Soft Tissue Pathology

Tips, Tricks, & Pearls

Jerad Gardner, MD

Dermatopathologist &

Section Head of Bone/Soft Tissue Pathology

Geisinger Medical Center

Danville, Pennsylvania

- **This ppt is adapted from a course created by myself and Nicole D. Riddle, MD, for the College of American Pathologists annual meeting.**
- **Dr. Riddle is awesome…be sure to follow her on Twitter!**

Nicole D. Riddle, MD
@NRiddleMD Follows you

@JMGardnerMD
@NRiddleMD

Disclosures

- **Revenue sharing: YouTube & KikoXP.com**
- **Paid consultant: Leica, Castle, BMS & KikoXP.com**
- **Stock: GOOG, APPL, Pathpresenter**
- **Publishing royalties: Elsevier, Innovative Science Press**
- **I do not own stock in Facebook, Twitter, or any other social media company**
- **More COI details: http://bit.ly/coi-jmg**

@JMGardnerMD
@NRiddleMD

Sarcomas

…many subtypes (growing list)

…much of the published literature and textbooks focus on diagnosis via immunostains and molecular

…what if these are not easily available to a pathologist?

Can one still diagnose soft tissue tumors without them?

@JMGardnerMD
@NRiddleMD

We must remember the Basics

- Which things matter for patient care/treatment?
  - MOST IMPORTANT
- Clinical info very helpful
- H&E morphology is King! (even when IHC available)
- Know & avoid the pitfalls

@JMGardnerMD
@NRiddleMD

How are sarcomas treated?

Wide local excision with negative margins (ideally)

- High & low grade sarcomas
- Amputation if too advanced to salvage limb
- If distant metastasis at initial diagnosis, surgery sometimes not performed (depends on scenario)

+/- **Radiation** if margins positive or close

+/- **Systemic chemotherapy** if stage IV
(most sarcomas have relatively limited response)

@JMGardnerMD
@NRiddleMD

How are sarcomas treated?

- Many sarcomas are treated similarly regardless of subtype
  - High grade vs low grade is usually important

- Exceptions exist; know the sarcomas that have specific therapy implications

- Establish good rapport with treating physician team
  - Ask them their plan for difficult cases
  - How will your diagnosis impact treatment?
  - I call my sarcoma surgeons several times/week to discuss cases

@JMGardnerMD
@NRiddleMD

Scenarios where sarcoma subtype DOES matter

- Osteosarcoma (often responds to specific chemo regimen) vs chondrosarcoma (does not respond to chemo)
- Angiosarcoma (very aggressive; certain chemo may help)
- Ewing sarcoma & round blue cell tumors of childhood (vs lymphoblastic lymphoma – different chemo needed)
- Pediatric rhabdomyosarcoma (alveolar vs embryonal vs other)

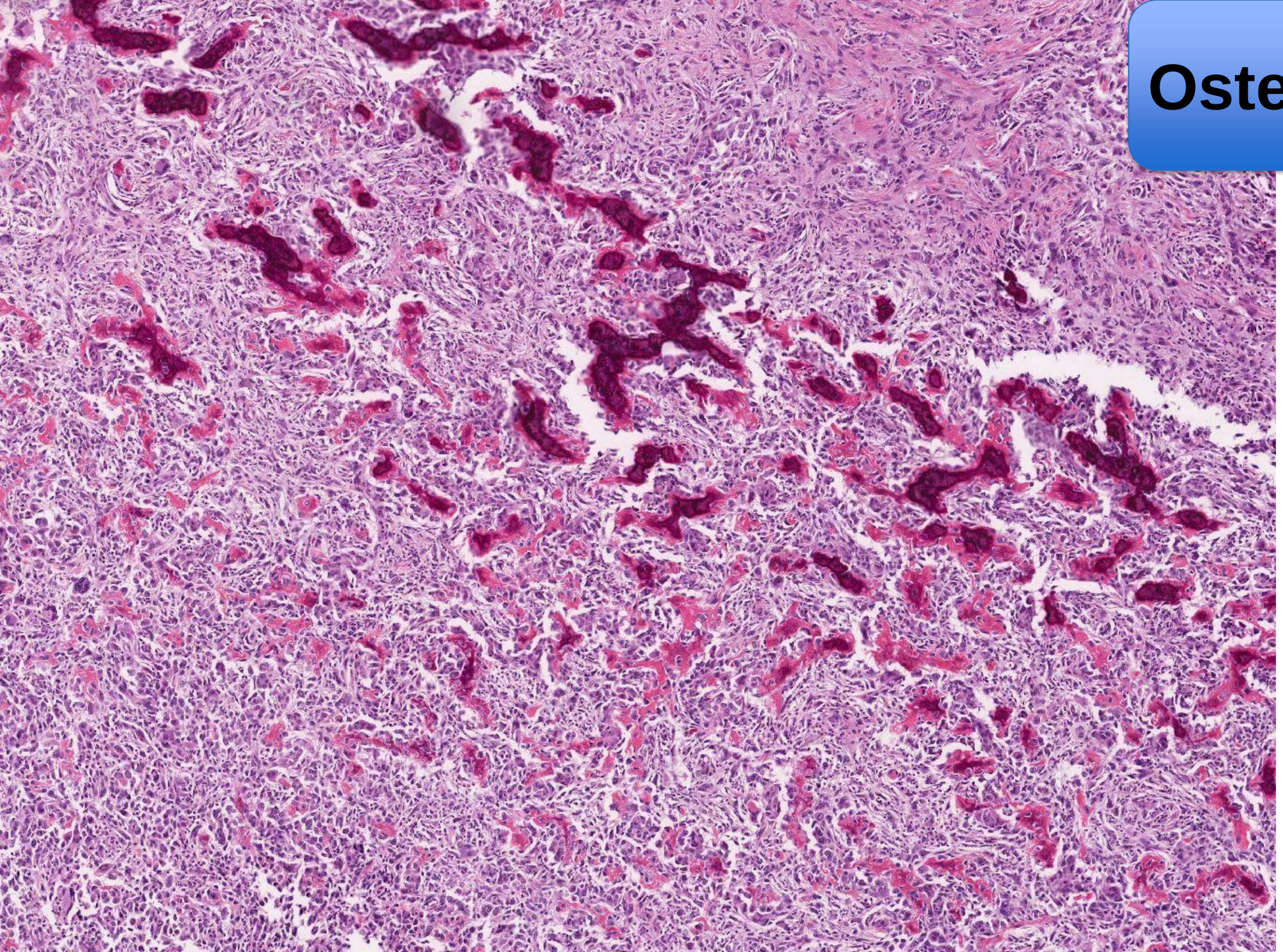
@JMGardnerMD
@NRiddleMD

Scenarios where sarcoma subtype DOES matter

- Synovial sarcoma: chemosensitive
- Myxoid liposarcoma: radiation-sensitive
- Very infiltrative sarcomas: negative margins often hard to achieve, local recurrence common problem
  - Myxofibrosarcoma
  - Myxoinflammatory fibroblastic sarcoma
  - DFSP

