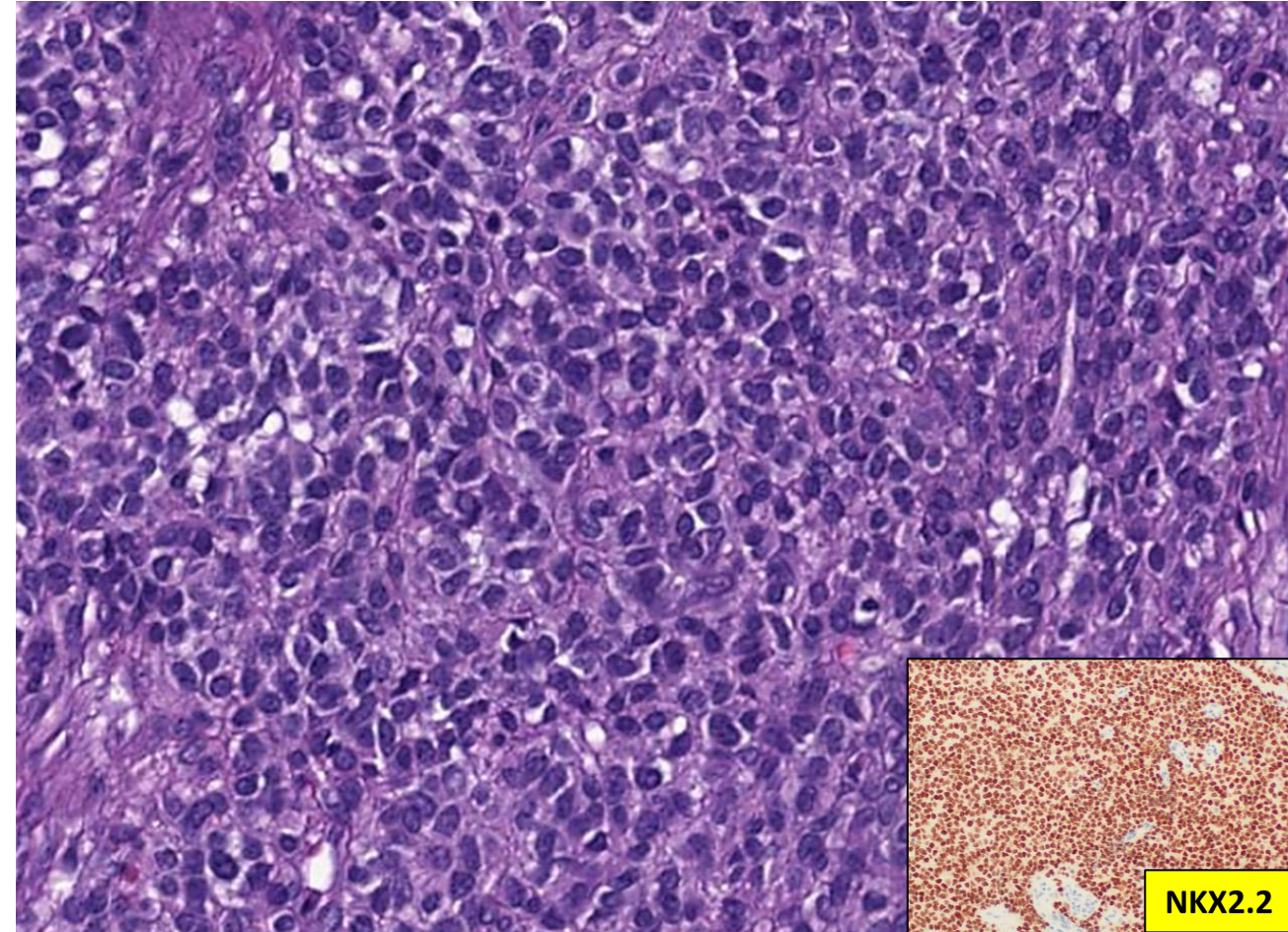
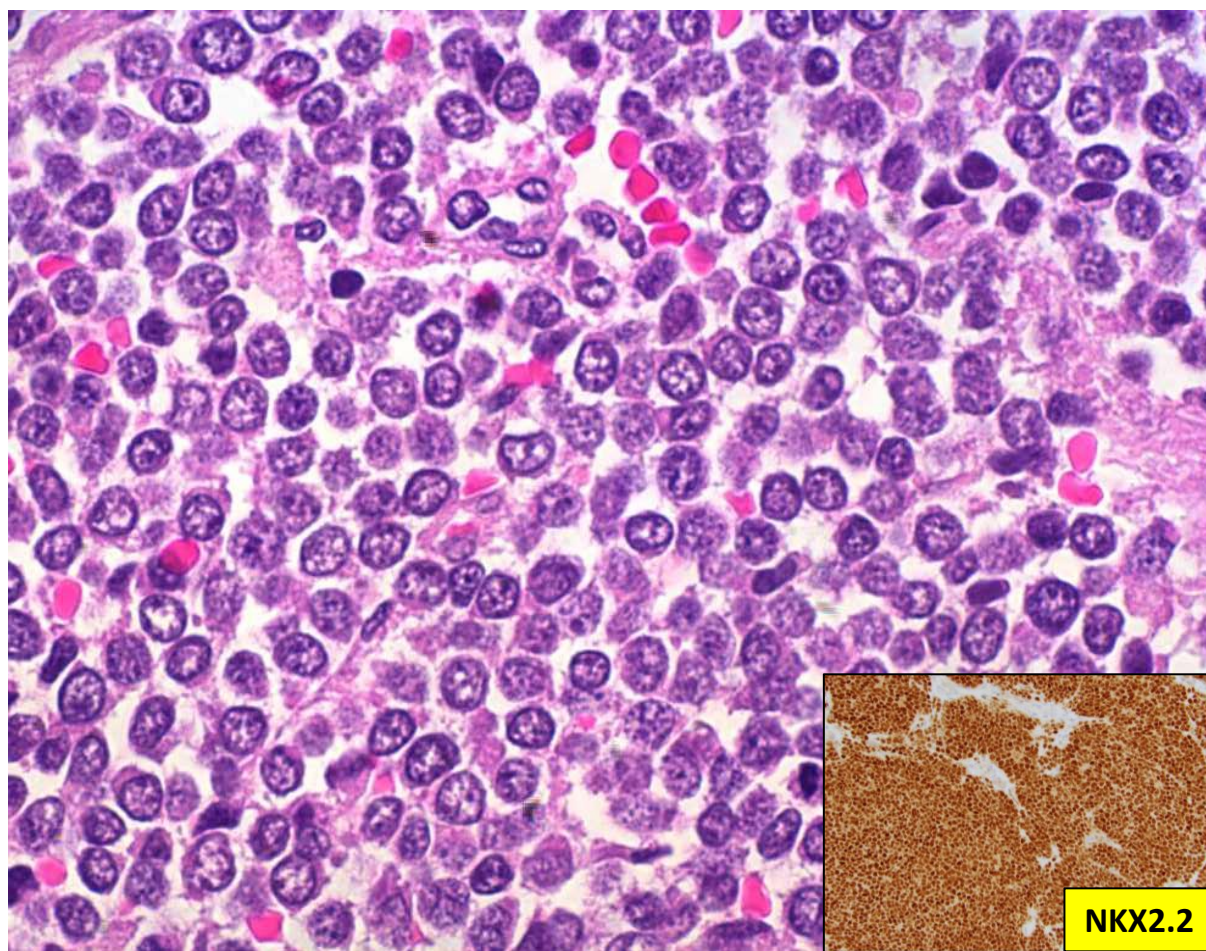
Folpe AL, Tetzlaff MT, Billings SD, Torres-Mora J, Borowsky AD, Santiago TC, Ameline B, Baumhoer D. Superficial Neurocristic EWSR1::FLI1 Fusion Tumor: A Distinctive, Clinically Indolent, S100 Protein/SOX10-Positive Neoplasm. Mod Pathol. 2024 Aug;37(8).

Dehner CA, Warmke LM, Umphress B, Malik F, Cloutier JM, Dermawan JK, Fritz M, Que SKT, Ameline B, Fritchie KJ, Kerr DA, Linos K, Baumhoer D, Billings SD, Folpe AL. Superficial Neurocristic FET::ETS Fusion Tumor: Expanding the Clinicopathological and Molecular Genetic Spectrum of a Recently Described Entity. Mod Pathol. 2025 Feb;38(2).

nmb/2/2/2026

Electronically Signed Out

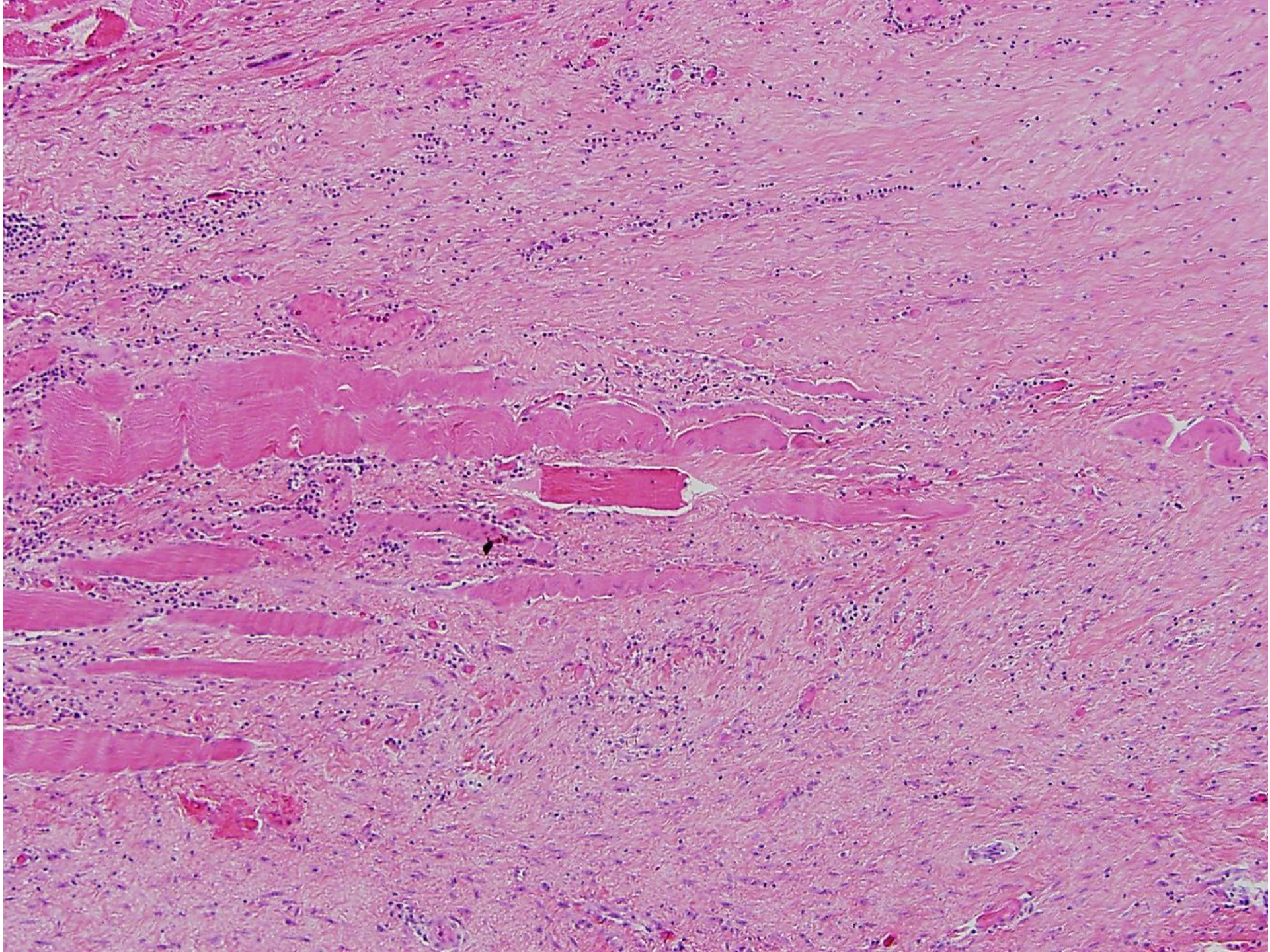
Eduardo Zambrano Tola, M.D.

