

Spindled, Infectious, and (Mostly) Interesting Cases in Breast Pathology

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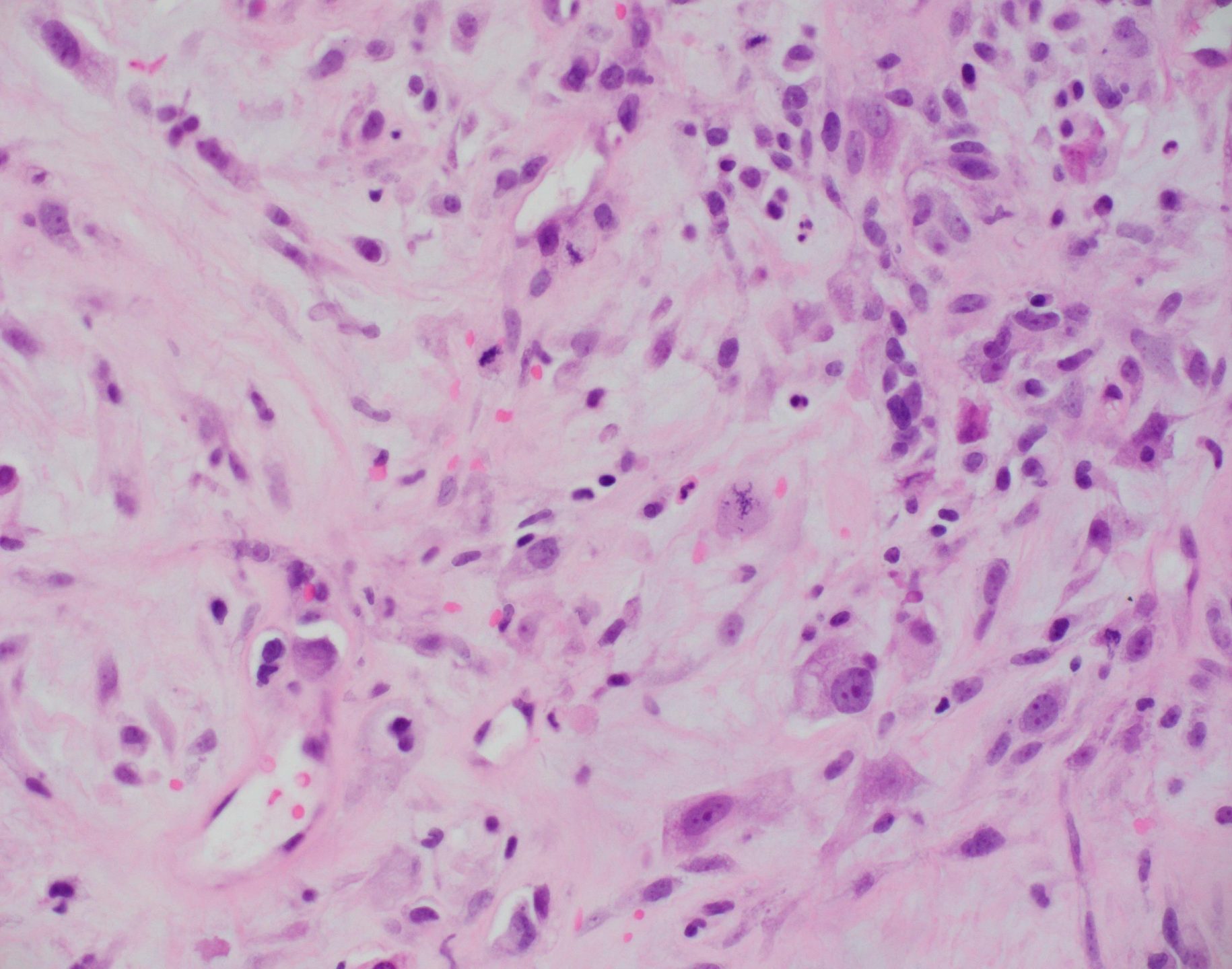


Learning Objectives

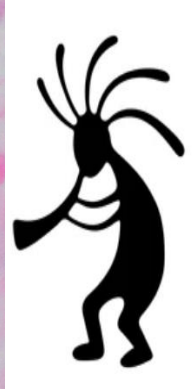
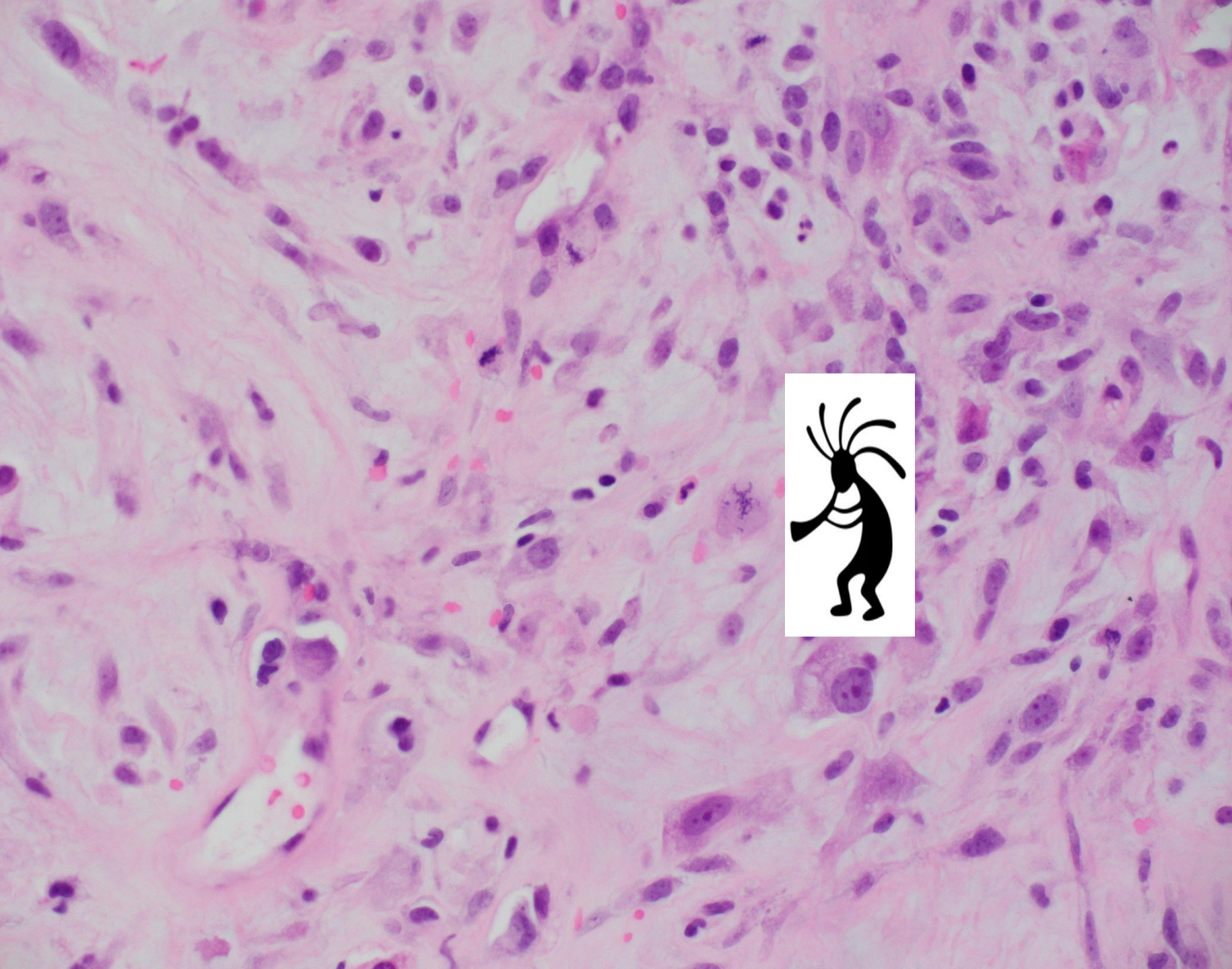
- Review a case-based selection of spindle cell breast lesions.
 - Acknowledge the importance and limitations of IHC in this endeavor
- Review a case-based selection of clinically relevant infectious findings in breast biopsies.
- Review some interesting and unexpected findings of (mostly) “interesting” cases in breast pathology.
 - Correlate these findings with anatomic distribution of breast tissue.

Case #1

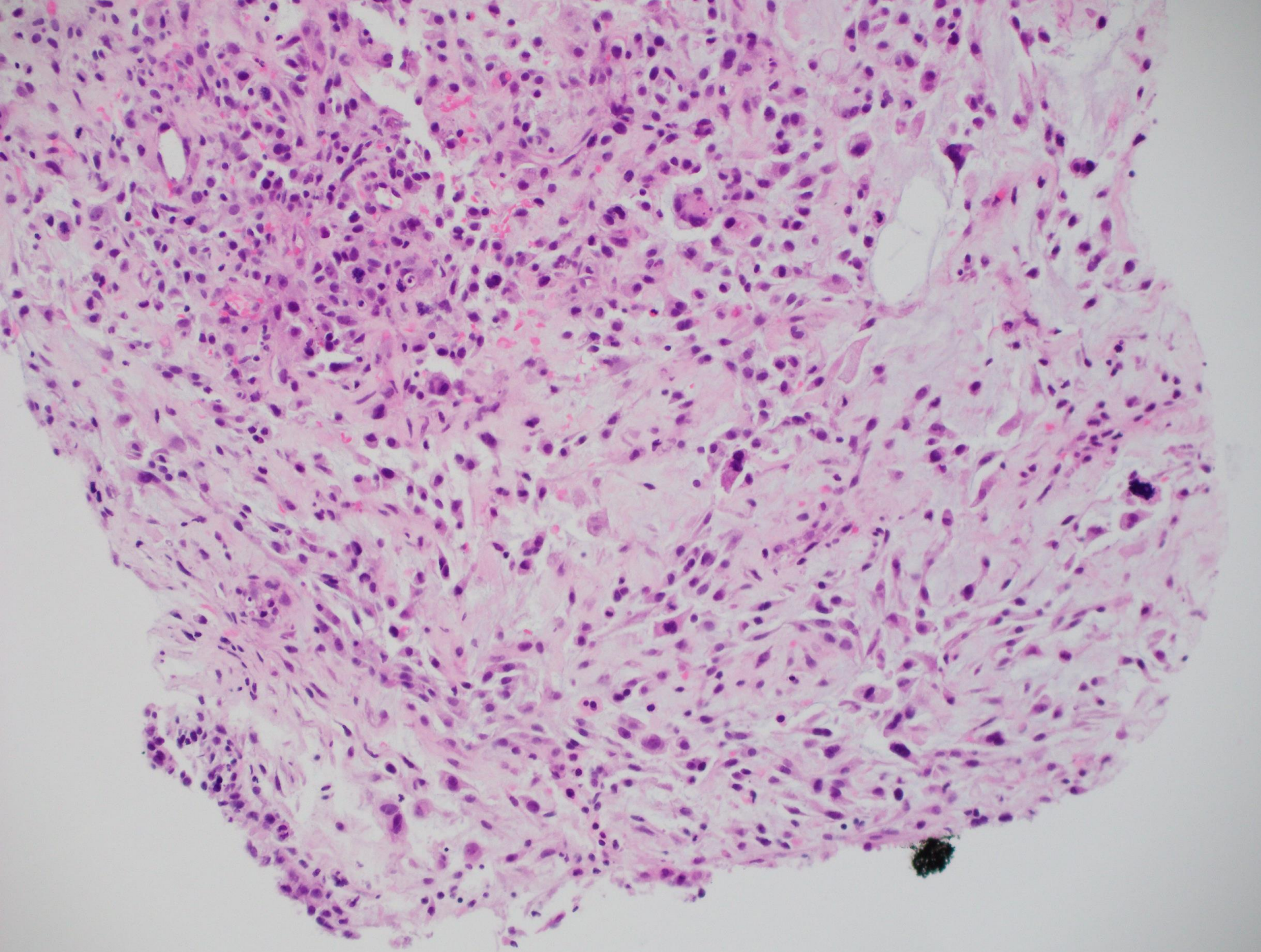




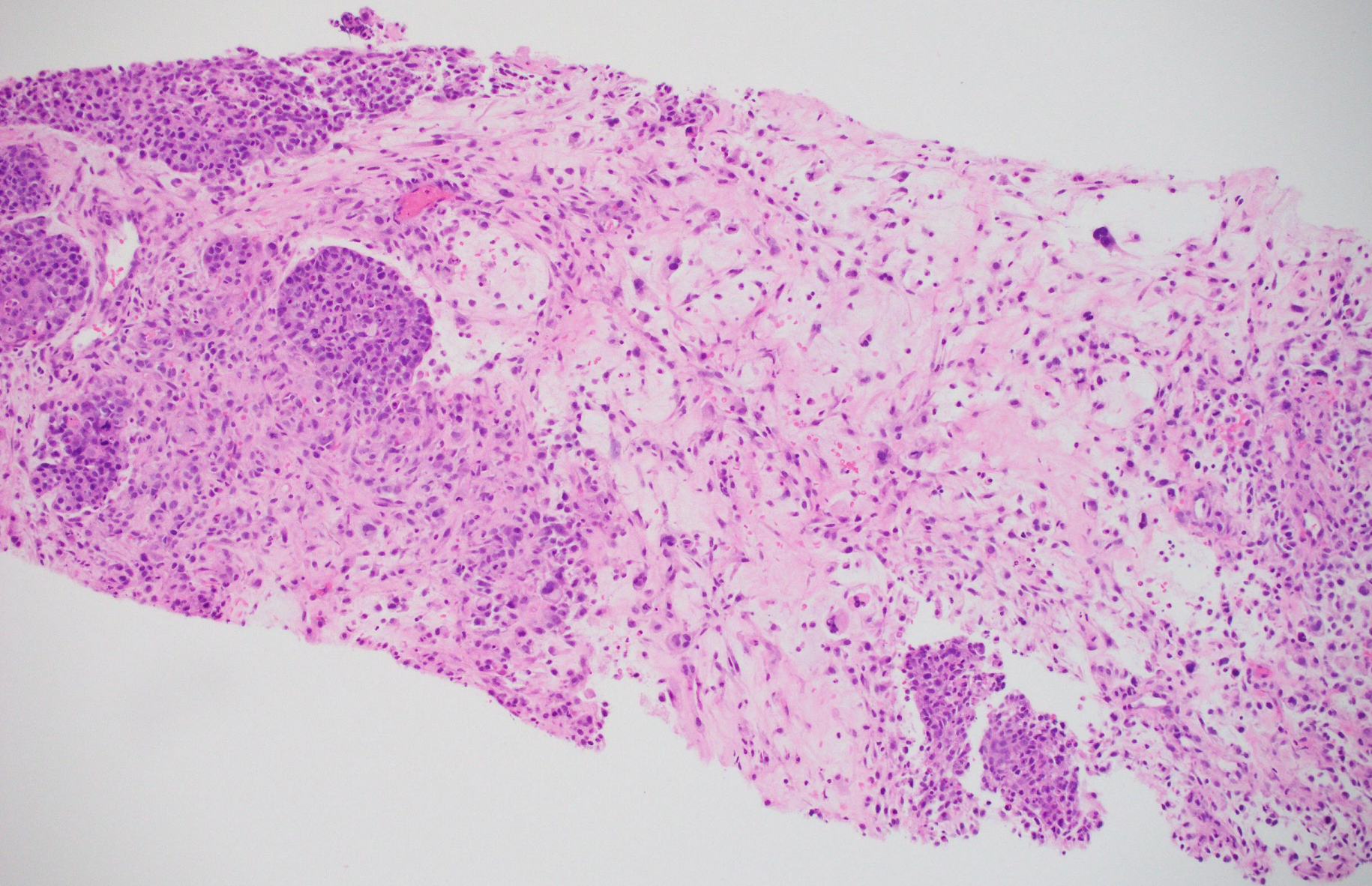
30F
Irregular Mass
1:00, Needle Core Biopsy



30F
Irregular Mass
1:00, Needle Core Biopsy



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Irregular Mass
1:00, Needle Core Biopsy



30F
Irregular Mass
1:00, Needle Core Biopsy

CAM5.2	AE1/3	K903 (HMWCK)	CK5/6	p63
H&E (biphasic)	ER	PR	HER2	
SMA	Desmin	CD34		

SMA positive in up to 2/3 of Metaplastic Breast Cancers

RIGHT BREAST, 1:00, CORE NEEDLE BIOPSY:

POORLY DIFFERENTIATED MALIGNANT BIPHASIC NEOPLASM, MOST CONSISTENT WITH METAPLASTIC CARCINOMA.

NO LYMPHOVASCULAR INVASION OR IN SITU CARCINOMA IDENTIFIED.

ANCILLARY STUDIES PERFORMED AT ARUP LABORATORIES WITH APPROPRIATELY REACTIVE CONTROLS DEMONSTRATE THE FOLLOWING STAINING PROFILE IN THE LESIONAL CELLS:

ESTROGEN RECEPTOR: NEGATIVE (0%)
PROGESTERONE RECEPTOR: NEGATIVE (0%)
HER2 (IHC): NEGATIVE (0)
HER2 (FISH): NEGATIVE

Tx: Neoadjuvant therapy with CPR

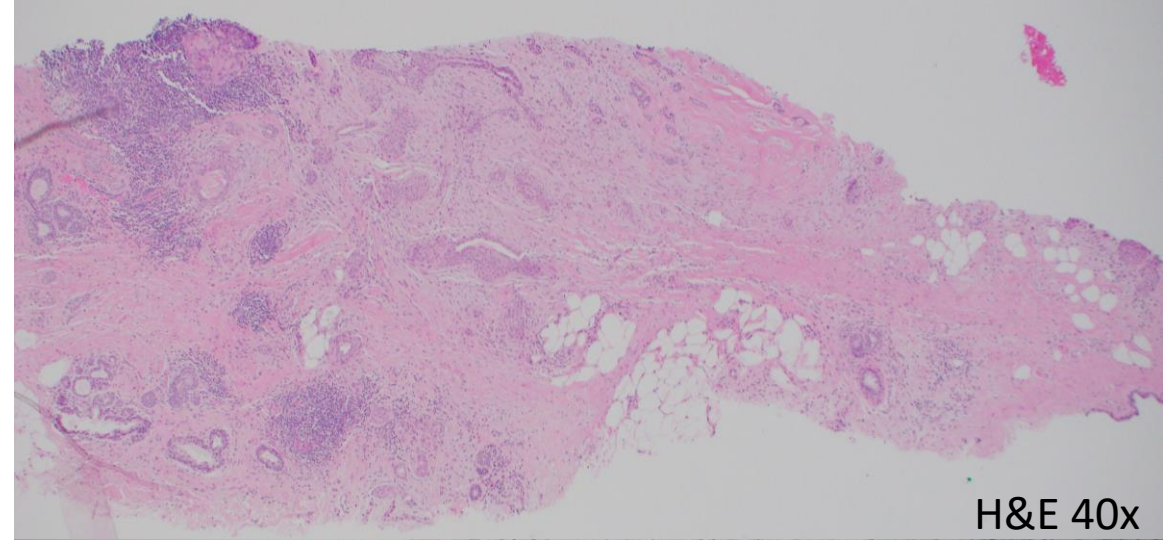
Metaplastic Carcinoma

- Highly diverse group of breast carcinomas that lack the classical adenocarcinoma appearance of breast cancer
 - Squamous
 - Adenosquamous (low grade)
 - Mesenchymal
 - Matrix producing
 - Spindled
- High in differential for ANY spindled breast lesion
- Keratins, Keratins, Keratins (x3) – at least one should be a particularly HMW CK (CK5/6, K903, etc.)
 - (P63)
 - 35-65% of MBC will express myoepithelial markers (p63, SMA, etc)
- Vast majority (>90%) Triple Negative
- Generally, very poor prognosis with some exceptions (LG Adenosquamous)

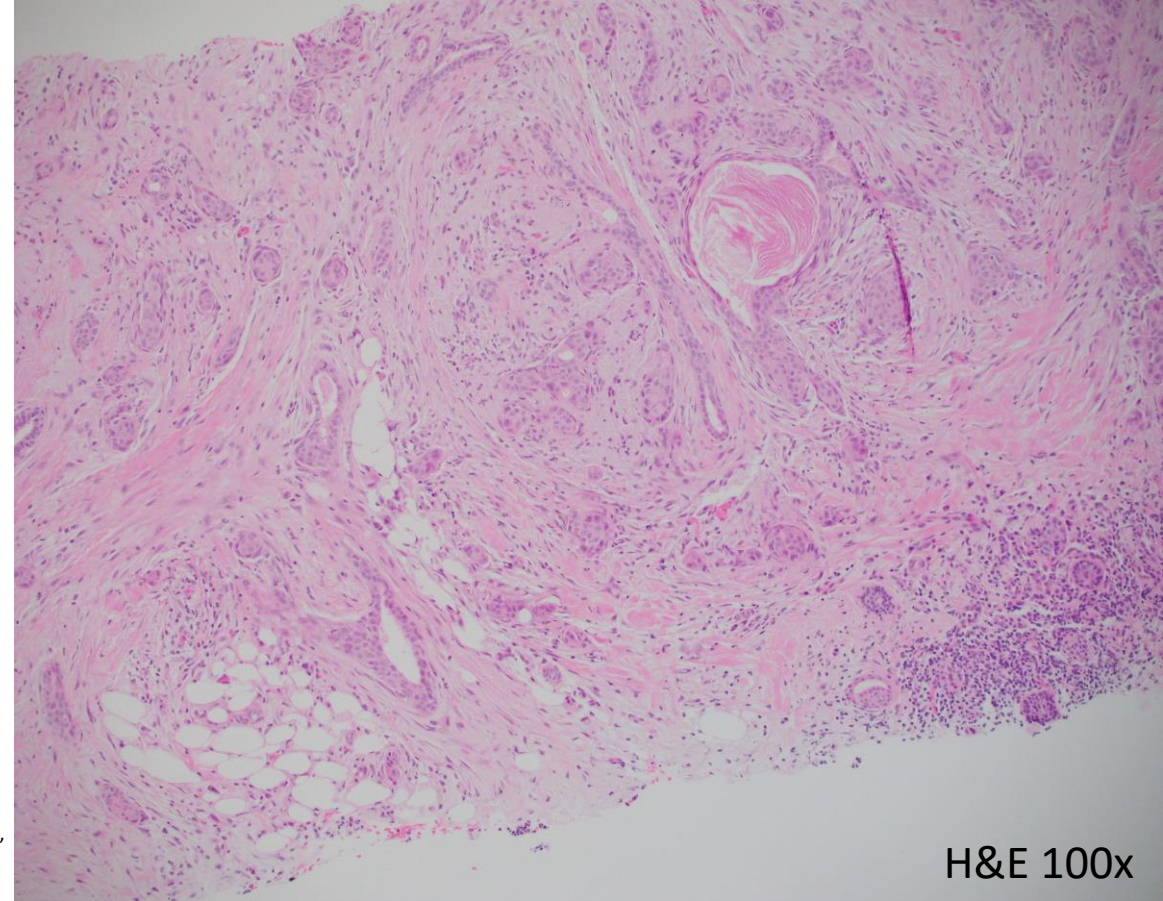
A Brief Diversion:

Low Grade Adenosquamous Carcinoma

- Well formed **glands** and **squamous nests** (+/- keratin)
- **Minimal atypia**, few if **ANY** mitoses
- Spindled component is typically not carcinomatous - but **reactive fibroblasts**
- **Smaller** (average 2.0 cm) and **slower growing** than typical MBC
- Predictably **unpredictable myoepithelial expression** (complicated by squamous profile CK5/6/p63)
- **Very favorable prognosis** from largest known cohort.
 - N=102 patients (follow-up ranging from 12 to 204 months.)
 - Local recurrence (10 cases, 10%)
 - Regional lymph node metastases (1 case, 1%)
 - Distant metastases (1 case, 1%)



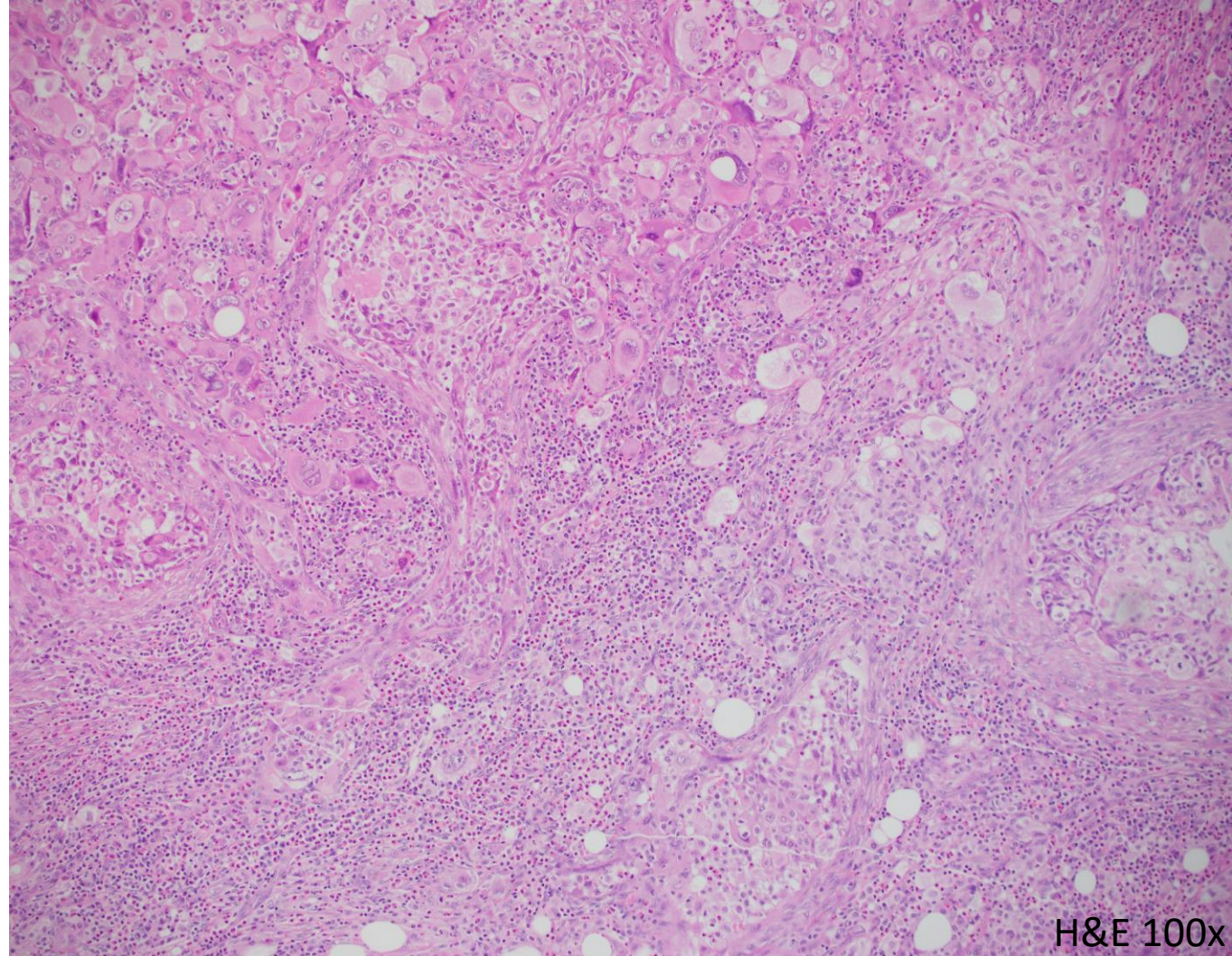
H&E 40x



H&E 100x

A Brief Diversion: Low Grade Adenosquamous Carcinoma

- Squamous differentiation alone **DOES NOT** automatically qualify for the low grade adenosquamous category.
- **MBC may frequently have some degree of HG squamous differentiation**
- **To be covered in detail in separate lecture**