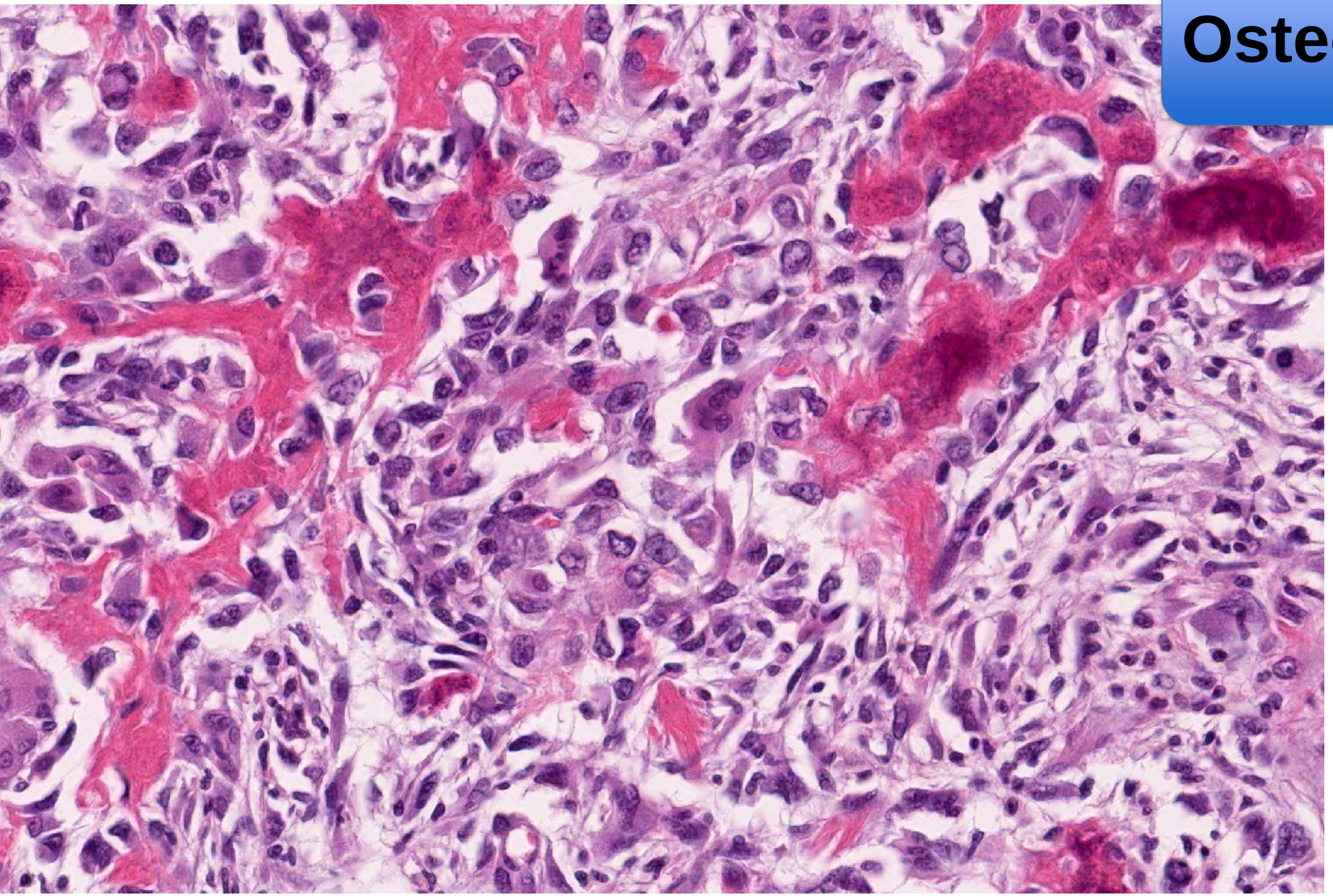
@JMGardnerMD
@NRiddleMD

Osteosarcoma

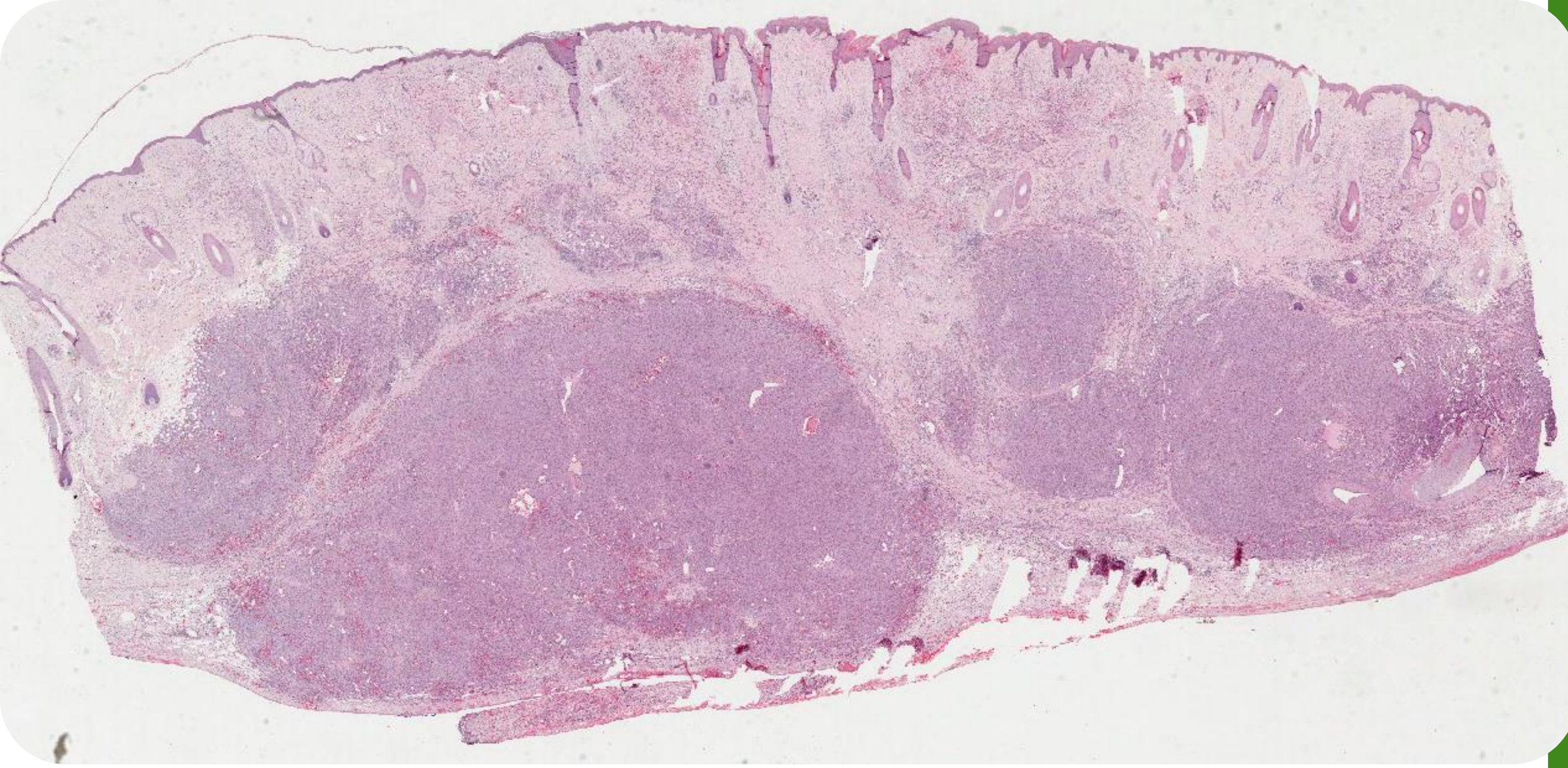


@JMGardnerMD
@NRiddleMD

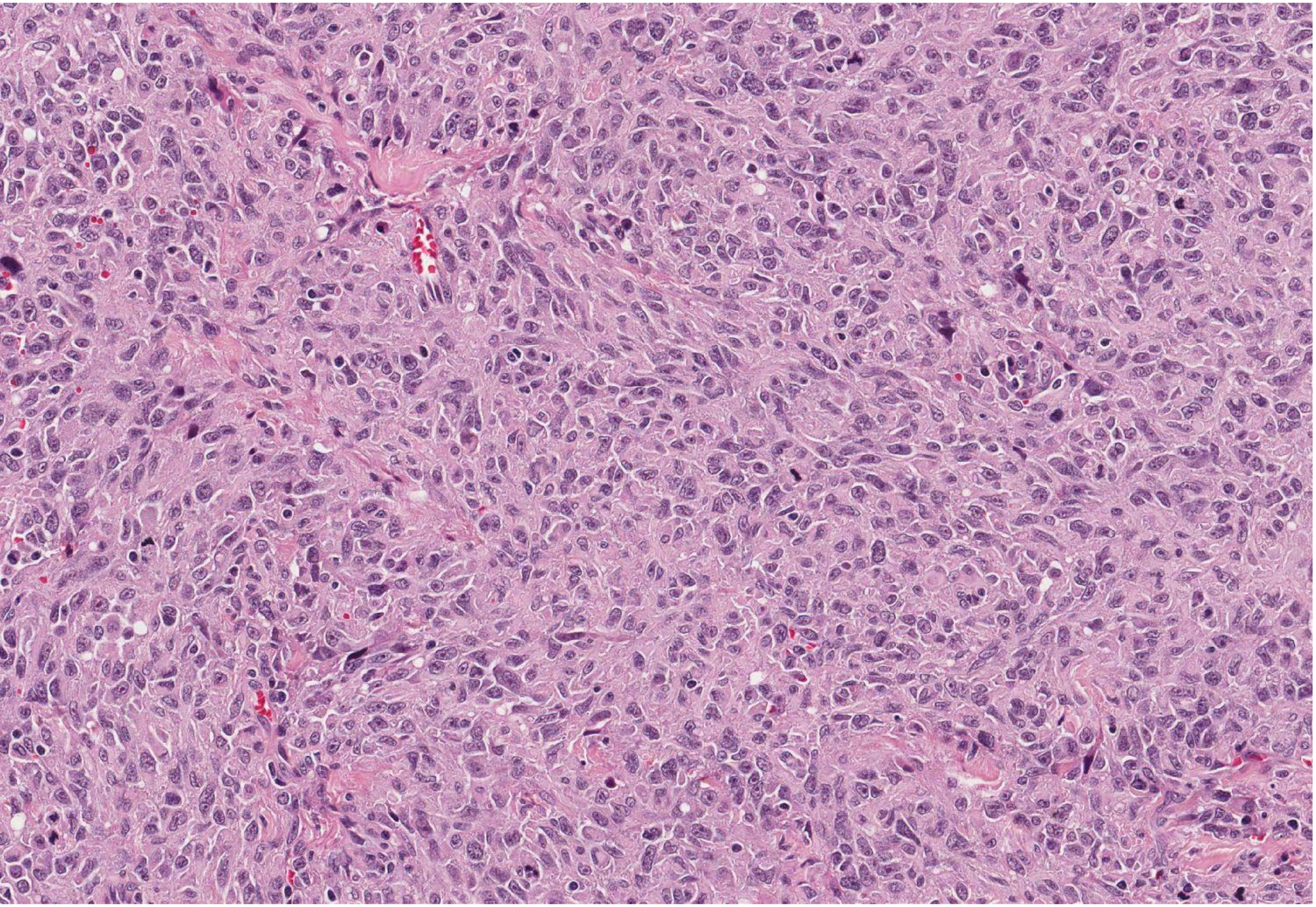
Osteosarcoma



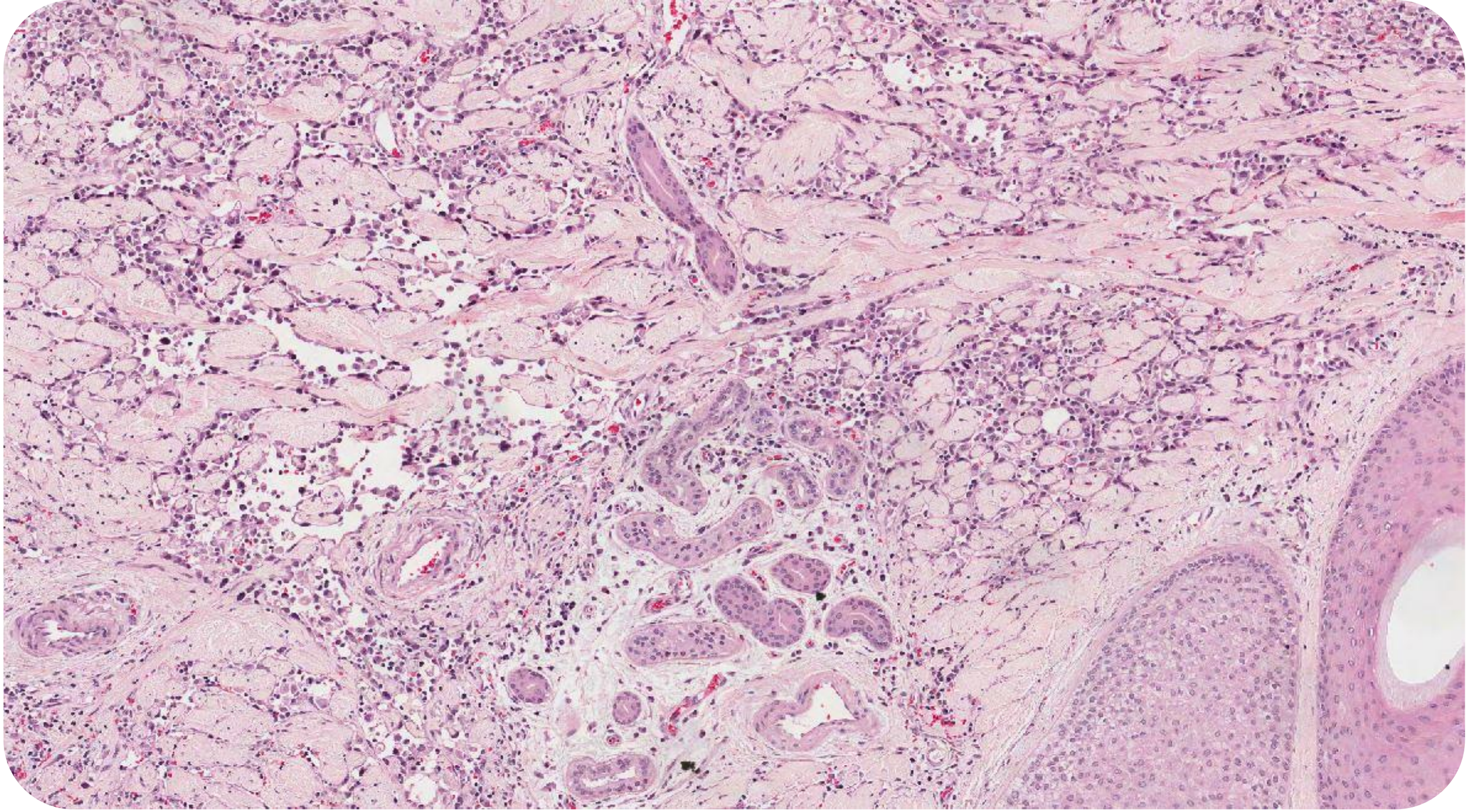
@JMGardnerMD
@NRiddleMD



@JMGardnerMD
@NRiddleMD

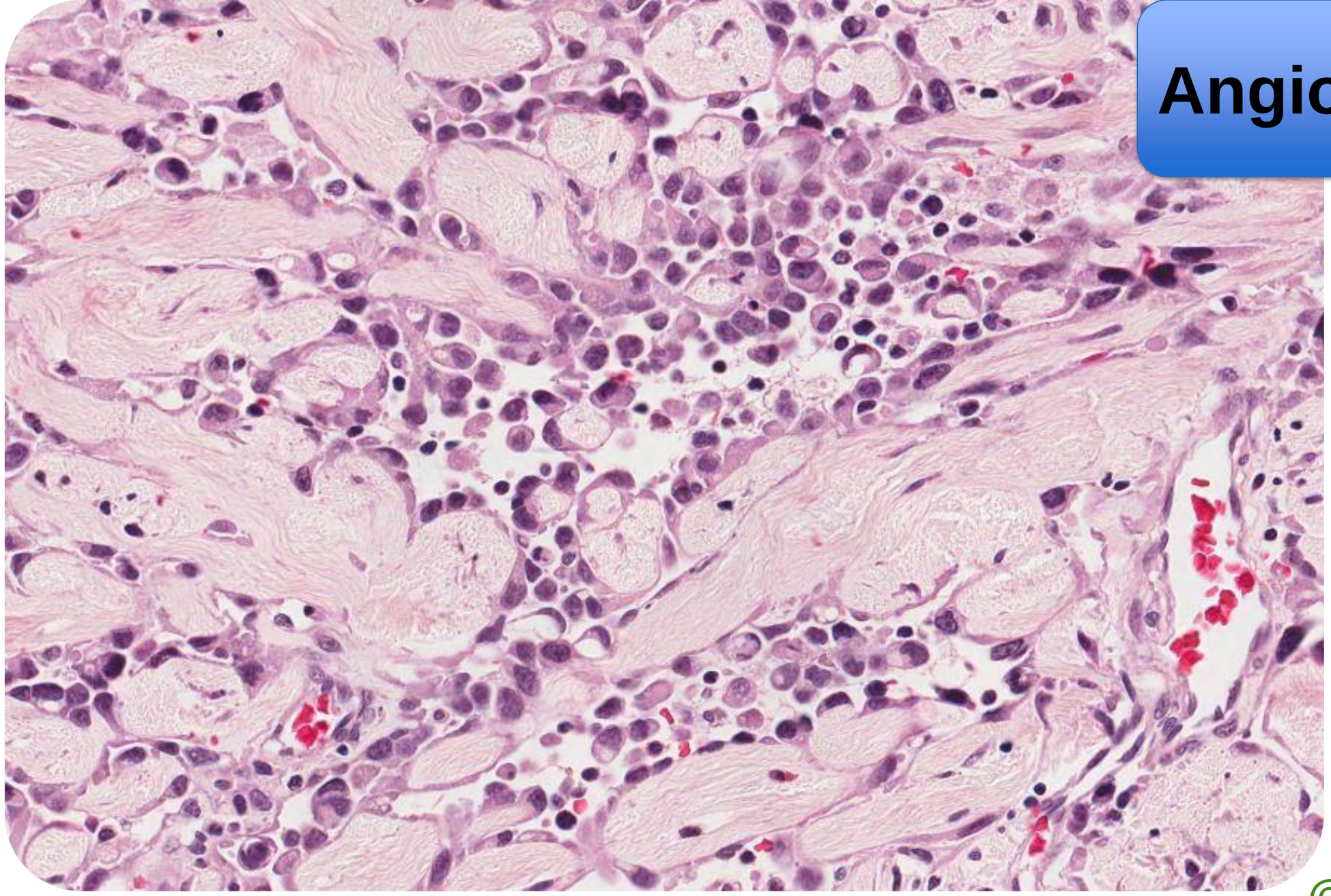


@JMGardnerMD
@NRiddleMD

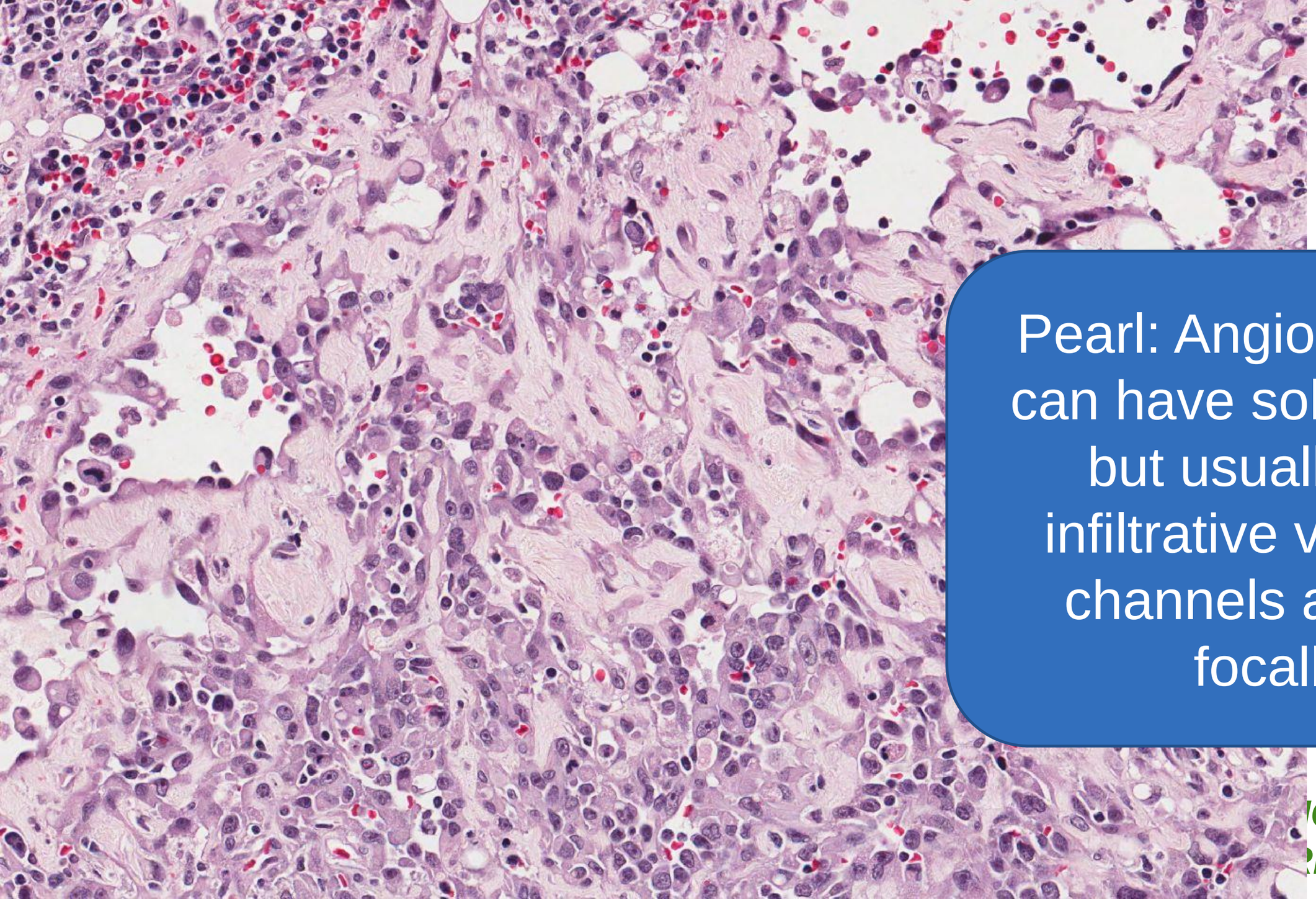


@JMGardnerMD
@NRiddleMD

Angiosarcoma



@JMGardnerMD
@NRiddleMD



Pearl: Angiosarcoma can have solid areas, but usually has infiltrative vascular channels at least focally

