Disclosures
July 6, 2015

The following planners and faculty had no financial relationships with commercial interests to disclose:

Presenters:

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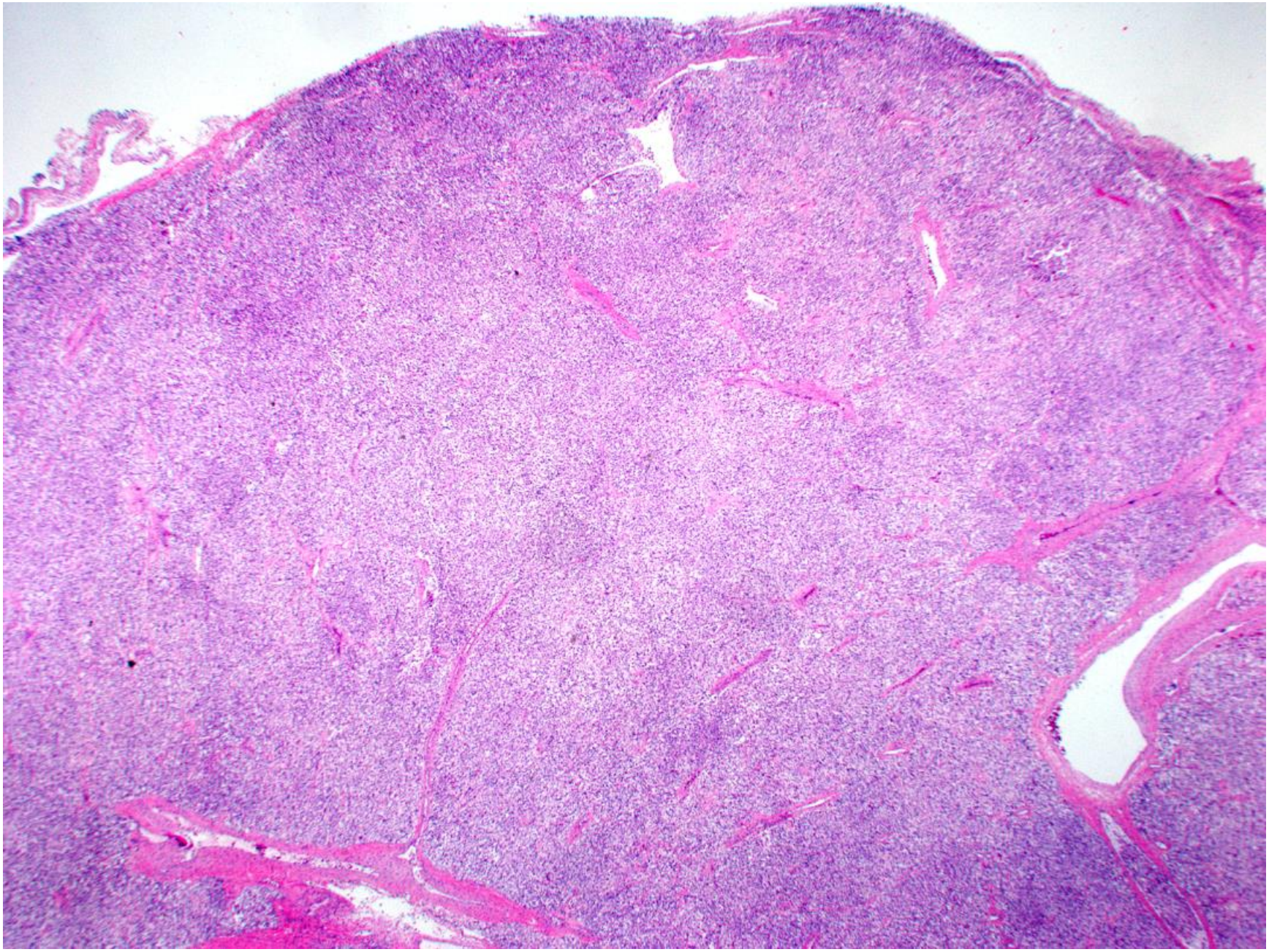
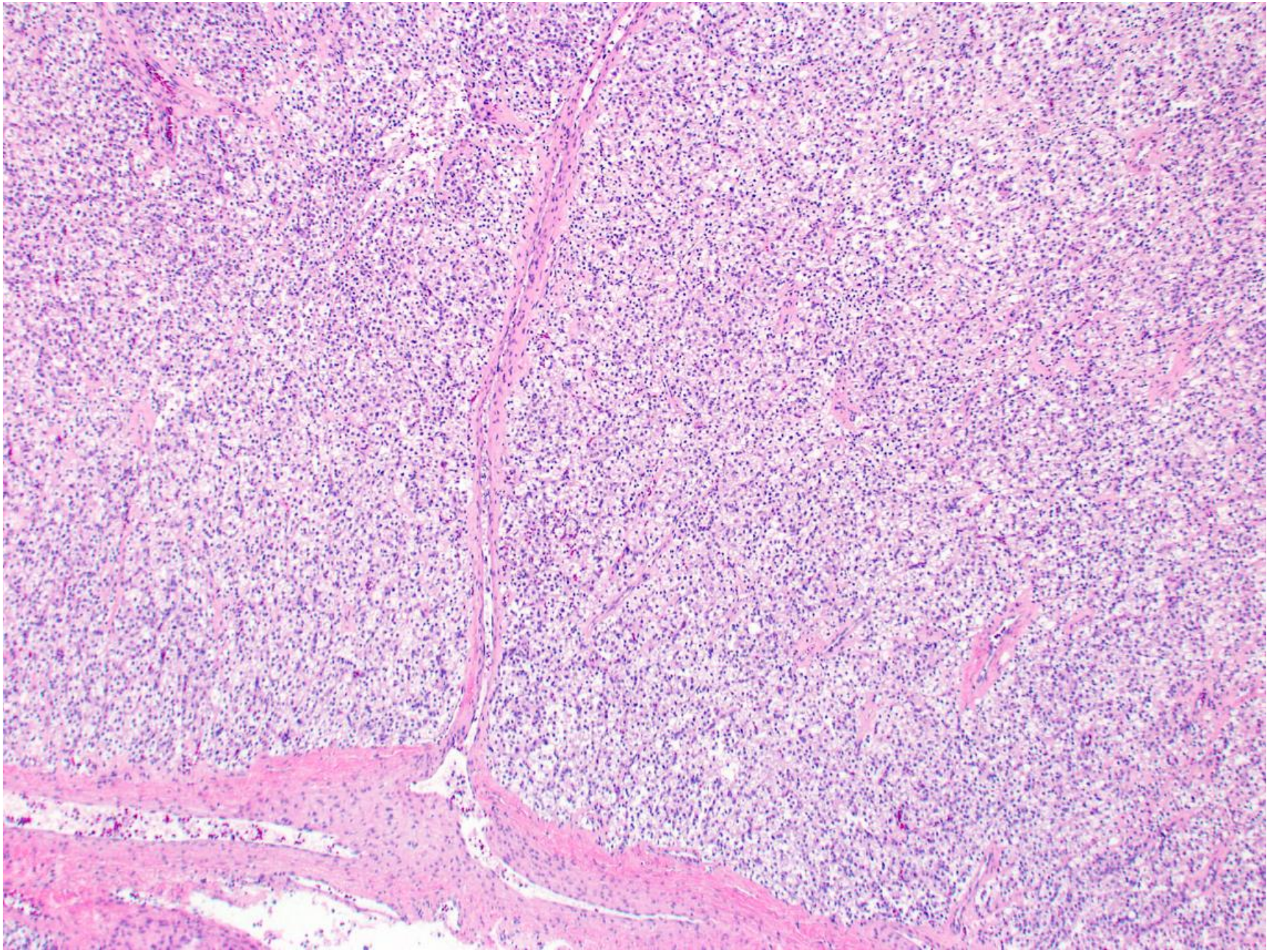