H&E 100x

What if all of the keratins are negative? (and so is p63)

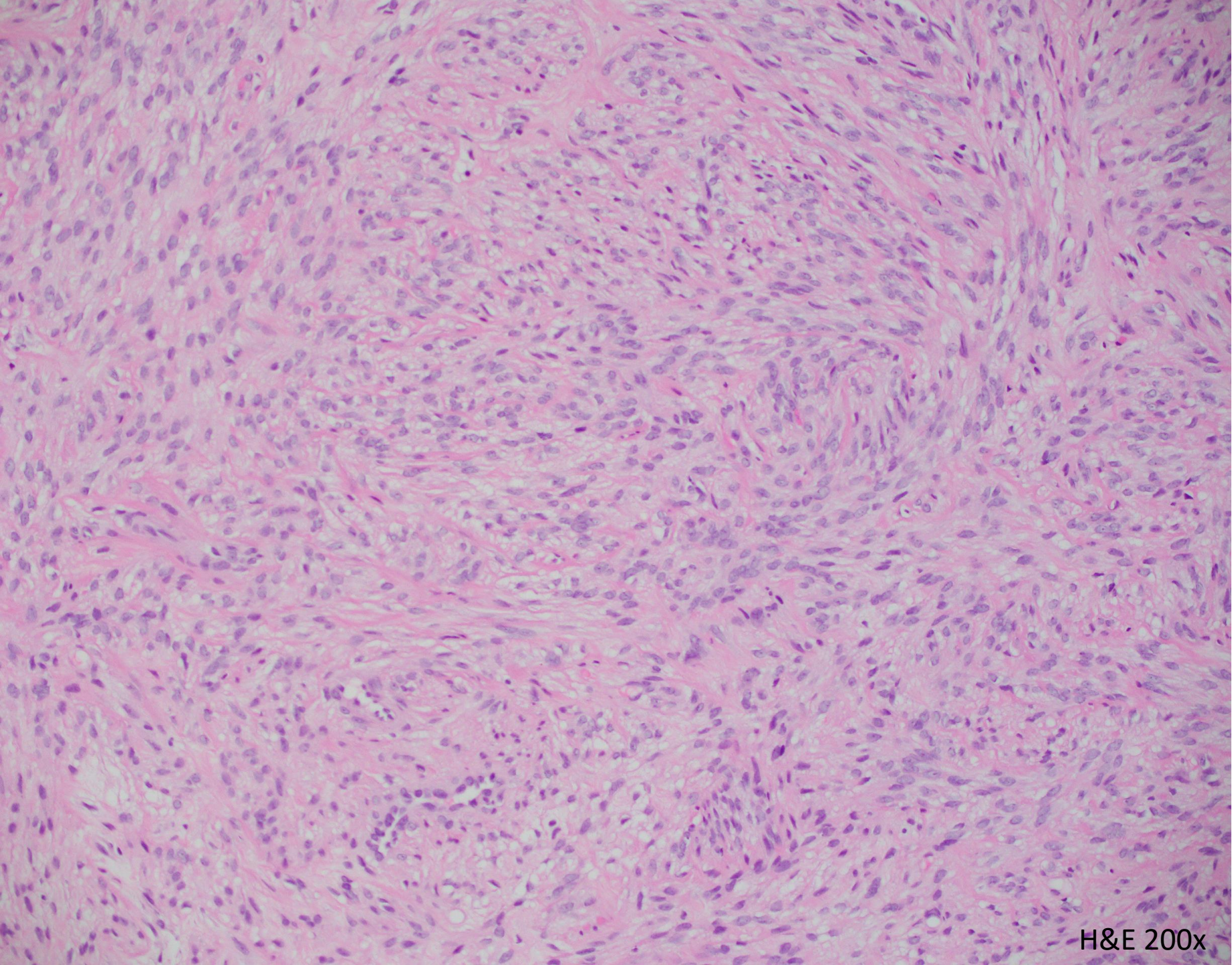
Diagnosis	Cytokeratins	p63	CD34	B-catenin (nuclear)	Malignant Mesenchymal Component
Metaplastic Carcinoma	Positive (possibly very focally)	Positive (possibly very focal)	Negative	20-30% Positive	Rare - possibly as part of biphasic tumor
Skin SCC	Positive	Positive	Negative	Negative	Absent
Phyllodes Tumor	Negative (rare)	Negative	Positive	Majority Positive (60-95%)	Possible / Expected
Fibromatosis	Negative	Negative	Negative	Majority Positive (>80%)	Absent
Nodular Fasciitis	Negative	Negative	Negative	Negative	Absent
Myofibroblastoma	Negative	Negative	Positive (90%)	Negative	Absent

**TURNING IS A
SIGN OF FEAR**
©LILAYEDMAN



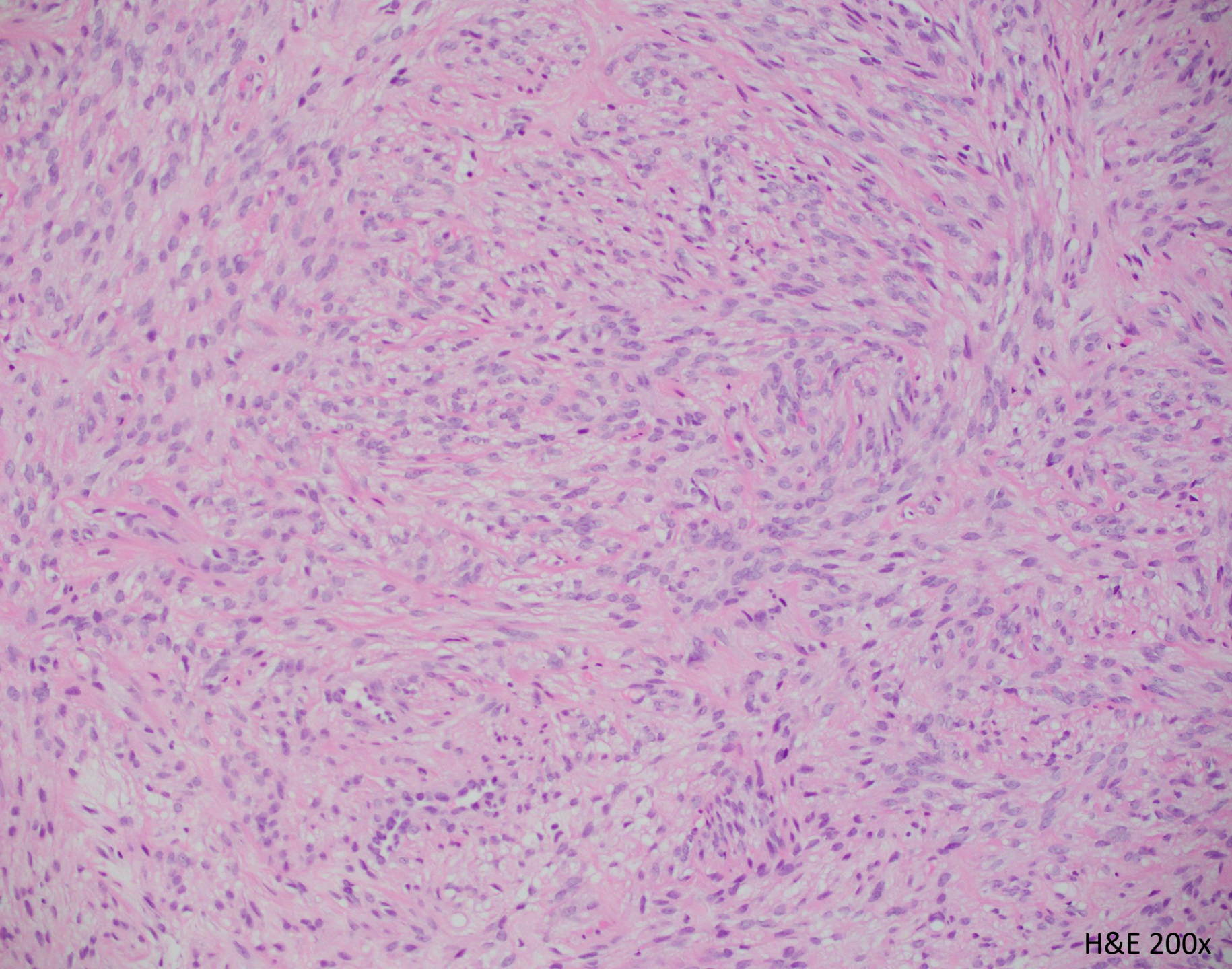


Case #2



60F, Breast Mass
Needle Core Biopsy

H&E 200x



60F, Breast Mass
Needle Core Biopsy

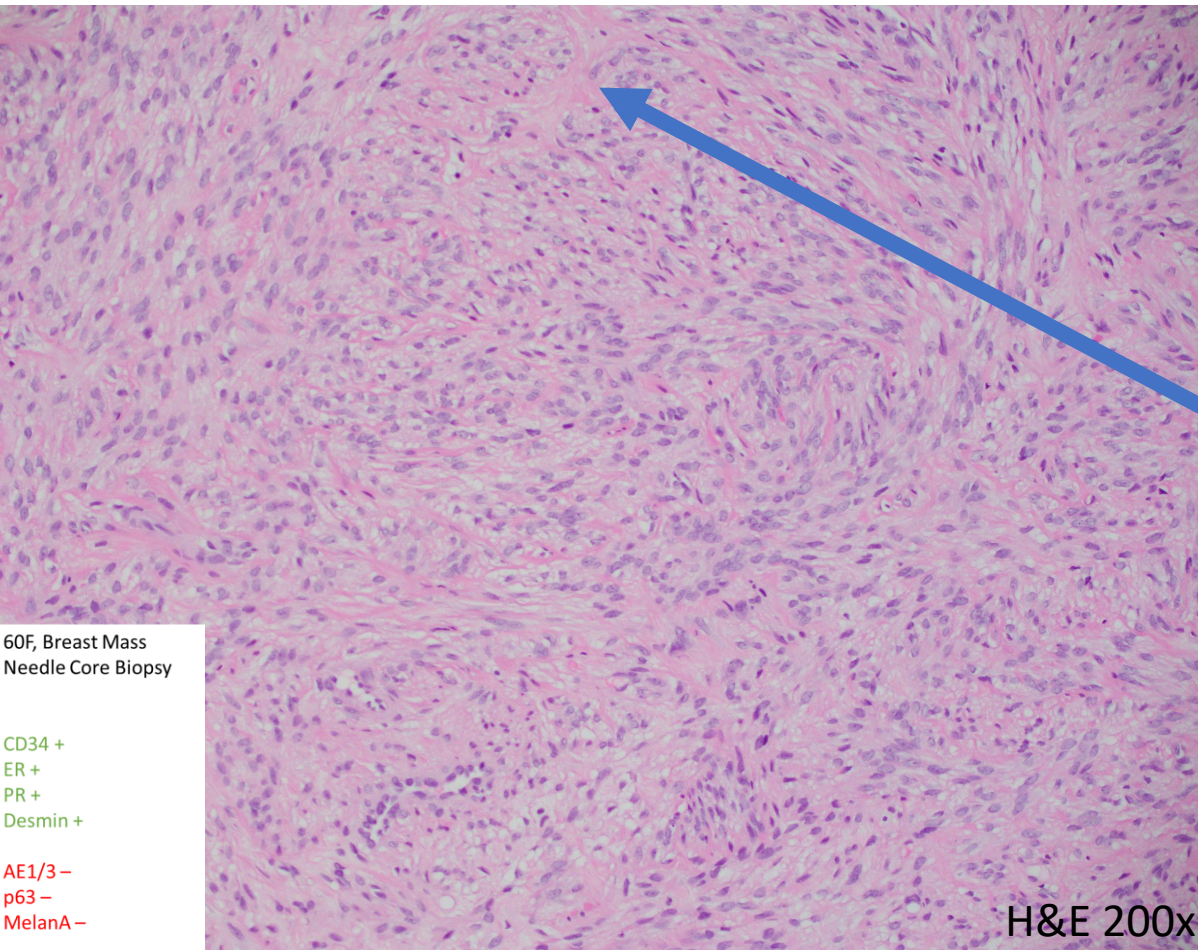
CD34 +
ER +
PR +
Desmin +

AE1/3 -
p63 -
MelanA -

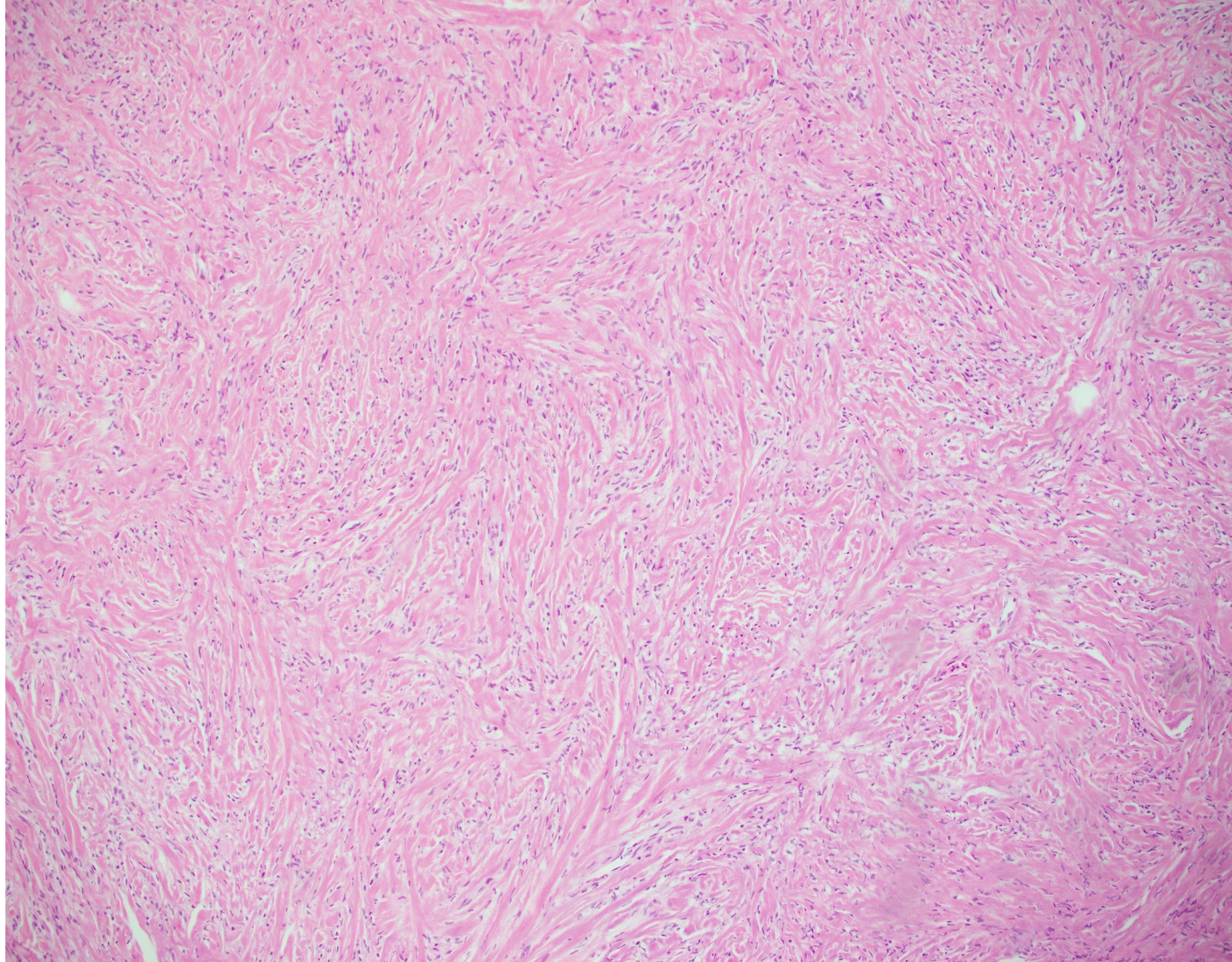
H&E 200x

(Mammary Type) Myofibroblastoma

- **Benign** - Uncommon (<1% of breast tumors)
- **Older Age Group** (peak = 50-75 yrs)
- Presents as **slow growing mass**
- **M=F Frequency** (Not historically)
- Closely related - morphologically and genetically - to spindle cell lipoma (**RB1 loss, 13q14**)
 - RB1 IHC (loss) can be confirmatory (if you have access)
 - We do not have access or order sendout RB1 IHC at ARUP
- Bland, monotonous spindle cell proliferation separated by variably **hyalinized collagen bundles**.
- Myofibroblastic IHC diff. with positive hormone receptors
- May occur in extramammary sites:
 - Back of neck, inguinal, genital, perianal
- Excised with complete excision with no recurrence or adjuvant therapy required.

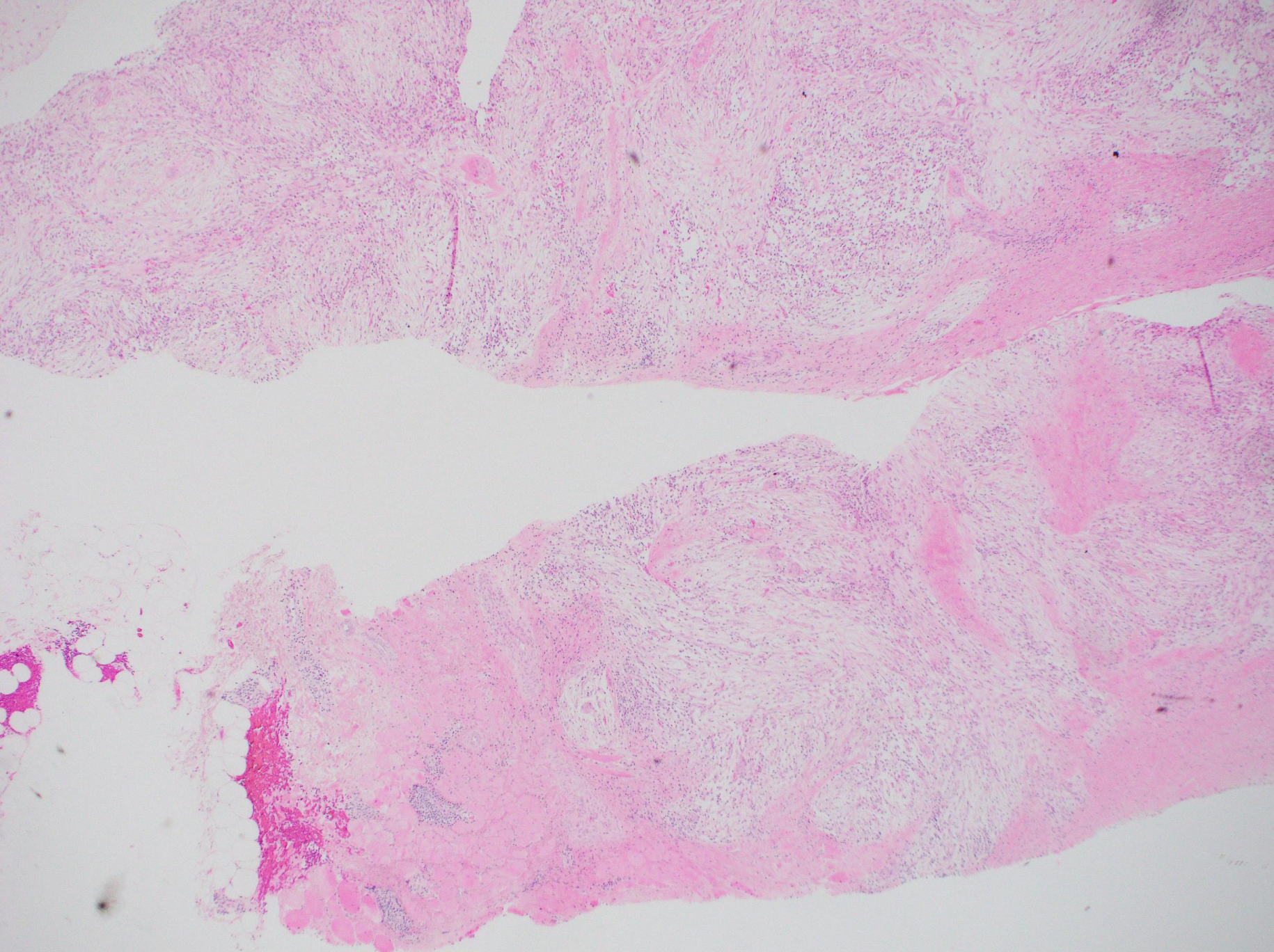


(Mammary Type) Myofibroblastoma



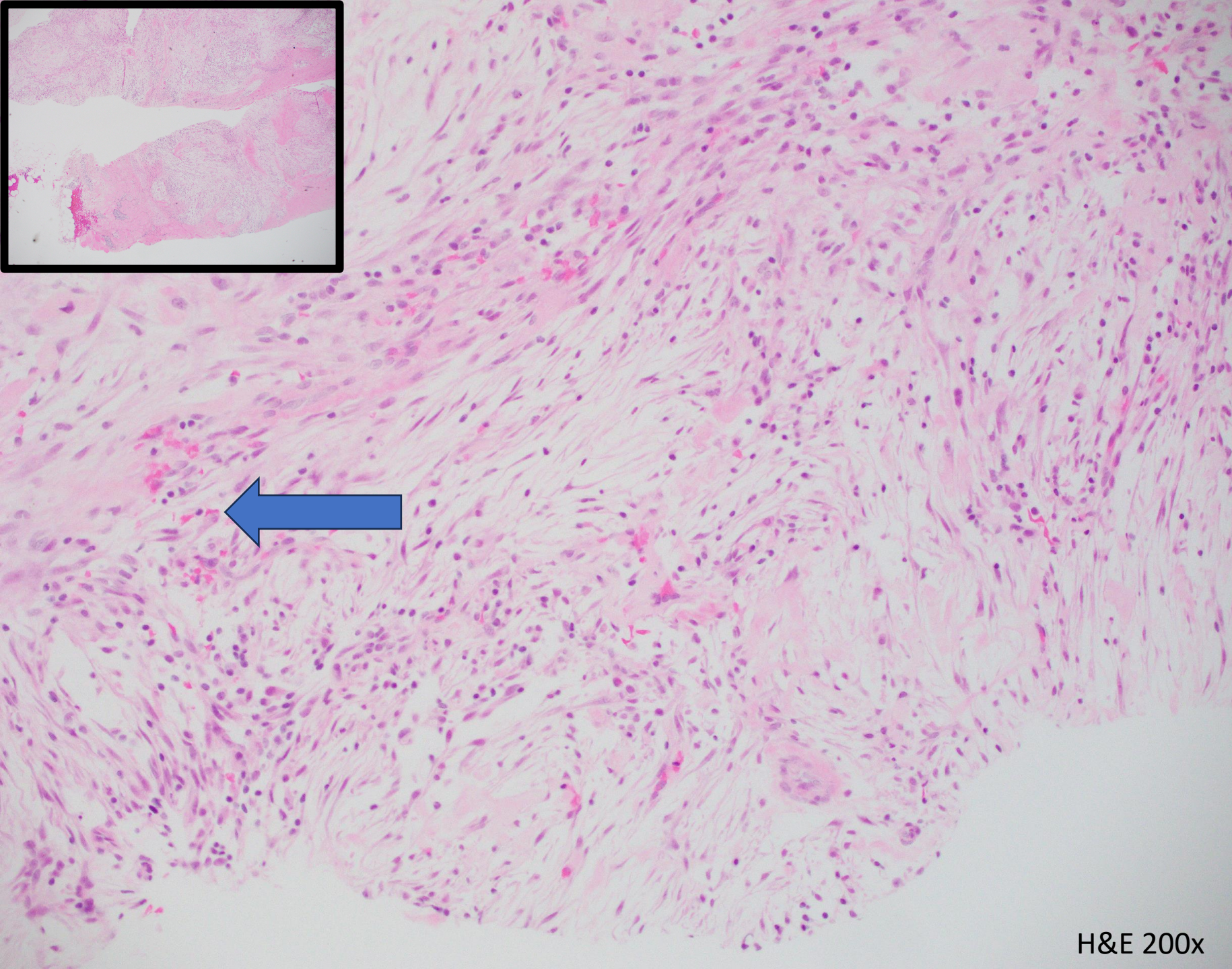
Case #3





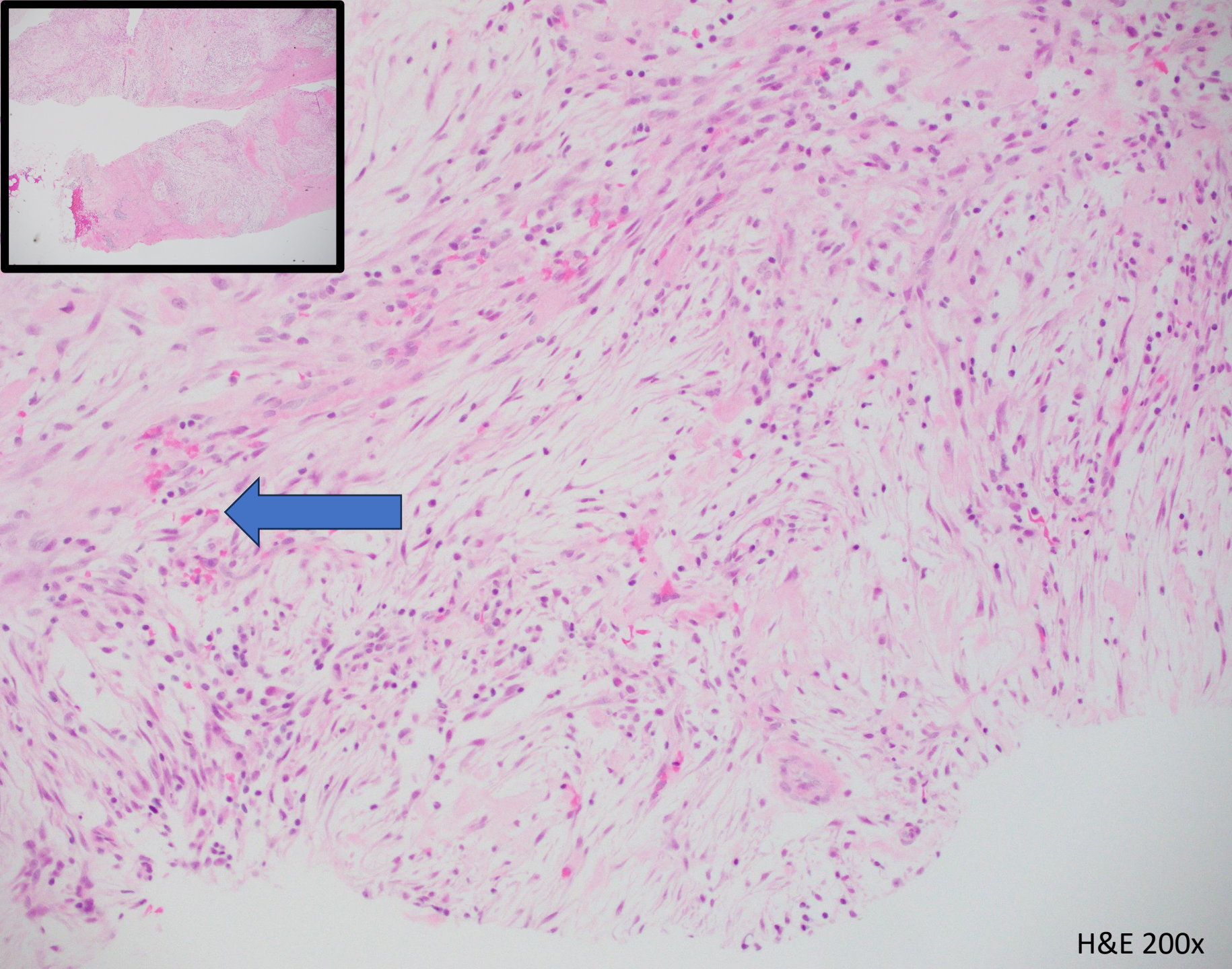
29F, Breast Mass,
Arising After Breast
Implant Surgery

H&E 40x



29F, Breast Mass,
Arising After Breast
Implant Surgery

H&E 200x



29F, Breast Mass,

Arising After Breast
Implant Surgery

SMA +

AE1/3 -

K903 -

P63 -

B-catenin - (no nuclear)

S100 -

CD34 -

Desmin -

ALK (d5f3) -

H&E 200x



Low Grade Spindle Cell Neoplasm, Favor Nodular Fasciitis

- Rapid growth (2-3 weeks)
- Tissue culture look varies significantly in older (more fibrotic lesions)
- No treatment necessary (spontaneous regression)
- USP6 overexpression (>90%), *USP6:MYH9*
- Diagnosis of exclusion of other more concerning or actionable entities.