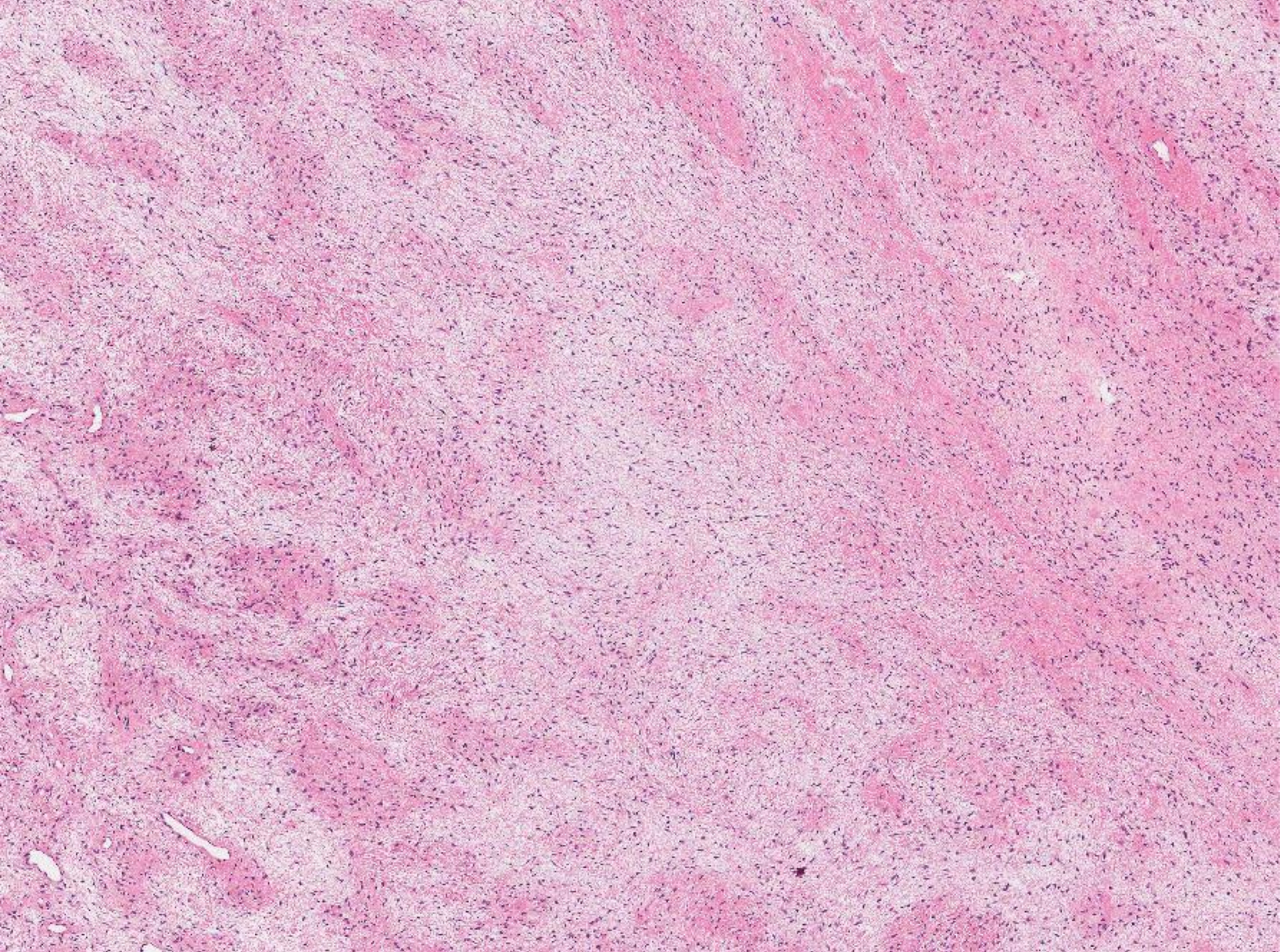
Diagnostic pitfalls

- Lymphoma, melanoma, or poorly differentiated carcinoma can mimic high grade sarcoma – treatment for each may be very different

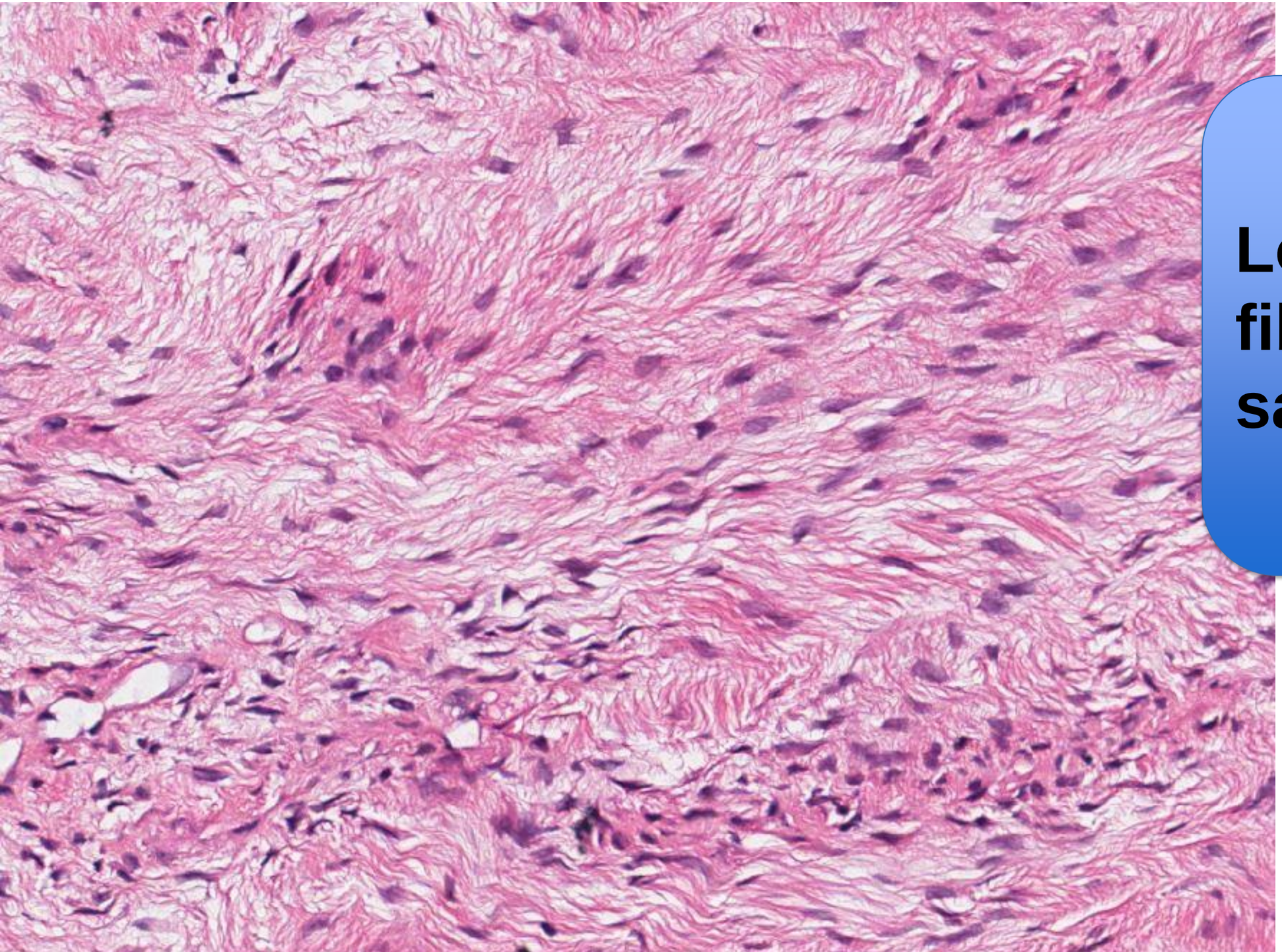
- Some sarcomas do not look cytologically malignant
  - Translocation associated sarcomas usually uniform/monotonous cells, sometimes even bland/banal, LACK pleomorphism
  - E.g. – low grade fibromyxoid sarcoma, dermatofibrosarcoma protuberans

- Some benign soft tissue tumors have pleomorphism
  - E.g. – pleomorphic lipoma, ancient schwannoma

@JMGardnerMD
@NRiddleMD



@JMGardnerMD
@NRiddleMD



Low grade fibromyxoid sarcoma

@JMGardnerMD
@NRiddleMD

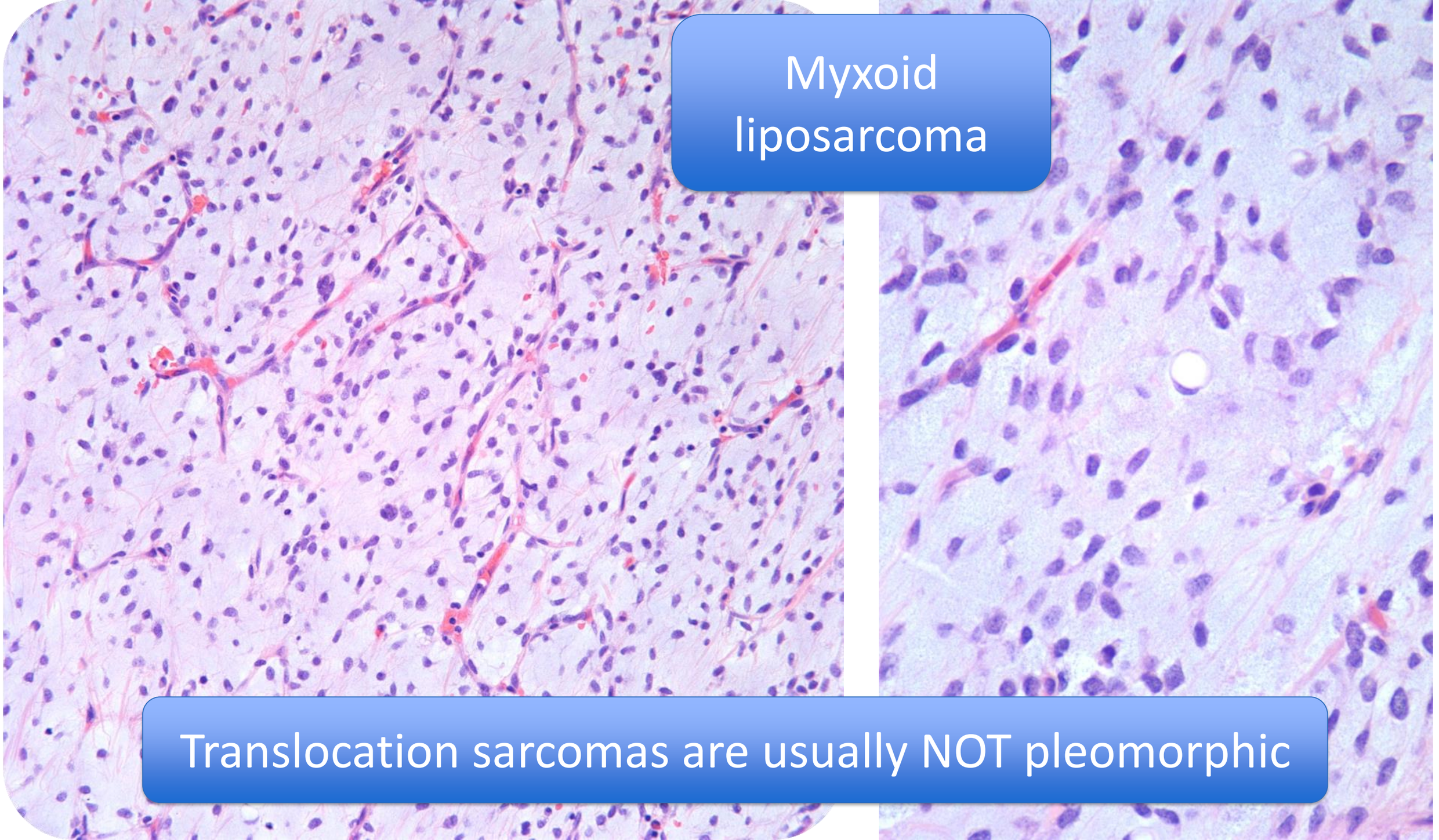
Soft Tissue Pathology ~~Look Alikes~~ Name Alikes

Low-grade fibromyxoid sarcoma

- **Fibrous (pink) > myxoid (blue)**
  - **FIBROmyxoid sarcoma**
- **Atypia/pleomorphism: RARE**
  - **Looks (deceptively) benign**
- **MUC4+ by IHC**

Myxofibrosarcoma, low grade (grade 1)

- **Myxoid (blue) > Fibrous (pink)**
  - **MYXOfibrosarcoma**
- **Atypia/pleomorphism: REQUIRED**
  - **Looks malignant**
- **No specific IHC marker**


Myxoid liposarcoma
Translocation sarcomas are usually NOT pleomorphic

Diagnostic Histopathology

Content All MP Journals Reader Info Subscribe

The pale blue slide: avoiding myx-ups and mishaps in cutaneous myxoid tumors

Nicole D Riddle

Jerad M Gardner

Abstract

Myxoid or mucinous background change is a common finding in a wide variety of cutaneous tumors and other diseases. Myxoid tumors often have overlapping features and may show significant heterogeneity from area to area within a given specimen and from individual case to case. As prognosis and treatment vary considerably between many of these entities, accurate diagnosis is essential. This article will discuss some of the more pertinent cutaneous myxoid mesenchymal tumors with a focus on key diagnostic features. Entities discussed include superficial angiomyxoma (cutaneous myxoma), superficial acral (digital) fibromyxoma, dermal nerve sheath myxoma (conventional neurothekeoma), myxoid dermatofibrosarcoma protuberans, giant cell fibroblastoma, low-grade fibromyxoid sarcoma, myxofibrosarcoma, and myxoinflammatory fibroblastic sarcoma.

Keywords low-grade fibromyxoid sarcoma; mucin; myxofibrosarcoma; myxoid; myxoinflammatory fibroblastic sarcoma; myxoma; sarcoma

Introduction

Purple epidermis and adnexae, pink dermal collagen, and white subcutaneous fat: these are comfortable and familiar colors to

like cutaneous myxoma and the other entities discussed be
This article will discuss some of the more pertinent cutan
myxoid mesenchymal tumors with a focus on how to tease
the correct diagnosis from other myxoid entities in the diffe
tial. A summary of the key diagnostic features of the cutan
myxoid tumors covered in this article is presented in Box 1.

Key diagnostic features of cutaneous myxoid tumors

Superficial angiomyxoma (cutaneous myxoma)
- Hypocellular myxoid proliferation with thin branching vessels
- Entrapped epithelial cysts in 25%
- Bland reniform nuclei with "belly" of eosinophilic cytoplasm
- Minimal nuclear atypia or mitotic activity
- Scattered neutrophils useful clue

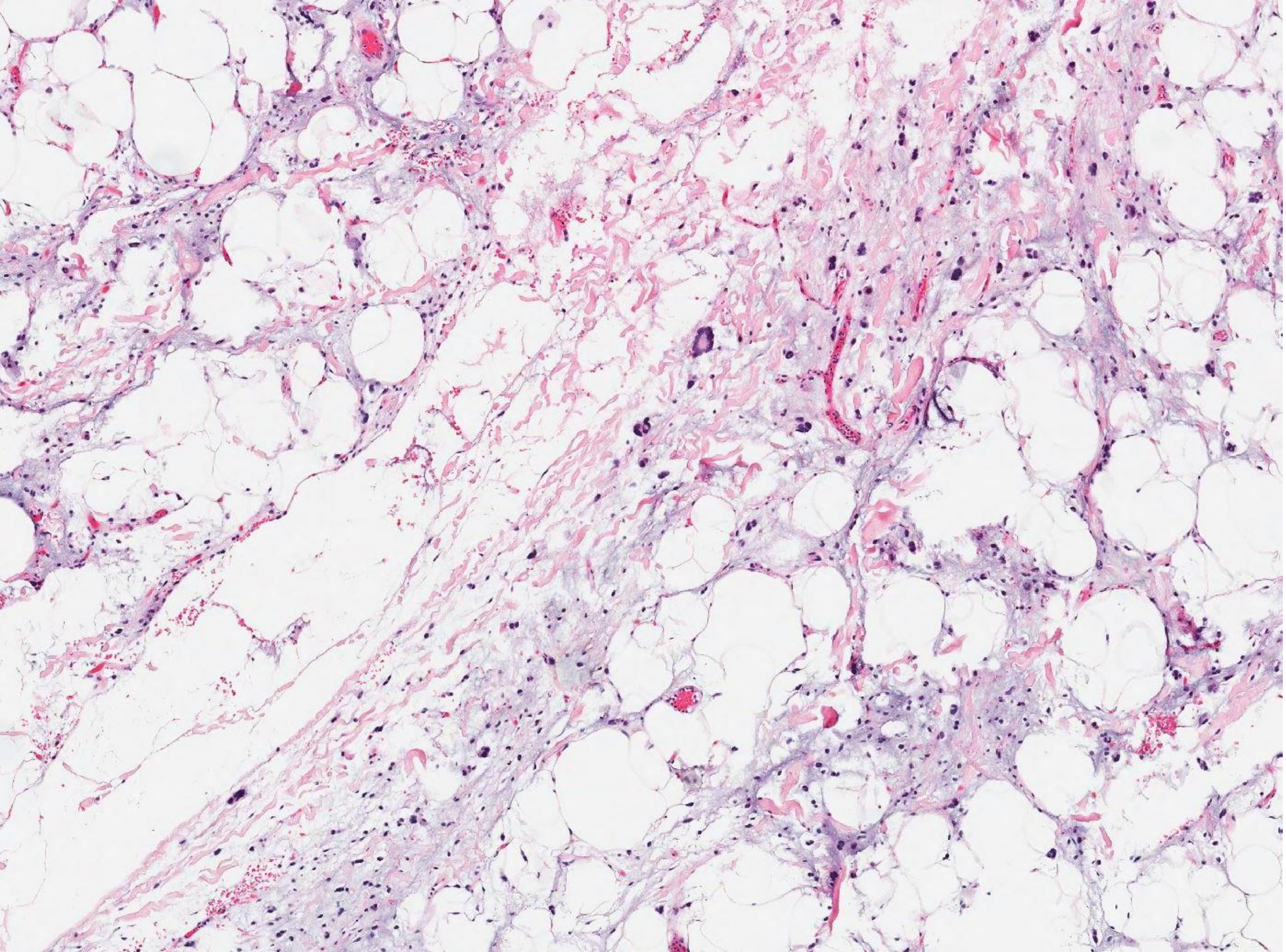
Superficial acral (digital) fibromyxoma
- Most occur on digits, usually periungual
- Bland spindle cells with variable myxoid/collagenous background
- Minimal nuclear atypia or mitotic activity
- CD34 (+)