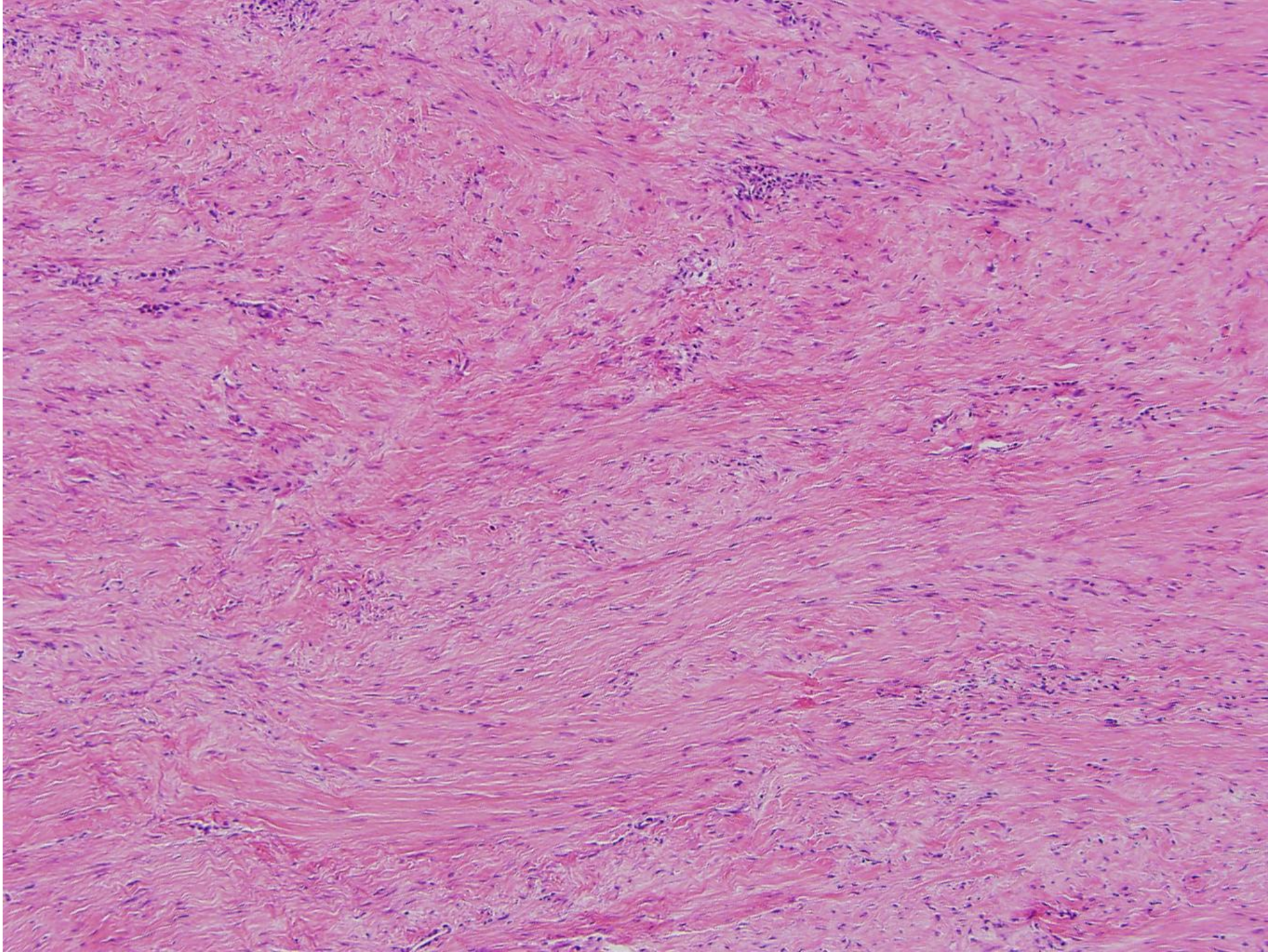


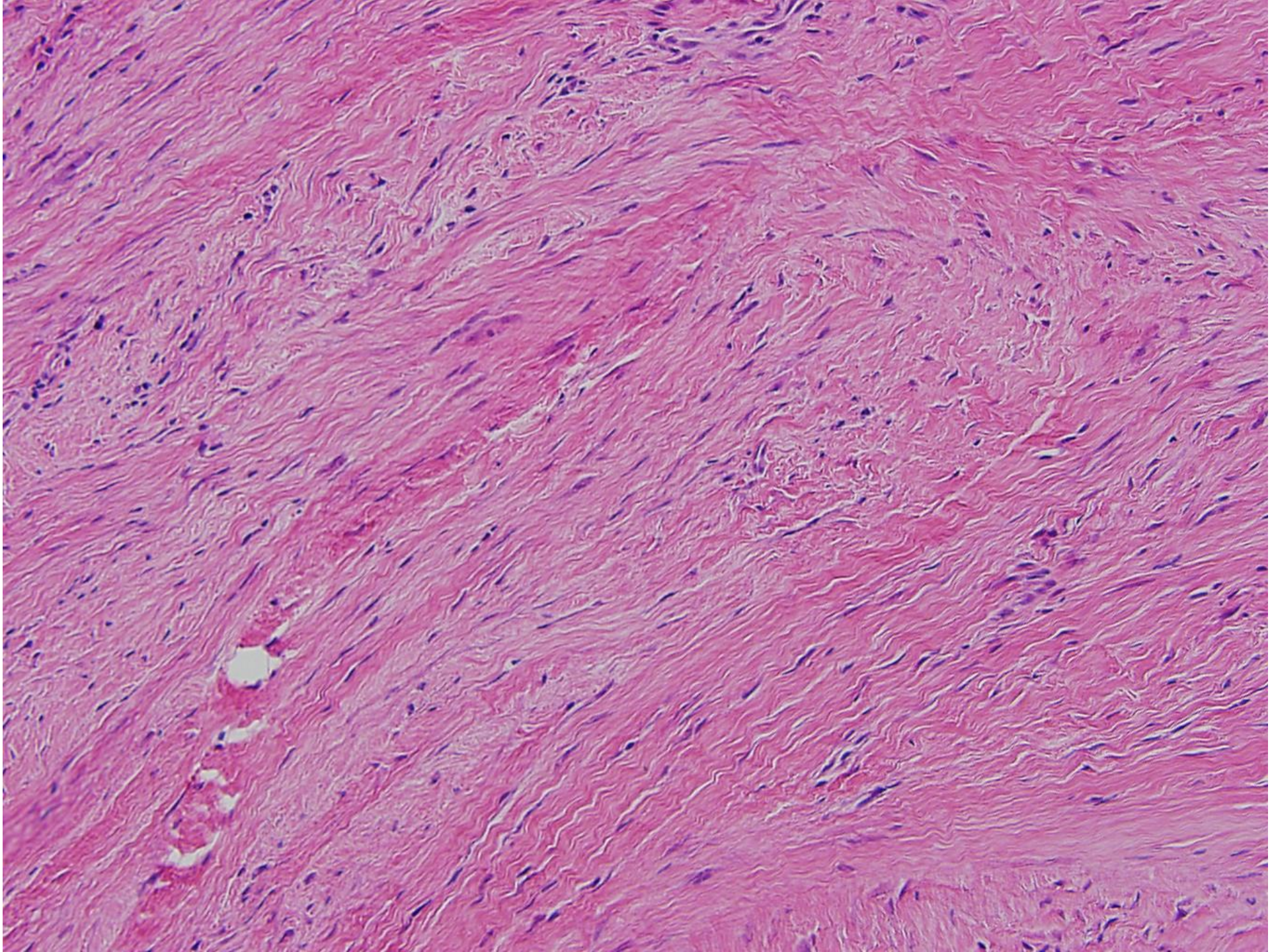
Location matters!

Clinical Case

- 62-year-old man presenting with left intra-abdominal soft tissue mass.
- Patient underwent surgery with intra-operative frozen section diagnosis.