29F, Breast Mass,

Arising After Breast
Implant Surgery

SMA +

AE1/3 -

K903 -

P63 -

B-catenin - (no nuclear)

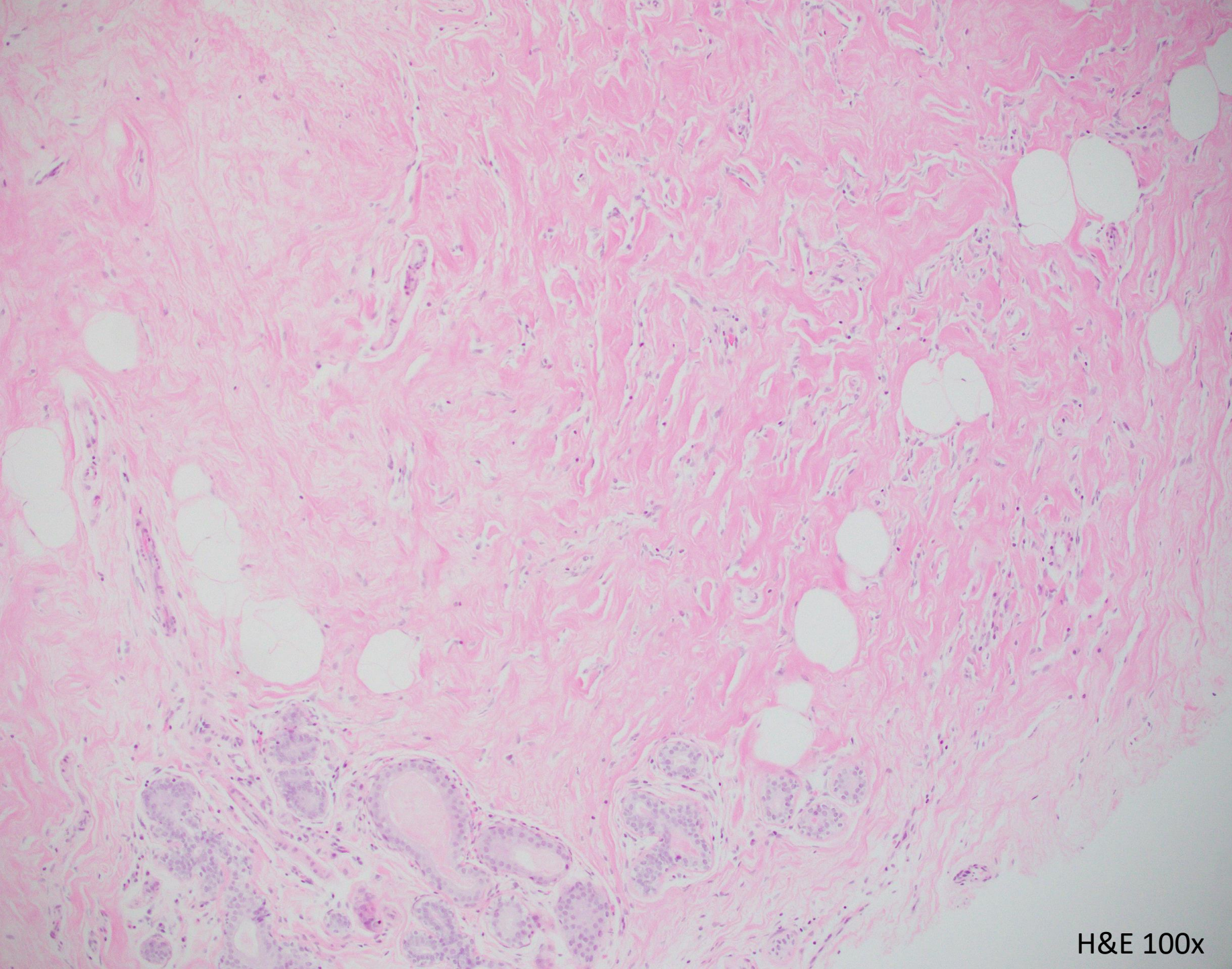
S100 -

CD34 -

Desmin -

ALK1 (d5f3) -

Case #4

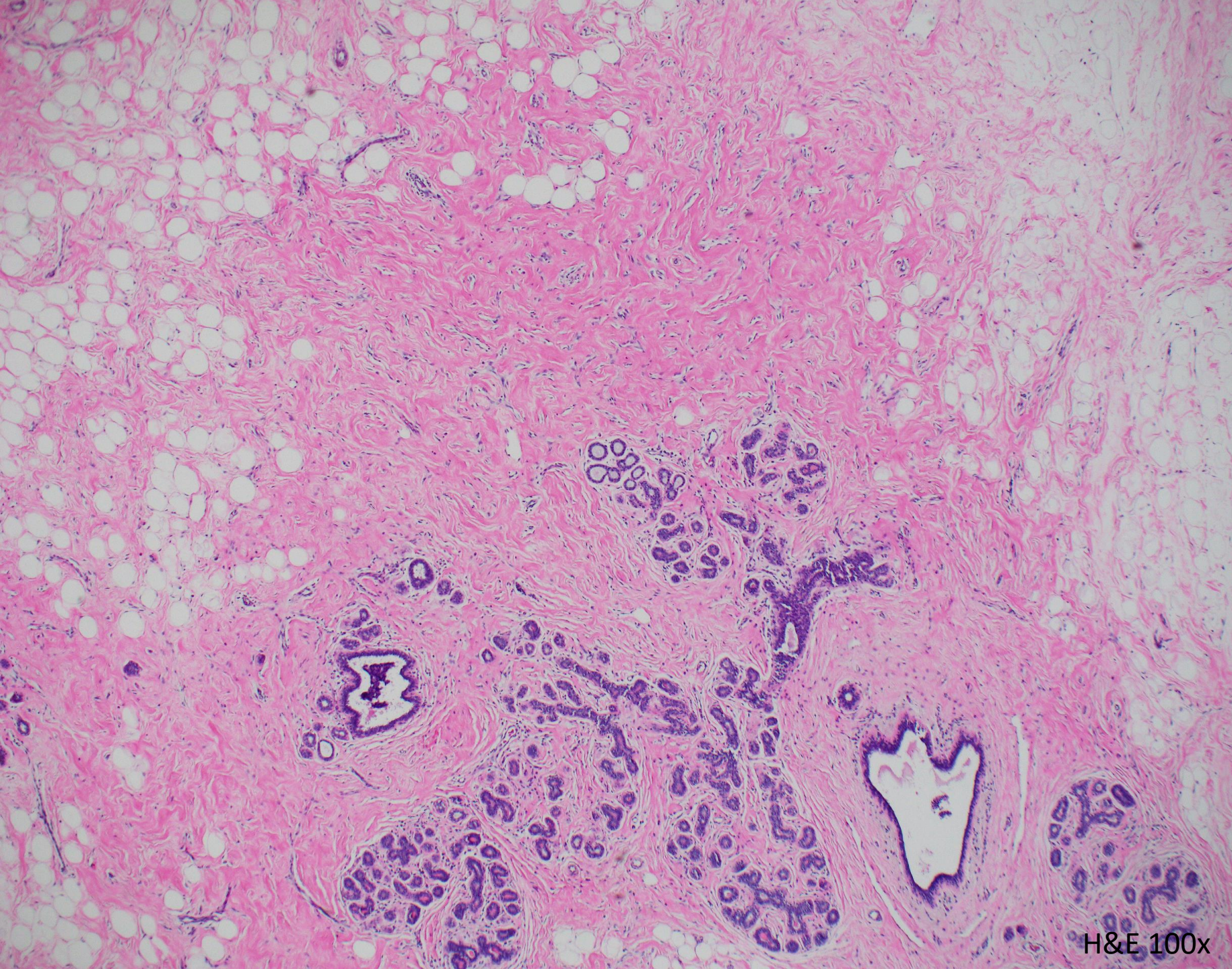


32F

STRONG family History
of breast cancer.

MRI Screening:
“Non-Mass
Enhancement”

H&E 100x

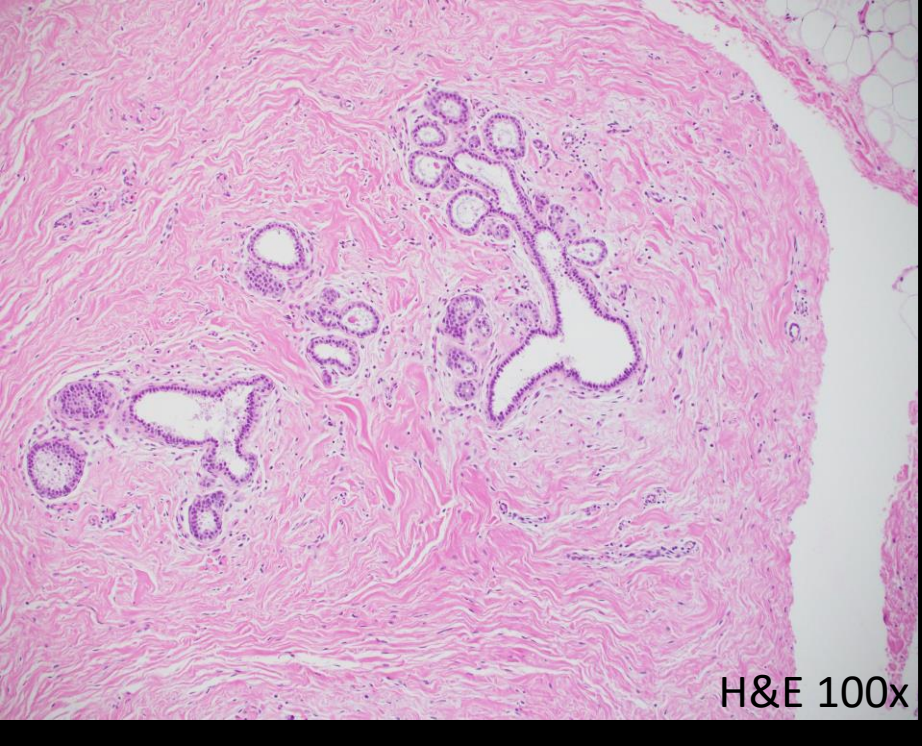


32F

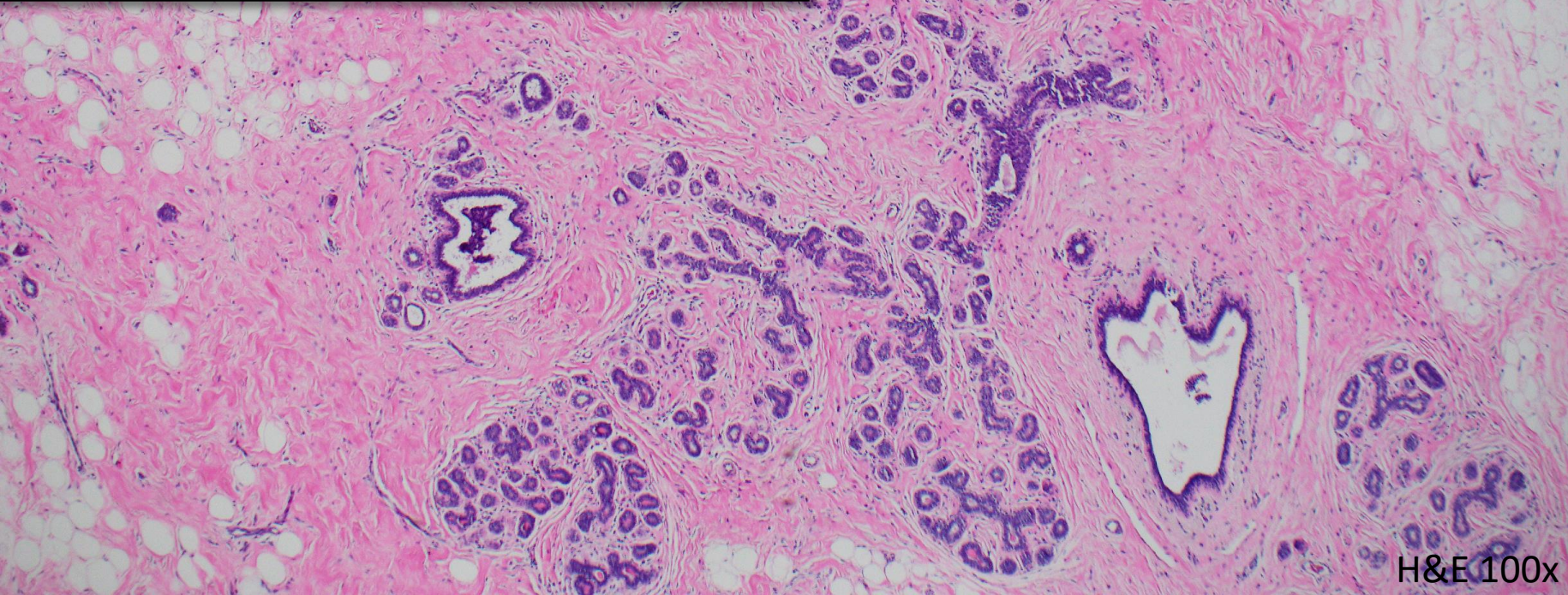
STRONG family History
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MRI Screening:
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Enhancement”

H&E 100x



H&E 100x



H&E 100x

32F

STRONG family History
of breast cancer.

MRI Screening:
“Non-Mass
Enhancement”

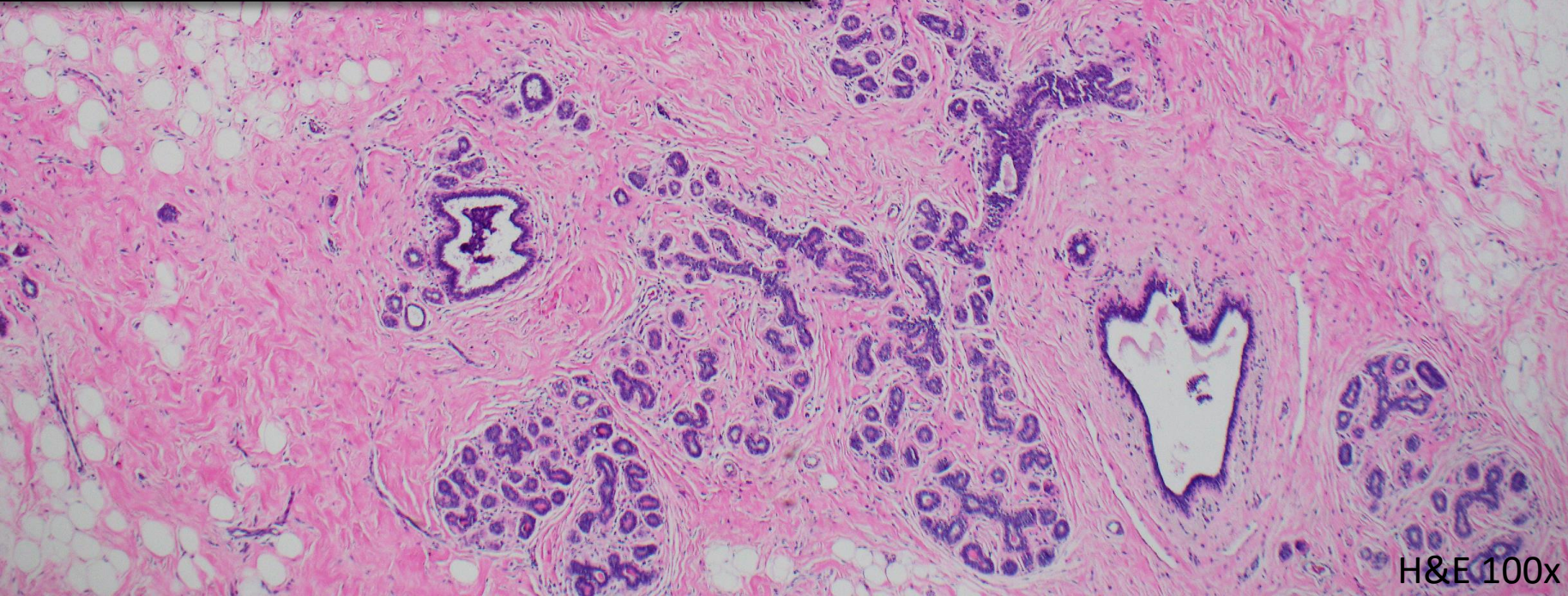
AE1/3 –

CD34 +

Pseudoangiomaticous stromal hyperplasia (PASH)



H&E 100x



H&E 100x

32F
(Typically pre-menopause)

STRONG family History of
breast cancer.
(No increased cancer risk -
Incidental finding – Pts
being screened early with
highly sensitive radiologic
techniques (MRI))

MRI Screening:
“Non-Mass Enhancement”

MRI: “Non-Mass Enhancement”

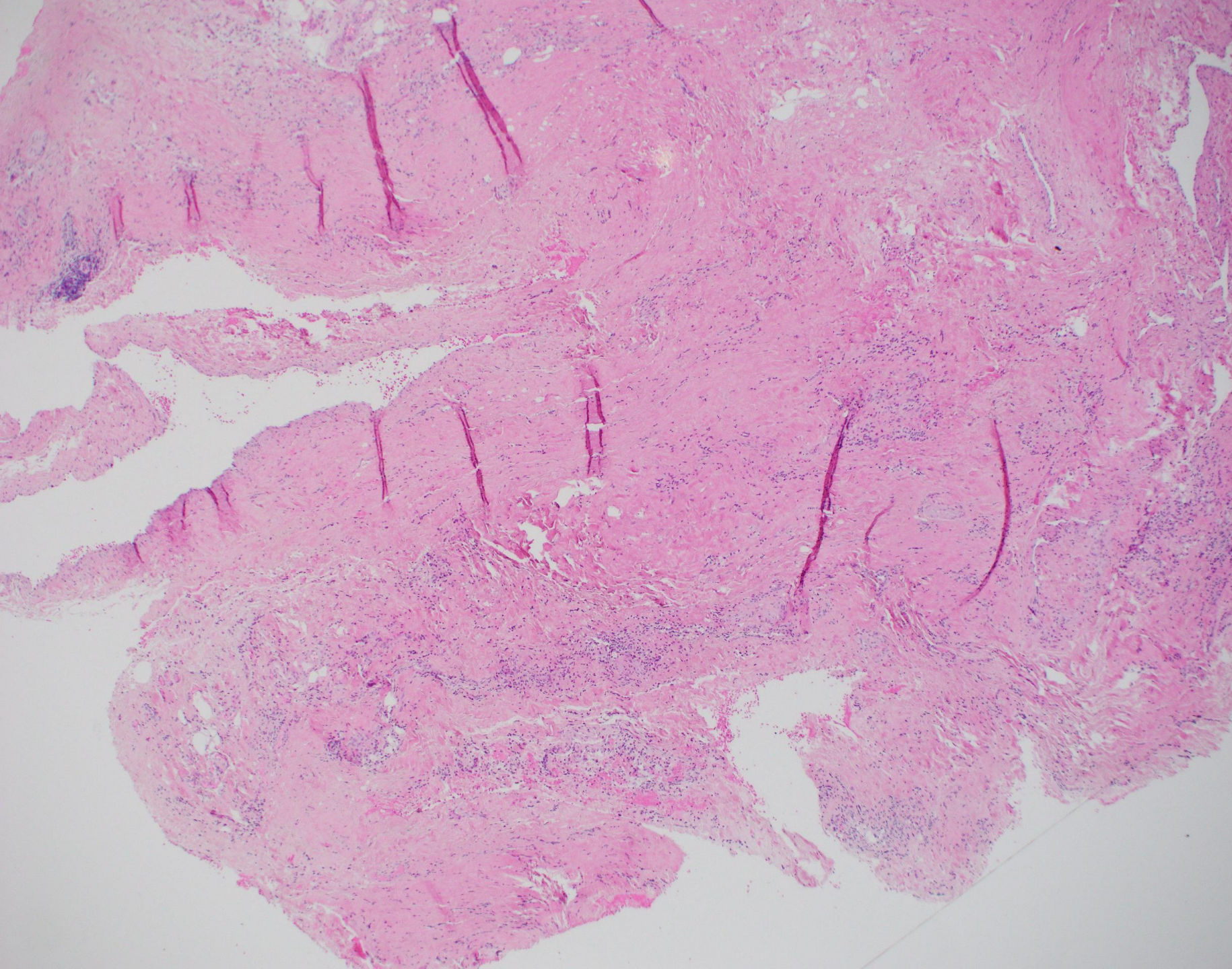
- Radiologic differential diagnosis:
 - PASH, apocrine metaplasia, intraductal papilloma, radiation effect
 - Flat epithelial atypia, intraductal papilloma, radiation effect, ADH, radial scar or complex sclerosing lesion
 - DCIS, IDC, and ILC
 - “When seen on MRI, biopsy most often is performed because there is substantial overlap in the imaging appearances among the varied benign and malignant causes.”
- Pathologic differential diagnosis:
 - PASH (and others).
 - 23% (35/149) of breast biopsies yielding PASH as the sole pathologic finding had no mammographic or USN finding on retrospective review of breast imaging within the prior year.

Chadashvili T, Ghosh E, Fein-Zachary V, Mehta TS, Venkataraman S, Dialani V, Slanetz PJ. Nonmass enhancement on breast MRI: review of patterns with radiologic-pathologic correlation and discussion of management. *AJR Am J Roentgenol*. 2015 Jan;204(1):219-27. doi: 10.2214/AJR.14.12656. PMID: 25539260.