Dermal nerve sheath myxoma (conventional neurothekeoma)
- Hypocellular myxoid nodules divided by fibrous septa
- Bland spindle cells, sometimes in swirling thin cords/chains
- S100, SOX-10, GFAP (+)

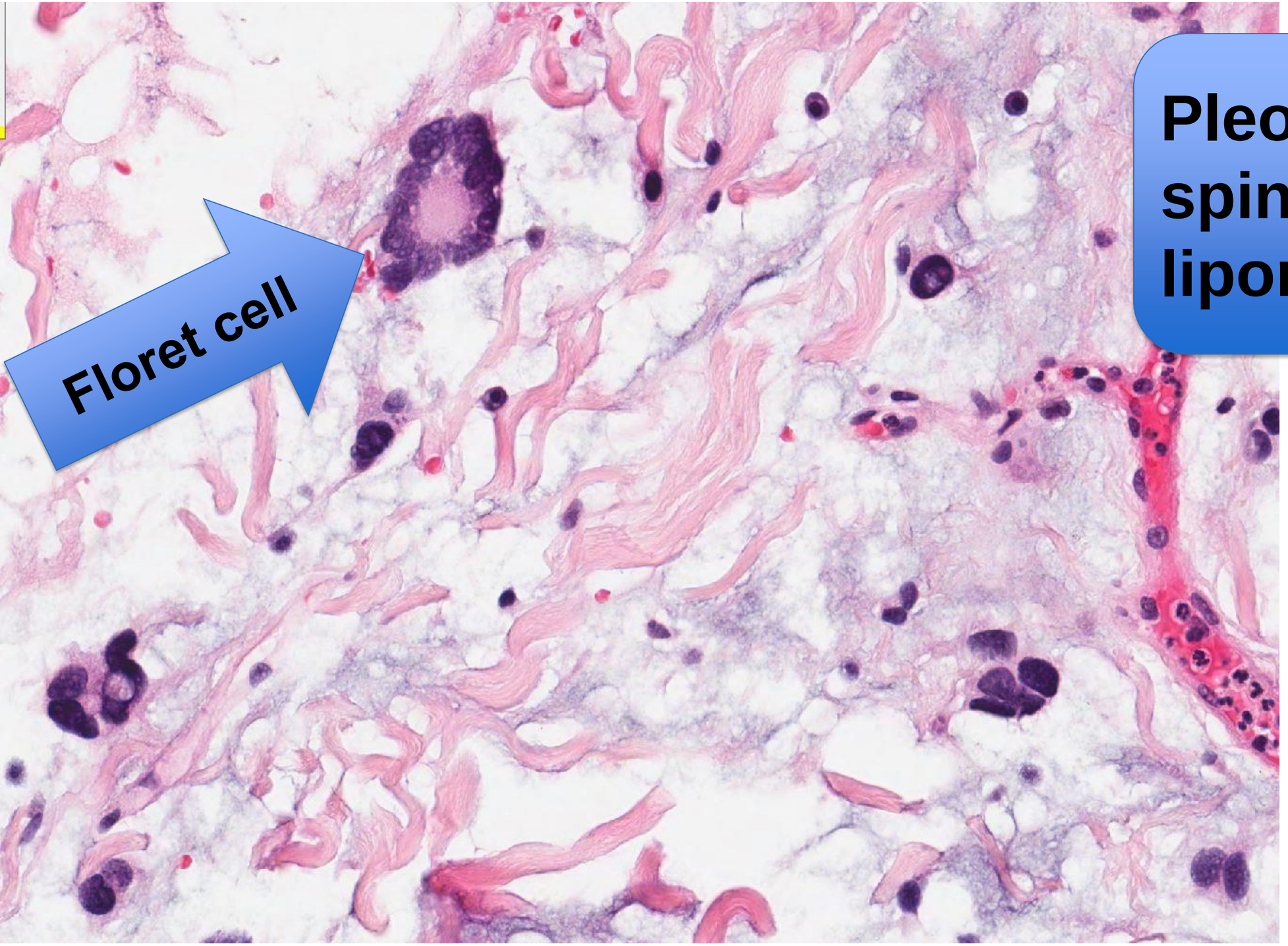
Myxoid dermatofibrosarcoma protuberans & giant cell fibroblastoma
- DFSP: bland spindle cells, storiform, "honeycomb" fat entrapment
- Myxoid foci in DFSP: hypocellular, plexiform vessels, multinucleated cells
- GCF: hypocellular myxoid lesion with bland spindle cells, pseudovascular spaces, hyperchromatic multinucleated cells (often around spaces)
- Hybrid tumors show both DFSP and GCF features

FREE COPY OF PAPER: http://bit.ly/myxoidtumors

@JMGardnerMD
@NRiddleMD



@JMGardnerMD
@NRiddleMD



Pleomorphic/ spindle cell lipoma

@JMGardnerMD
@NRiddleMD

H&E morphology is KING

- Immunostains & molecular are wonderful…but they can make us lazy!

- Always push yourself to figure out diagnosis on H&E only before ordering IHC (good practice!)

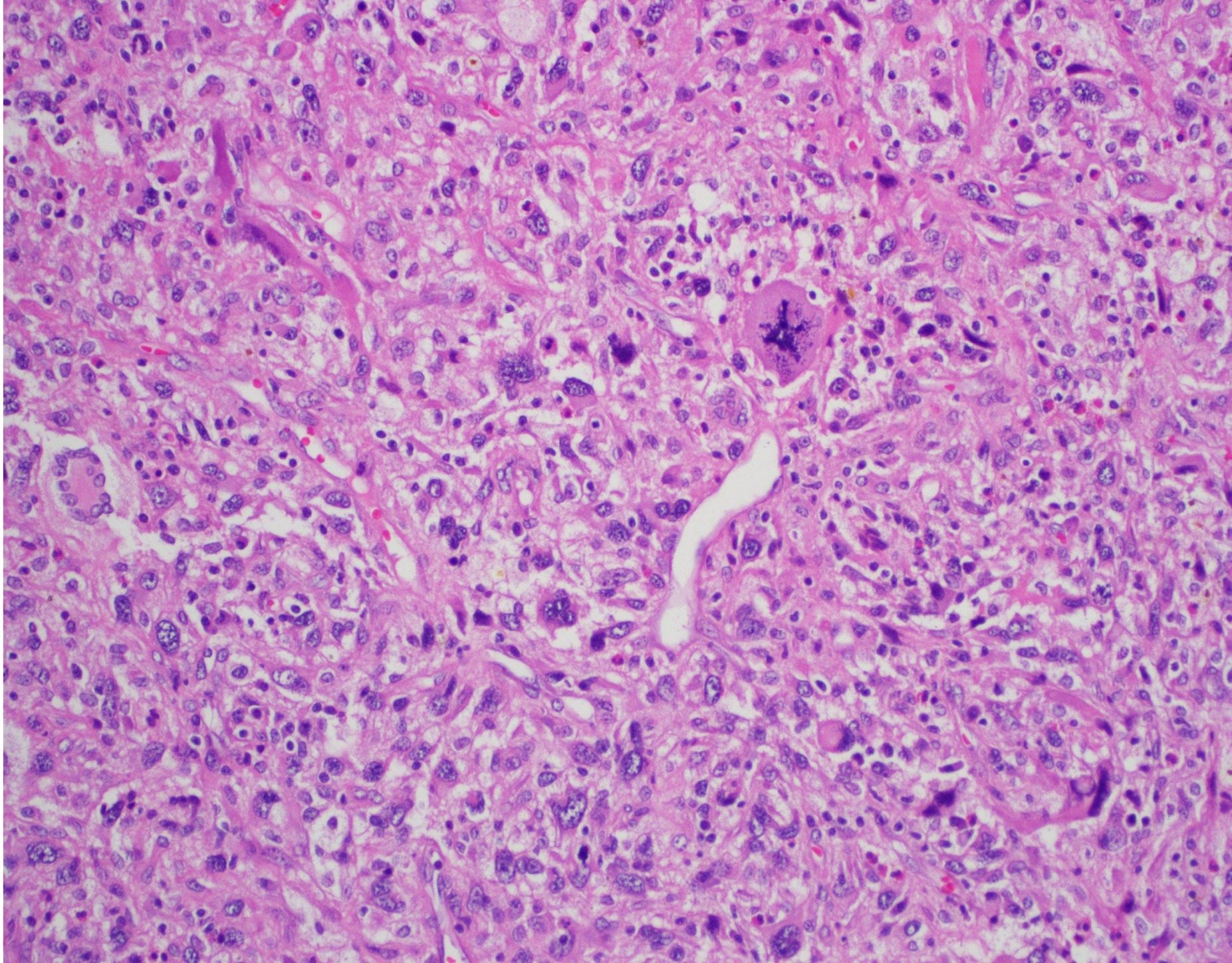
@JMGardnerMD
@NRiddleMD

Clinical info helps a lot

- Age of patient
- Anatomic site
- Superficial vs Deep
- Size
- Duration

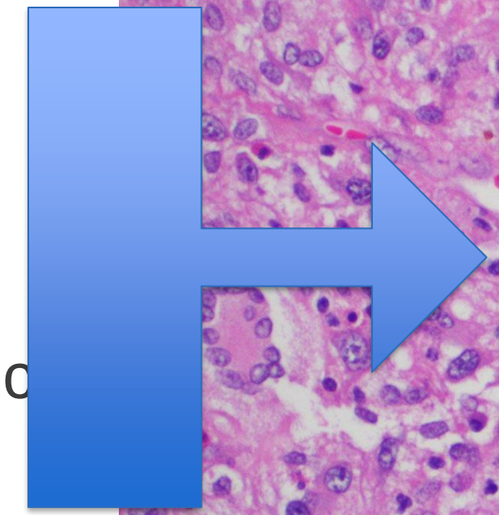
@JMGardnerMD
@NRiddleMD

65 year old woman with 15 cm deep thigh mass. No history of previous cancer. Chest/abdomen/ pelvis CT scan negative.



H&E differential:

- Undifferentiated Pleomorphic sarcoma
- Other pleomorphic sarcomas
- ~~Metastatic poorly-differentiated carcinoma~~
- ~~Metastatic melanoma~~



Possible, but treatment is essentially the same

Possible, but very unlikely clinically

Clinical info helps a lot

- IHC & molecular are very helpful in sarcoma pathology, but not always required
- Reasonable diagnosis (or at least differential diagnosis) can often be provided using combination of clinical scenario, H&E features, and a good biopsy sample.
- Larger repeat biopsy or excision sometimes makes a huge difference

@JMGardnerMD
@NRiddleMD

Diagnostic approach to Sarcomas (simplified)

So you think you have a high grade sarcoma under your scope. What now?

Specific histologic clues to line of differentiation?

- **Adipocytic: lipoblasts, mature fatty component**
- **Smooth muscle: abundant pink cytoplasm, fascicular growth, perinuclear vacuoles**
- **Skeletal muscle: rhabdomyoblasts**
- **Neural: arising in nerve or neurofibroma (or patient has NF-1)**
- **Vascular: vascular channels, blister cells**

@JMGardnerMD
@NRiddleMD

Diagnostic approach to Sarcomas (simplified)

Clinical info (age, site, size) – narrows ddx a lot

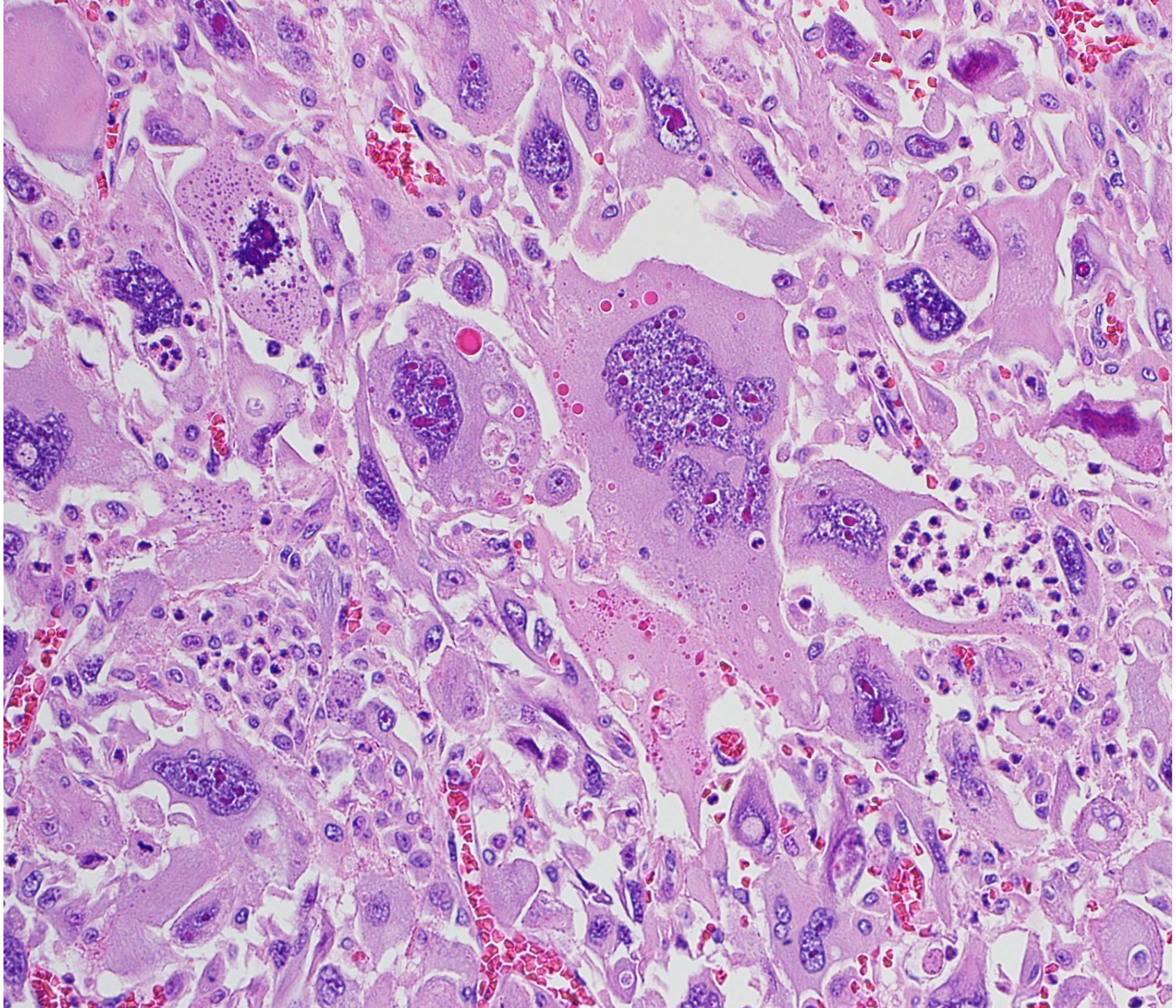
Distinct pattern (looks like you *should* be able to classify it)