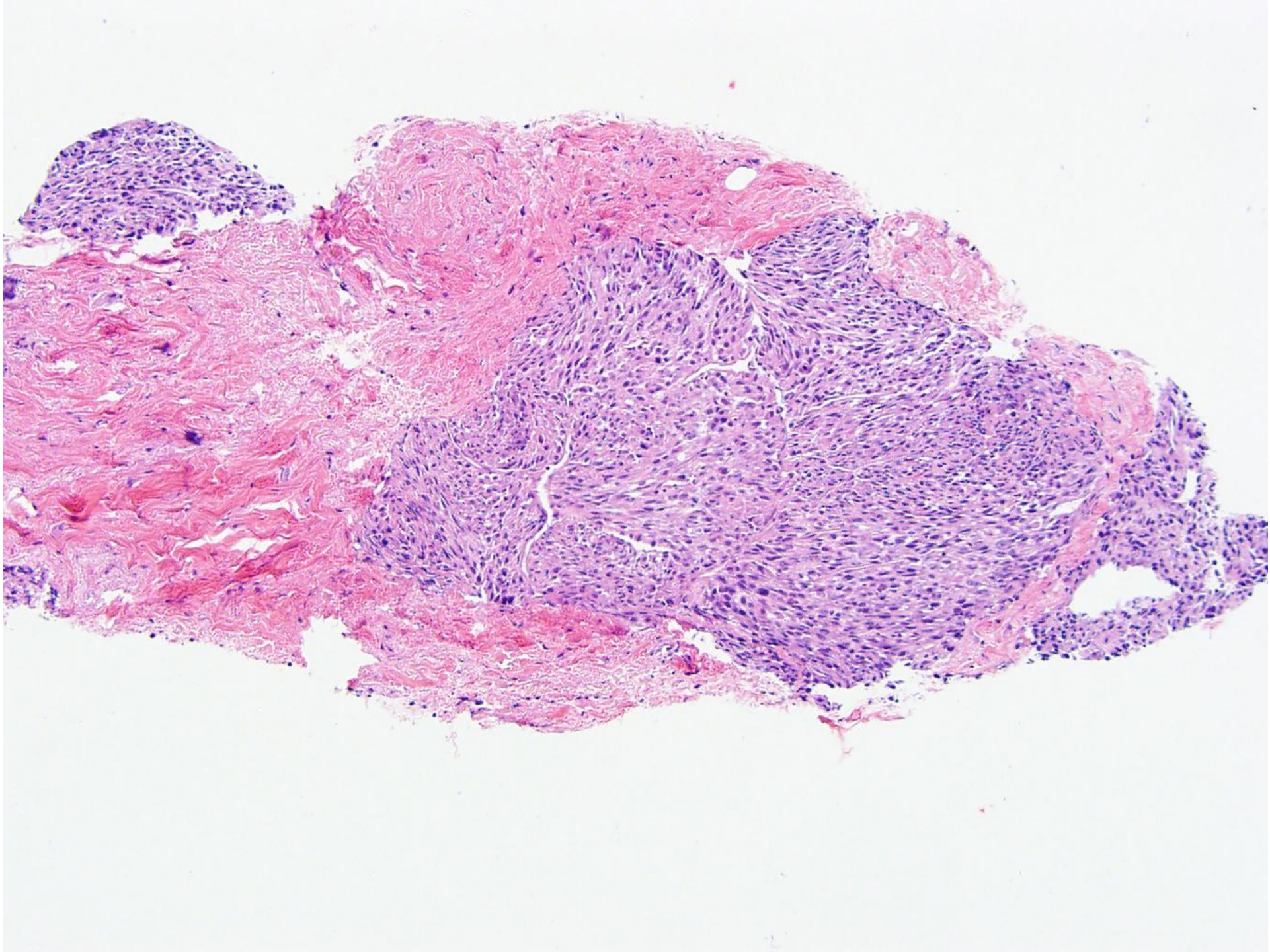


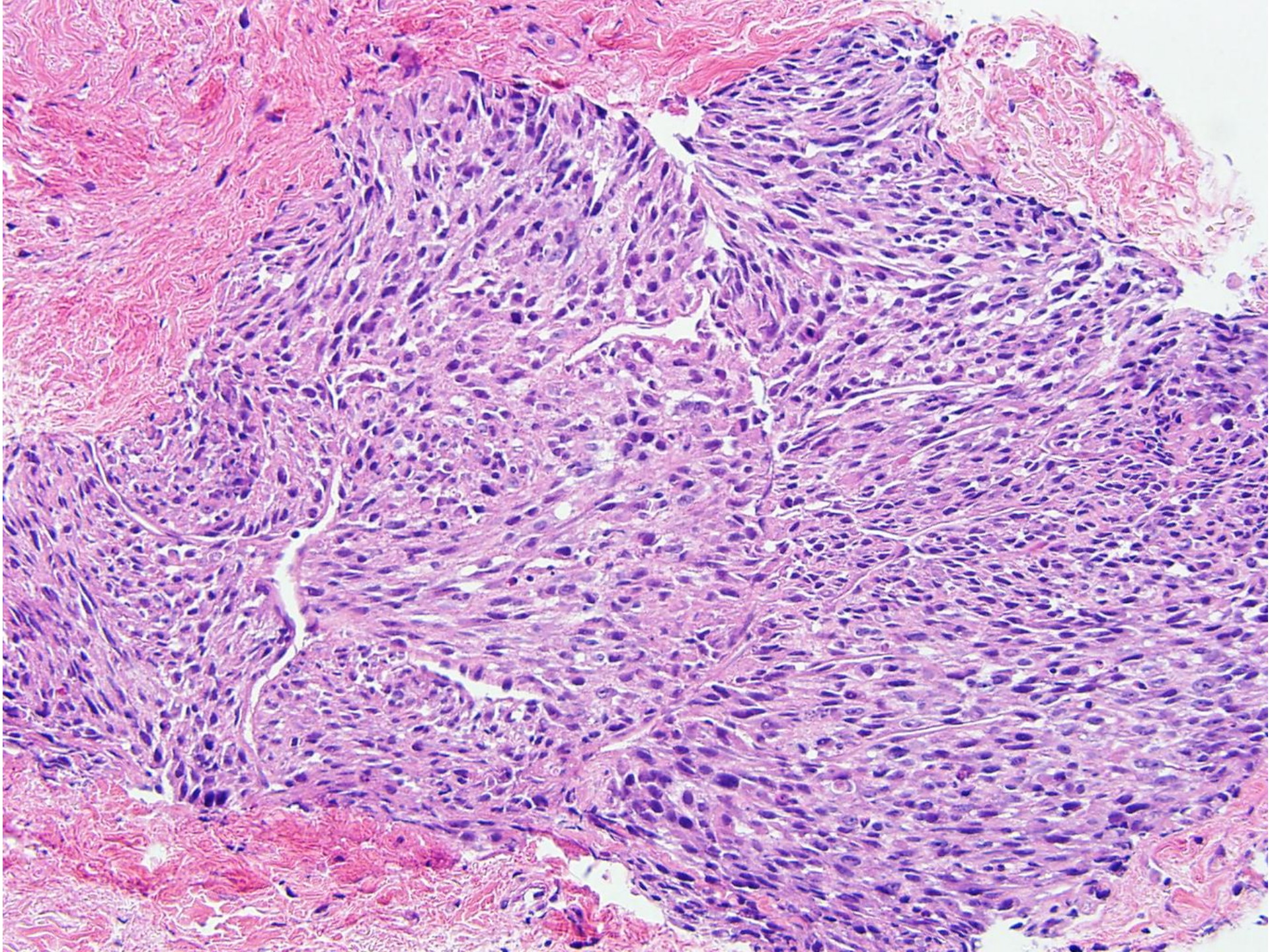


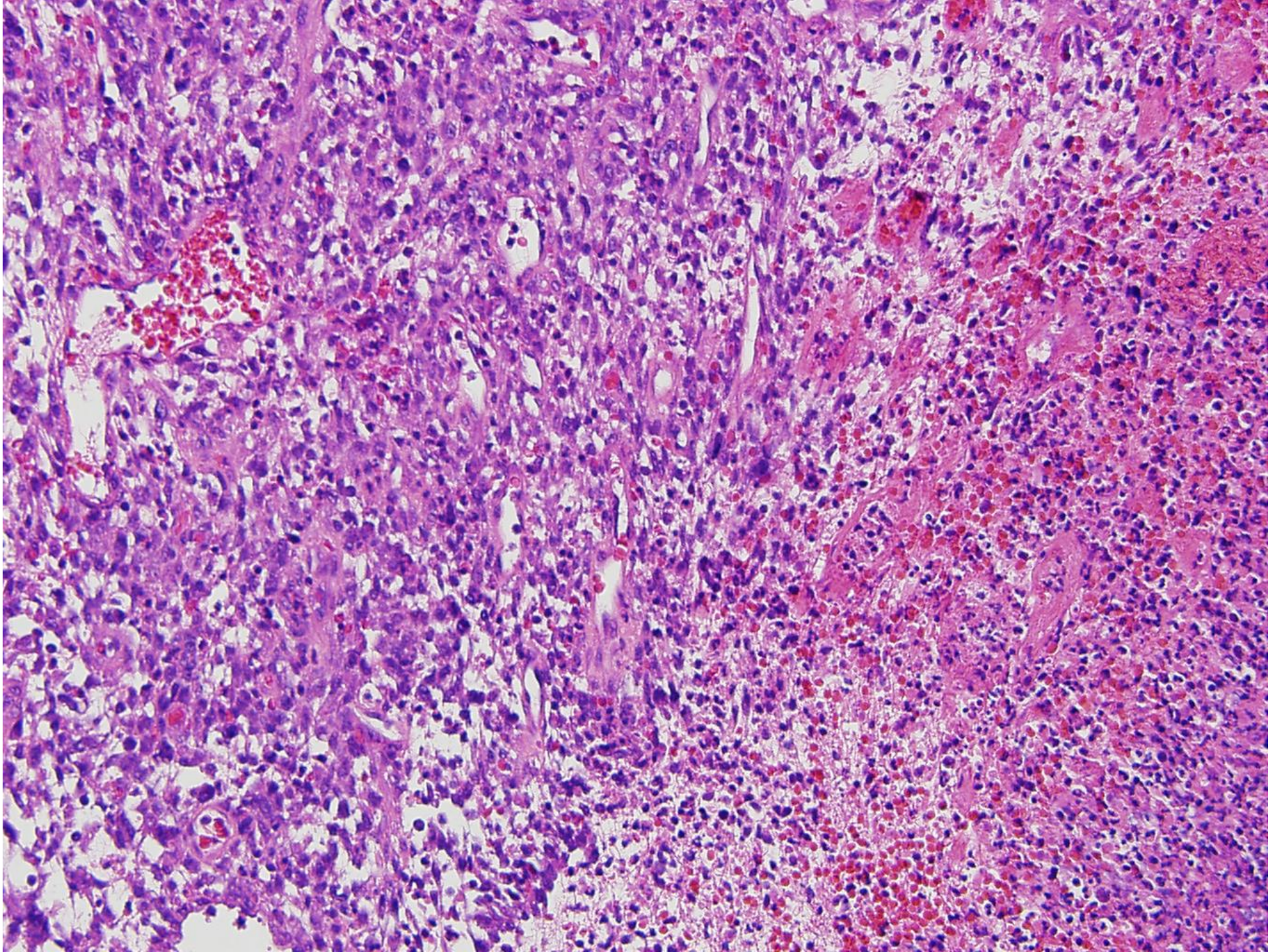


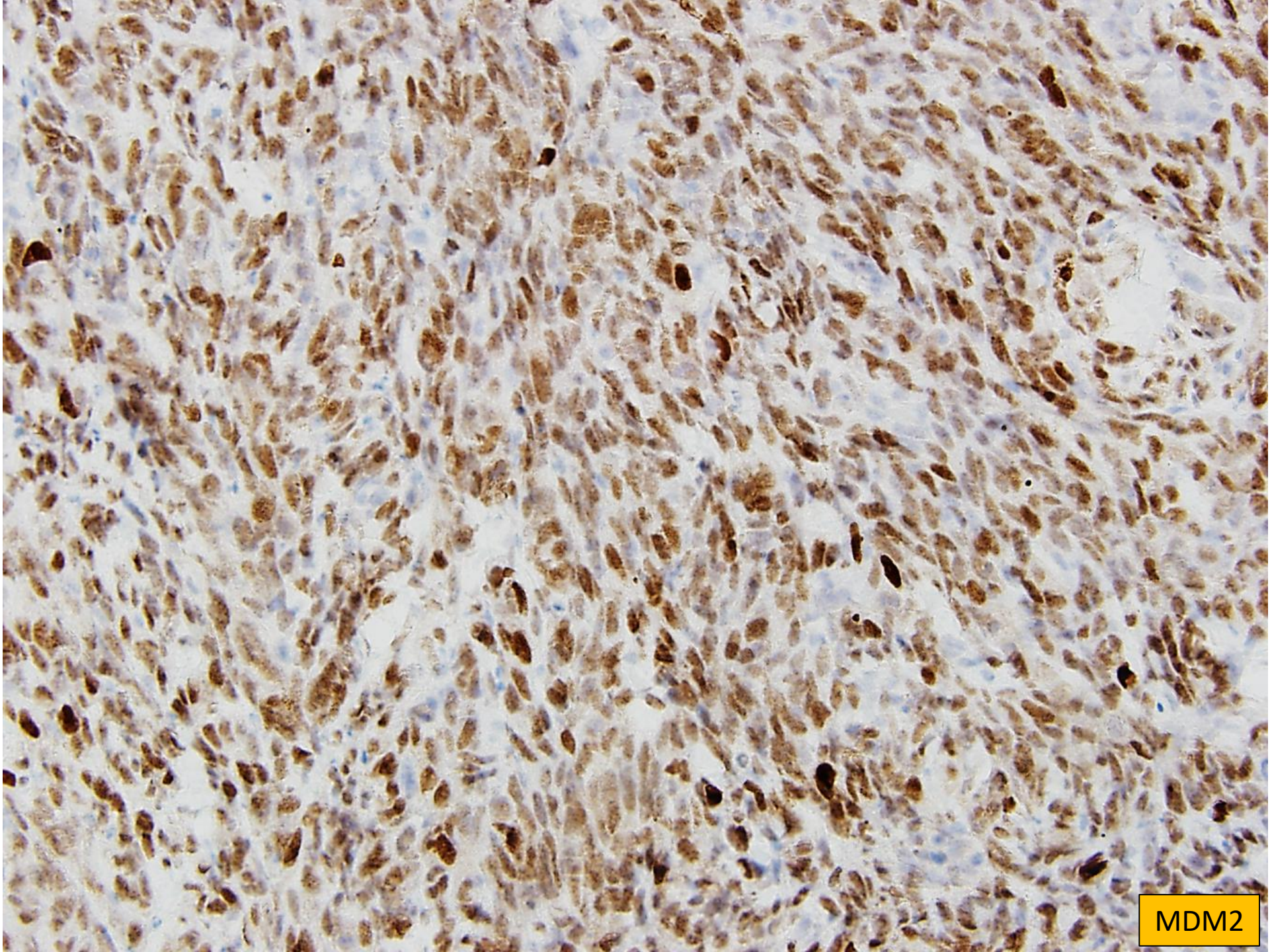
- The case was interpreted as *desmoid-type fibromatosis*, extending to resection margins.
- No further treatment was given, and the patient was scheduled for periodic follow-ups.

- Six years later, patient presented with left (ipsilateral) pelvic/perineal soft tissue mass, clinically suspicious for recurrent desmoid tumor.
- Perineal mass was biopsied, followed by pelvic mass excision.