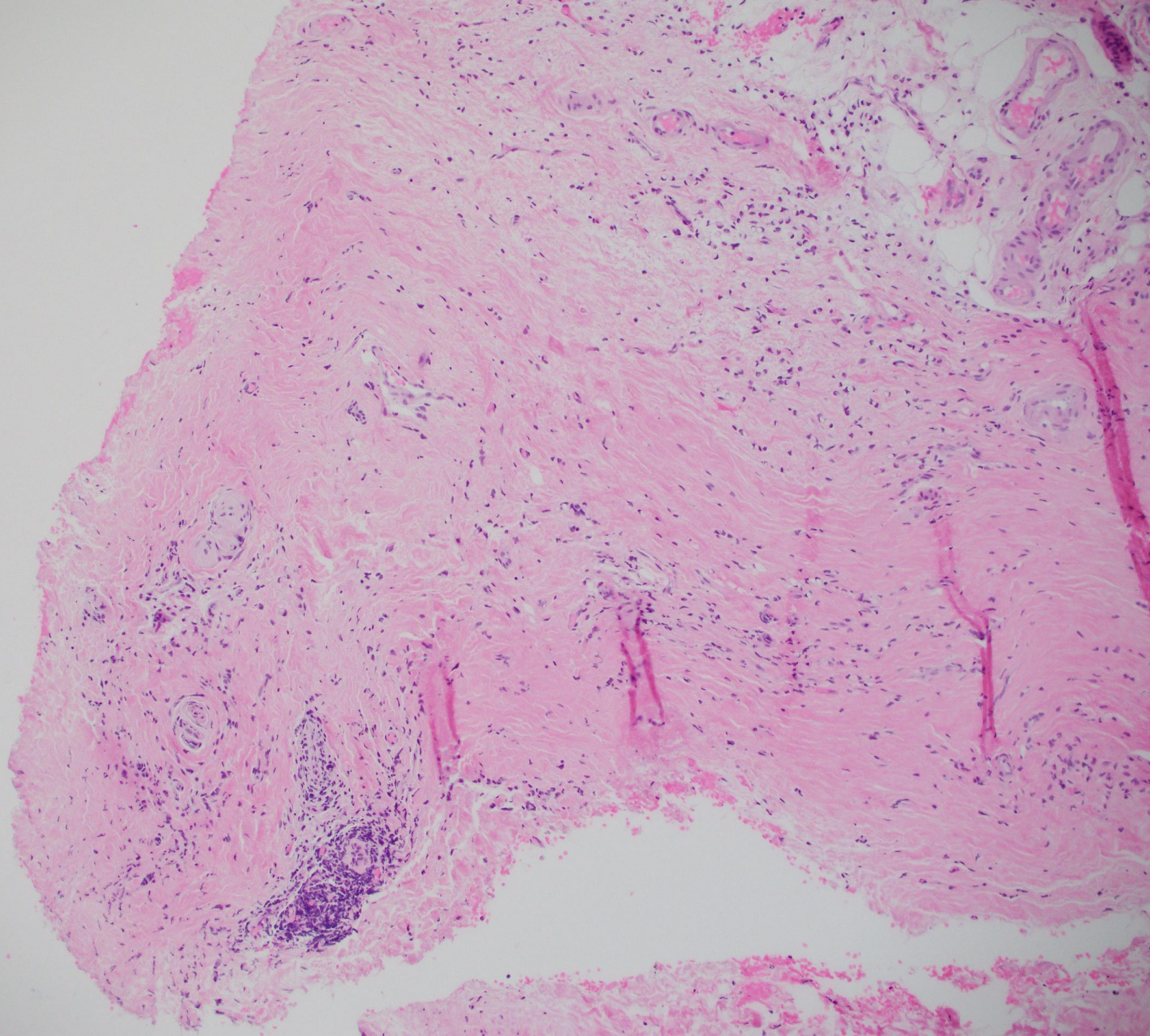
Hargaden GC, Yeh ED, Georgian-Smith D, et al. Analysis of the mammographic and sonographic features of pseudoangiomatous stromal hyperplasia. *AJR Am J Roentgenol* 2008;191(2):359-363.

Case #5

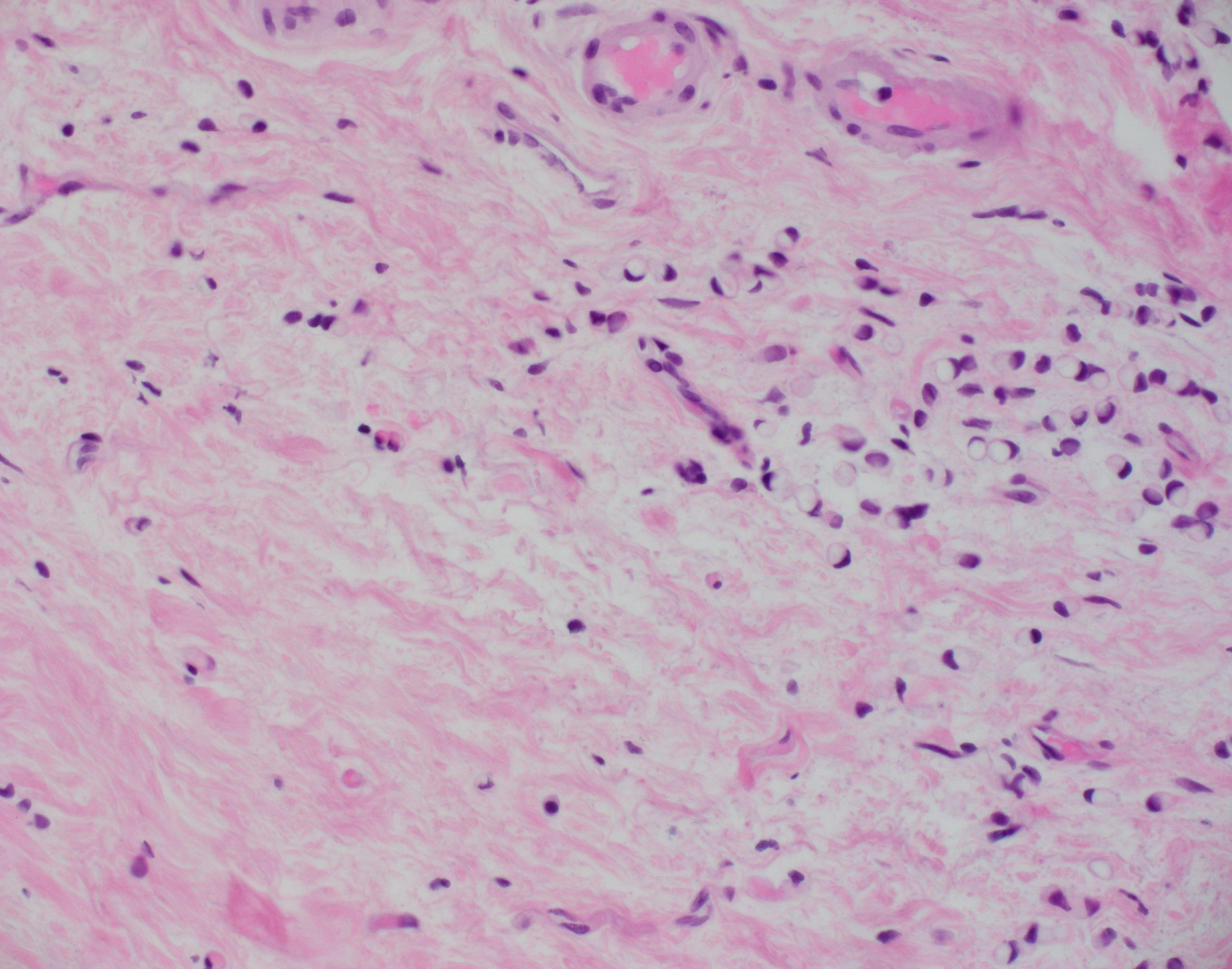




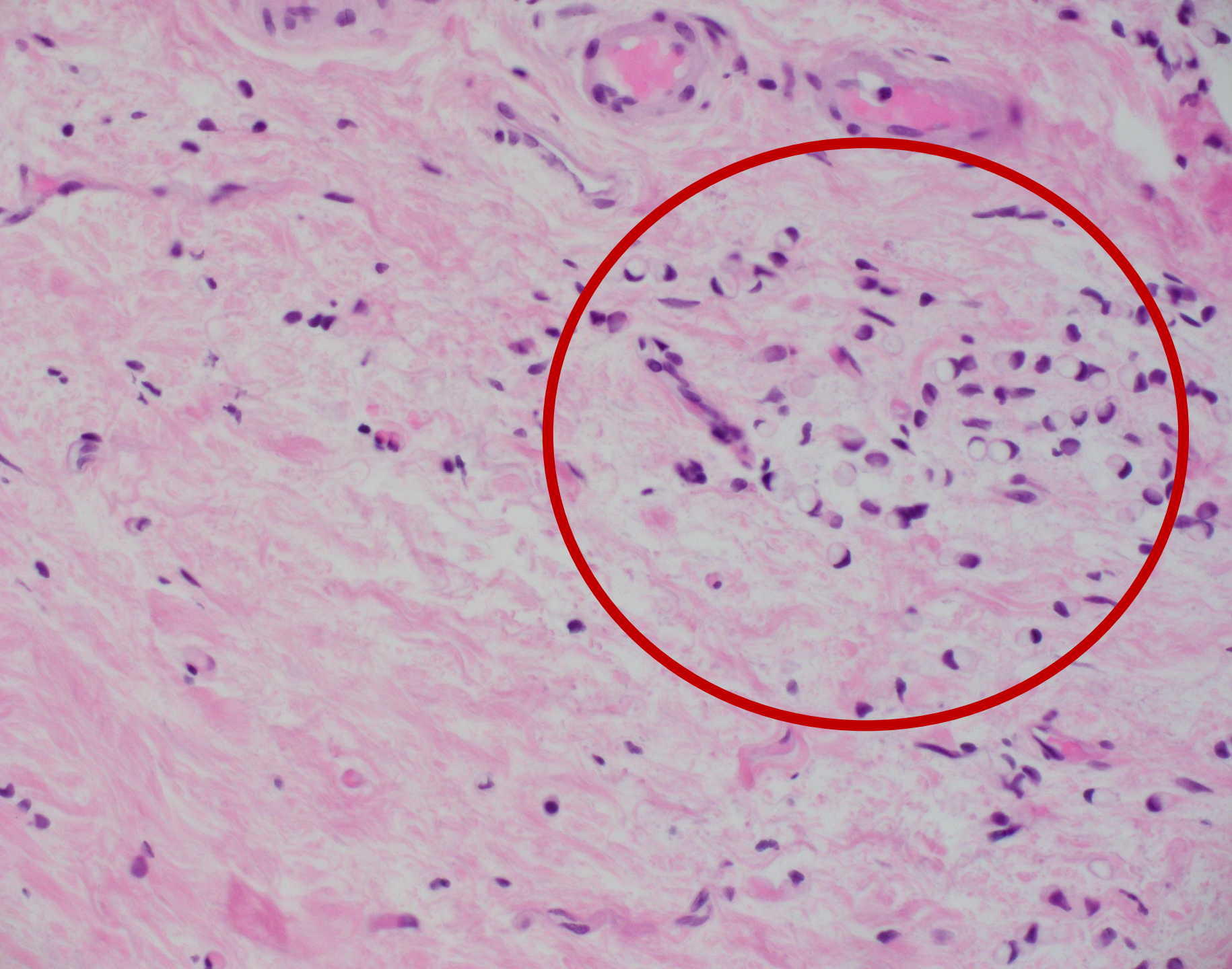
68F
Periocular Soft Tissue, Biopsy
H&E 40x



68F
Periocular Soft Tissue, Biopsy
H&E 100x



68F
Periocular Soft Tissue, Biopsy
H&E 100x



68F
Periocular Soft Tissue, Biopsy
H&E 100x

GATA3 +

ER +

PR +

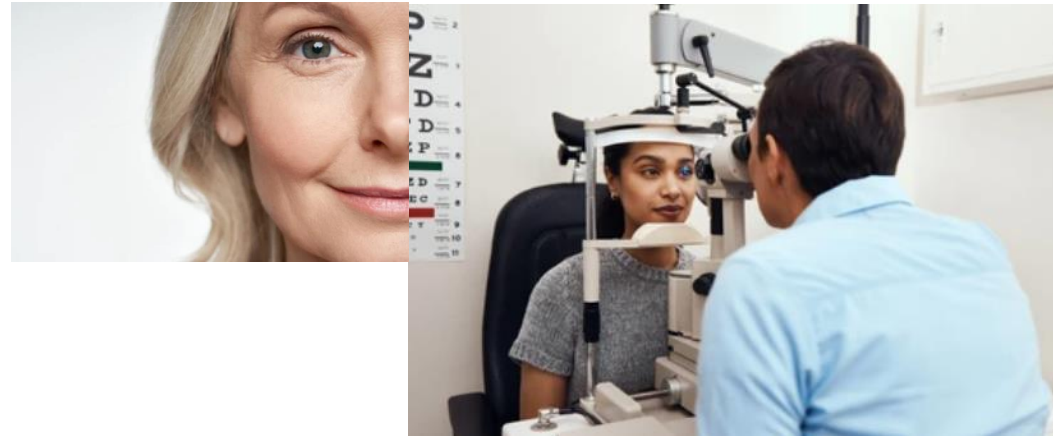
Her2 -

E-cadherin - Lost

Orbital/Ocular Breast Mets

- Breast cancer: The most common malignancy involving the eye/orbit. Depending on the series, breast cancers account for 29–53% of ocular metastasis.
- Still a rare presentation (case reports, meta analysis identified 94 published cases) – “Estimated at 1-2 cases / year at “larger institutions (Mayo)”

Number of cases	94 (100%)
Age	
- Median	56
- Range	(33–76)
Histopathology	
- IDC ^a	51 (54.3%)
- ILC ^b	28 (29.8%)
- Rare histology	11 (11.7%)
- Unknown	4 (4.2%)
Immunohistochemical subtype	
- Hormonal receptors positive	75 (80%)
- HER2 neu enriched	9 (1%)
- Triple negative	19 (2%)
- Not identified	16 (17%)



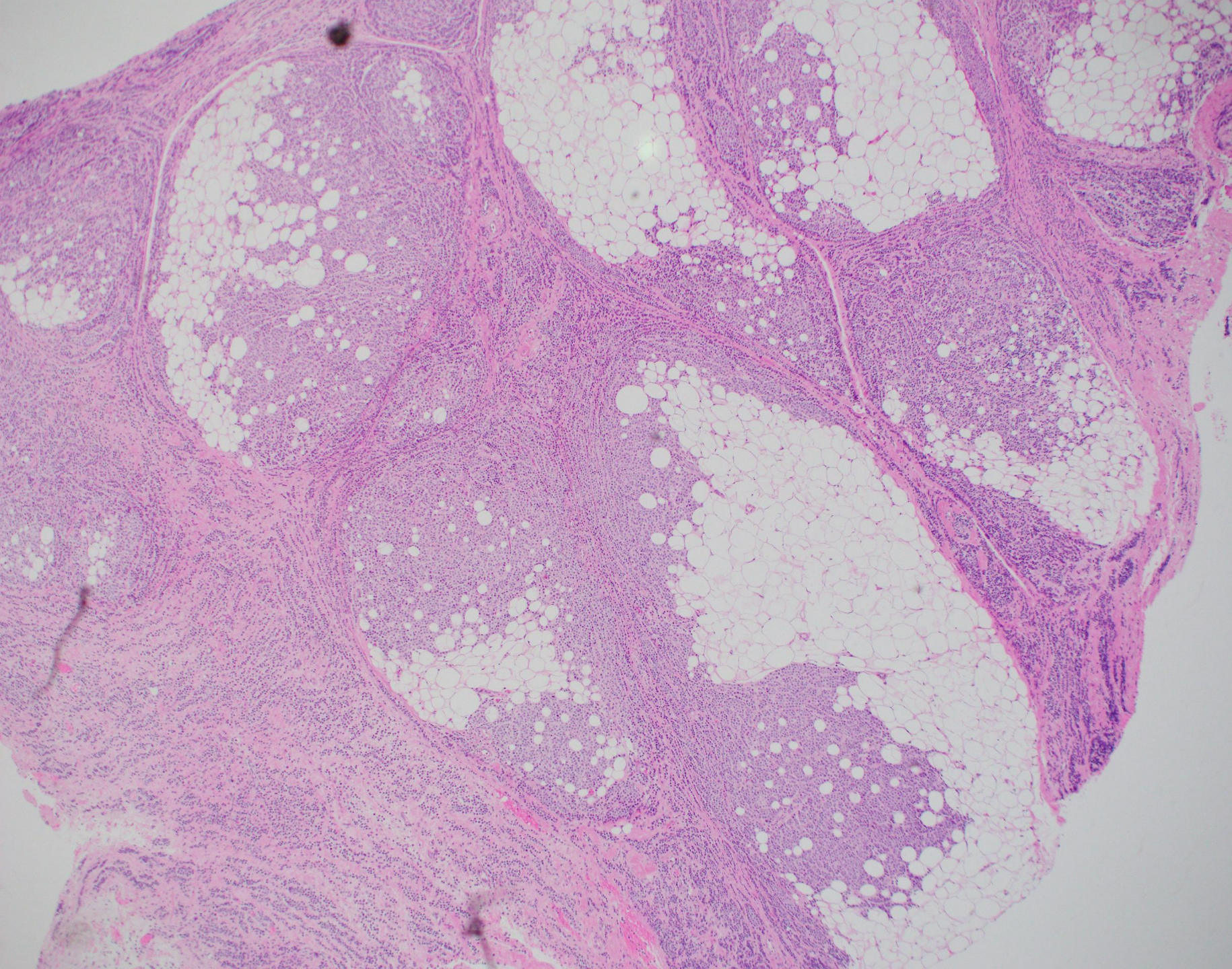
Valenzuela AA, Archibald CW, Fleming B, Ong L, O'Donnell B, Crompton JJ, et al. Orbital metastasis: clinical features, management and outcome. *Orbit*. 2009;28:153–159.

Henderson JW, Campbell RJ, Farrow GM. *Metastatic carcinomas orbital tumors*. 3rd ed. New York, NY: Raven Press; 1994. pp. 361–376.

Shields JA, Shields CL, Brotman HK, Carvalho C, Perez N, Eagle RC., Jr Cancer metastatic to the orbit: the 2000 Robert M. Curts Lecture. *Ophthalmol. Plast. Reconstr. Surg*. 2001;17:346–354.

Saad ESP, Bakri HM, Rayan A, Barakat D, Khalel MM. Eye metastasis in breast cancer: case report and review of literature. *Ecancelmedicalscience*. 2022 Feb 10;16:1353. doi: 10.3332/ecancer.2022.1353. PMID: 35510138; PMCID: PMC9023307.

Raap M, Antonopoulos W, Dämmrich M, Christgen H, Steinmann D, Länger F, Lehmann U, Kreipe H, Christgen M. High frequency of lobular breast cancer in distant metastases to the orbit. *Cancer Med*. 2015 Jan;4(1):104-11. doi: 10.1002/cam4.331. Epub 2014 Oct 30. PMID: 25355547; PMCID: PMC4312124.

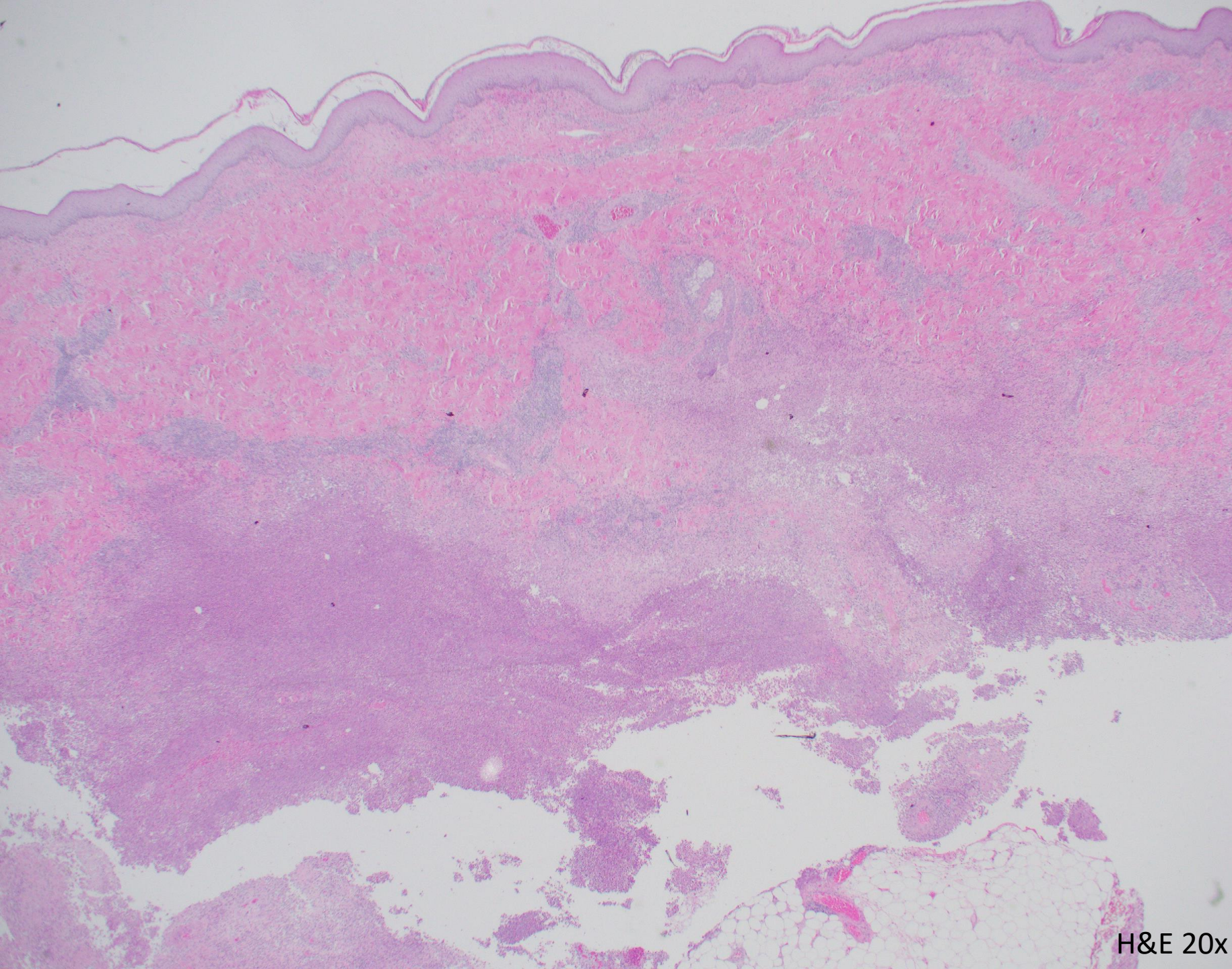


71F

Requisition: "Metastatic
Lobular Breast Cancer"

- 85% Ocular Mets have known history of breast cancer
- Cream colored retinal plaque
- If vision threatened: Radiation therapy – maintain good vision
- Endocrine therapy - hormone receptor positive