Use ancillary tests to rule in/out your diagnostic possibilities

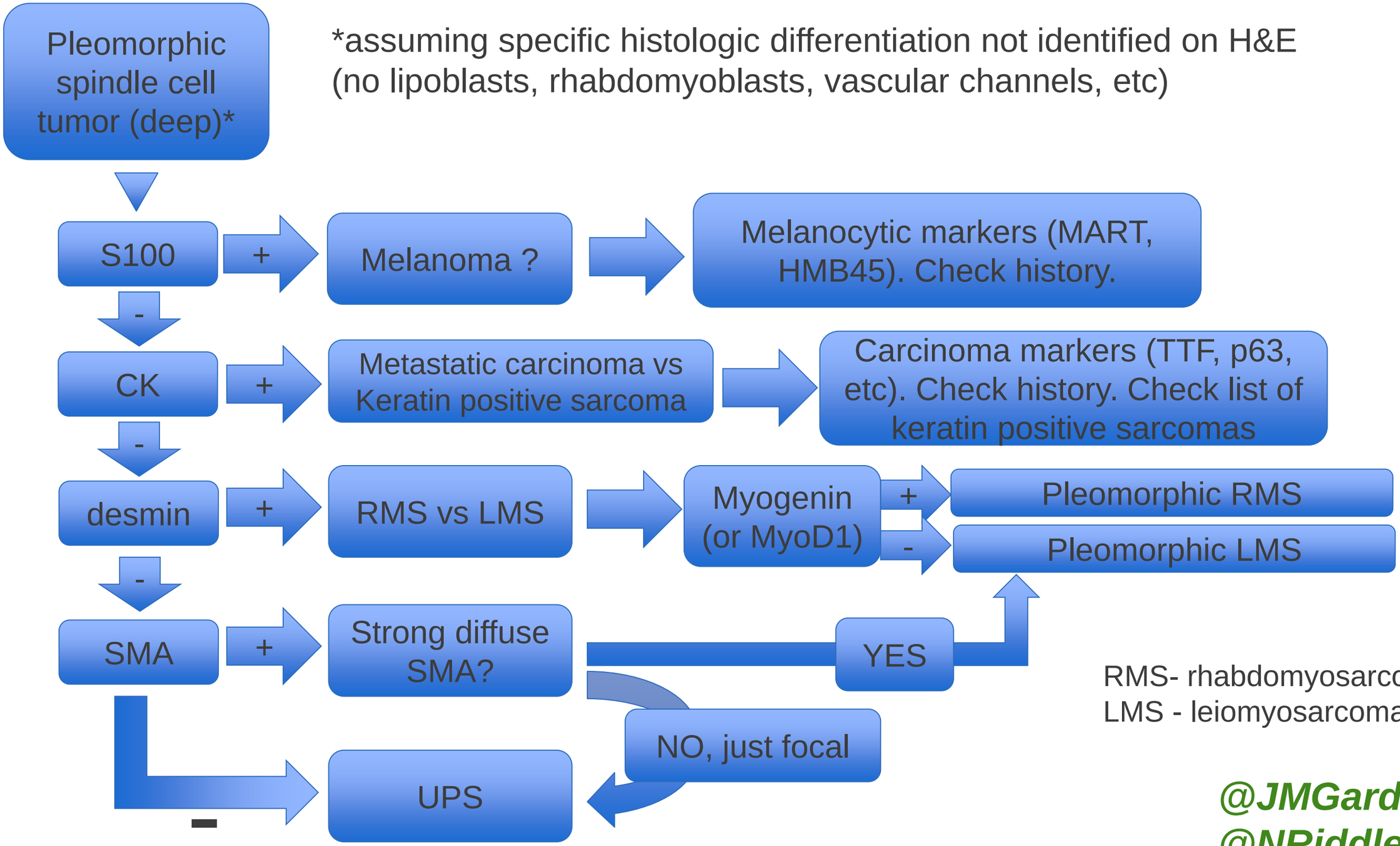
Ancillary tests must make sense in context of histology and clinical

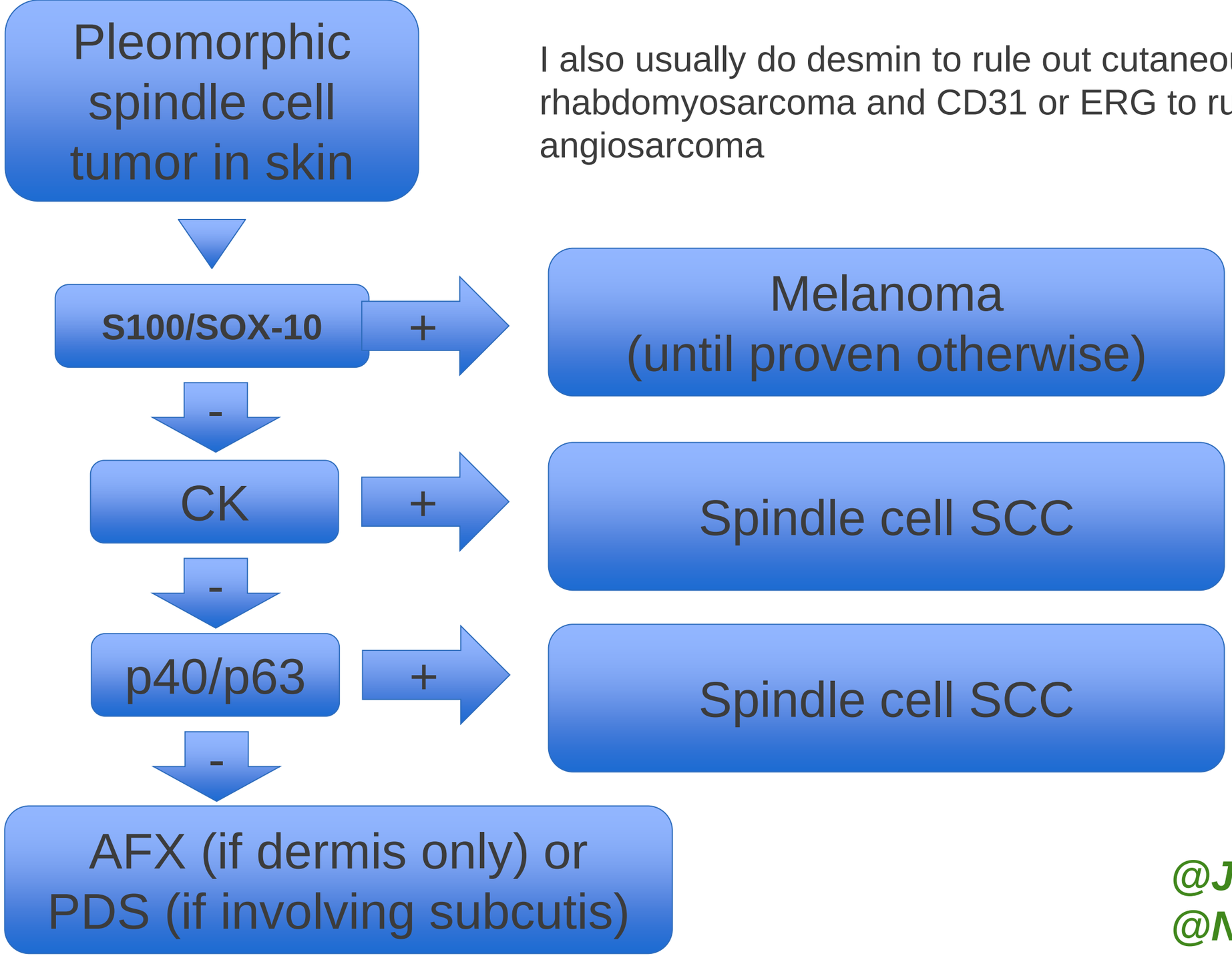
<u>Cannot use IHC or molecular blindly!</u>

@JMGardnerMD
@NRiddleMD



@JMGardnerMD
@NRiddleMD


Pleomorphic spindle cell tumor (deep)*
*assuming specific histologic differentiation not identified on H&E (no lipoblasts, rhabdomyoblasts, vascular channels, etc)
S100
+
Melanoma ?
Melanocytic markers (MART, HMB45). Check history.
-
CK
+
Metastatic carcinoma vs Keratin positive sarcoma
Carcinoma markers (TTF, p63, etc). Check history. Check list of keratin positive sarcomas
-
desmin
+
RMS vs LMS
Myogenin (or MyoD1)
+
Pleomorphic RMS
-
Pleomorphic LMS
-
SMA
+
Strong diffuse SMA?
YES
NO, just focal
-
UPS
RMS- rhabdomyosarcoma
LMS - leiomyosarcoma
@JMGardnerMD
@NRiddleMD



I also usually do desmin to rule out cutaneous rhabdomyosarcoma and CD31 or ERG to rule out angiosarcoma

@JMGardnerMD
@NRiddleMD

Highly useful soft tissue IHC stains

- **P63/P40**
- **S100**
- **SOX-10**
- **Cytokeratins (AE1/AE3, CK7, CK20, CK5/6, CAM 5.2)**
- **Desmin +/- SMM**
- **CD31 & ERG**
- **CD34 (in select scenarios; be careful…it stains a lot of things, including normal dermis!)**
- **MUC4**
- **HHV-8**
- **INI-1**

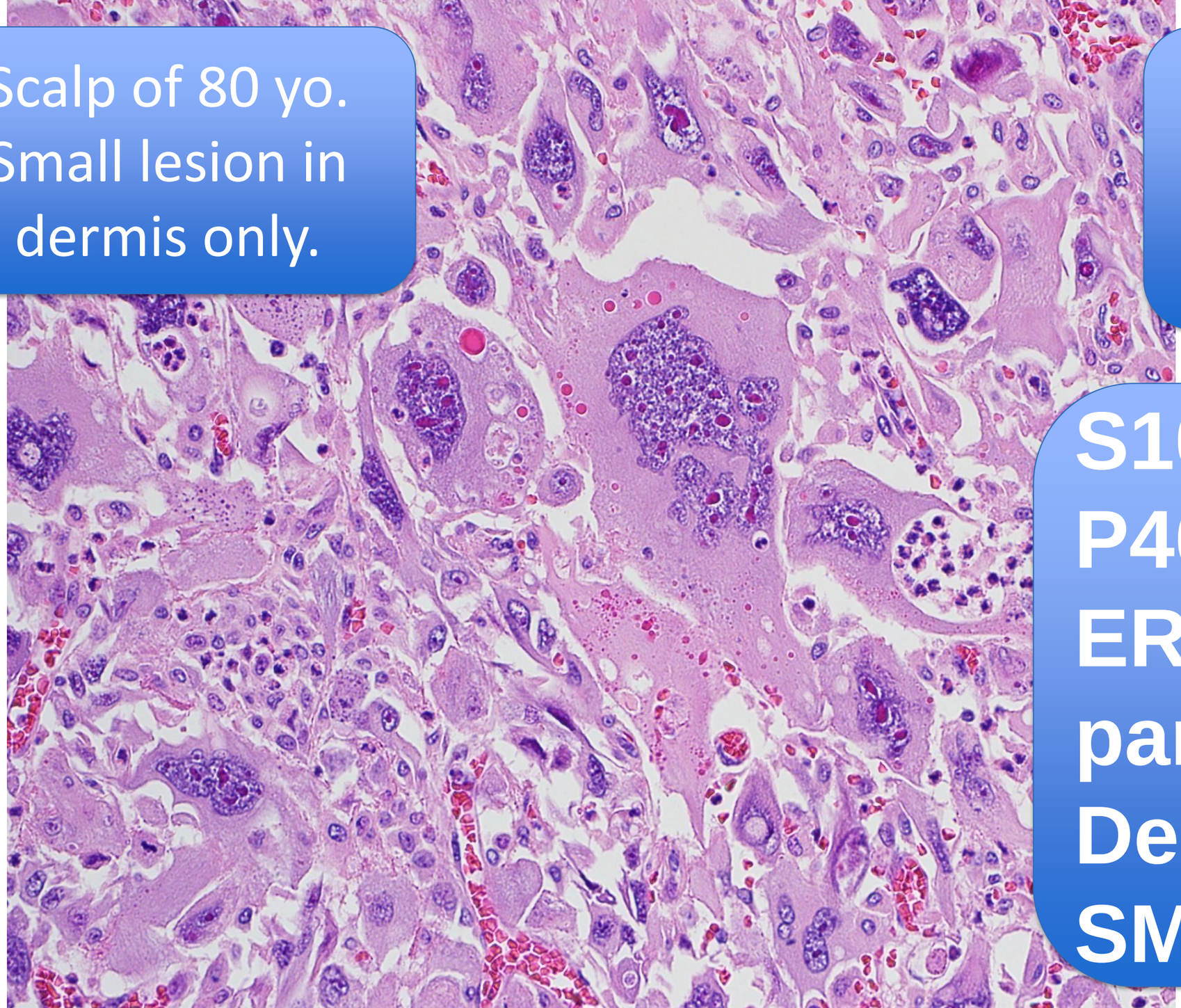
@JMGardnerMD
@NRiddleMD

Soft tissue IHC stains I don't find very helpful

- **Vimentin (totally non-specific; I've NEVER seen it change a diagnosis! Don't do it!)**
- **Factor XIIIa**
- **CD68 (I do use it sometimes in dermpath)**
- **CD10**
- **Procollagen 1**
- **CD99* (useful only in very select settings)**
  - **If negative, probably not Ewing. Otherwise, not very helpful as it stains many things**

@JMGardnerMD
@NRiddleMD

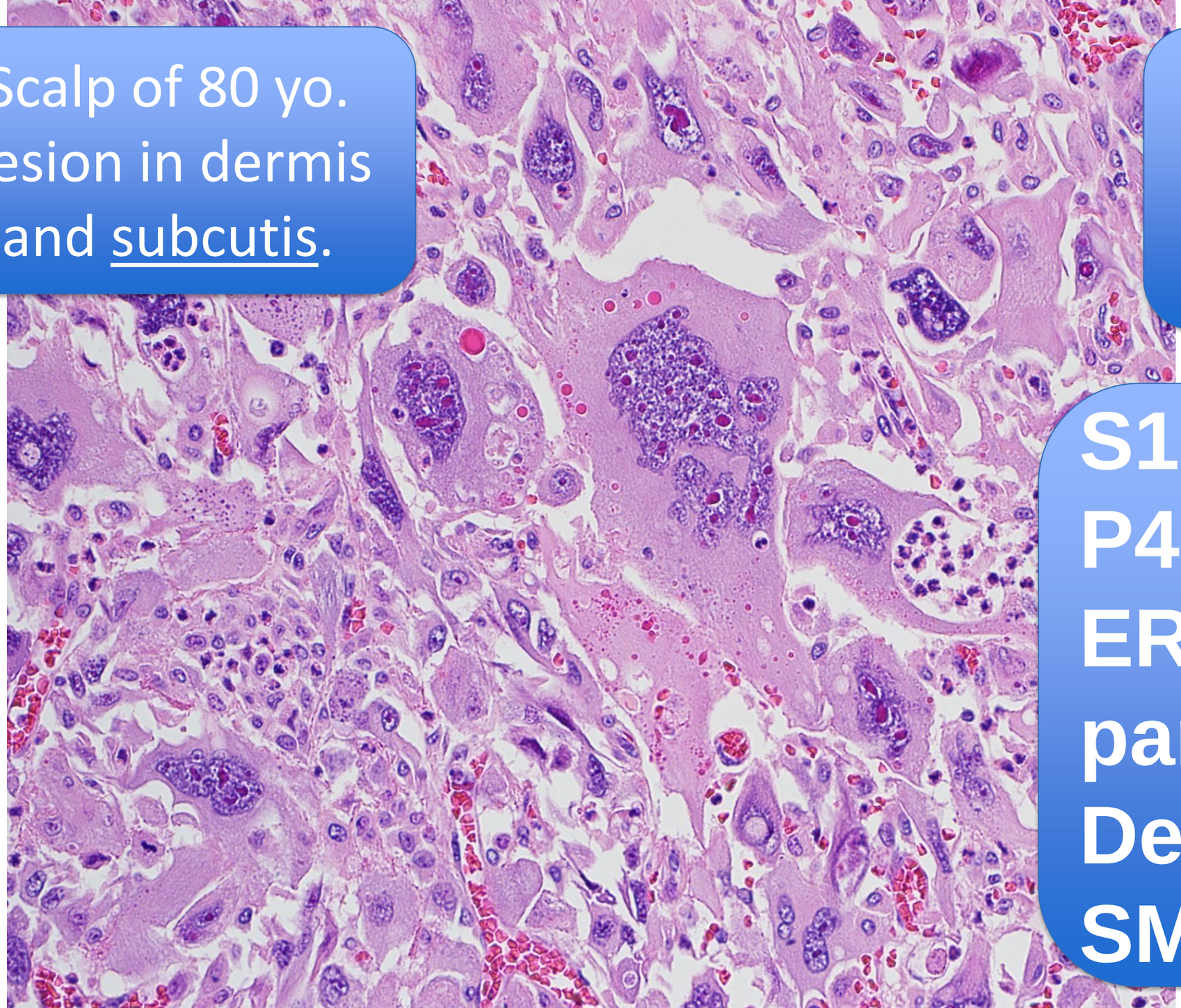
Scalp of 80 yo. Small lesion in dermis only.