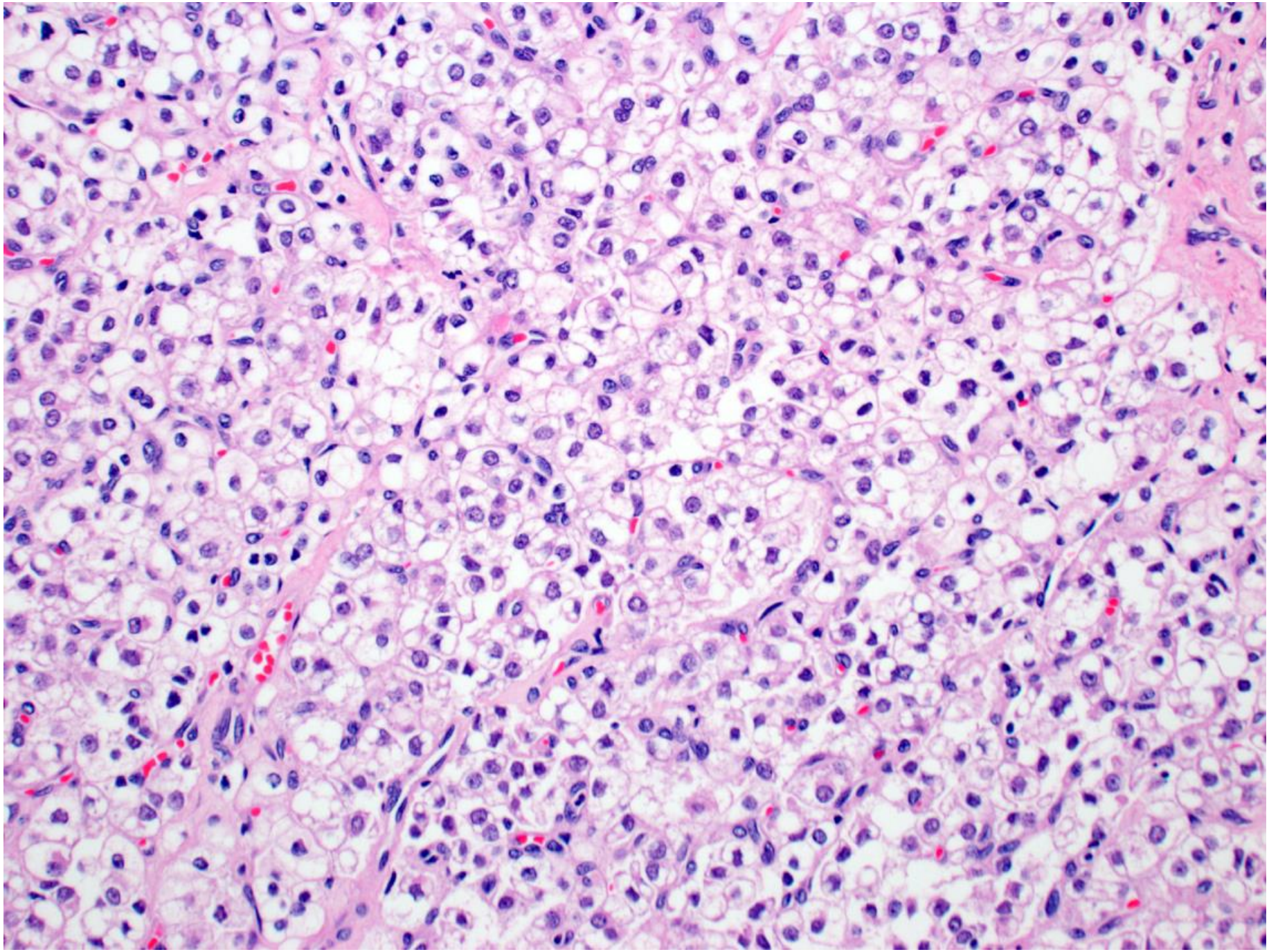
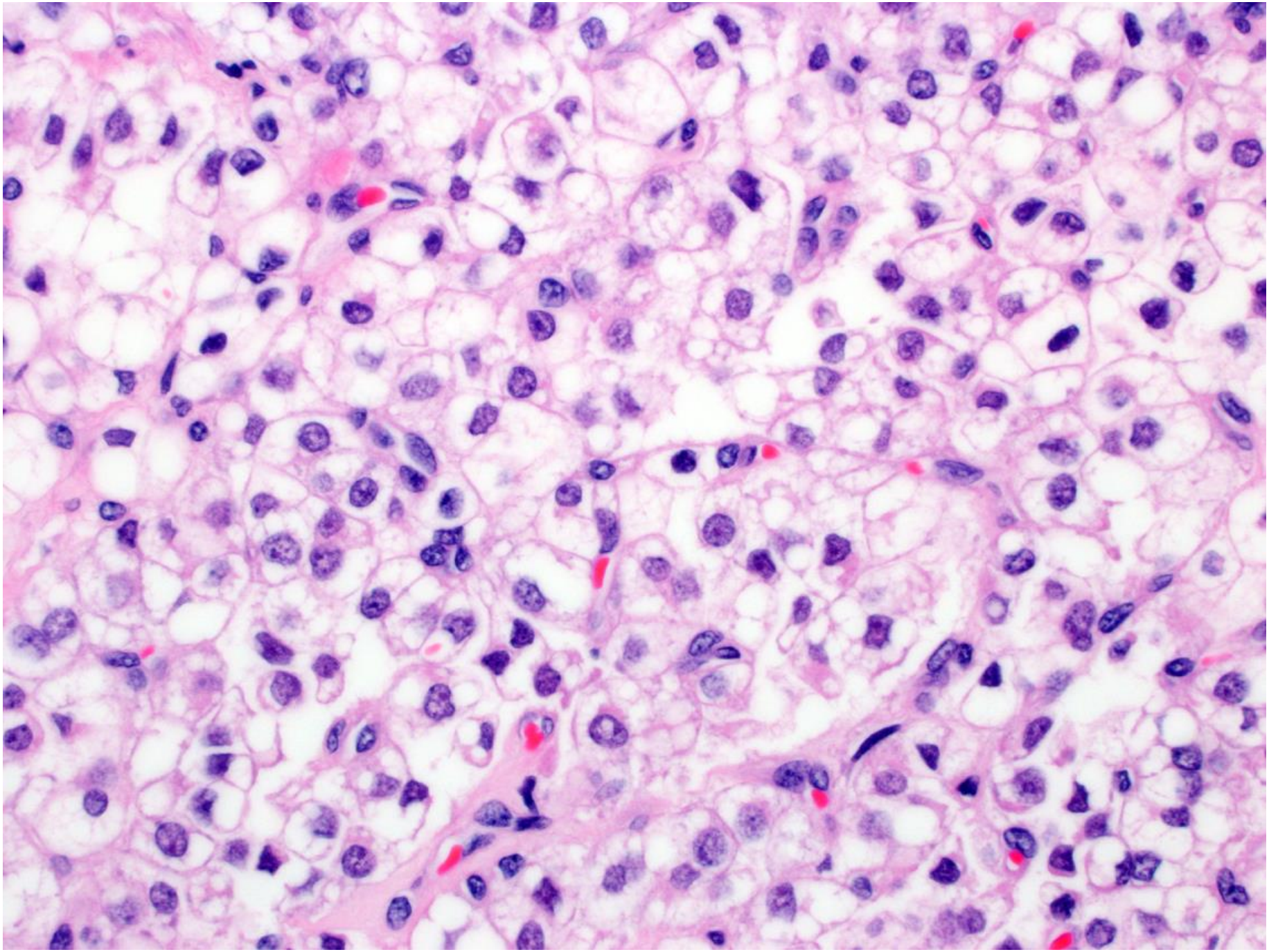
SB 5951
Joe Rabban; UCSF