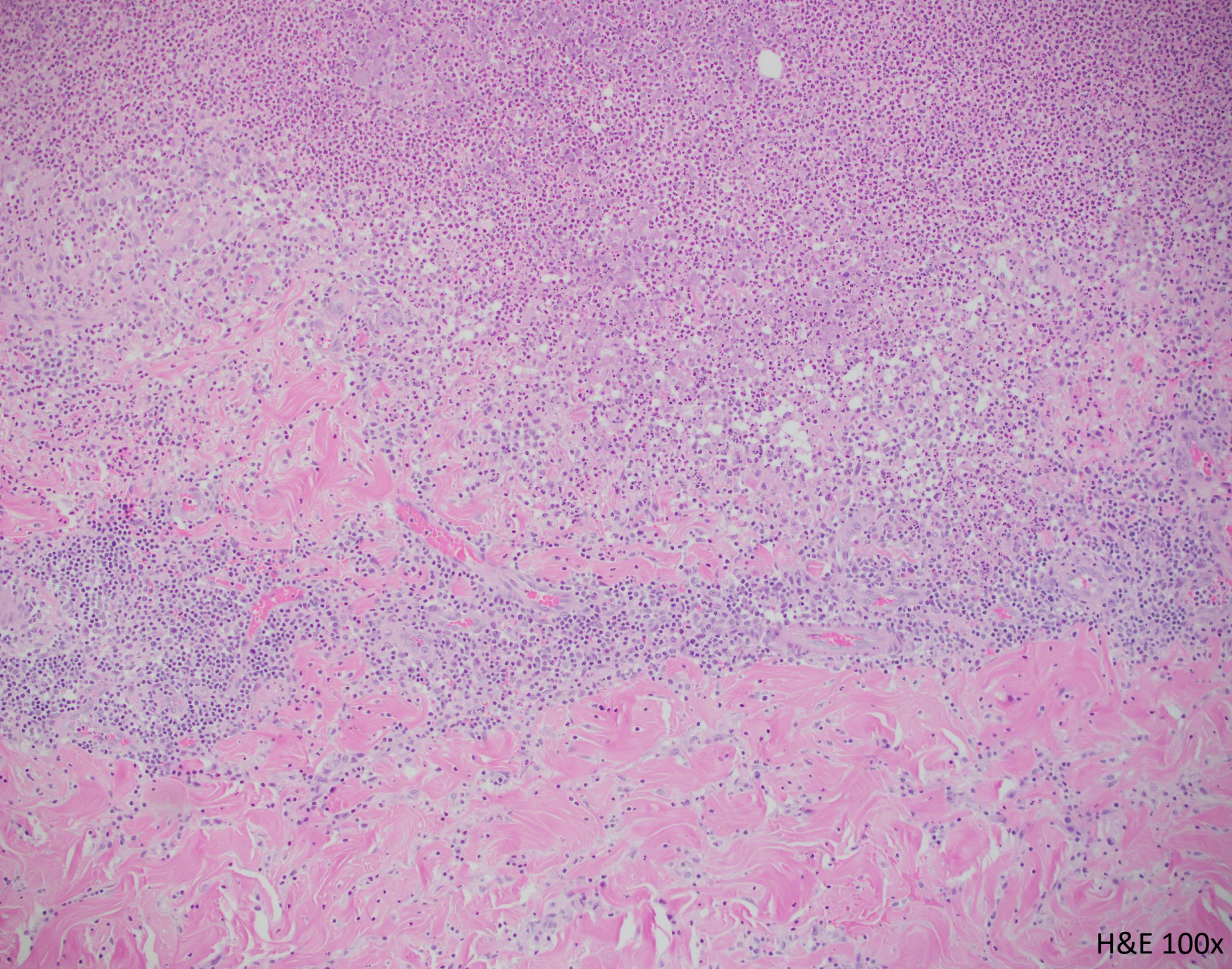
Case #6



27F, Excision

Three-year
history of breast
abscess

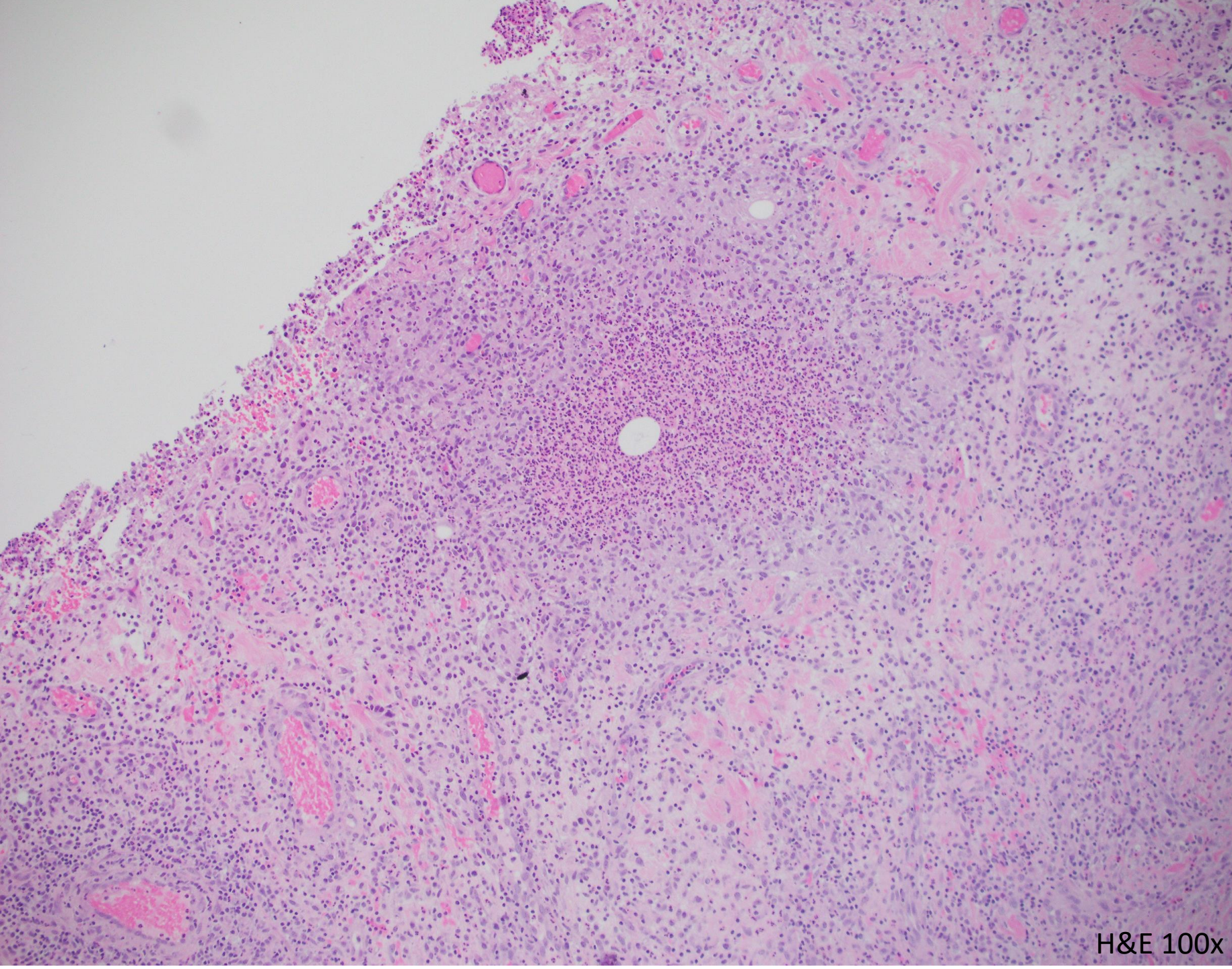
H&E 20x



27F, Excision

Three-year
history of breast
abscess

H&E 100x

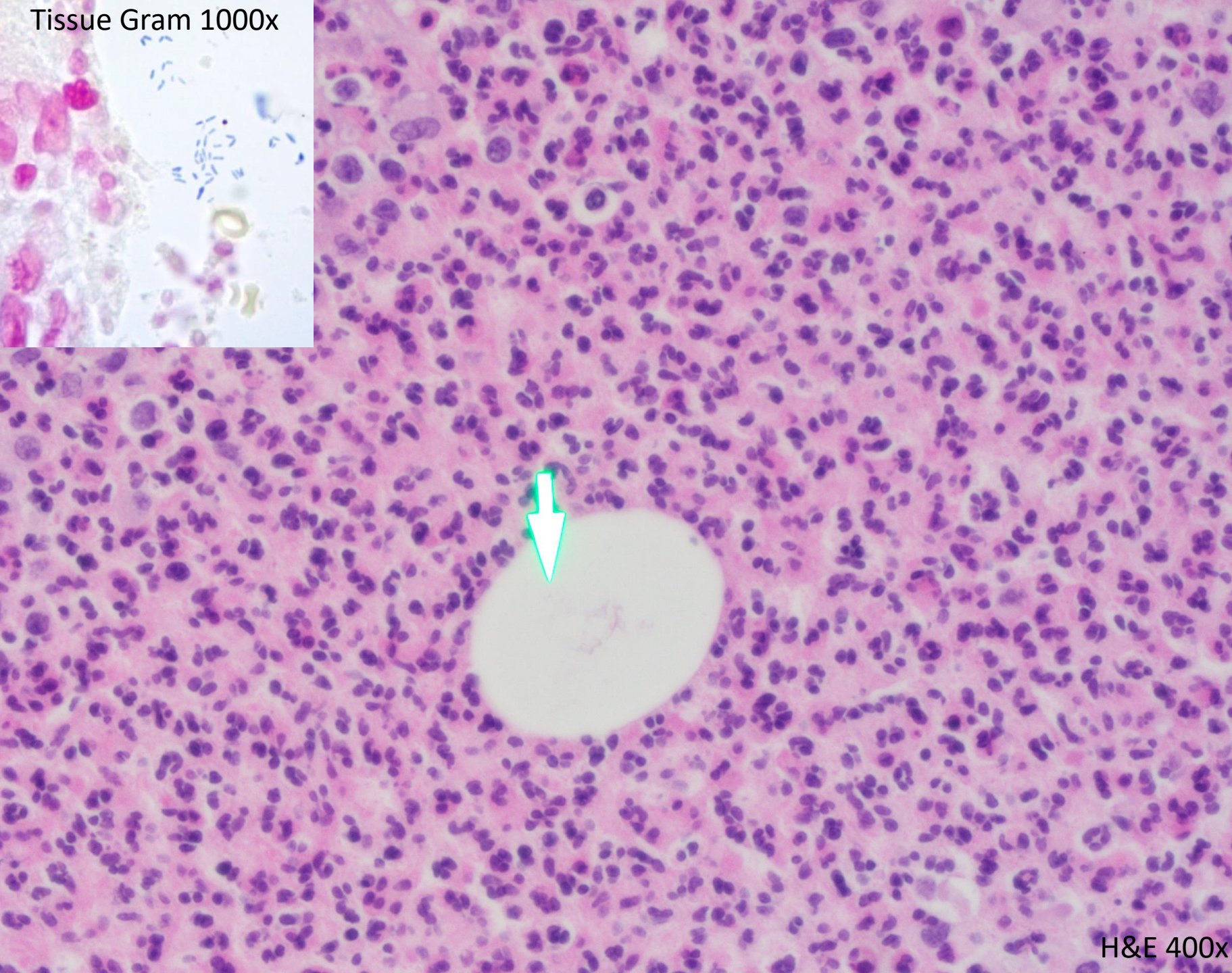


27F, Excision

Three-year
history of breast
abscess

H&E 100x

Tissue Gram 1000x



27F, Excision

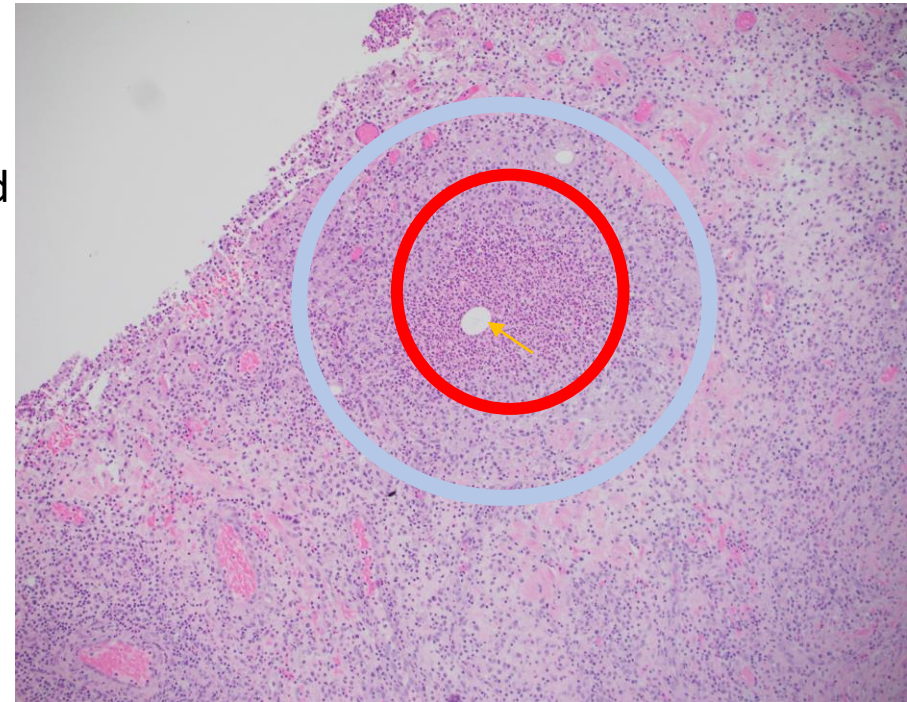
Three-year
history of breast
abscess

H&E 400x

1000x Oil Image From:
Gautham I, Radford DM, Kovacs CS, Calhoun BC, Procop GW,
Shepardson LB, Dawson AE, Downs-Kelly EP, Zhang GX, Al-Hilli Z,
Fanning AA, Wilson DA, Sturgis CD. Cystic neutrophilic
granulomatous mastitis: The Cleveland Clinic experience with
diagnosis and management. Breast J. 2019 Jan;25(1):80-85. doi:
10.1111/tbj.13160. Epub 2018 Nov 17. PMID: 30449049.

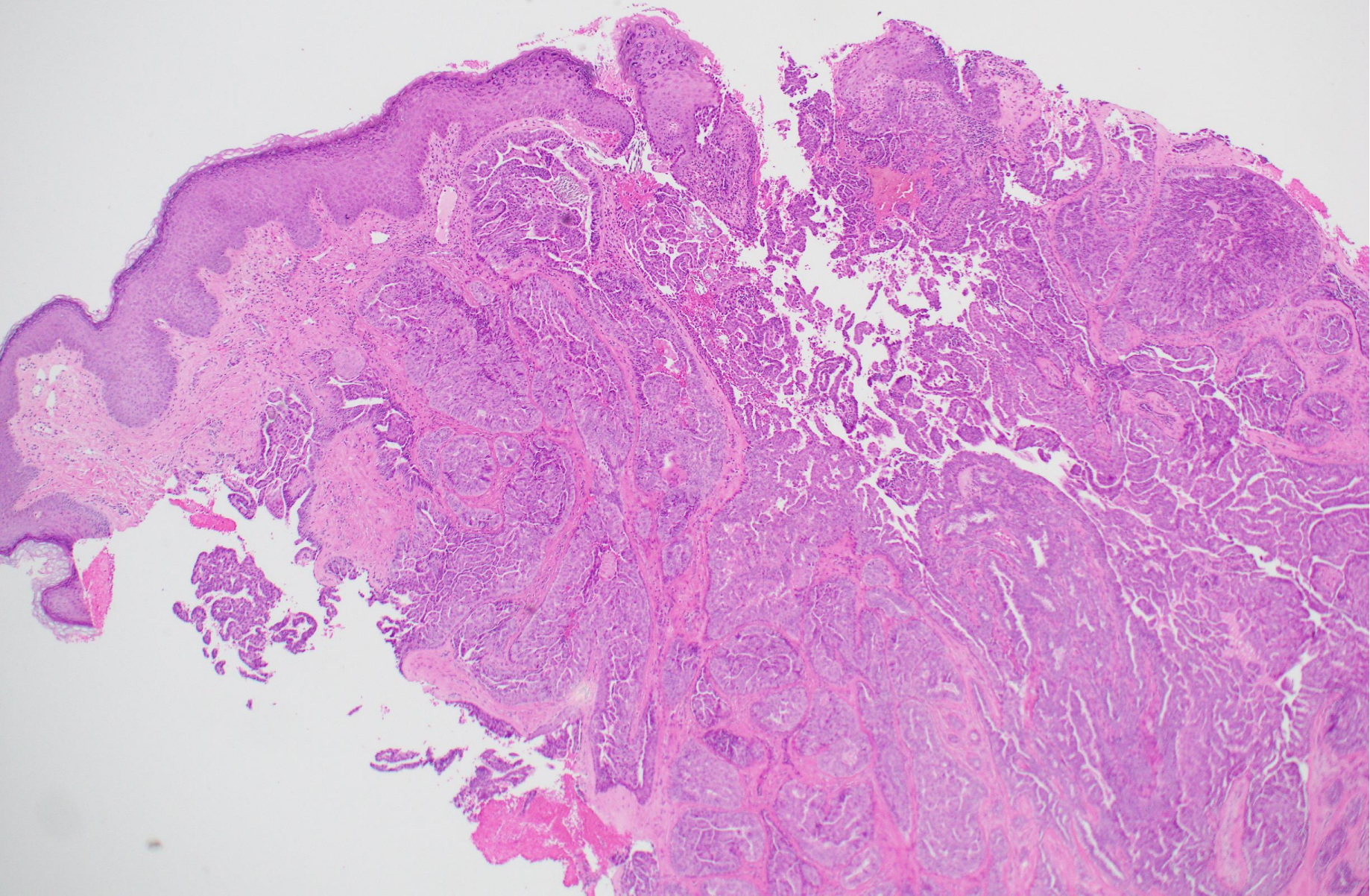
Cystic Neutrophilic Granulomatous Mastitis (CNGM)

- A (non-idiopathic) cause of **granulomatous mastitis** with distinct and reproducible morphology.
- **Gram Positive Bacilli** (mostly invisible on H&E) – *Corynebacterium sp.*
- Focal zonation of **palisading histiocytes**, **ringing neutrophilic inflammation**, and **“empty space”** (potentially filled with Gram + Rods and lipid).
- Tissue Gram Stain will (sometimes (1/3)) highlight organisms.
 - **Number of organisms is low.**
 - Morphologic pattern is highly suggestive.
- Ideal antimicrobial therapy will follow culture and susceptibility testing.
 - Lipophilic show some increased efficacy (lipid vacuoles)
 - Multi-drug resistant strains have been reported
- Standard empiric mastitis Abx therapy may not be effective – hence the **need to distinguish from classical mastitis.**
- Typically no breast feeding history (vs classical mastitis), 30-40 years, **unresponsive to initial Abx therapy, protracted course (years is common).**