Atypical fibroxanthoma (AFX)

S100 –
P40 –
ERG –
panCK –
Desmin –
SMA focal +

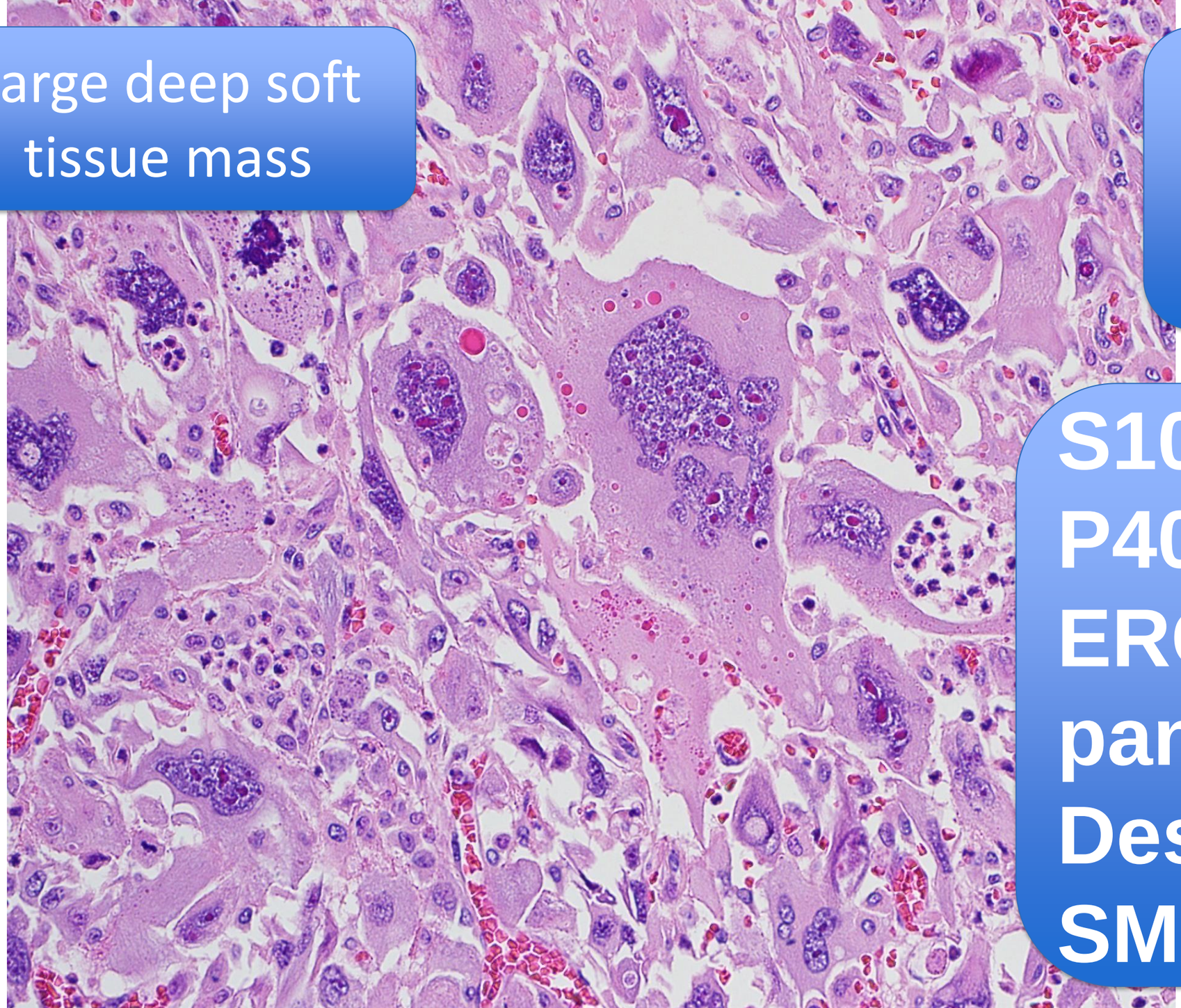
Scalp of 80 yo. Lesion in dermis and subcutis.



Pleomorphic Dermal Sarcoma (PDS)

S100 –
P40 –
ERG –
panCK –
Desmin –
SMA focal +

Large deep soft tissue mass



Undifferentiated pleomorphic sarcoma (UPS)

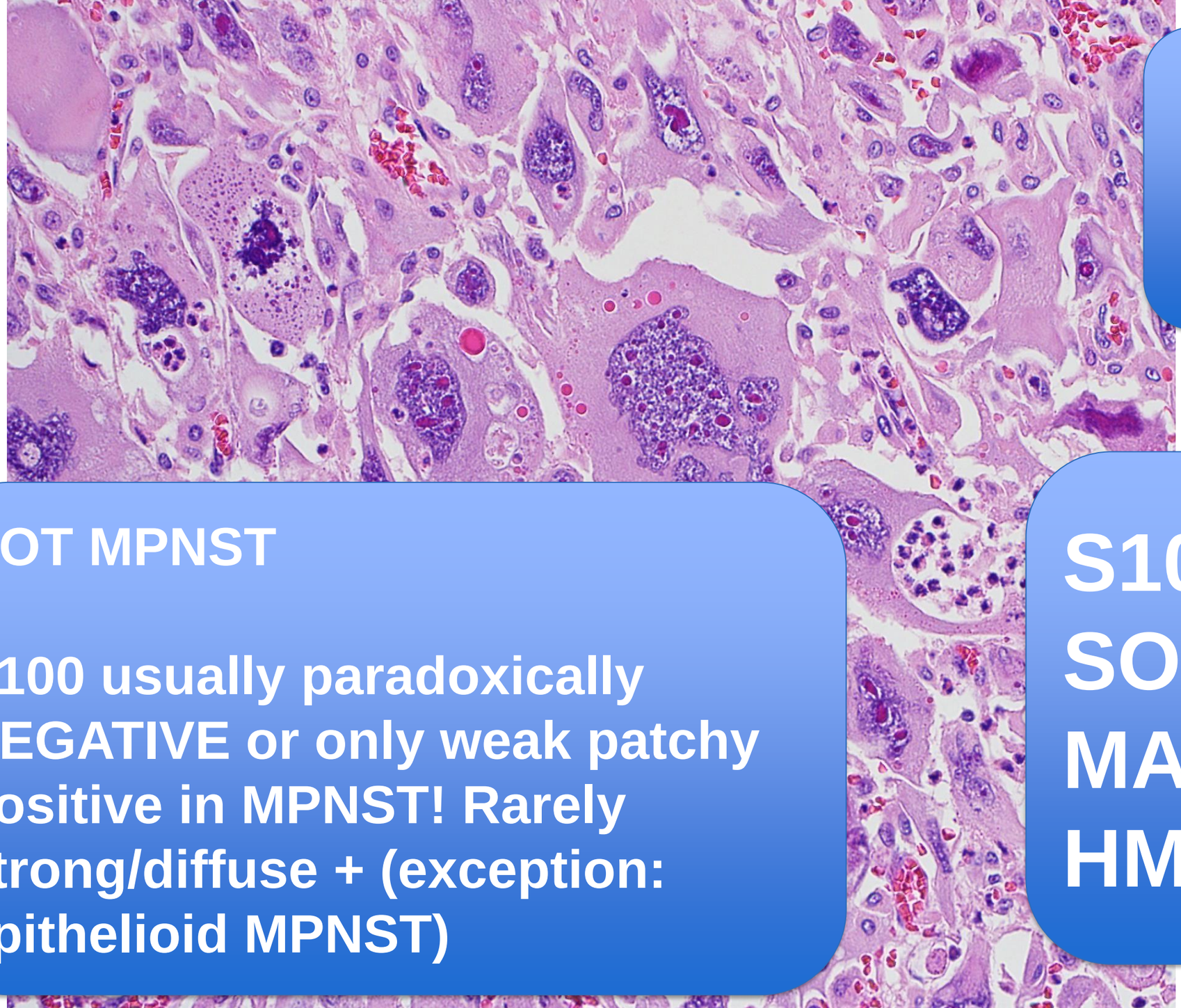
S100 –
P40 –
ERG –
panCK –
Desmin –
SMA focal +

Looks/stains like UPS on needle biopsy, I say…

“High grade pleomorphic sarcoma”

Comment: This could be UPS, but ddx includes other adult pleomorphic sarcomas. Correlate with excision specimen.