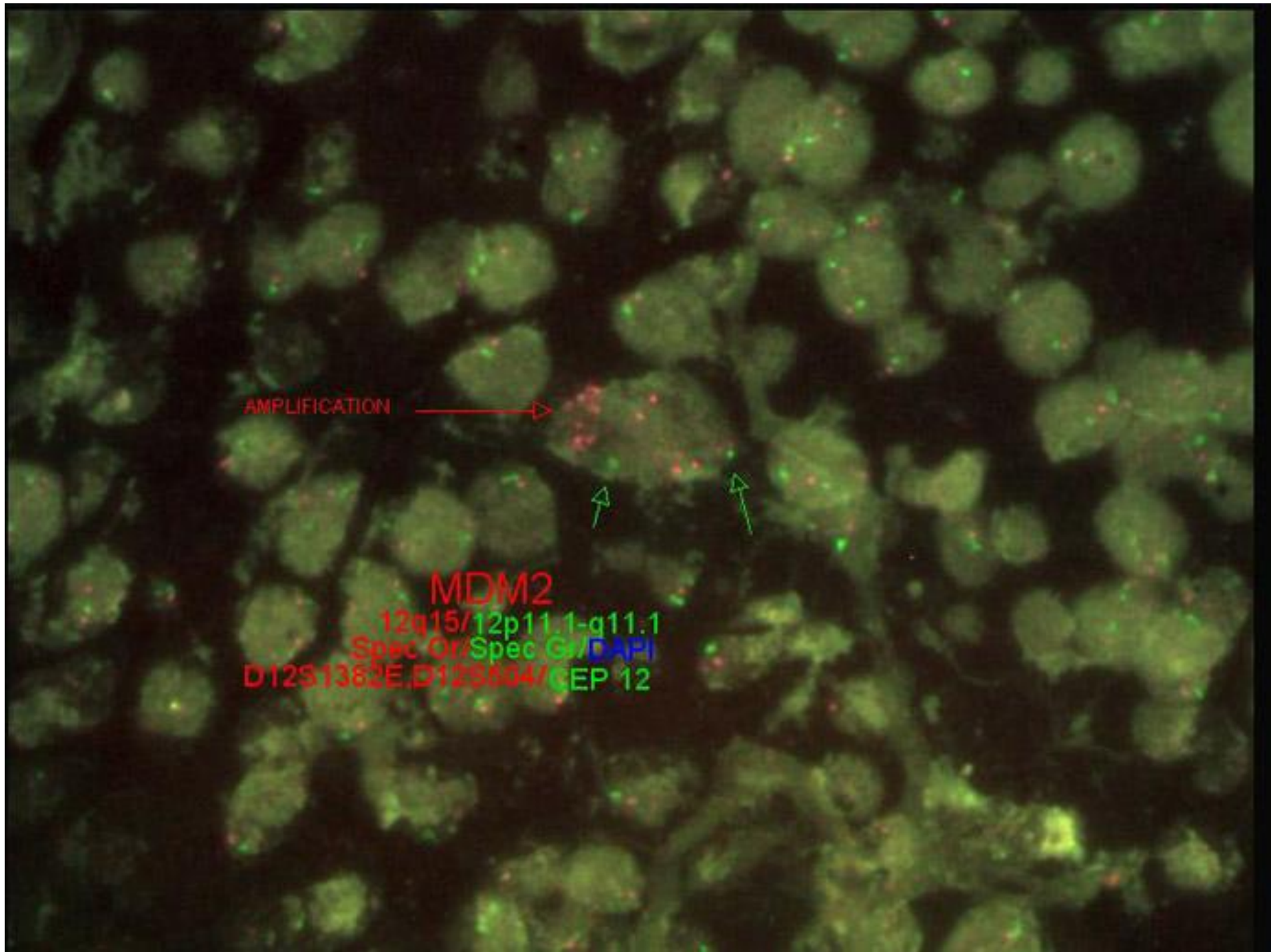








MDM2

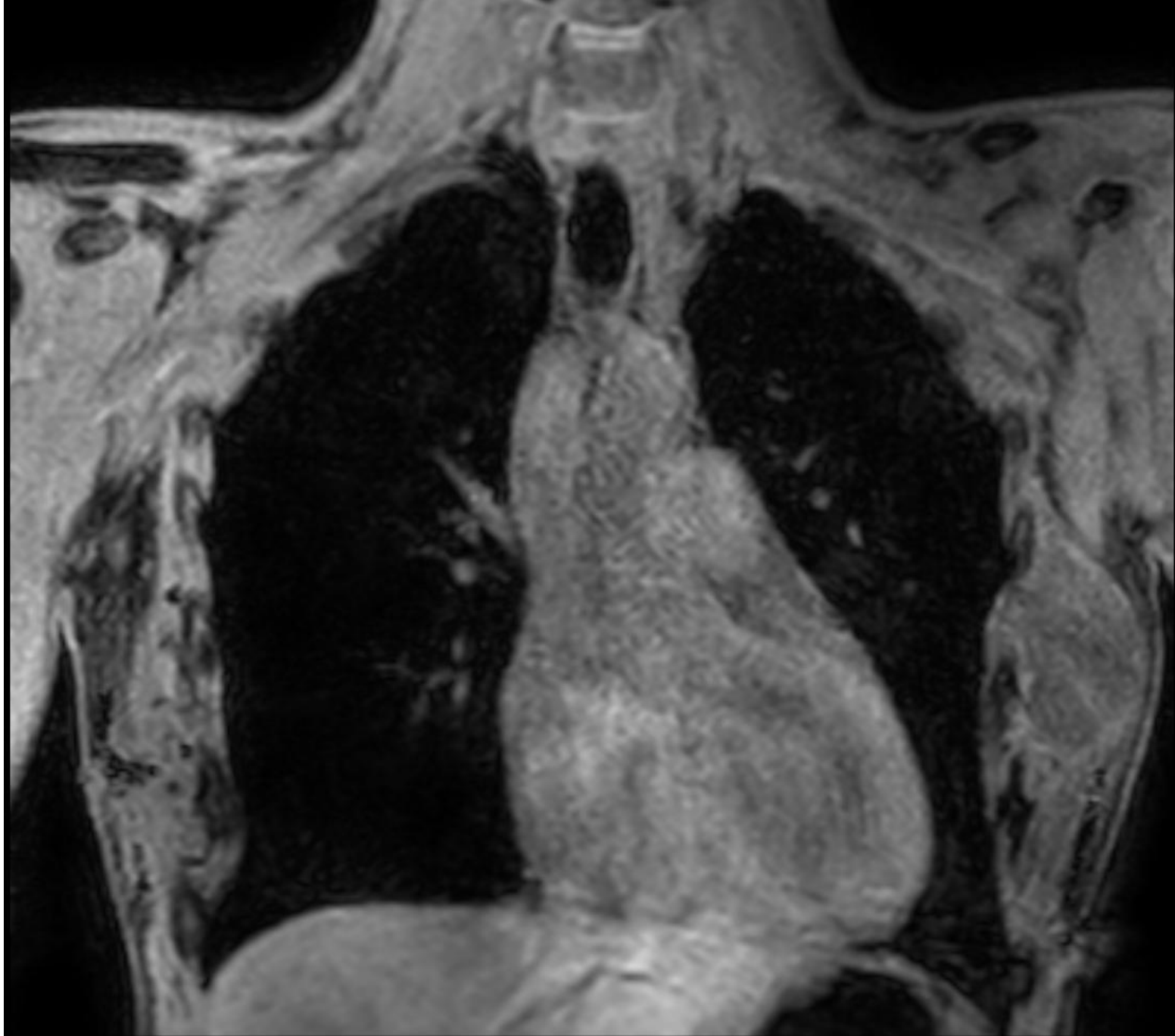


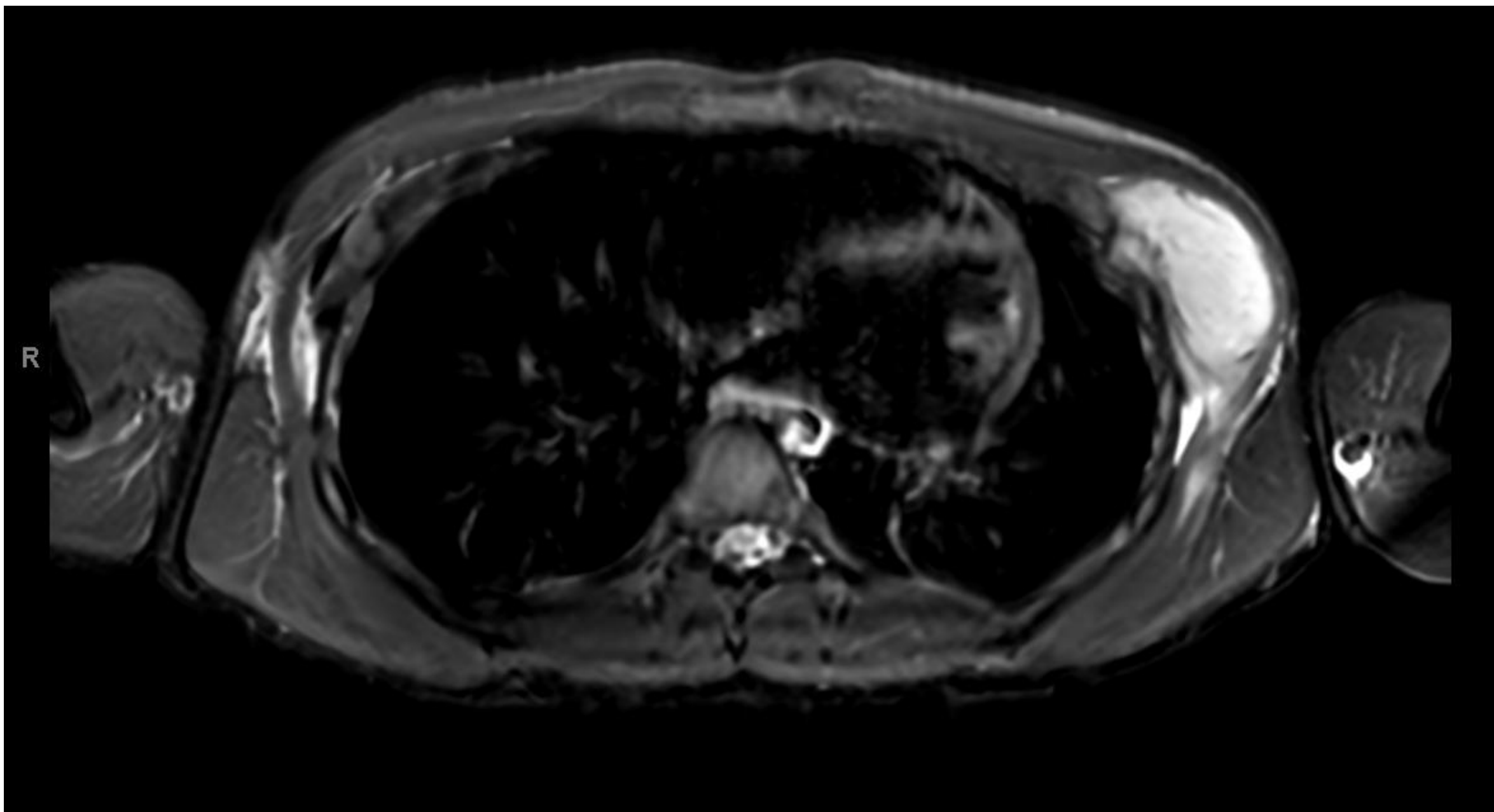
Diagnosis:

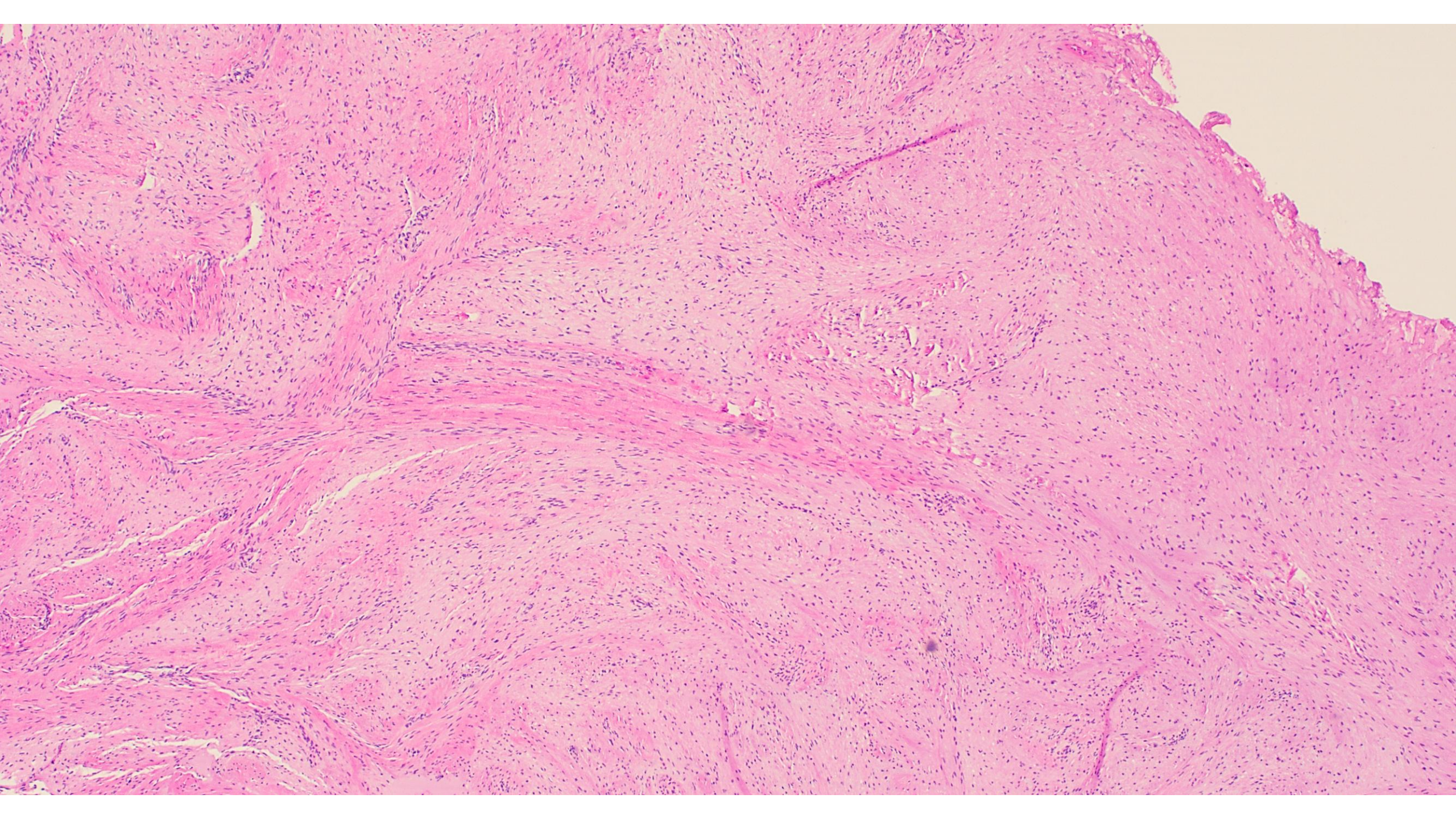
High-grade Dedifferentiated Liposarcoma

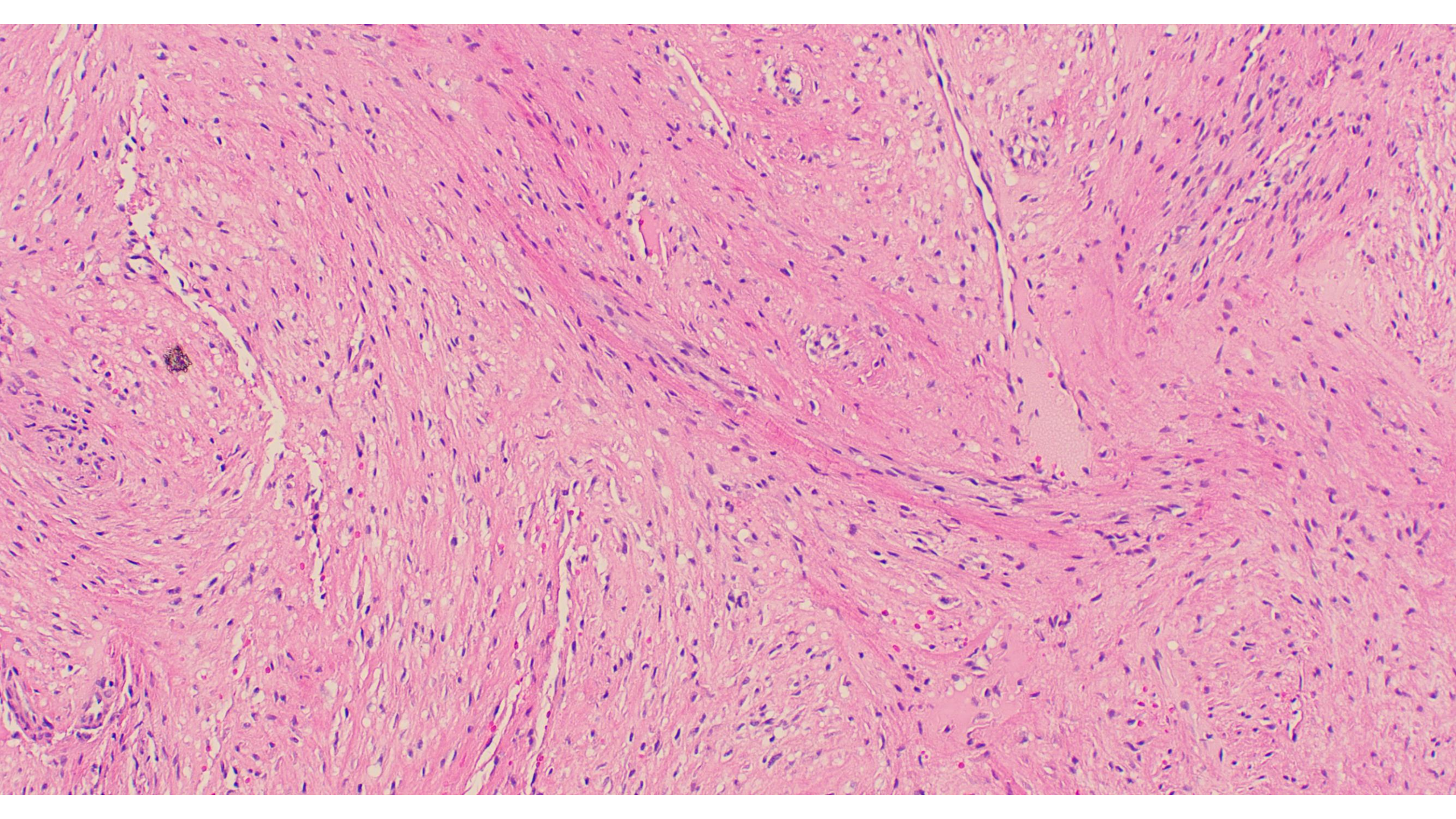
Clinical Case

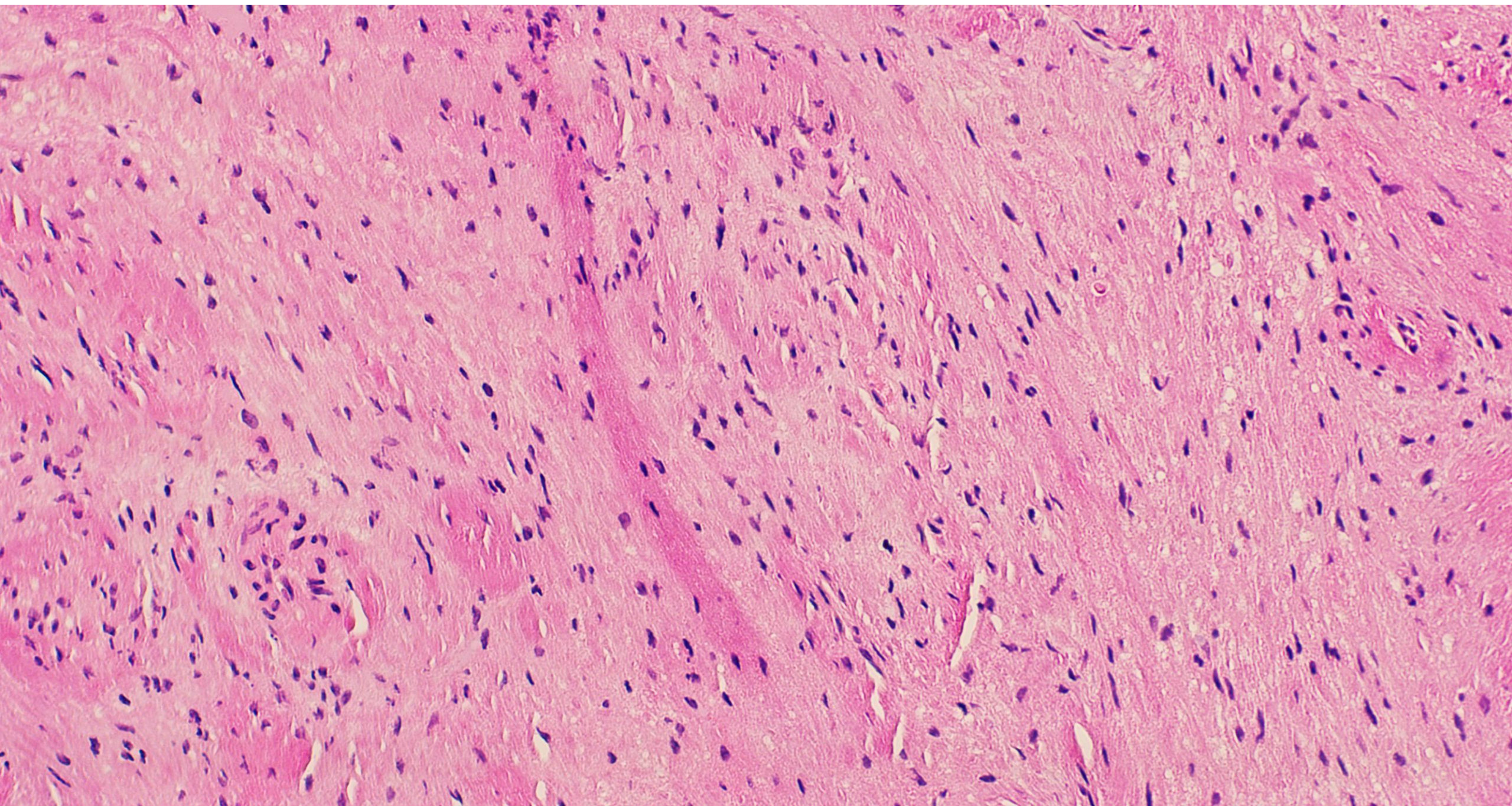
- 17-year-old boy with 9 x 7 cm left chest wall mass adjacent to Nuss bar for pectum excavatum.