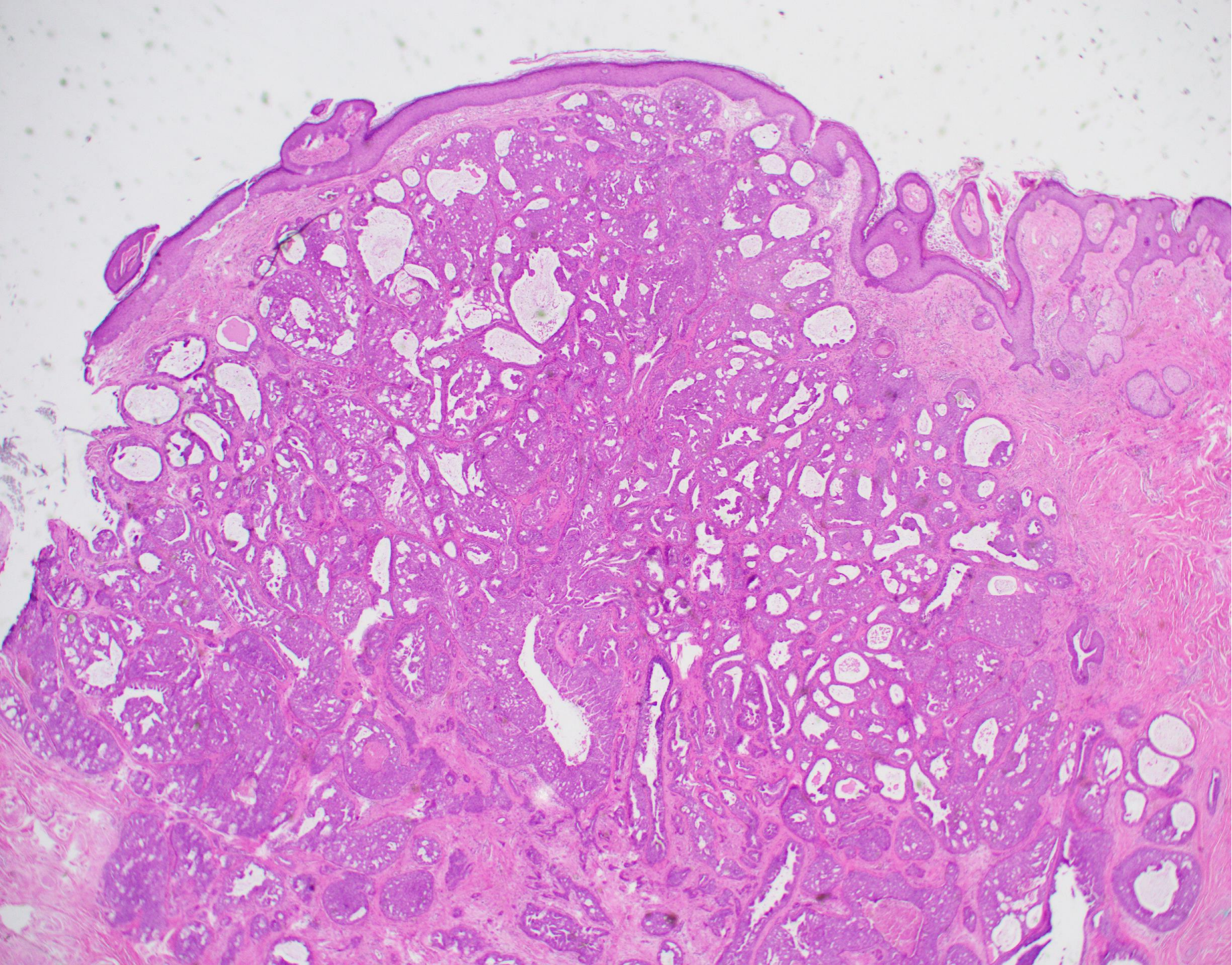
Case #7





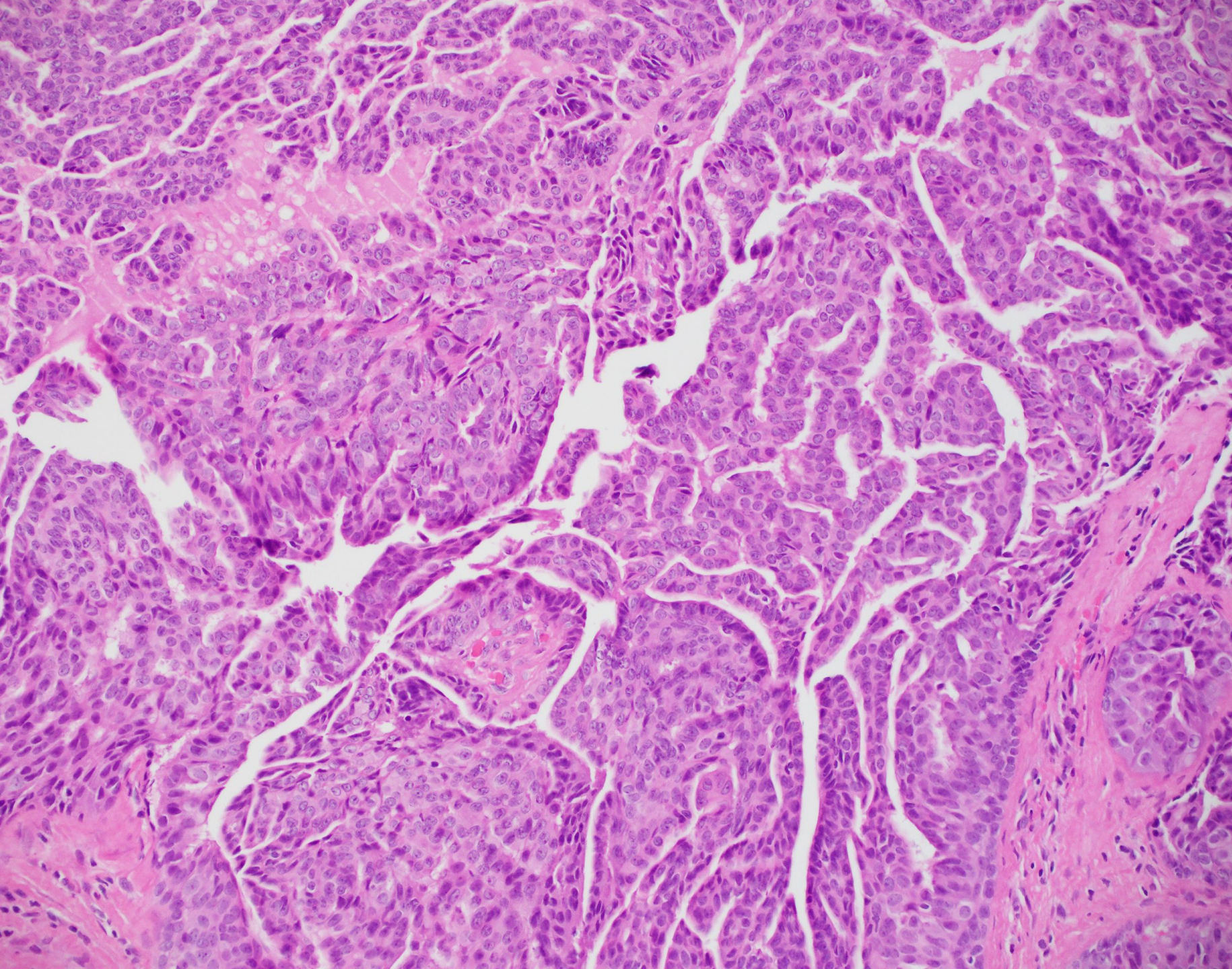
36F

Bloody Nipple Discharge
Nipple Ulceration / Crusting



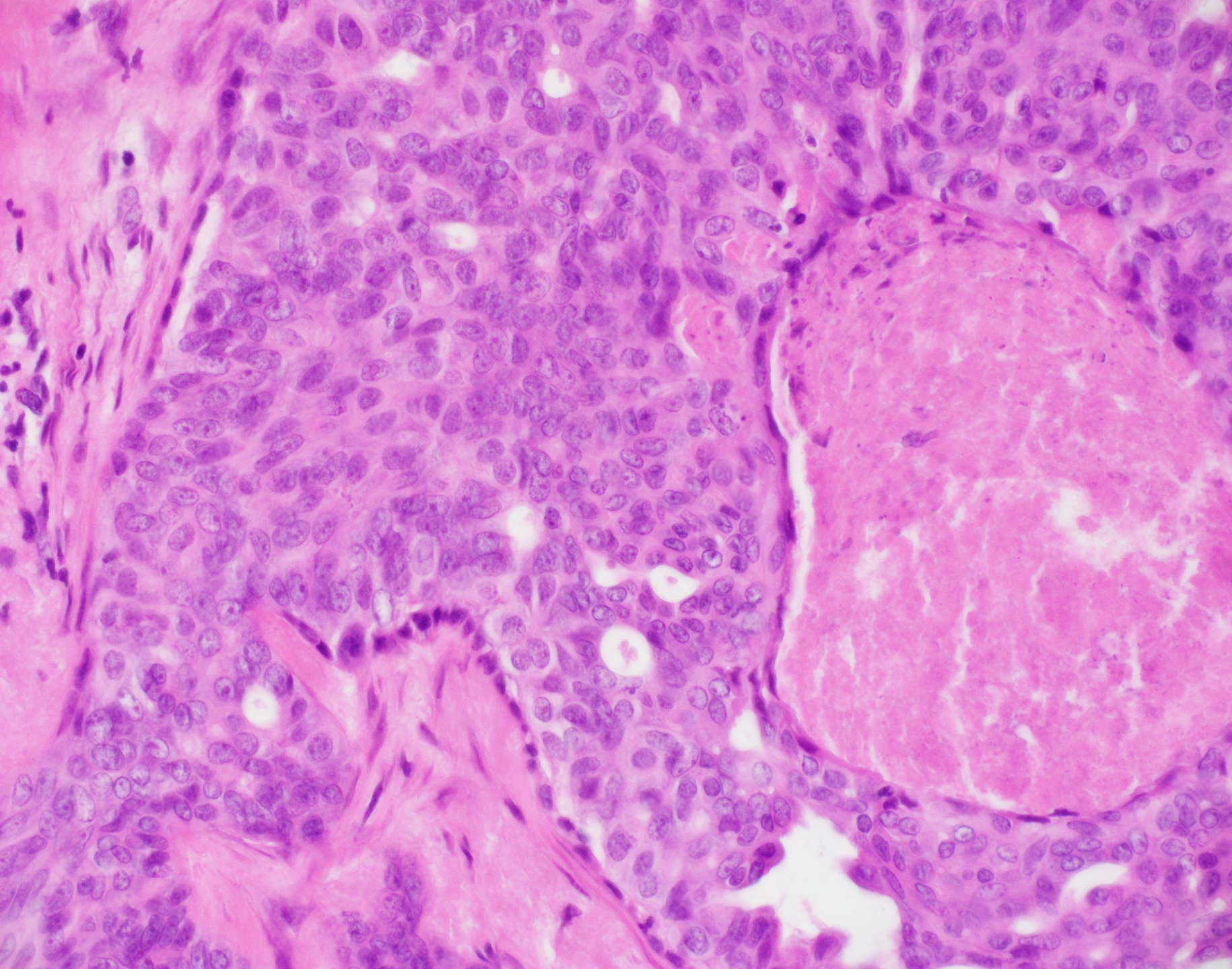
36F

Bloody Nipple Discharge
Nipple Ulceration / Crusting



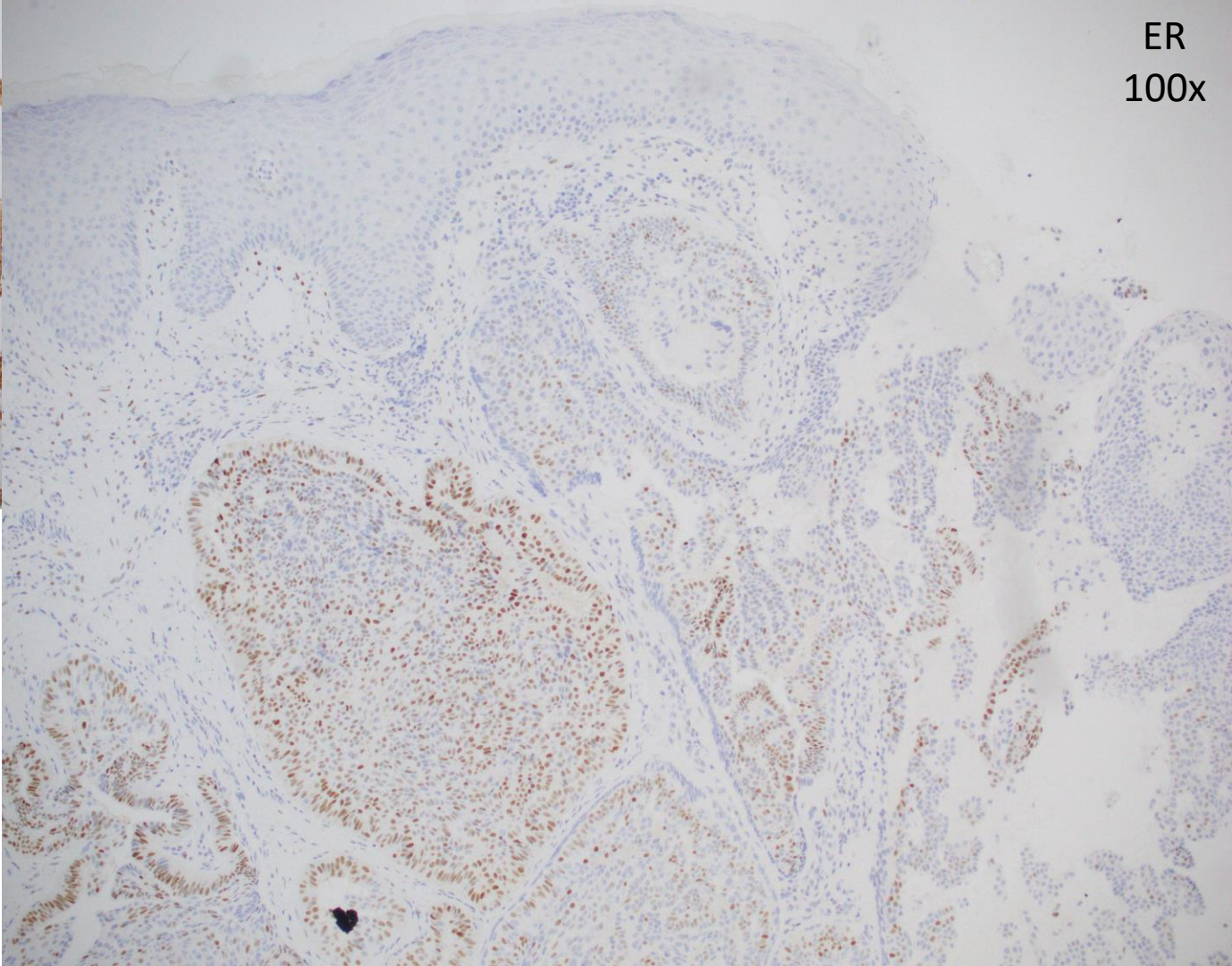
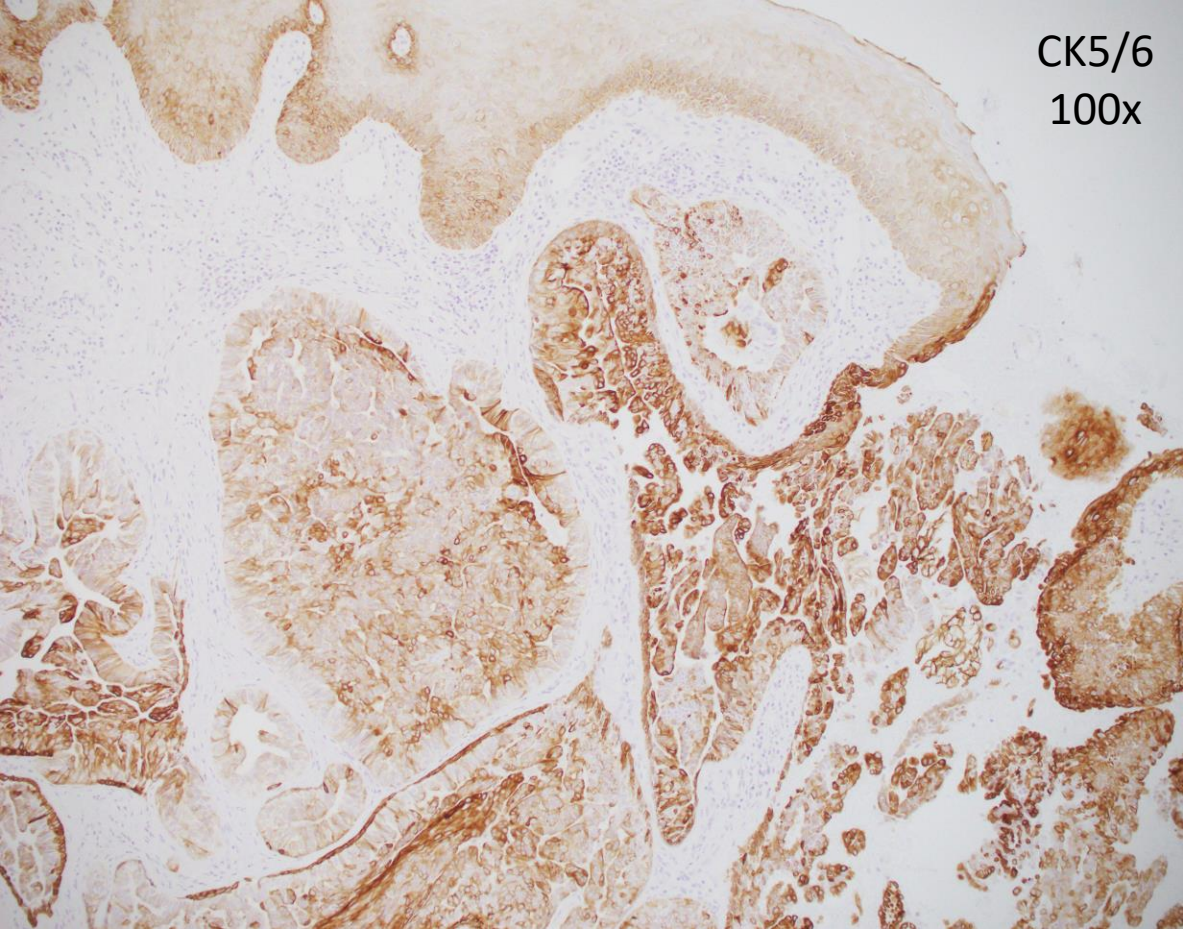
36F

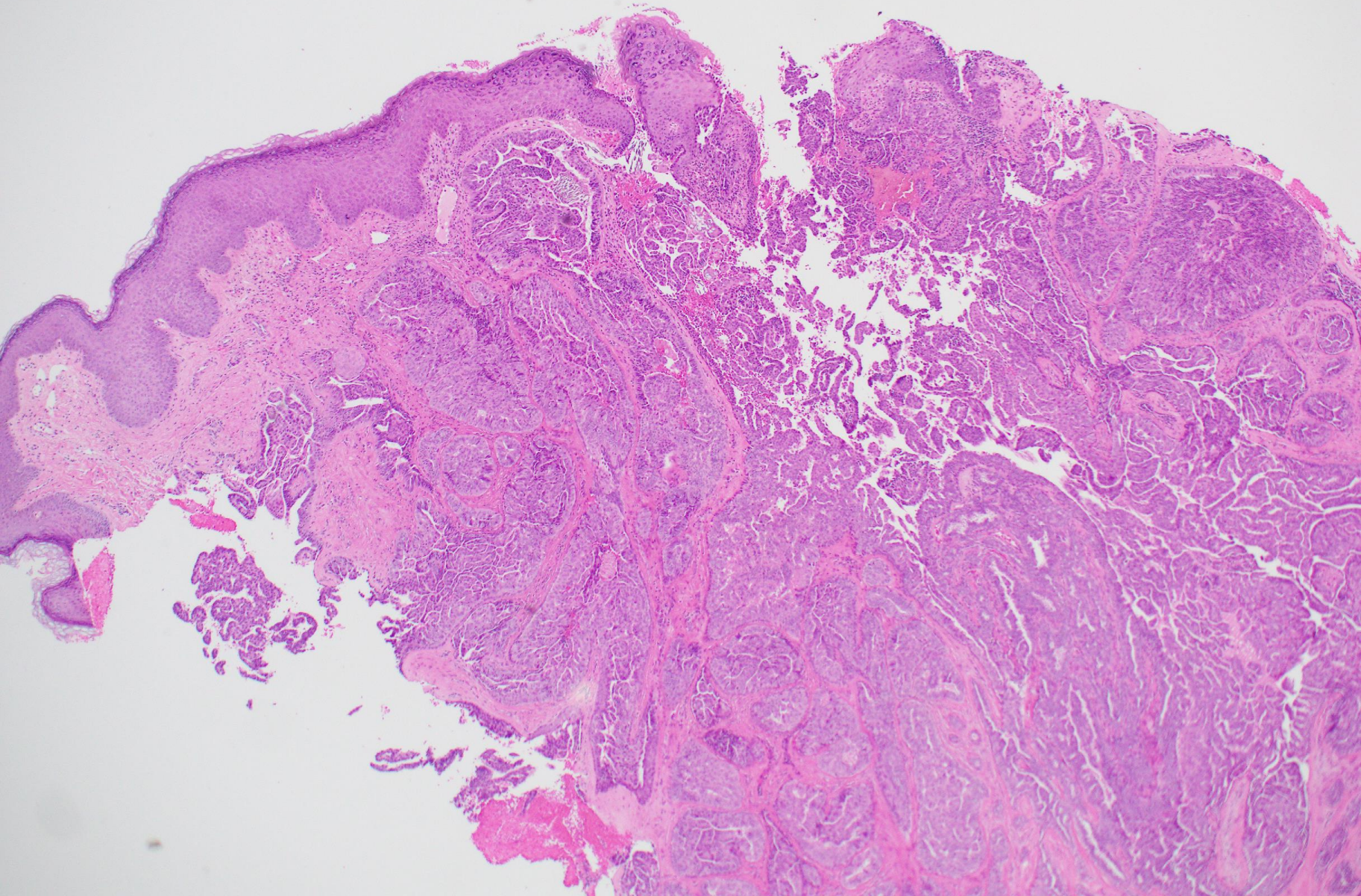
Bloody Nipple Discharge
Nipple Ulceration / Crusting



36F

Bloody Nipple Discharge
Nipple Ulceration / Crusting

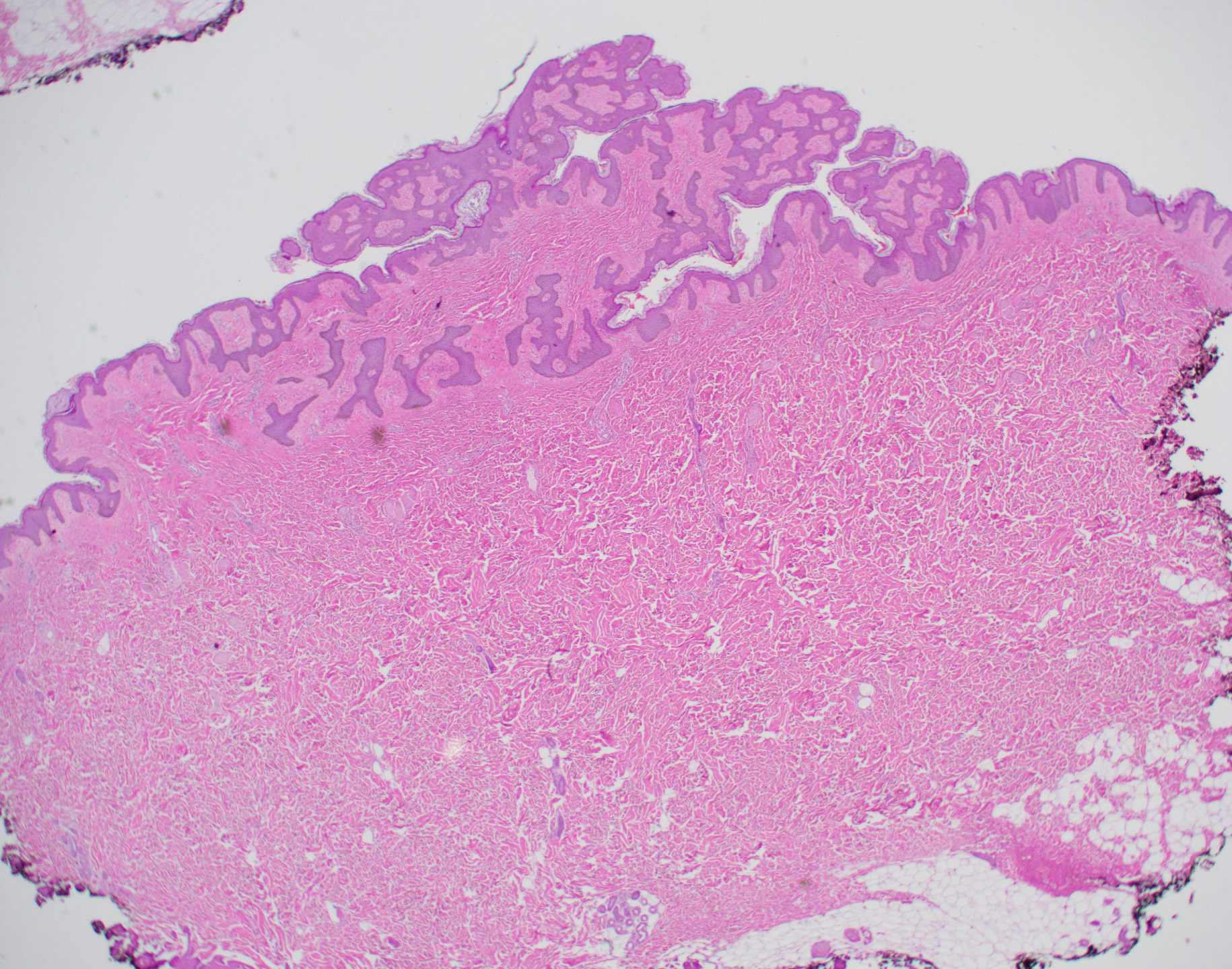




Nipple Adenoma (Florid UDH of Lactiferous Duct)

- Easily mistaken for DCIS
- Cured with limited excision
- Ulceration and nipple crusting (clinically concerning for Paget's not uncommon).
- Mosaic ER/CK5/6 is key in markedly florid cases or those with necrosis.
- Retained myoepithelial markers.

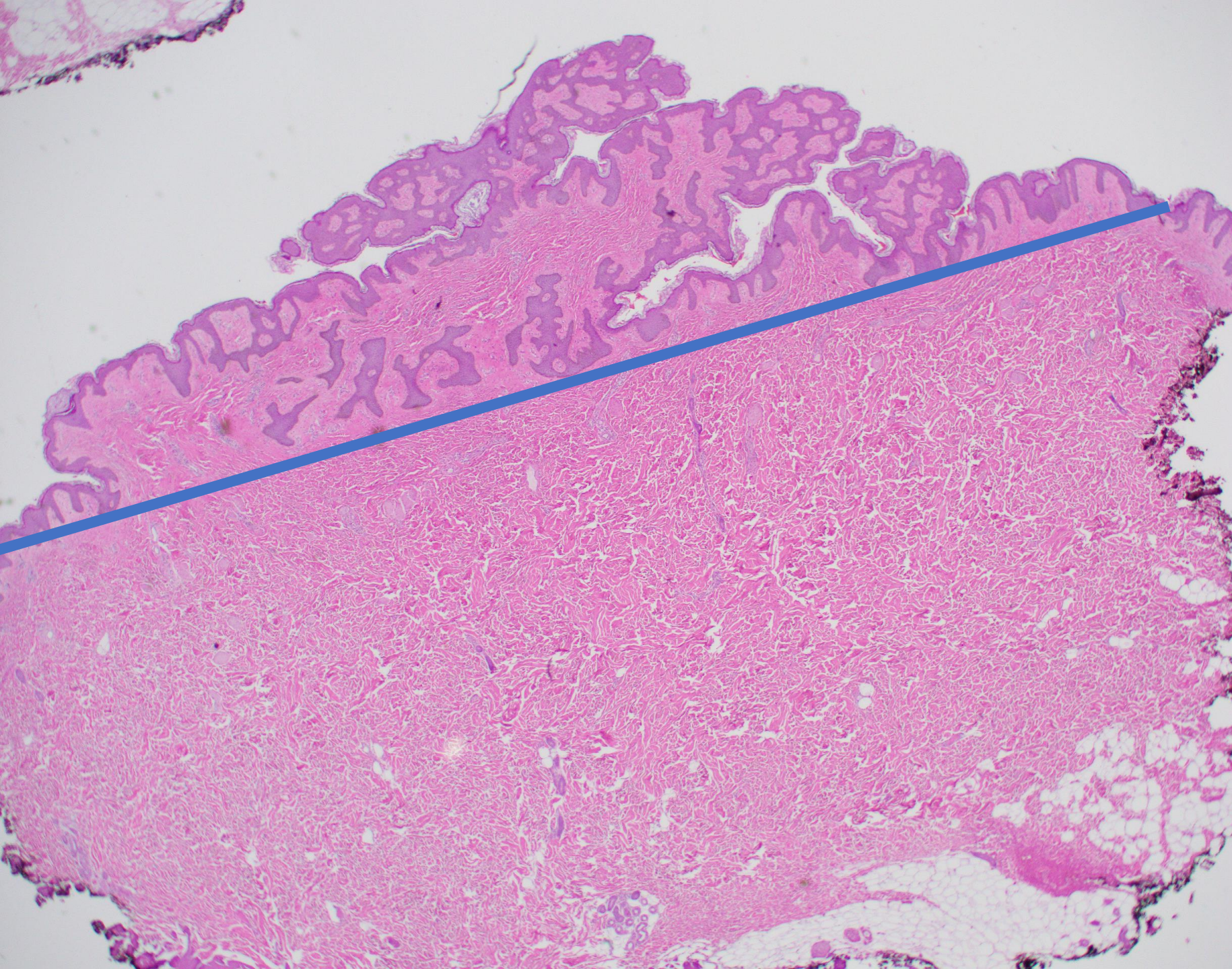
Case #8



34F

Personal (and family) history of melanoma.

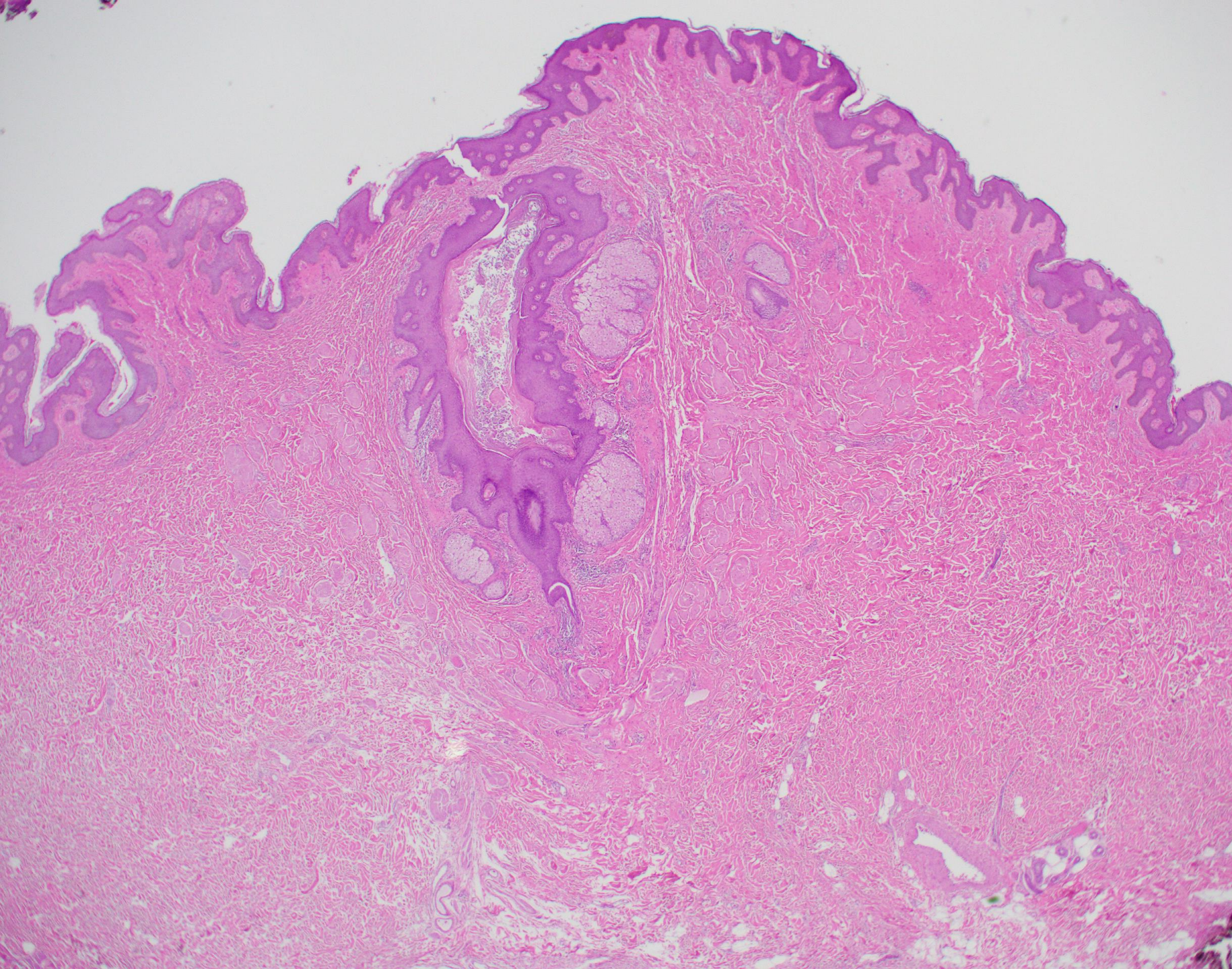
Pigmented abdominal skin lesion.



34F

Personal (and family) history of melanoma.

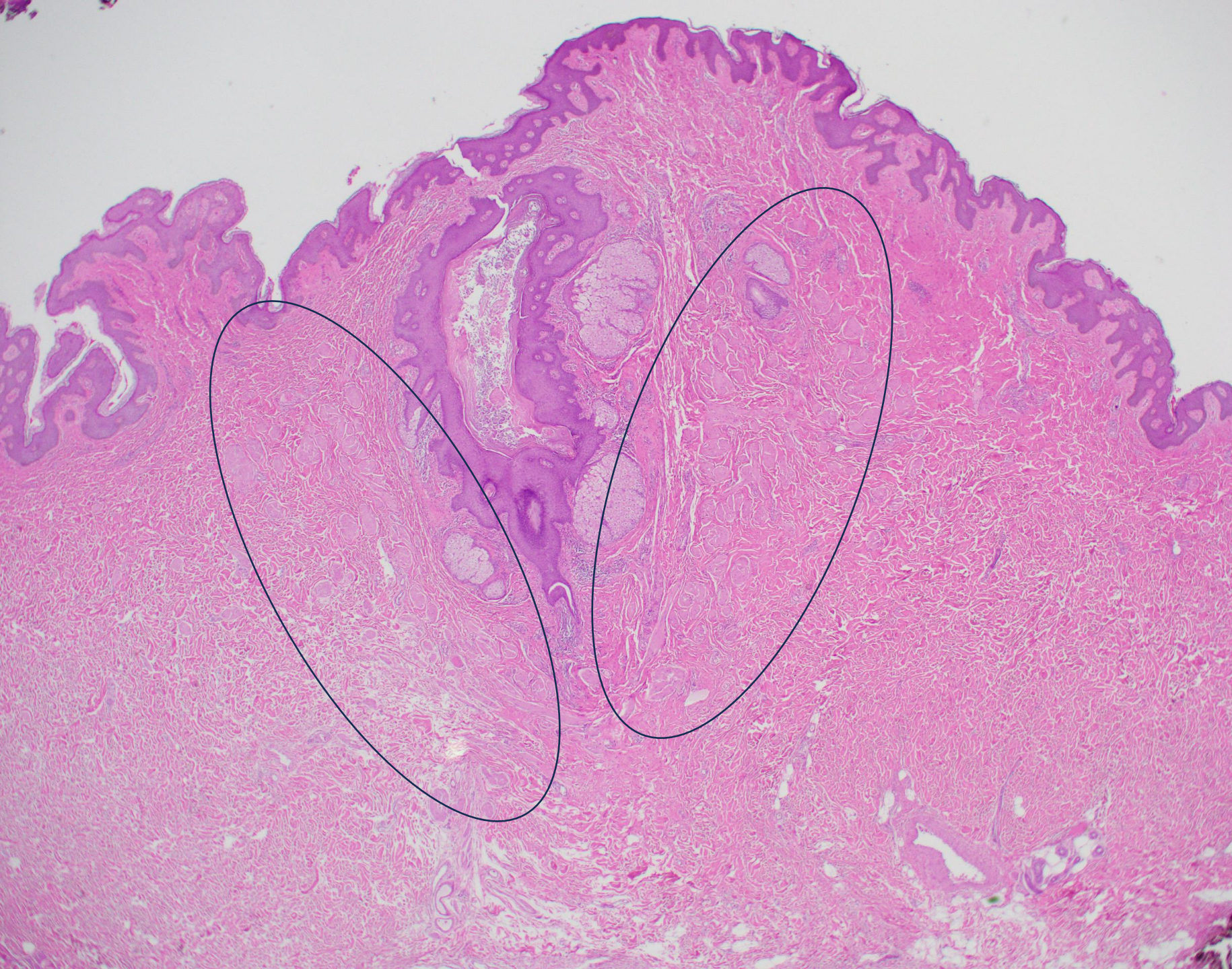
Pigmented abdominal skin lesion.