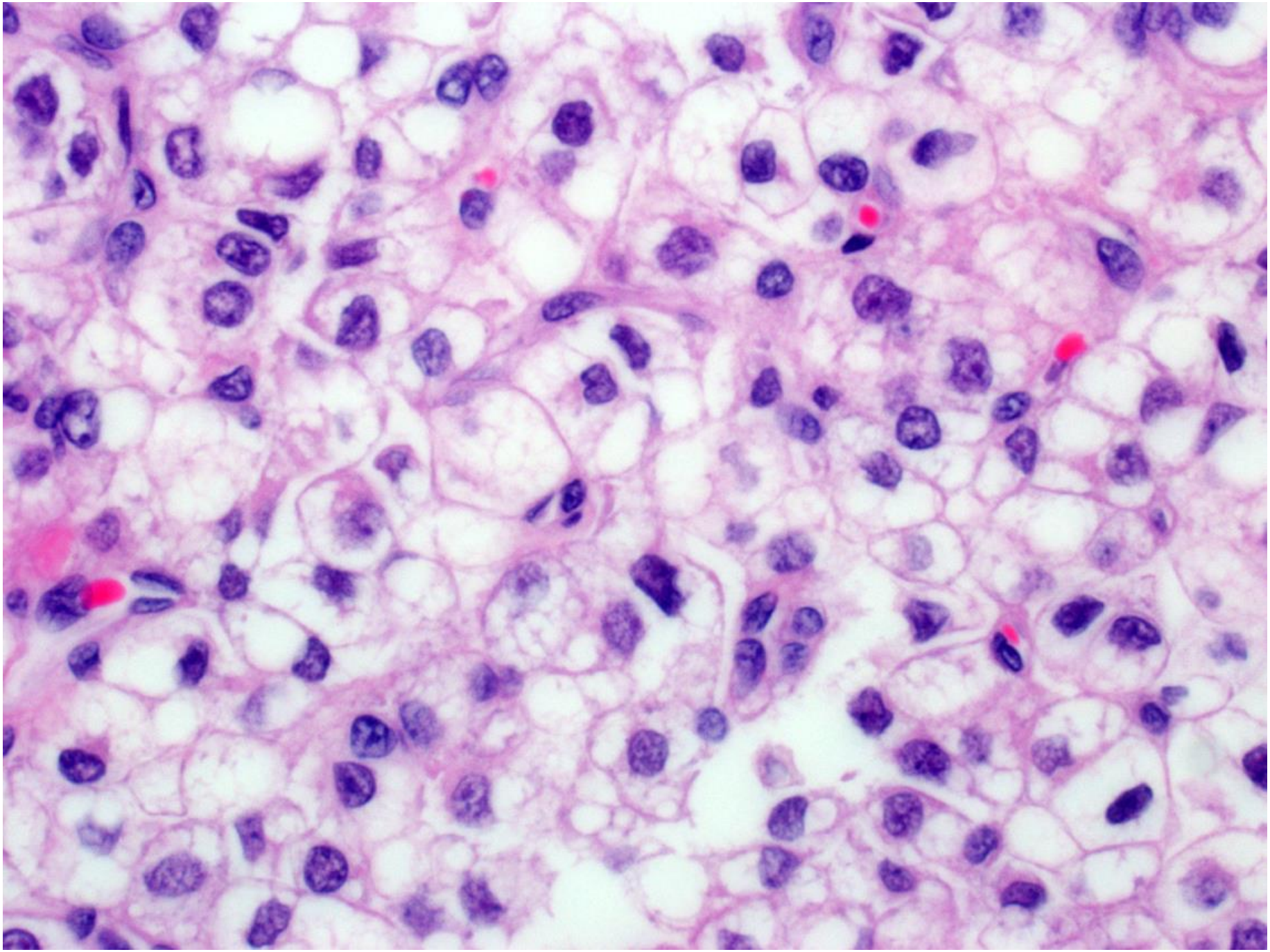
25-year-old woman was found to have an asymptomatic 8 cm pelvic mass during routine GYN physical exam. Imaging showed a circumscribed solid ovarian mass. She underwent salpingo-oophorectomy. Grossly the tumor was a 10 cm homogenously solid, slightly multinodular, yellow orange mass without necrosis or cysts.