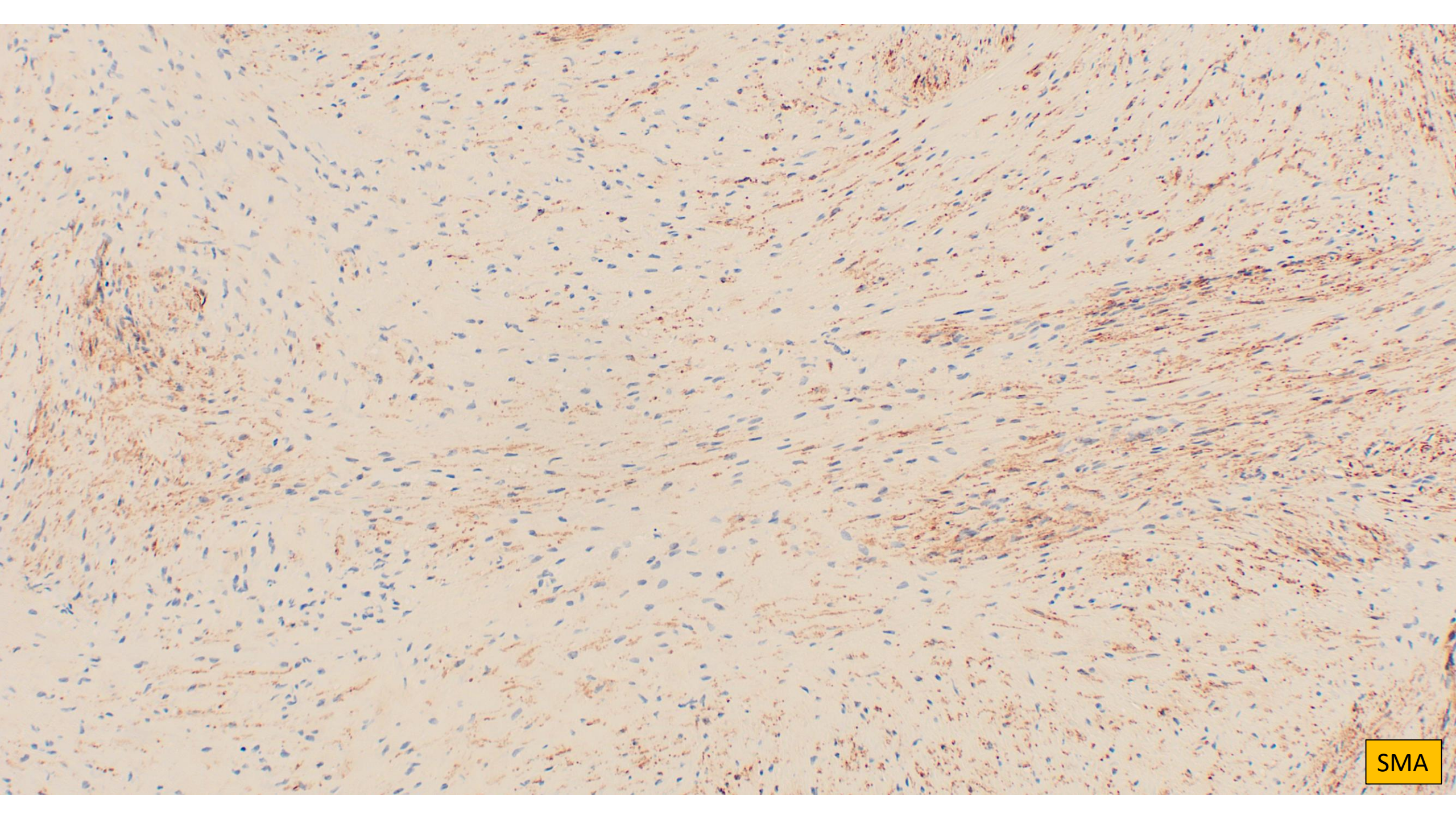




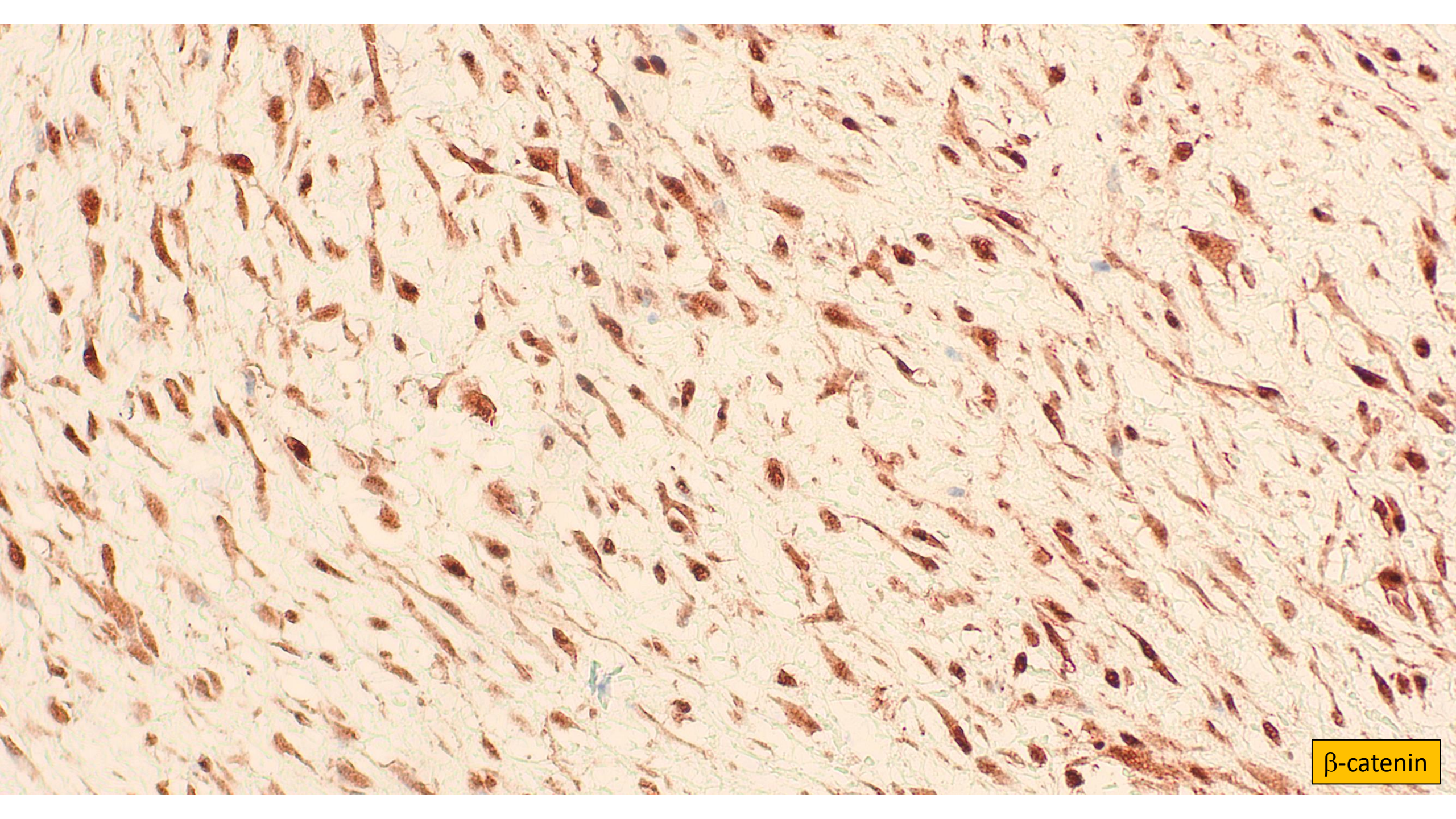








SMA



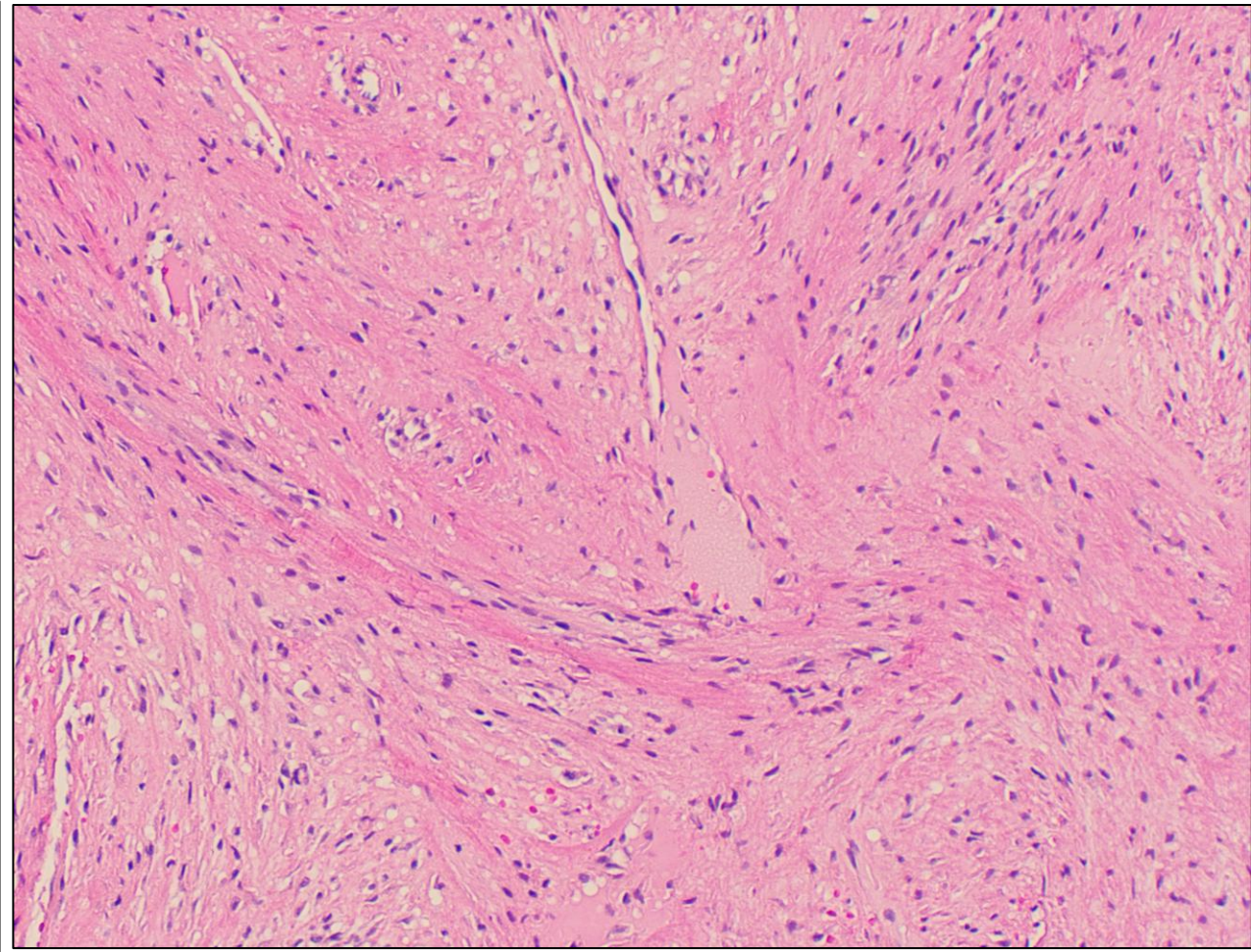
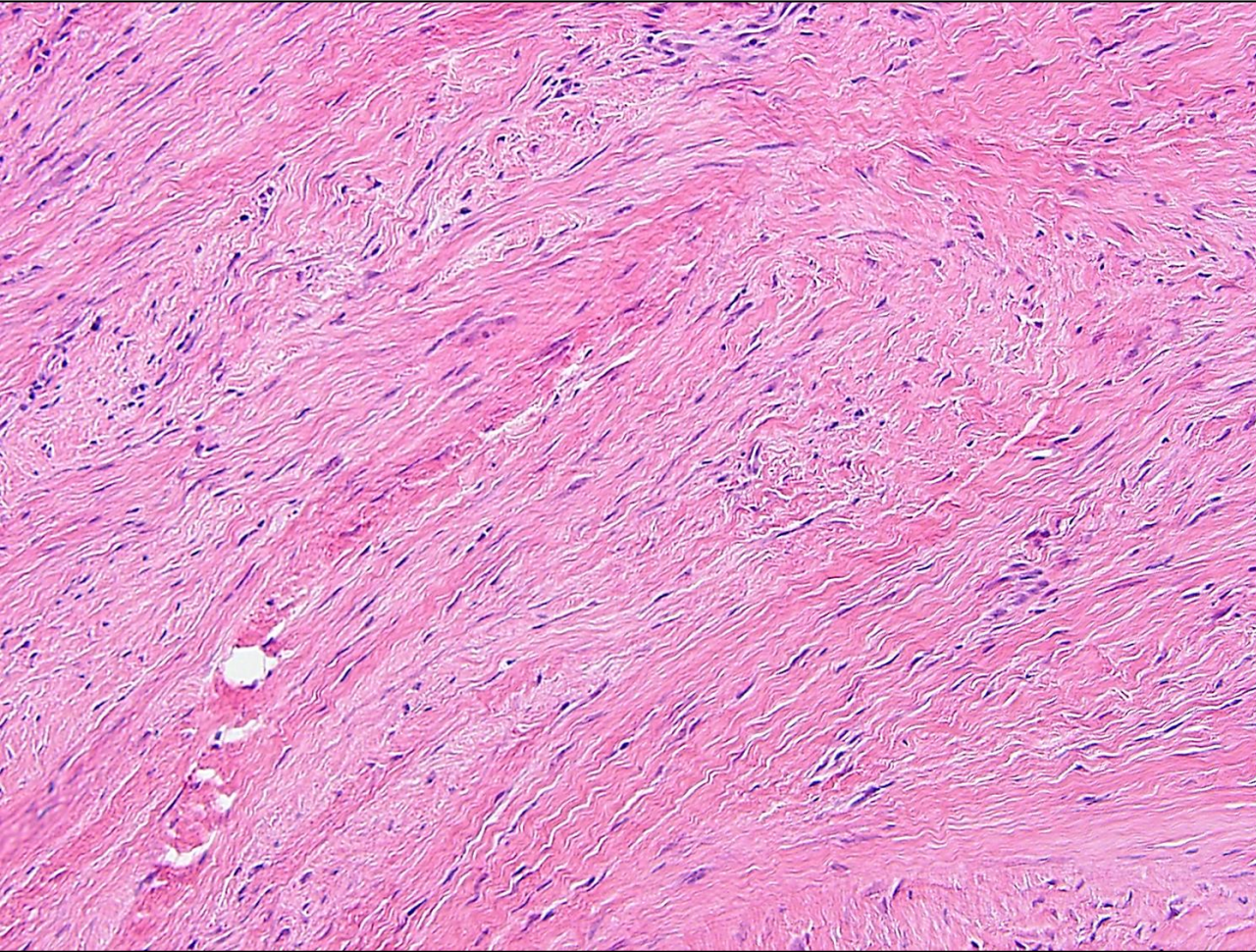
β-catenin

Genes Tested with Pathogenic or Likely Pathogenic Alterations

Gene	Method	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency %
CTNNB1	Seq	DNA-Tumor	Pathogenic Variant	p.D32Y	3	c.94G>T	31

Diagnosis:

Desmoid-type Fibromatosis

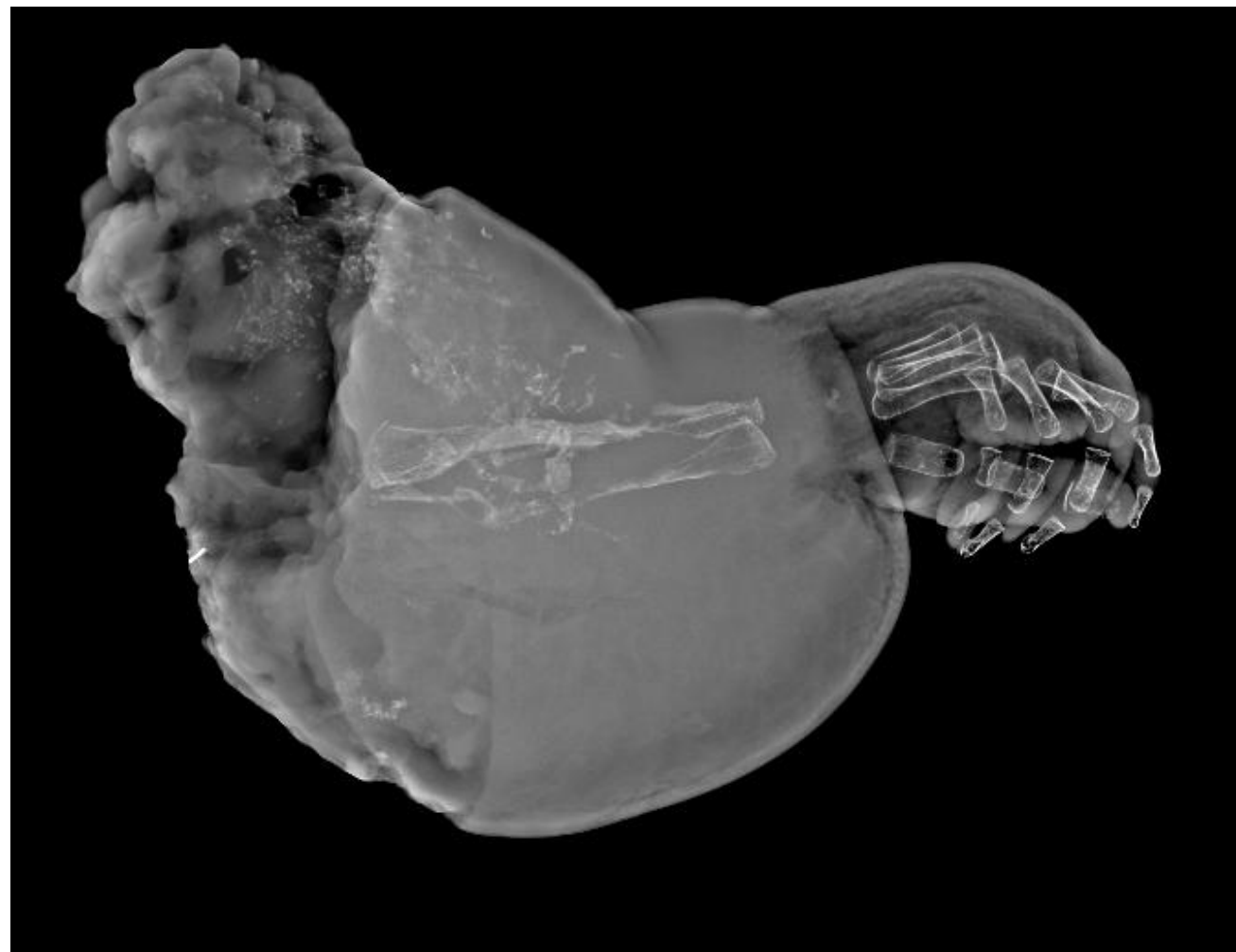
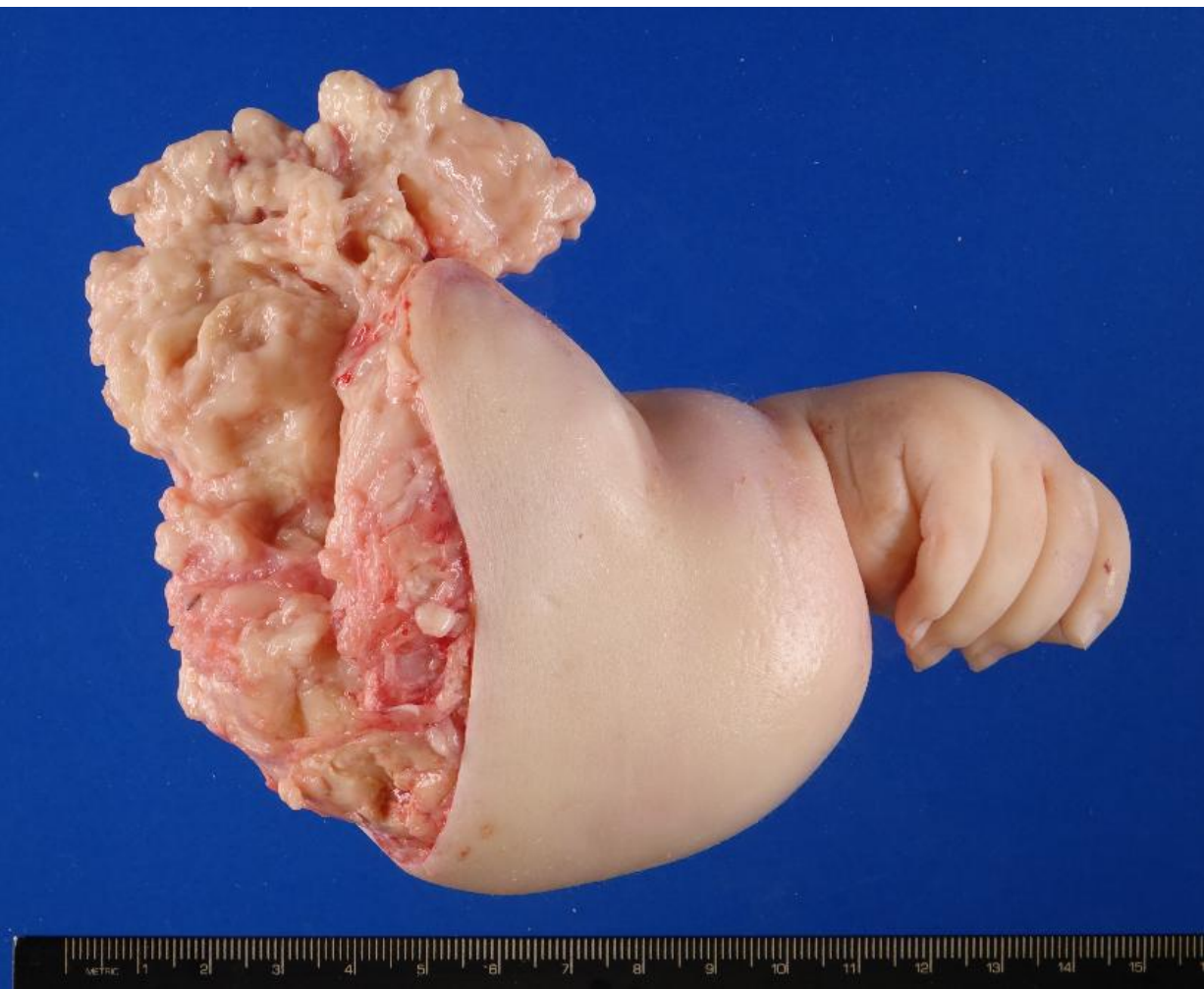


Age matters!