34F

Personal (and family) history of melanoma.

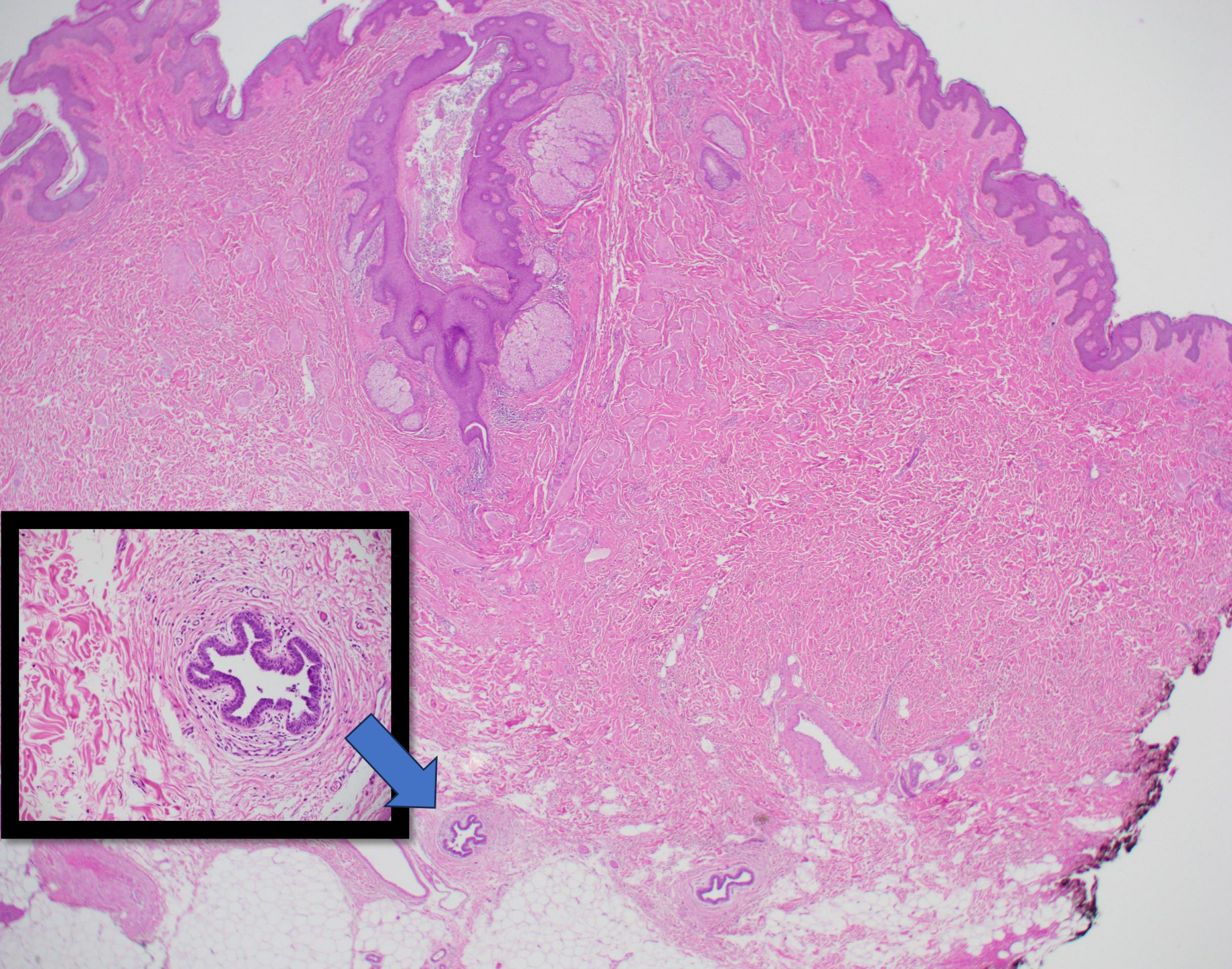
Pigmented abdominal skin lesion.



34F

Personal (and family) history of melanoma.

Pigmented abdominal skin lesion.



34F

Personal (and family) history of melanoma.

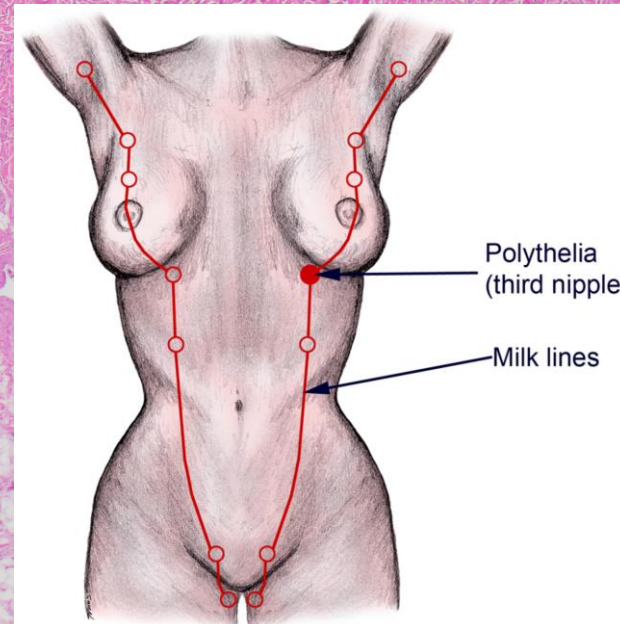
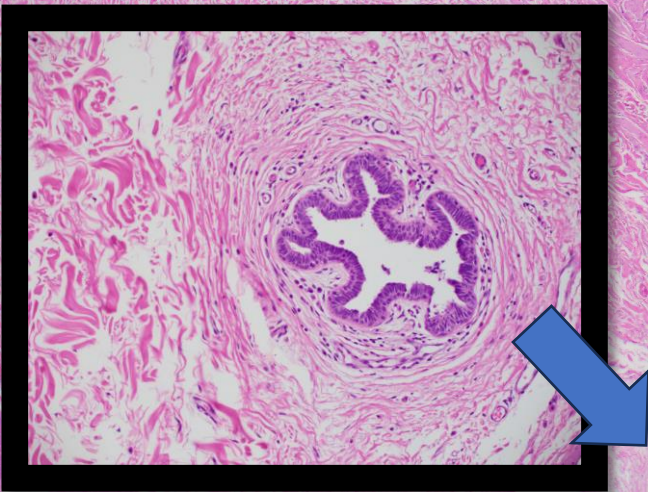
Pigmented abdominal skin lesion.

Benign Skin with Supernumerary Nipple

34F

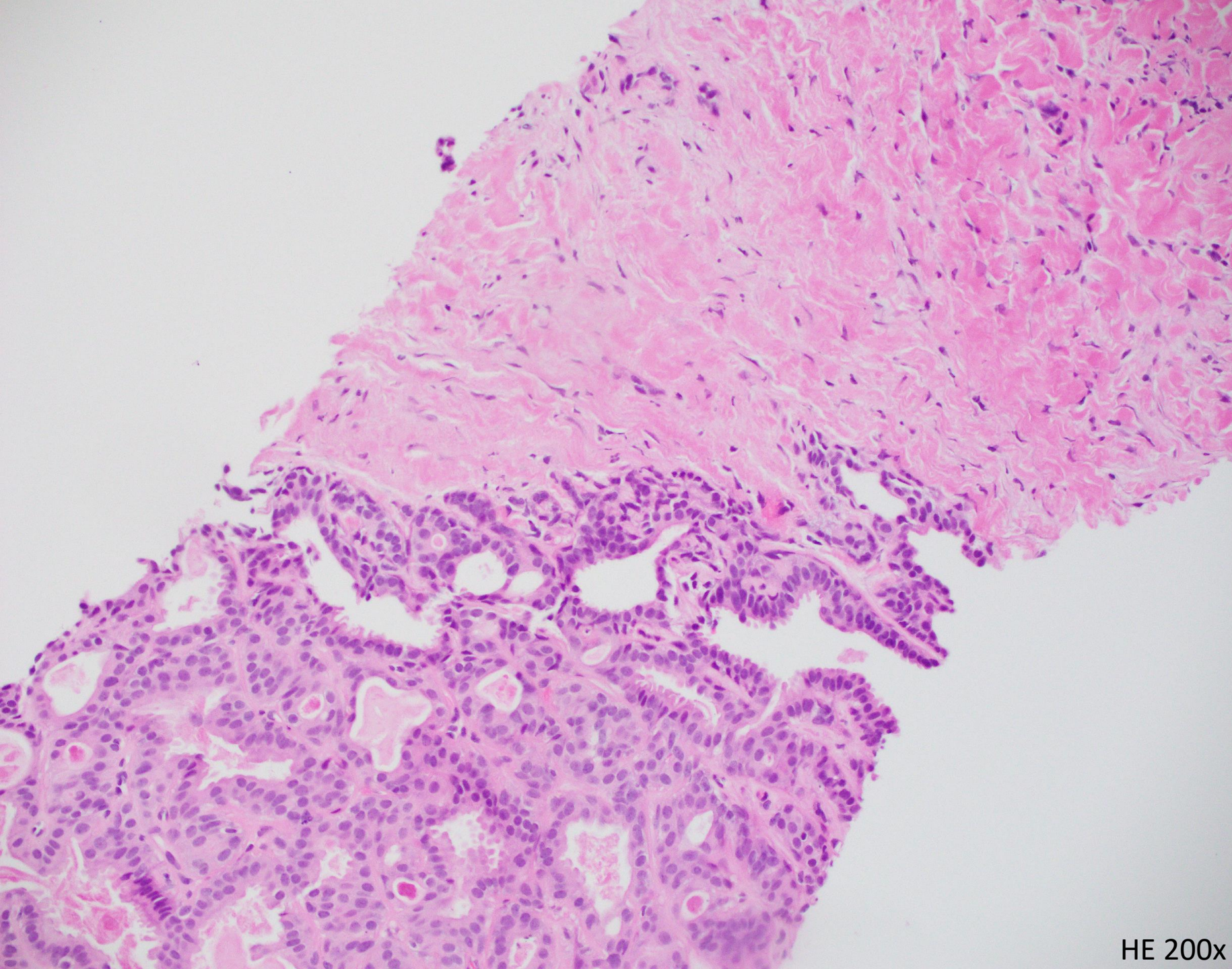
Personal (and family) history
of melanoma.

Pigmented abdominal skin
lesion.



Case #9



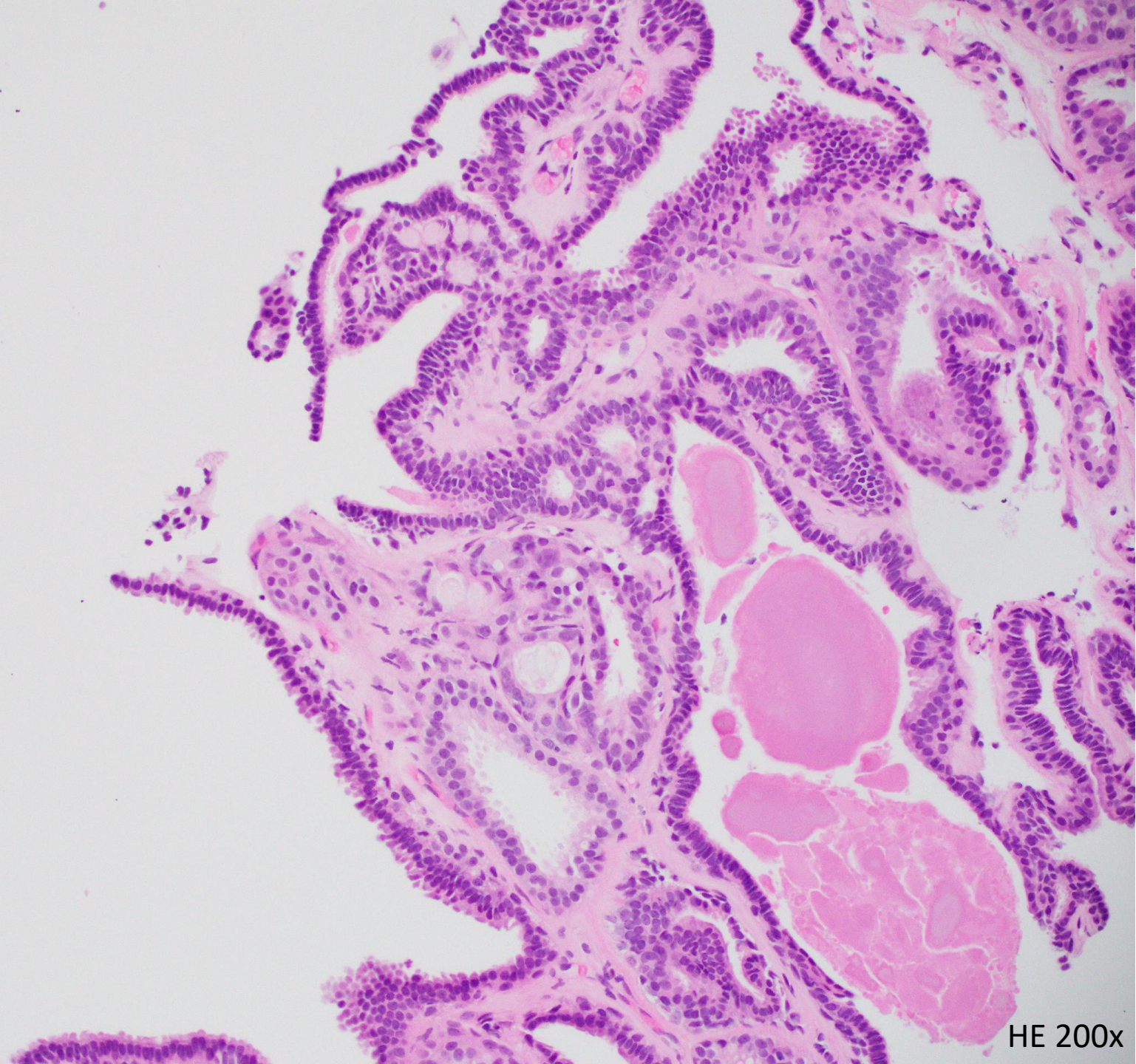


Presumed
Dermis?

74F

"Shallow" Axillary Mass,
Needle Core Biopsy

HE 200x



← Papillary?

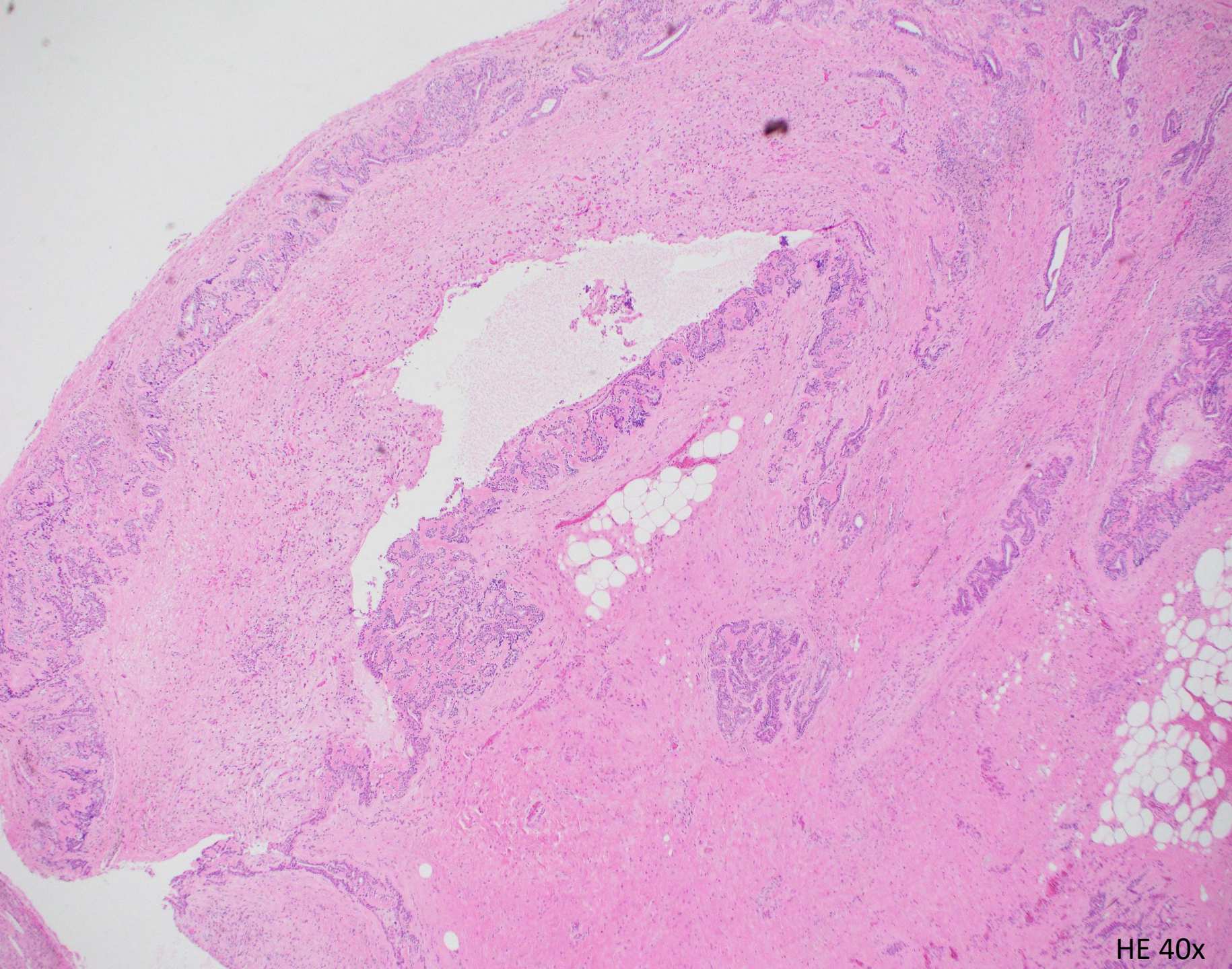
74F

“Shallow” Axillary Mass,
Needle Core Biopsy

Myosin +
P63 +

ER: Mostly
positive

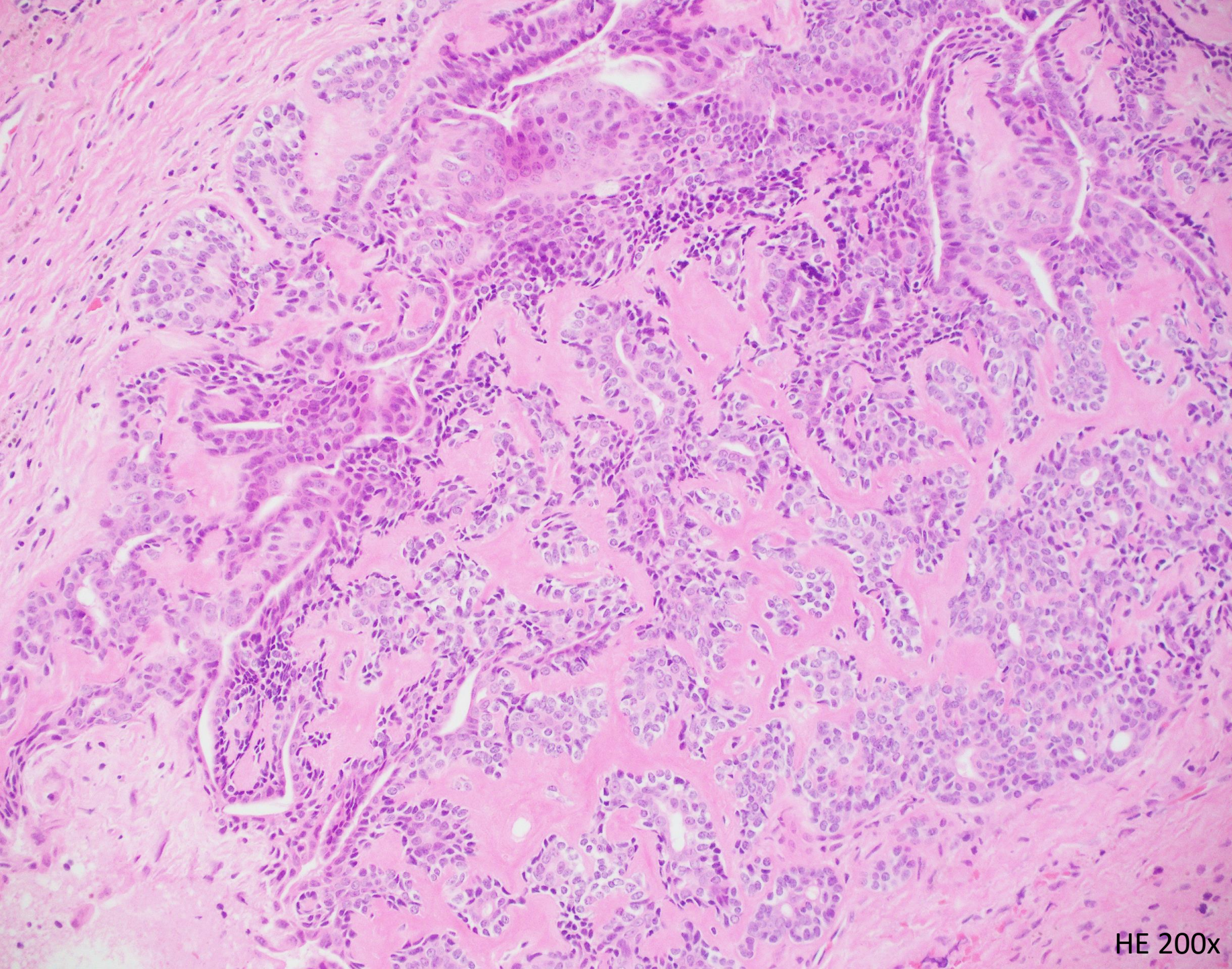
HE 200x



74F

“Shallow” Axillary Mass,
Excision

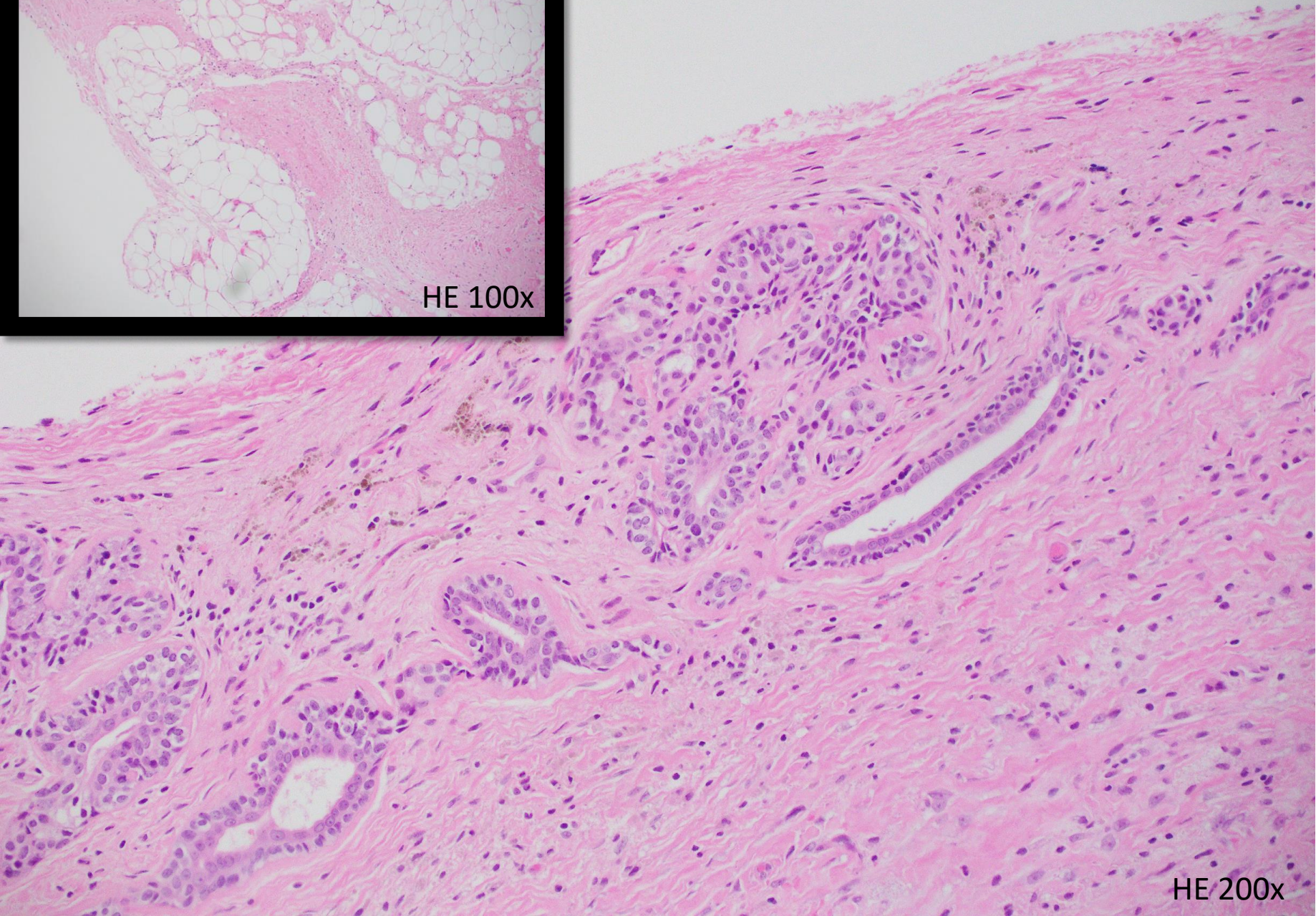
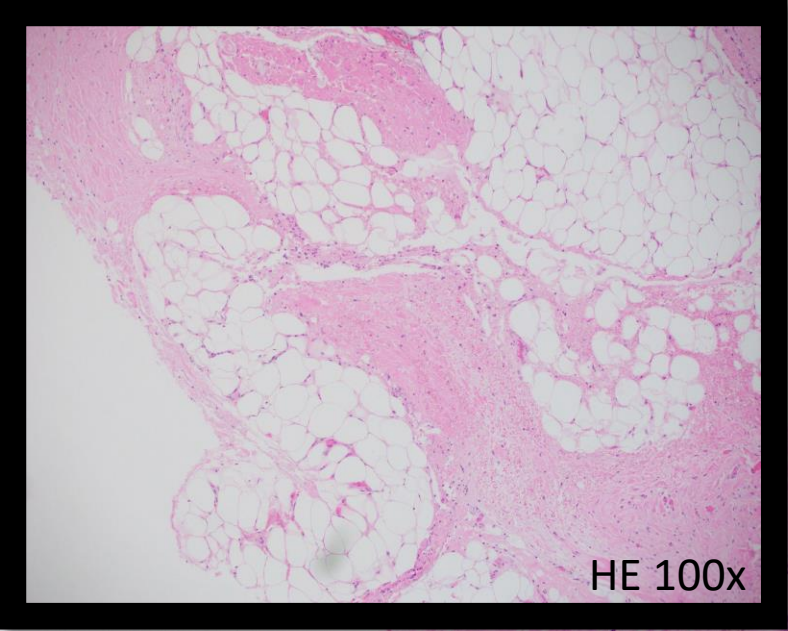
HE 40x