@JMGardnerMD
@NRiddleMD



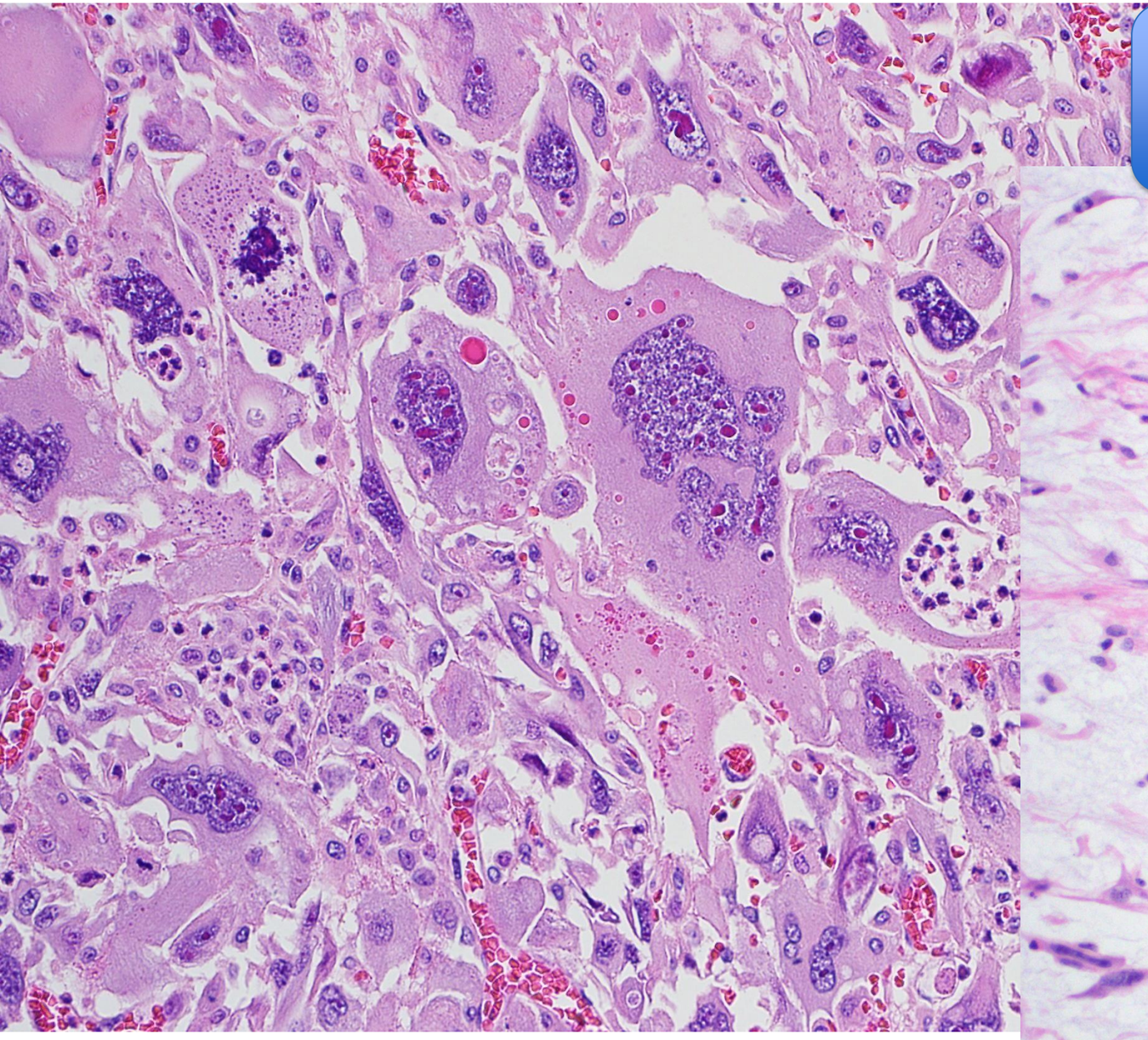
Spindle Cell Melanoma

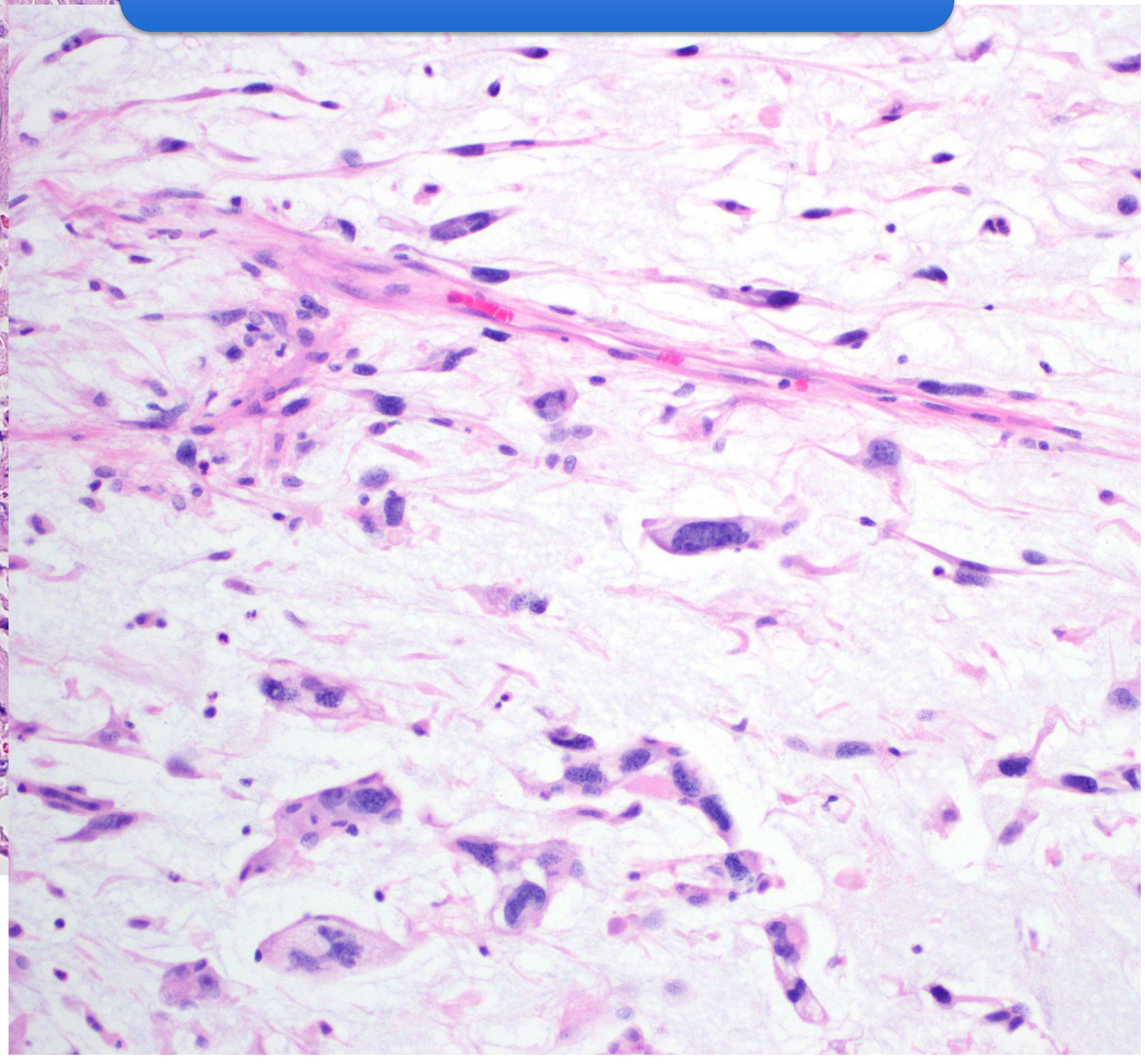
NOT MPNST

S100 usually paradoxically NEGATIVE or only weak patchy positive in MPNST! Rarely strong/diffuse + (exception: epithelioid MPNST)