Clinical Case

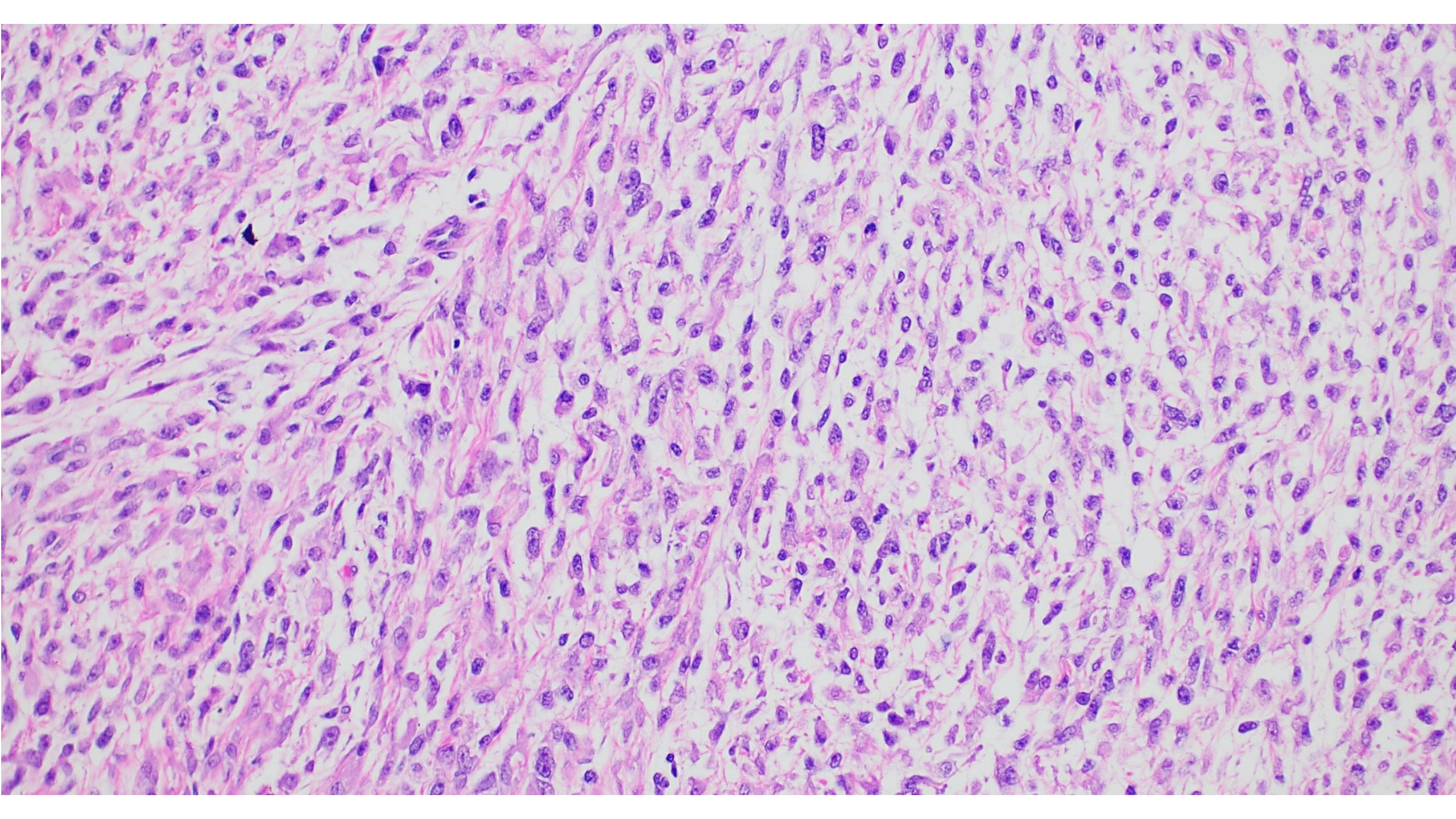
- 2-month-old boy presents with a large congenital mass involving his right arm since birth.
- The mass was initially biopsied yielding nonspecific results.
- Due to massive involvement of upper extremity an amputation was performed.

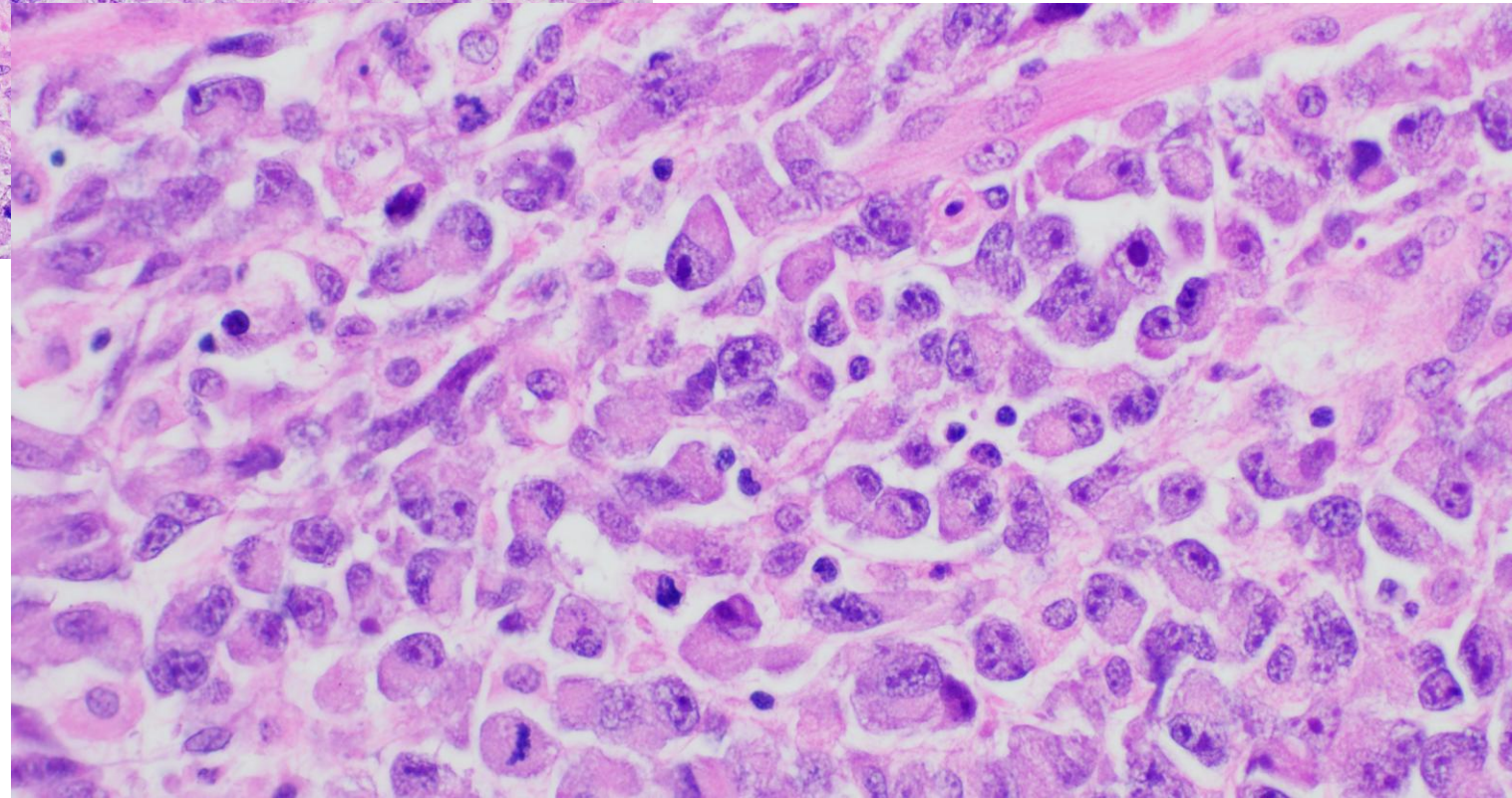
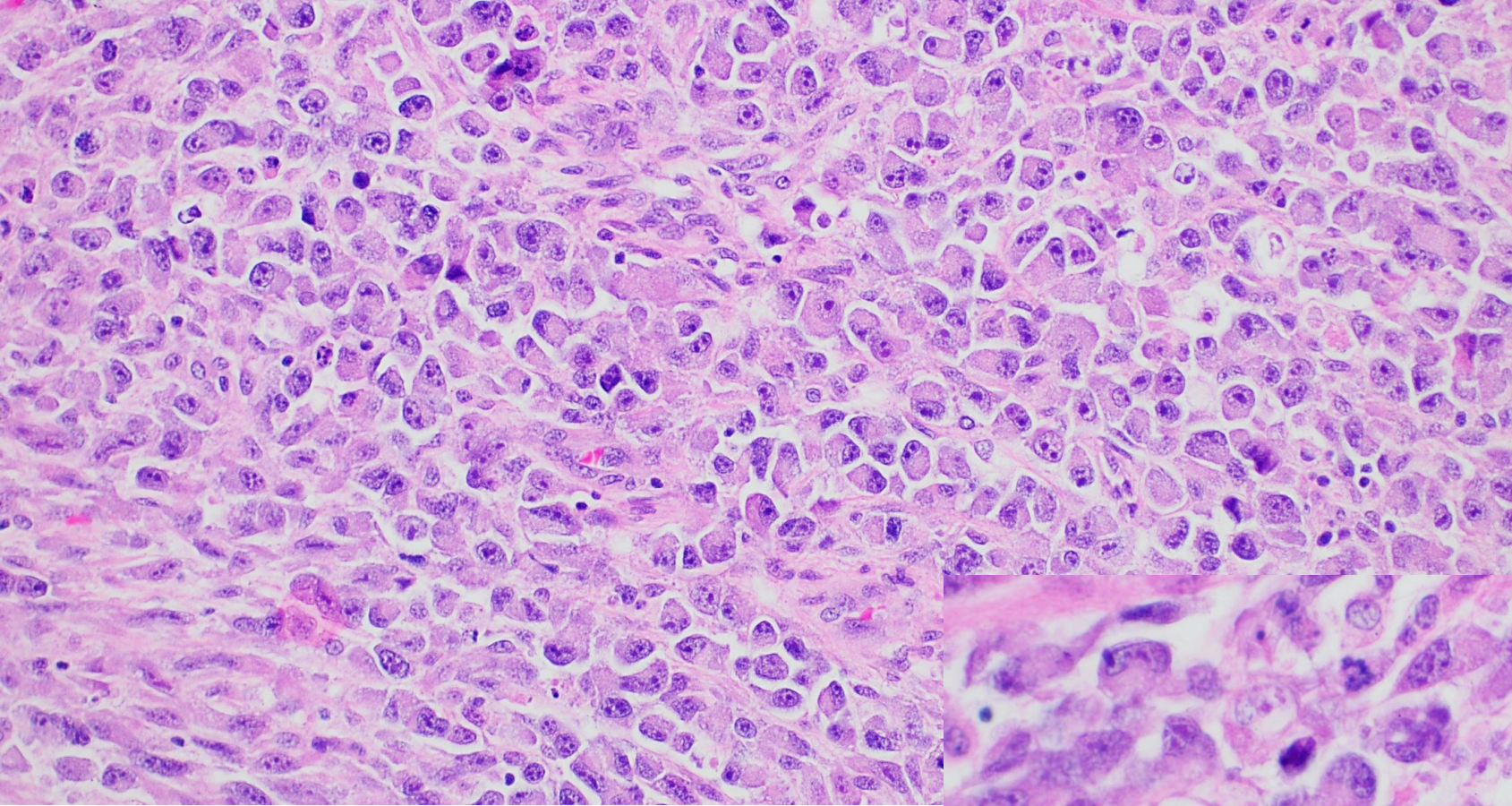