74F

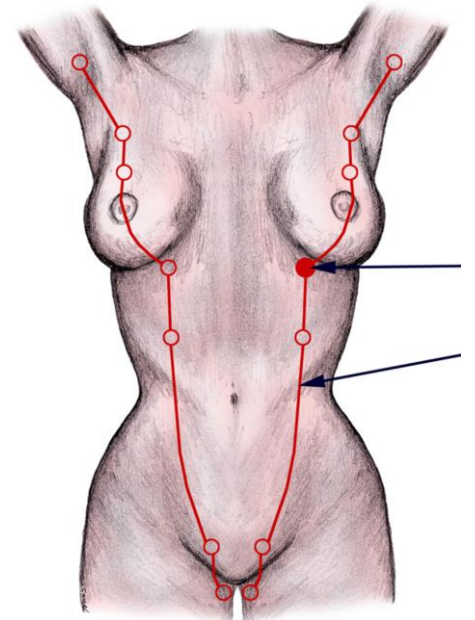
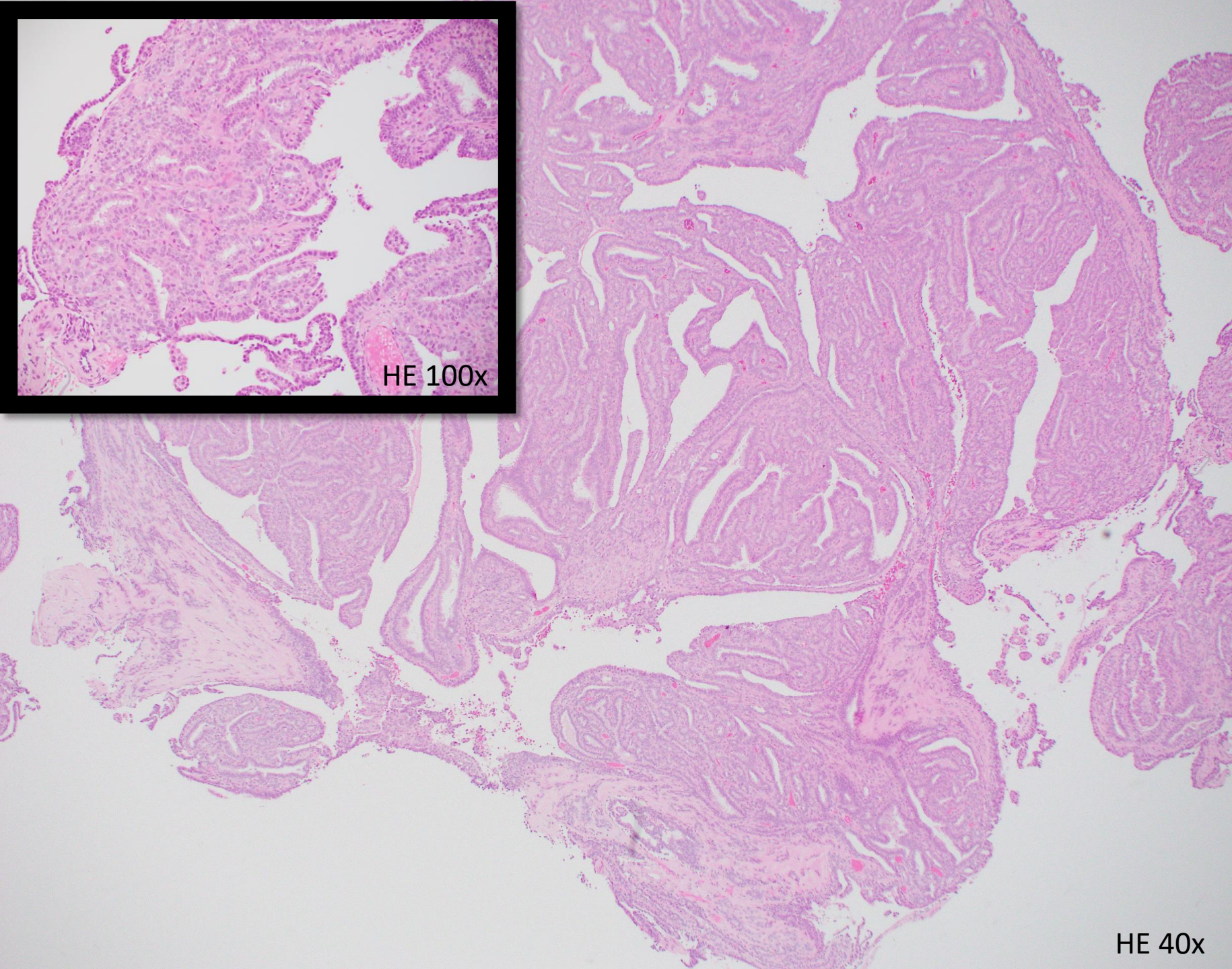
“Shallow” Axillary Mass,
Excision

HE 200x



74F

“Shallow” Axillary Mass,
Excision



Same Lesion? Example from GYN – Vulva

Sketch From: The Geneva Foundation for Medical Education and Research
Photo Courtesy of Dr. Lesley Lomo, Univ. of Utah, GYN Pathology



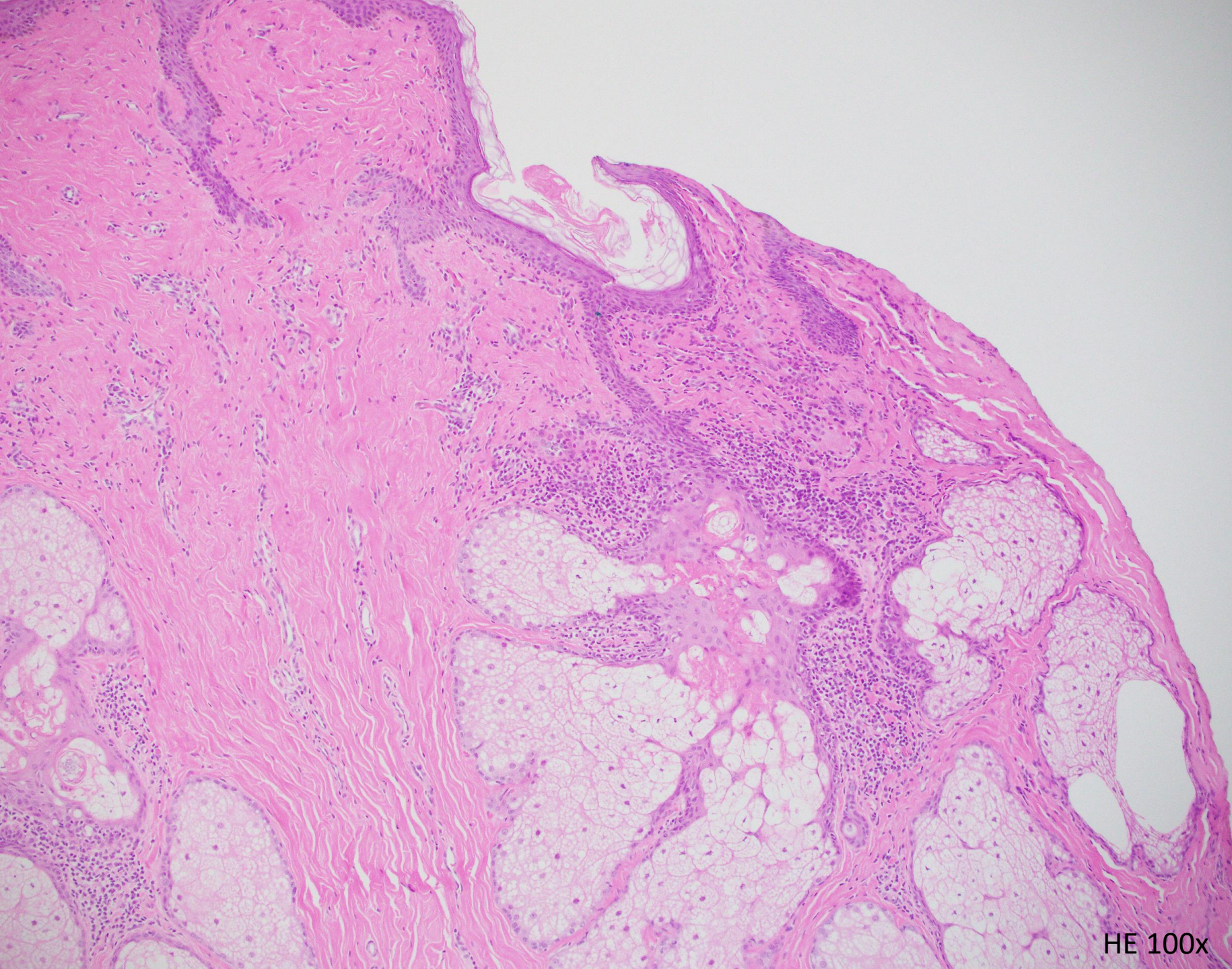
Benign Papillary Lesion, Favor Hidradenoma Papilliferum

Ddx: Ectopic axillary breast tissue with sclerosed intraductal papilloma

BENIGN

HE 200x

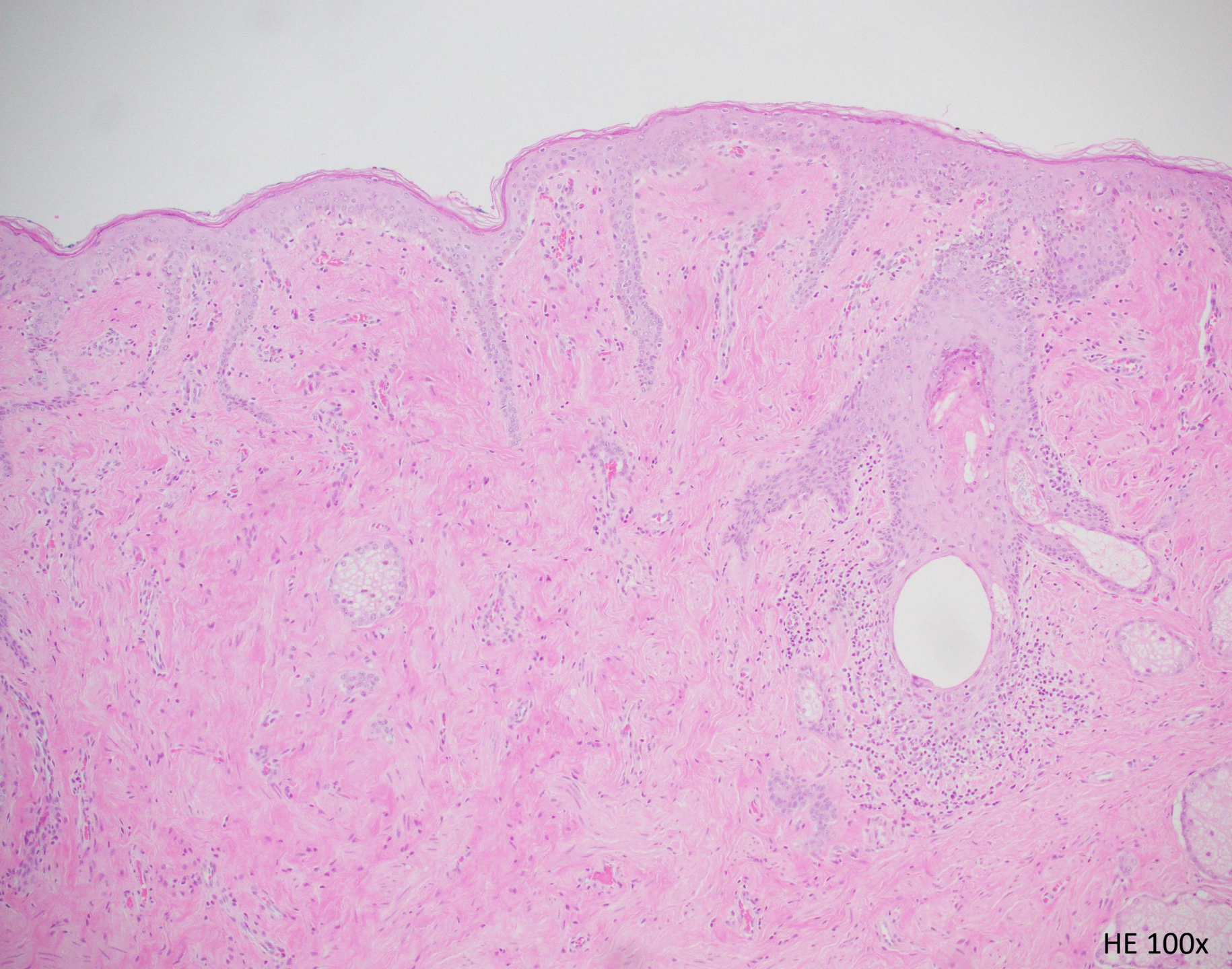
Case #10



55F, Nipple/Skin Biopsy

“Nipple Crusting and Irritation,
r/o Paget’s

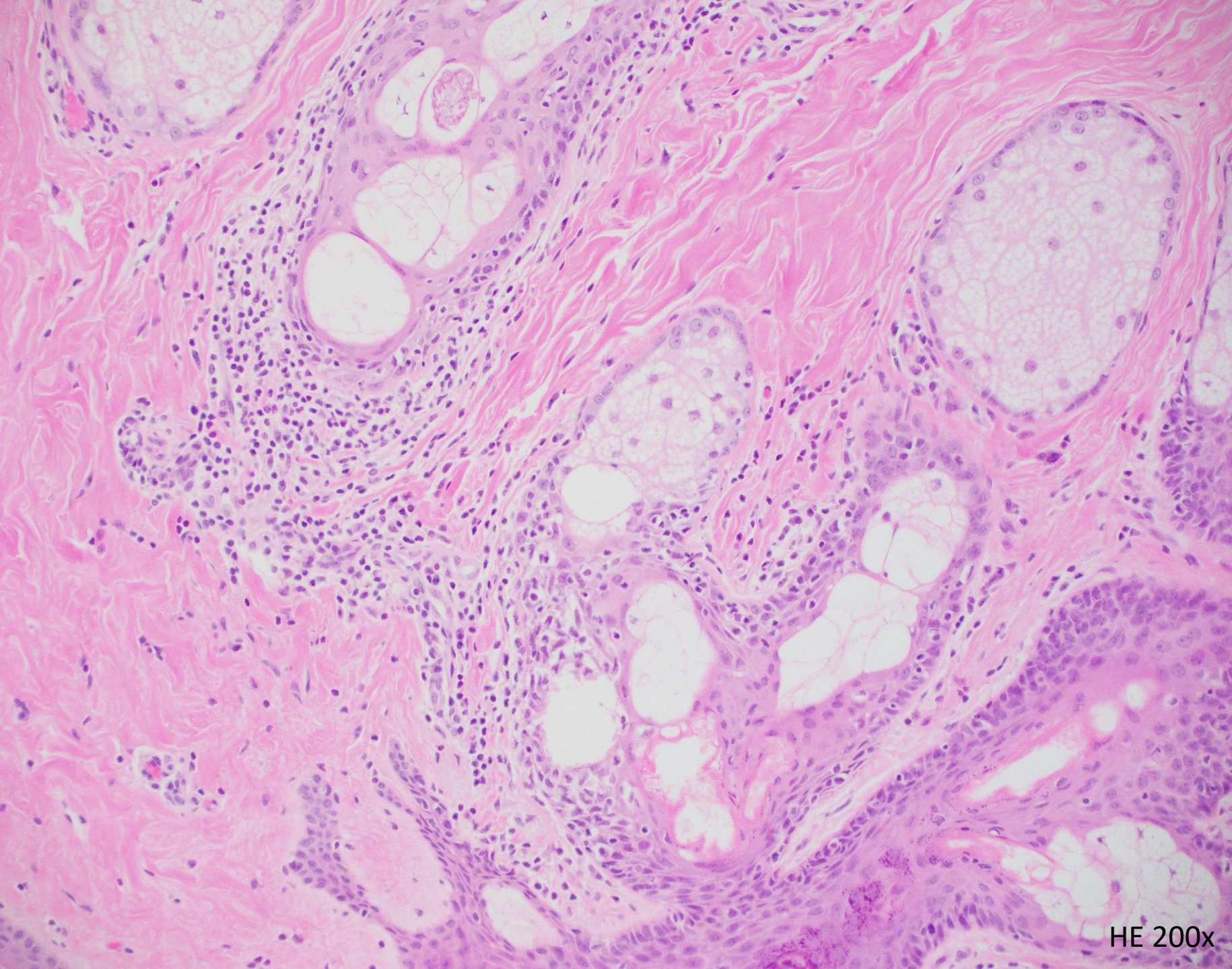
HE 100x



55F, Nipple/Skin Biopsy

“Nipple Crusting and Irritation,
r/o Paget’s”

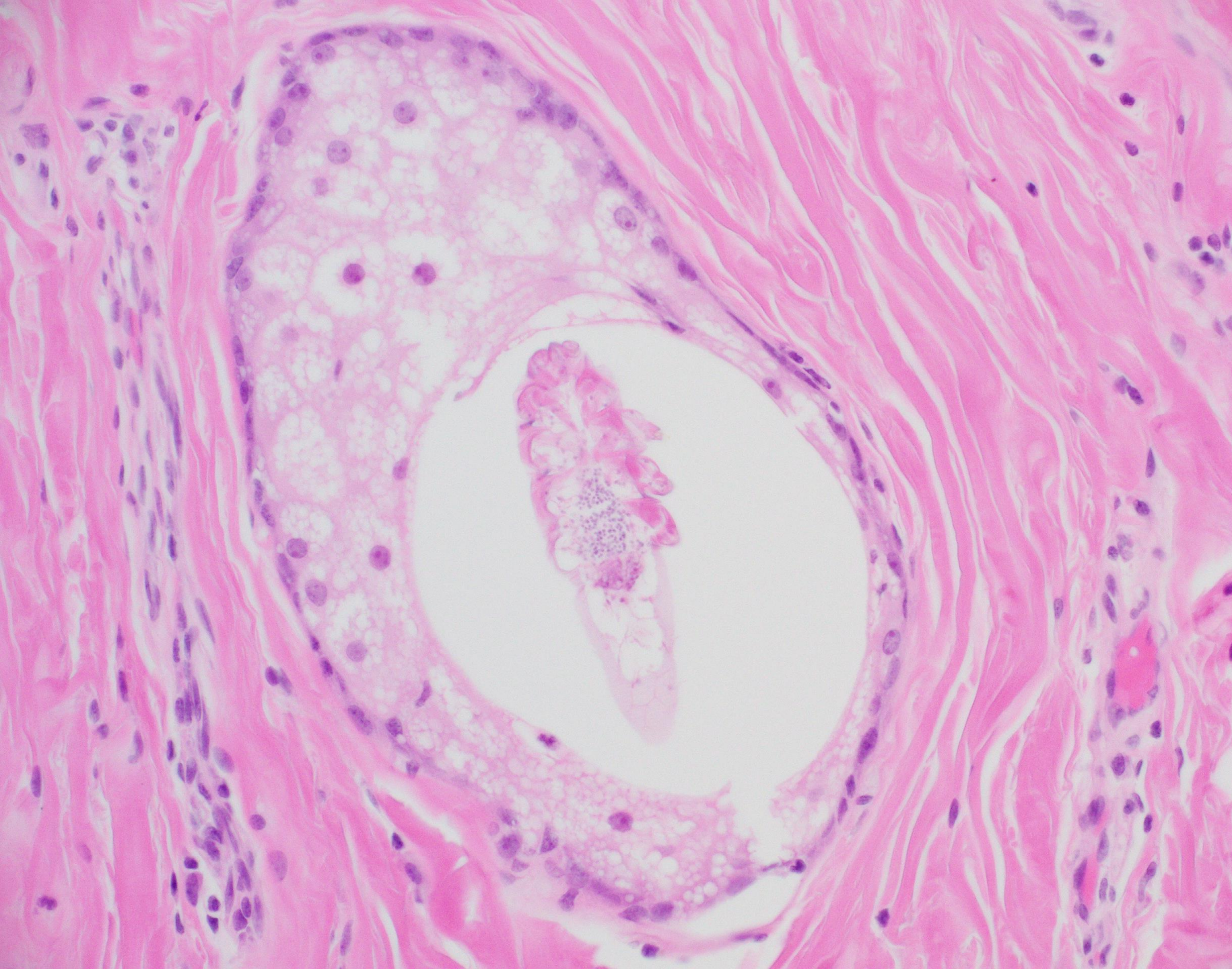
HE 100x



55F, Nipple/Skin Biopsy

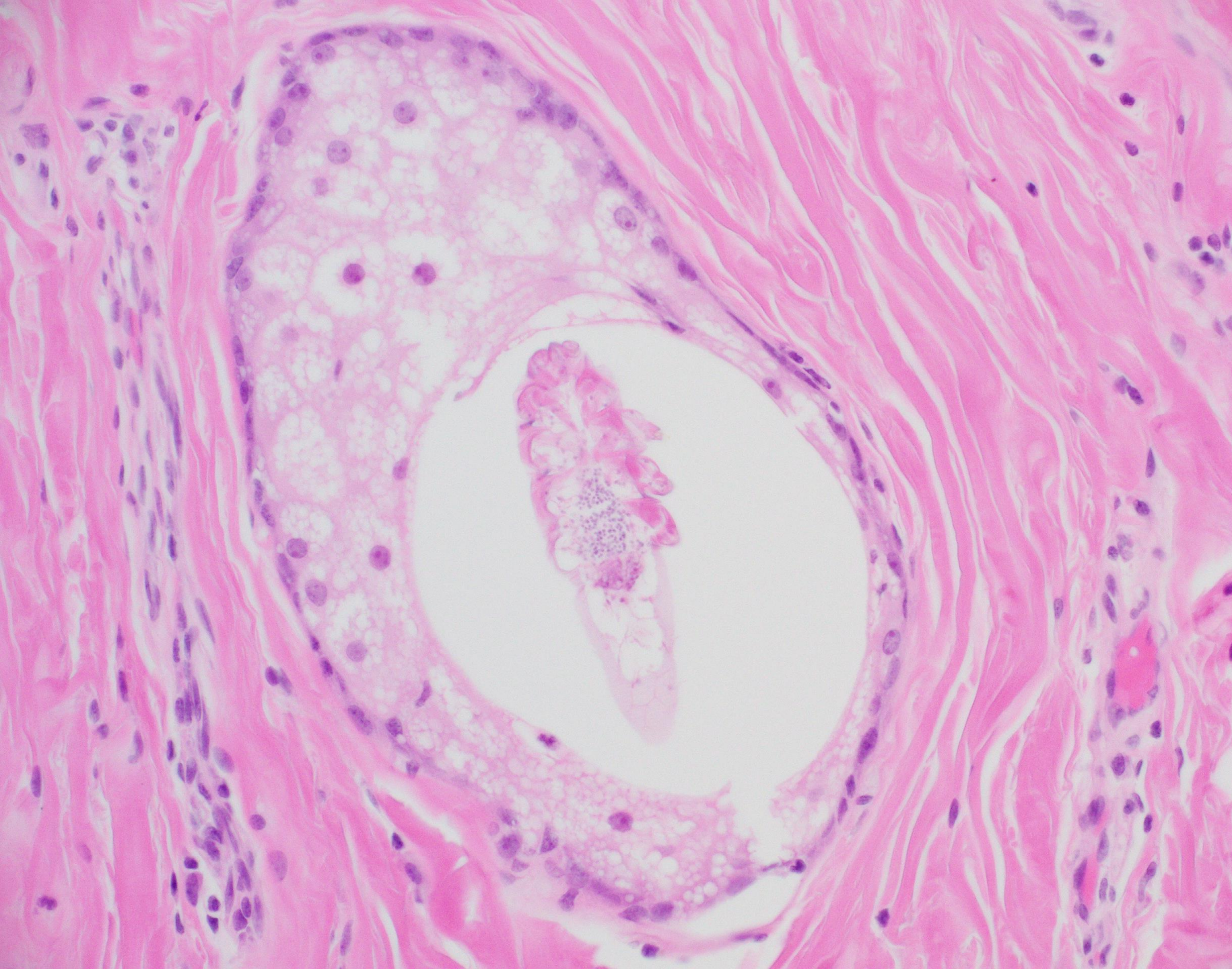
“Nipple Crusting and Irritation,
r/o Paget’s”

HE 200x



55F, Nipple/Skin Biopsy

“Nipple Crusting and Irritation,
r/o Paget’s”



Demodex Folliculitis



55F, Nipple/Skin Biopsy

“Nipple Crusting and Irritation,
r/o Paget’s”

41.4% of all nipple
biopsies! (Spain)

Val-Bernal JF, Diego C, Rodriguez-Villar D, Garijo MF. The nipple-areola complex epidermis: a prospective systematic study in adult autopsies. *Am J Dermatopathol.* 2010 Dec;32(8):787-93. doi: 10.1097/DAD.0b013e3181ddbec5. PMID: 20802299.

Questions?

A microscopic image showing a cross-section of a biological structure, likely a developing embryo or a specific tissue. The image is stained with pink and purple dyes. A prominent feature is a large, clear, circular space in the center, surrounded by a thick, pink-stained layer. Within this layer, there is a smaller, elongated, pink-stained structure. A blue callout bubble is overlaid on the image, containing the text "Enjoy your day in Park City!!!".

Enjoy your day in
Park City!!!