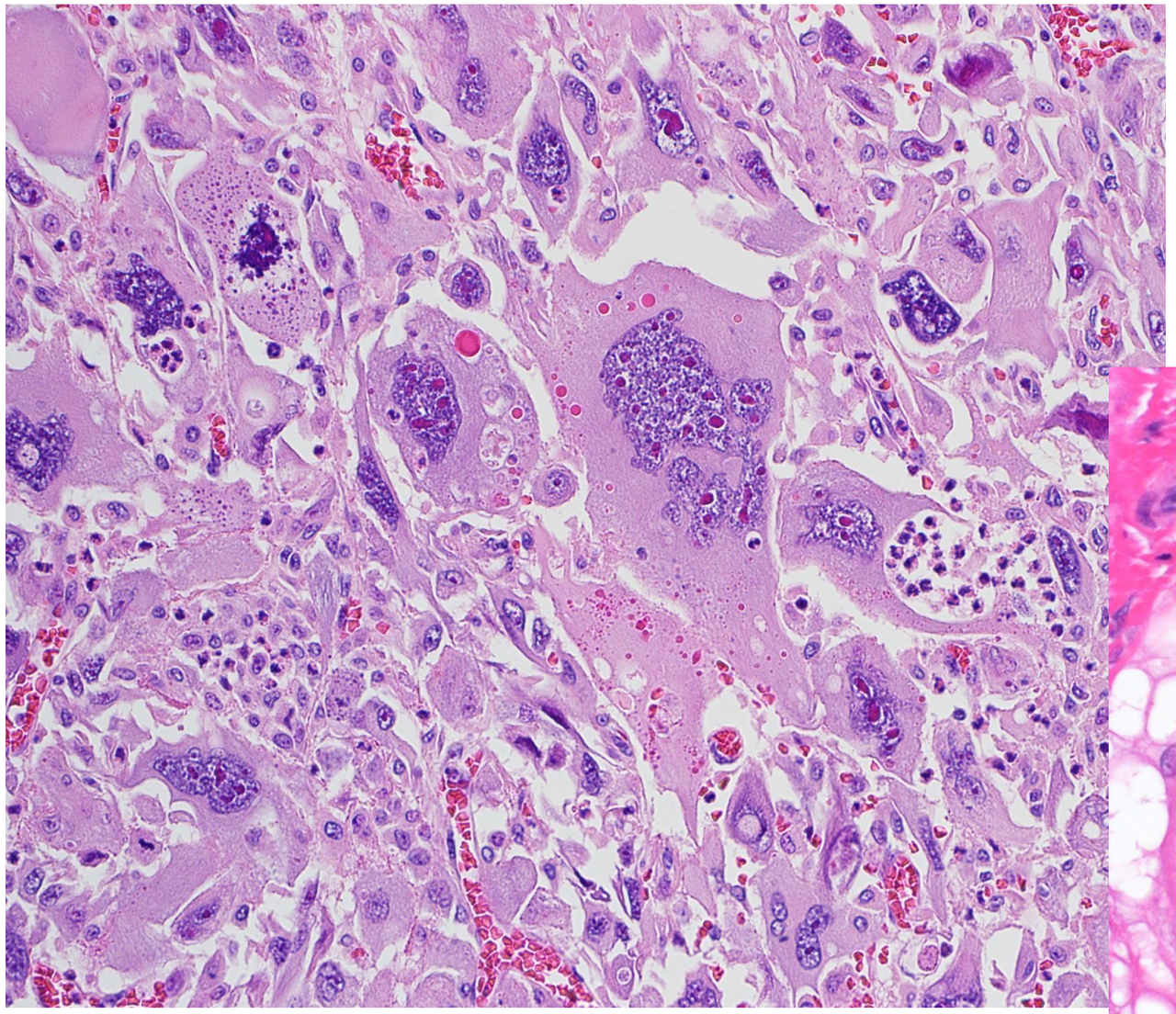
S100 +++
SOX-10 +++
MART-1 –
HMB-45 –

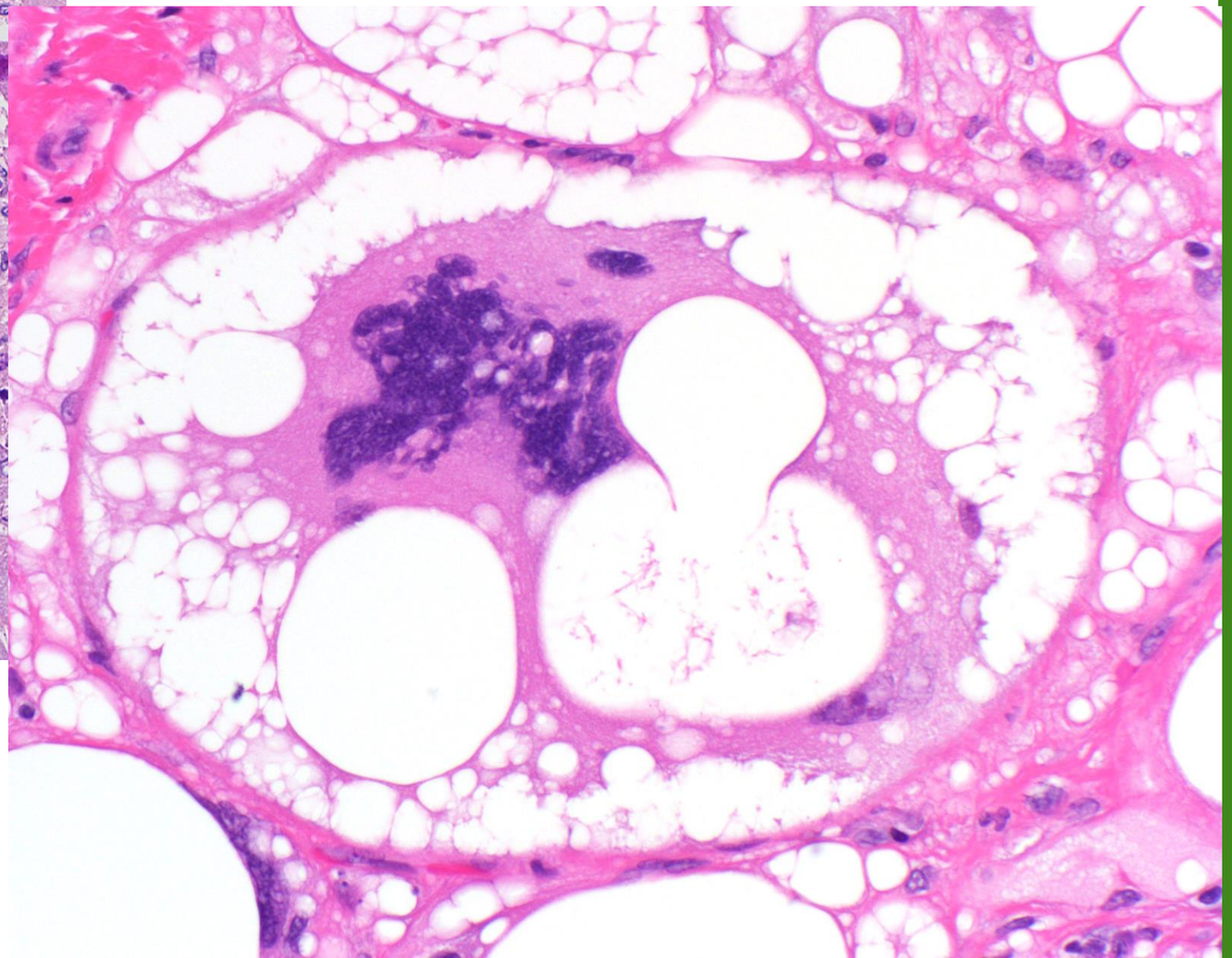
Myxofibrosarcoma

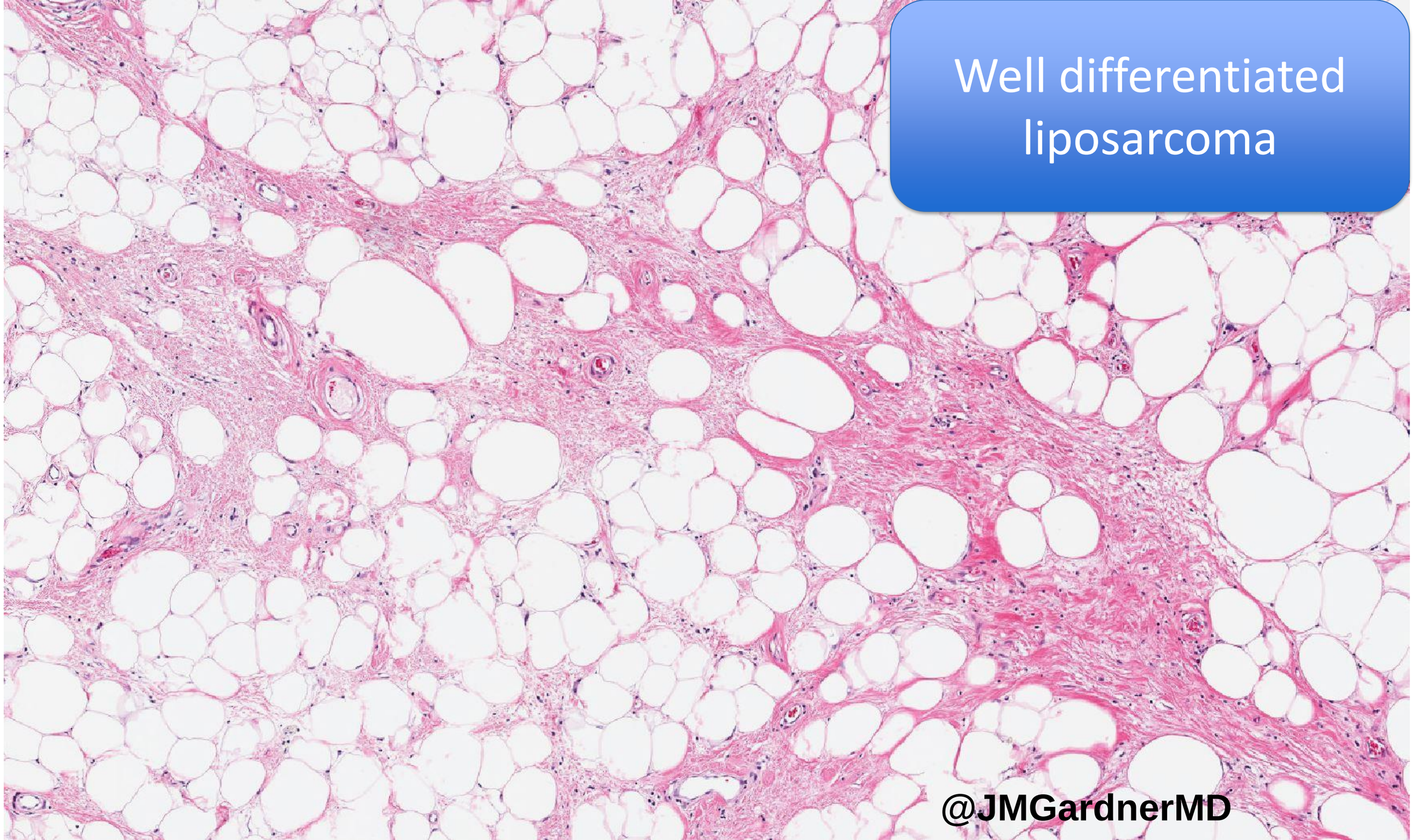


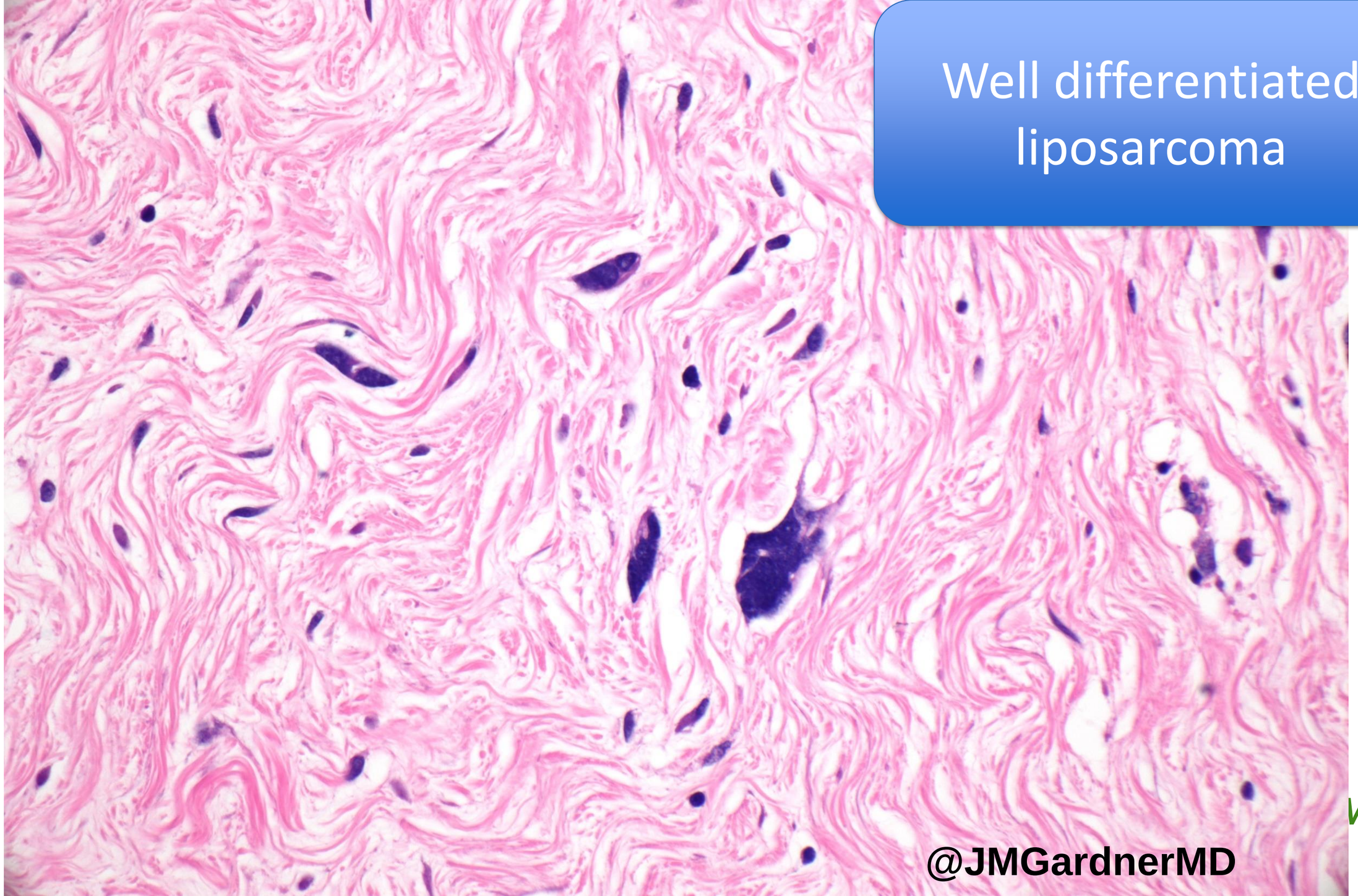


Pleomorphic liposarcoma

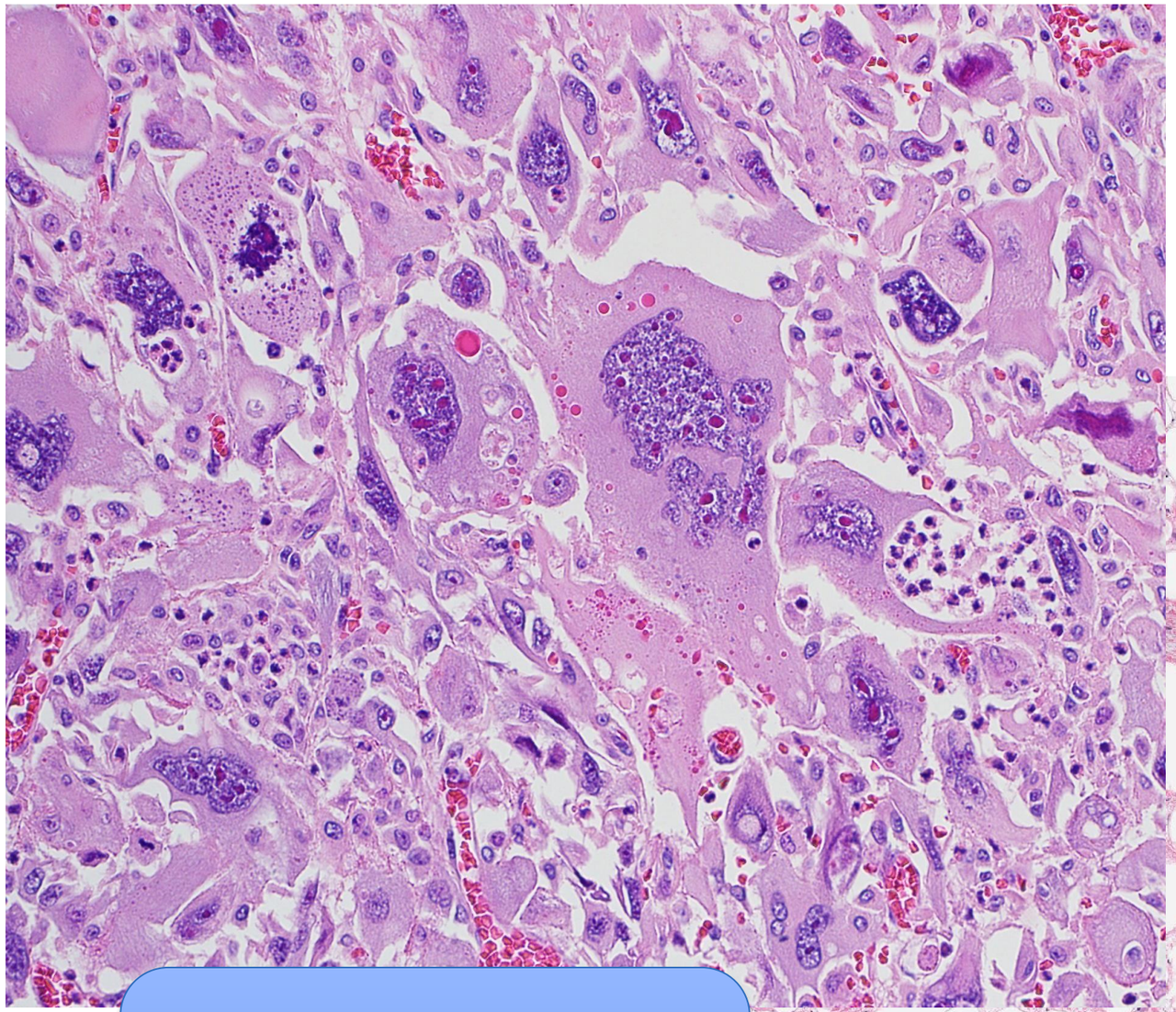





Well differentiated liposarcoma
@JMGardnerMD

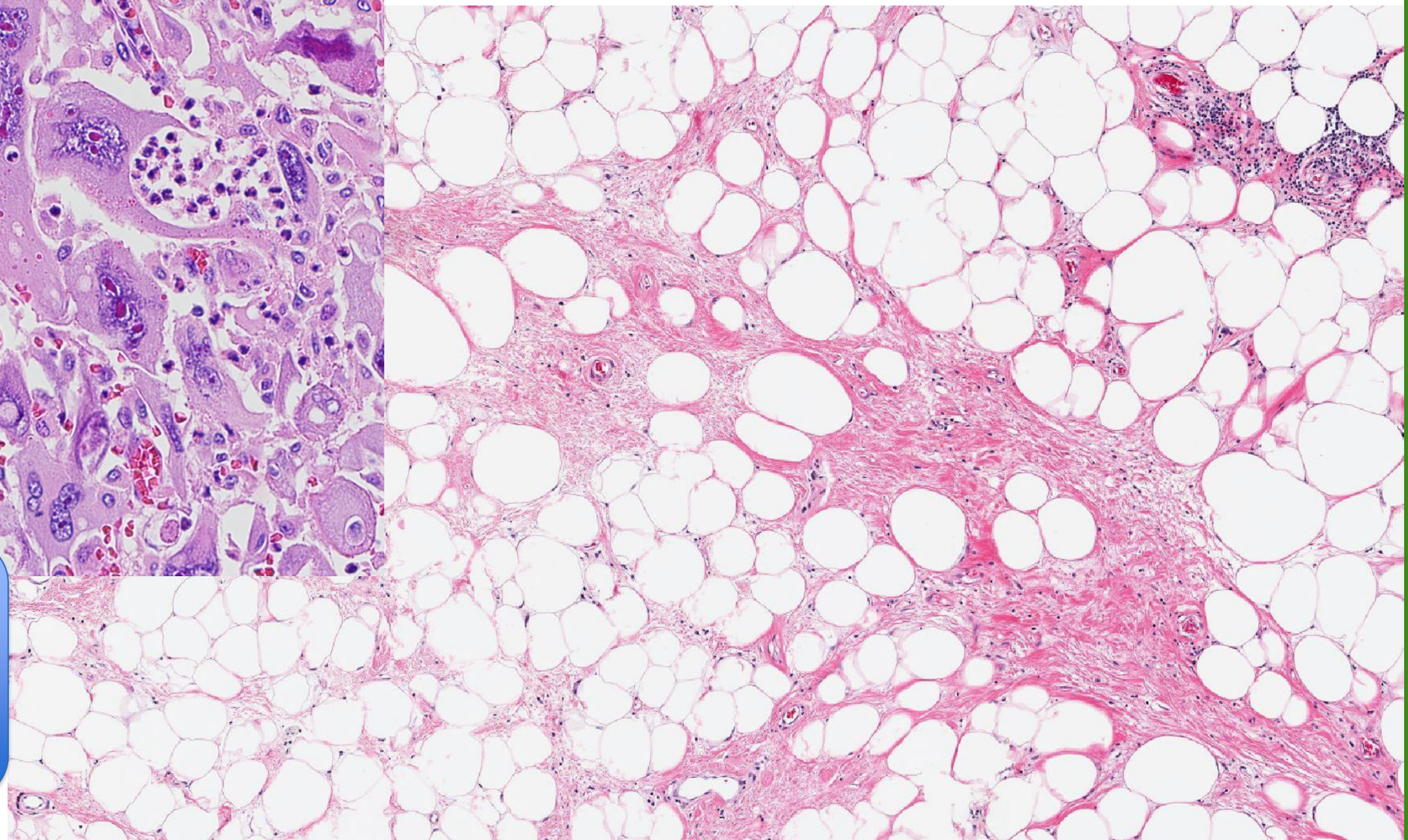


Well differentiated liposarcoma



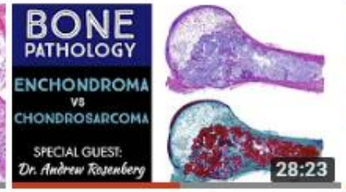
Most cases lack lipoblasts

Dedifferentiated liposarcoma



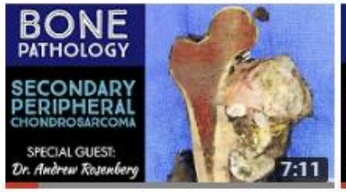
Melanocytic Dermpath Basics: Melanoma

4.5K views • 4 months ago



Chondrosarcoma vs Enchondroma: Bone...

2.1K views • 5 months ago



Chondrosarcoma (Secondary Peripheral): Bone Pathology...

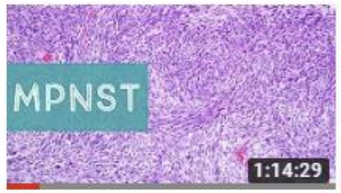
737 views • 5 months ago

Normal Bone Histology & Embryology with Dr. Andrew...

2.5K views • 5 months ago

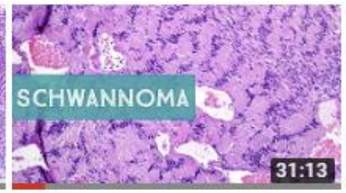
954 views • 5 months ago

5.4K views • 5 months ago



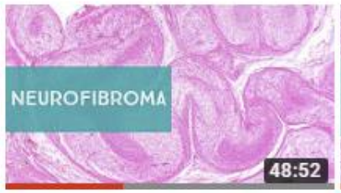
Malignant Peripheral Nerve Sheath Tumor...

3.5K views • 5 months ago



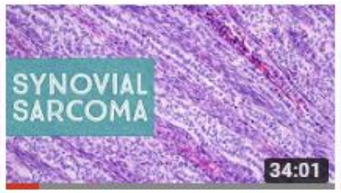
Schwannoma (Neurilemmoma)...Explaine...

2.6K views • 5 months ago



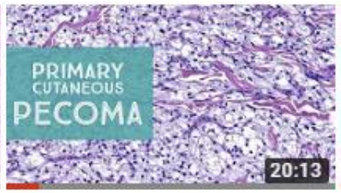
Neurofibroma, Neurofibromatosis-1, and...

3.4K views • 5 months ago



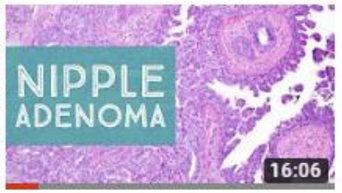
Synovial Sarcoma...Explained by a Soft Tissue Pathologist

3.9K views • 5 months ago



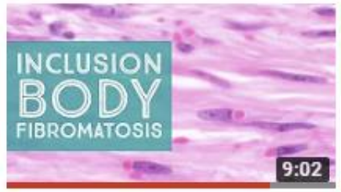
Primary Cutaneous PEComa...Explained by a...

1.1K views • 6 months ago



Nipple Adenoma (Erosive Adenomatosis of the Nipple)

584 views • 6 months ago



Inclusion Body Fibromatosis (Infantile Digital...

552 views • 6 months ago

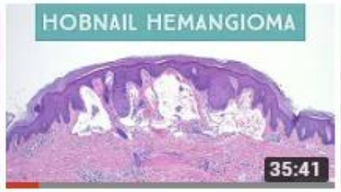
CC

Melanocytic Dermpath Basics: Benign Nevus

7.1K views • 6 months ago

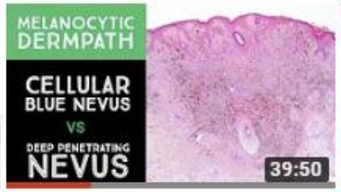
Extranodal Rosai-Dorfman Disease...Explained by a...

1.6K views • 6 months ago



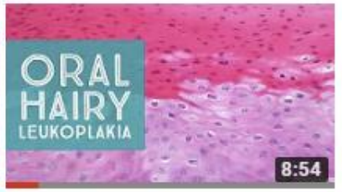
Hobnail Hemangioma, Retiform...

1.2K views • 6 months ago



Melanocytic Dermpath: Cellular Blue Nevus vs Deep...

2.1K views • 7 months ago



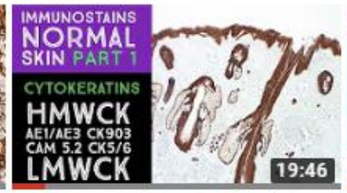
Oral Hairy Leukoplakia...Explained by ...

1.3K views • 7 months ago

CC

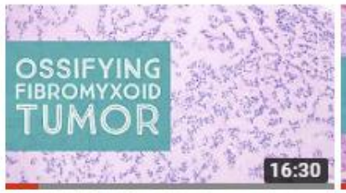
Immunohistochemistry in Normal Skin 2: p63, EMA,...

1.5K views • 8 months ago



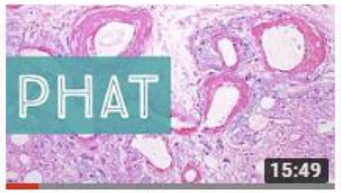
Immunohistochemistry in Normal Skin 1: Cytokeratins

1.9K views • 8 months ago



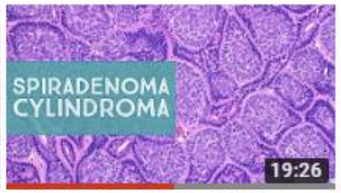
Ossifying Fibromyxoid Tumor (OFMT) of Soft Parts

1K views • 8 months ago



PHAT: Pleomorphic Hyalinizing Angiectatic...

784 views • 8 months ago



Spiradenoma & Cylindroma...Sweat Gland...

2.6K views • 8 months ago

Vasculitis...Explained by a Dermatopathologist

2.3K views • 8 months ago

@JMGardnerMD
@NRiddleMD