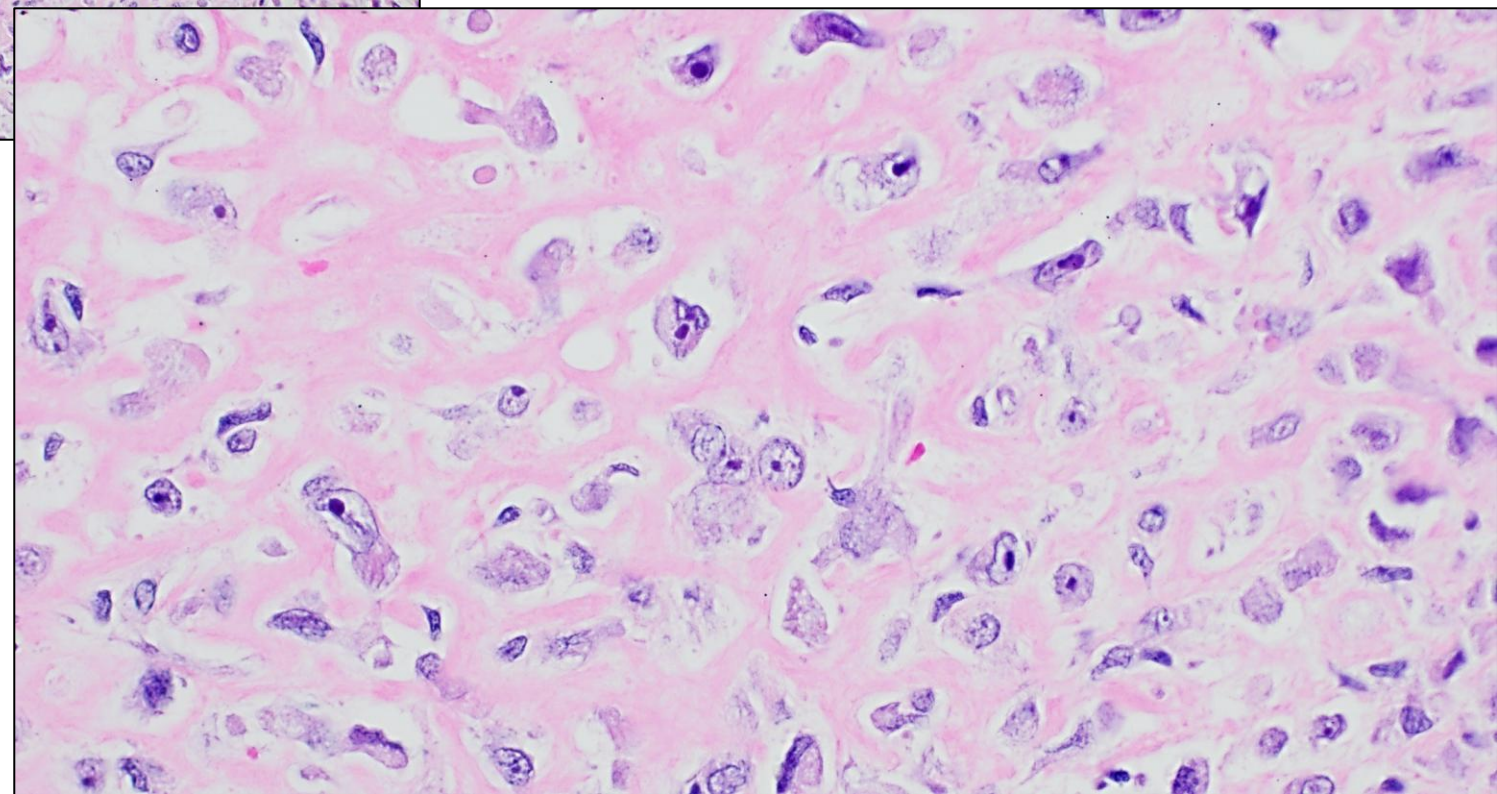
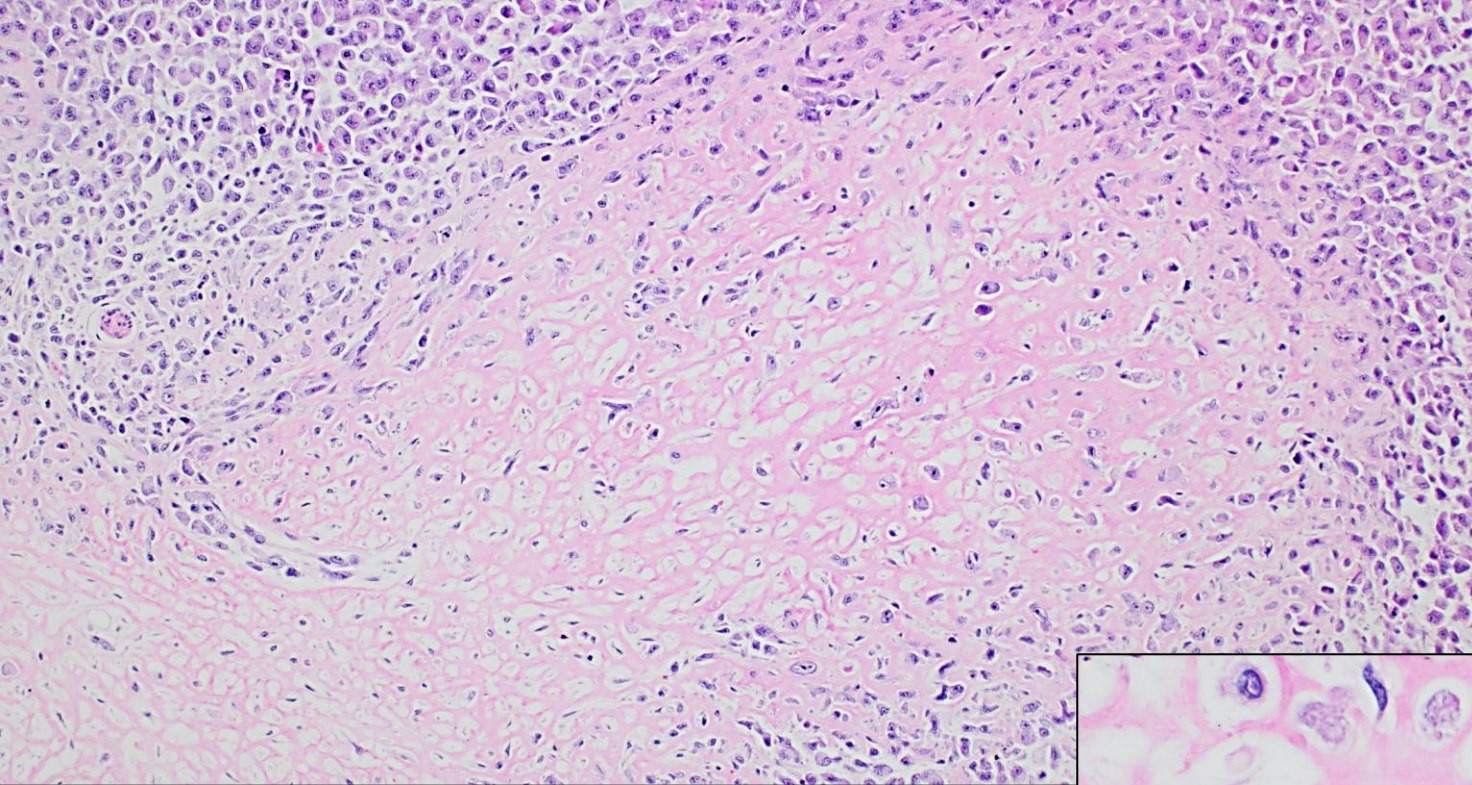


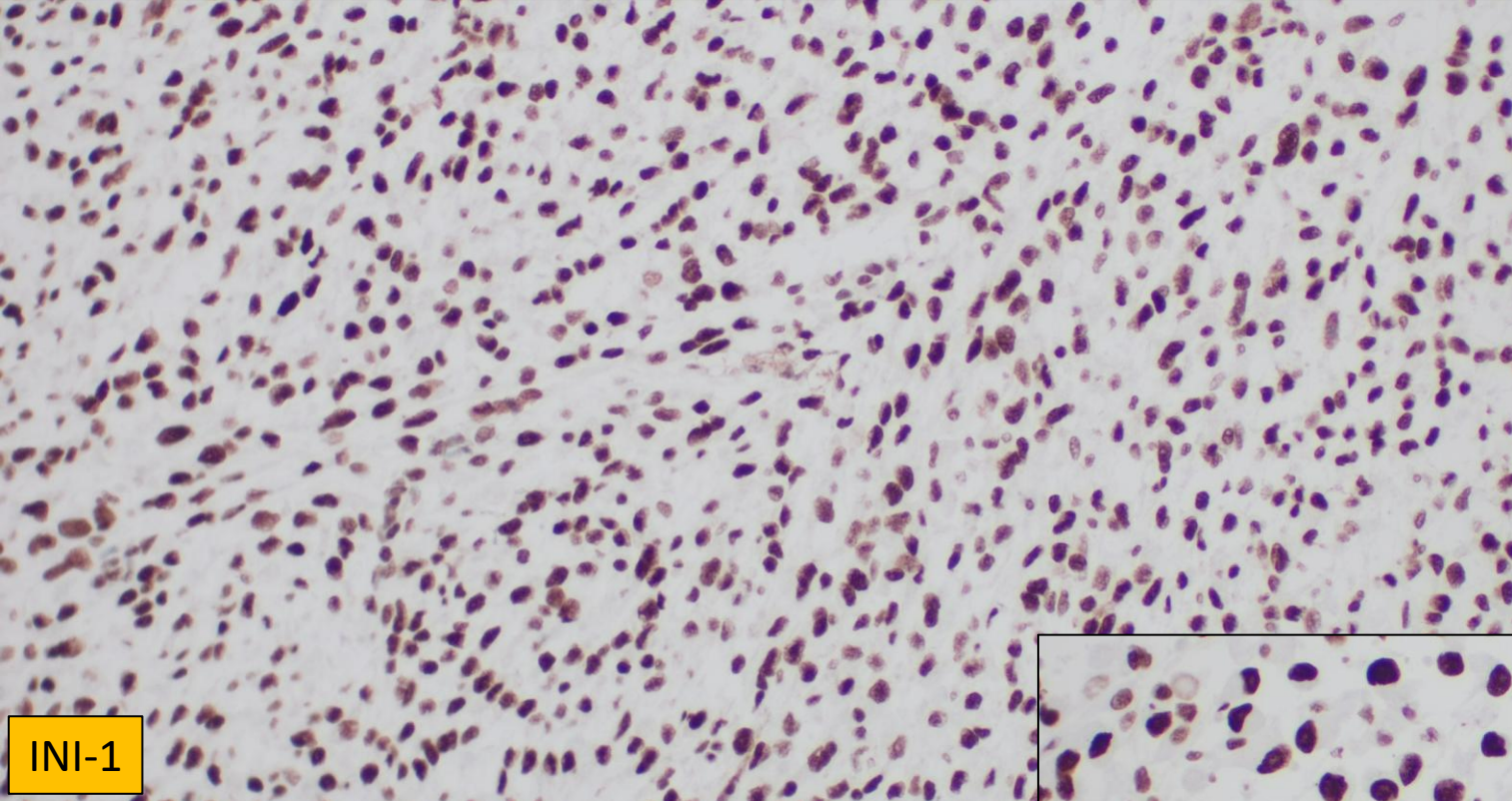




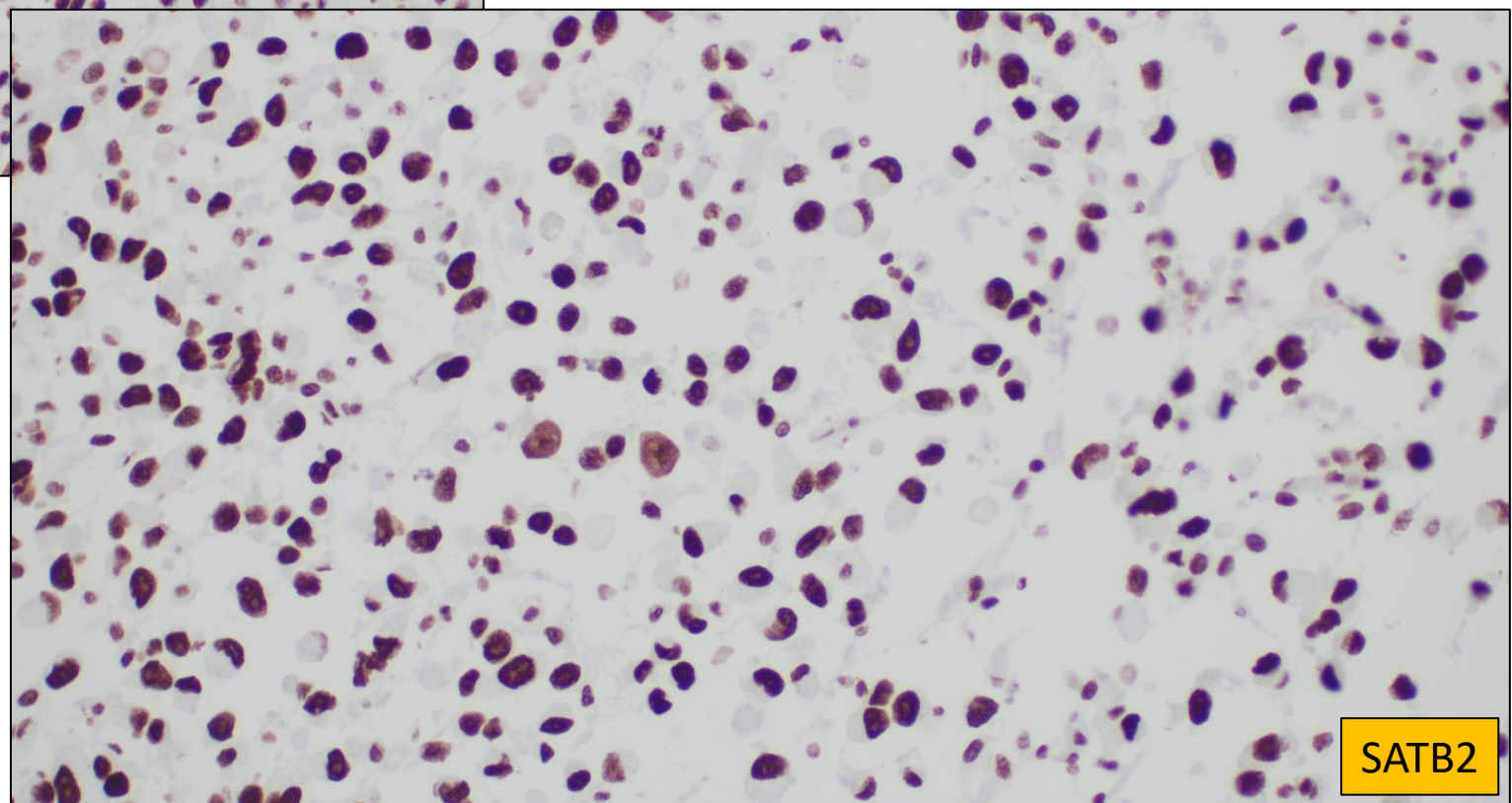








INI-1



SATB2

Final Pathologic Diagnosis

A. Right arm, excision:

HIGH GRADE CONGENITAL SARCOMA WITH OSTEOSARCOMATOUS DIFFERENTIATION (SEE COMMENT).

PROXIMAL SKIN AND SOFT TISSUE MARGINS INVOLVED BY TUMOR.

B. Right humerus, excision:

POSITIVE FOR TUMOR, EXTENDING TO MARGIN.

- Subsequently, NGS revealed a c.3727 C>T point mutation (p.R1243W) in exon 27 of the *SMARCA4* gene.
- We rendered an integrated diagnosis of *Extrarenal rhabdoid tumor*.

Molecular correlation matters!



Gross Examination: The PA Perspective

- Orientation and margins
- Measurements and relationship to fascia/bone/other structures (critical for staging!)
- Necrosis, hemorrhage, calcification
- Radiographs (when applicable)
- Photographs, including before and after inking specimen
 - Gross relationship of tumor to inked margins
 - Mapping of sections (important in most specimens; crucial in osteosarcoma and Ewing sarcoma → full cross section)
- Strategic tissue sampling
 - Sample generously from viable, non-necrotic tumor for fusion testing
 - When dedifferentiation is suspected, target the transition zone specifically

Take-Home Messages

- Clinical context matters.
- Radiology is part of pathology.
- Gross examination drives diagnosis.
- Sample generously and thoughtfully.
- Preserve tissue for molecular testing.
- Molecular findings complement morphology.
- Pathologists' Assistants are essential members of the diagnostic team.
- *Your work at the gross bench directly shapes diagnostic accuracy downstream.*

Thank you!



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