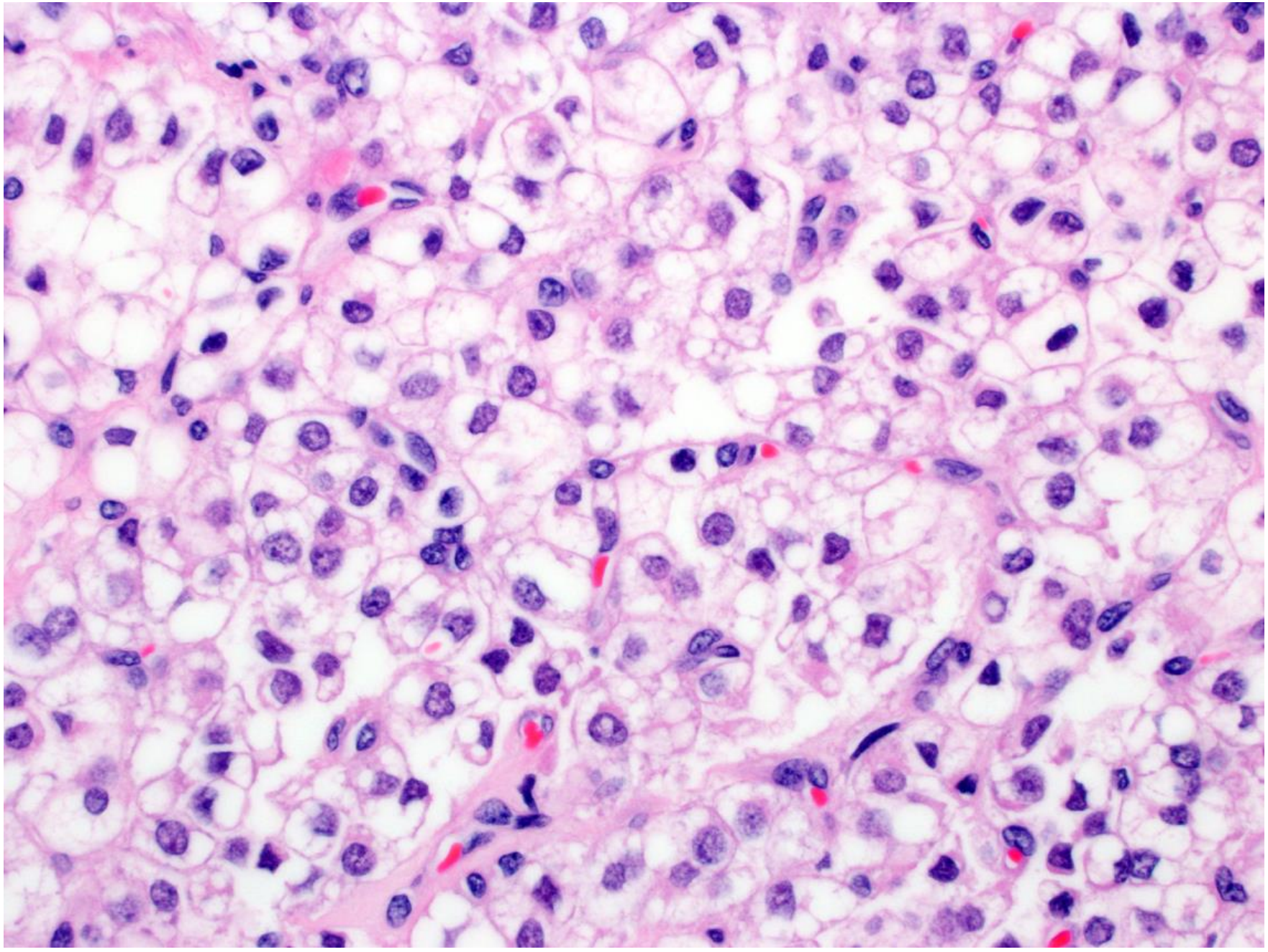




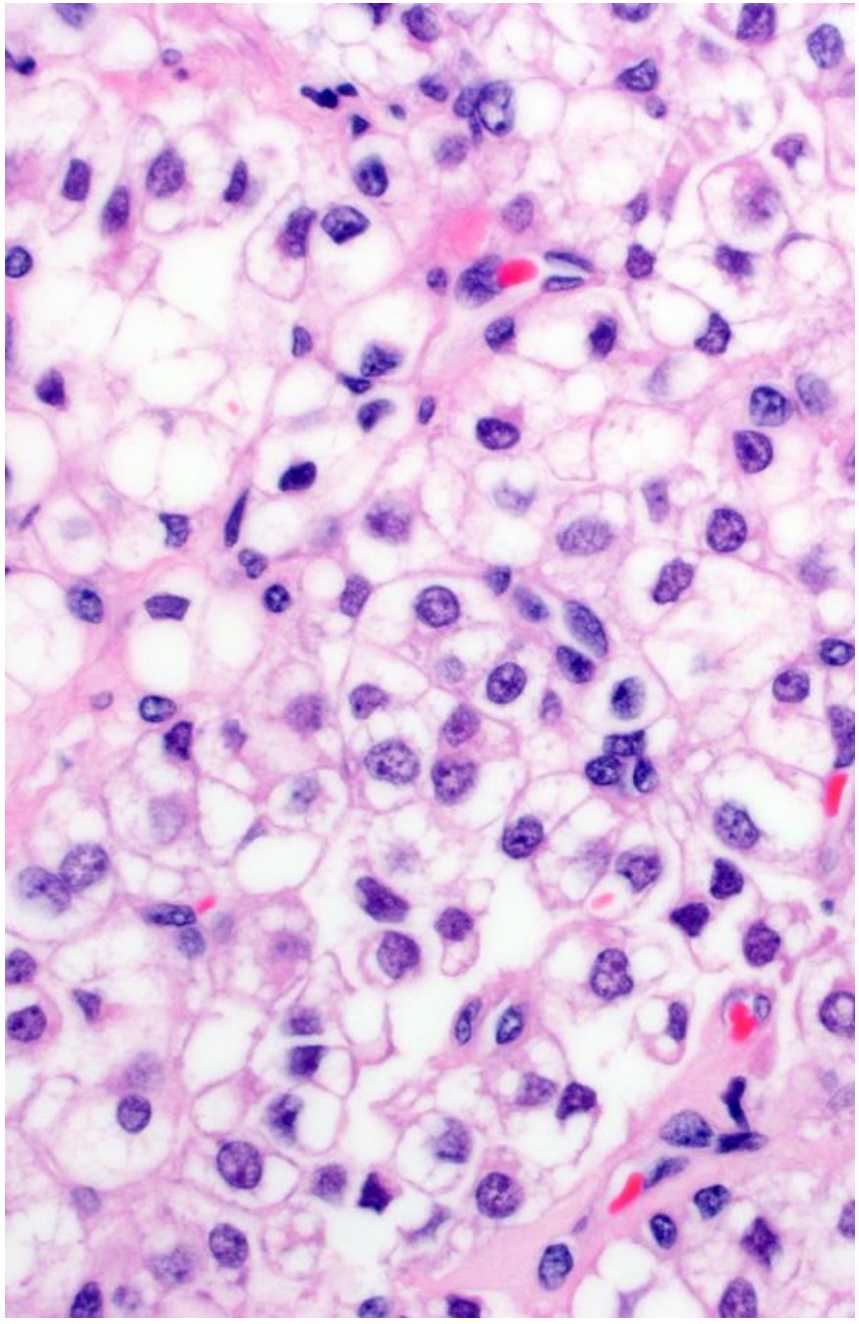



Diagnosis?

Clear cell rich tumor; solid, nested pattern



Clear cell rich tumor; solid, nested pattern



Consult requested: Is this a PEComa ?

HMB45: Negative
MelanA: Positive

Clear cell rich tumor; solid, nested pattern

Epithelial Tumors
Clear cell carcinoma
Endometrioid adenocarcinoma, clear cell rich
High grade serous carcinoma, clear cell rich

IHC	
EMA	Negative
CK7, Keratin	Negative
PAX8	Negative
ER	Negative

Clear cell rich tumor; solid, nested pattern

Epithelial Tumors
Clear cell carcinoma
Endometrioid adenocarcinoma, clear cell rich
High grade serous carcinoma, clear cell rich

Germ Cell Tumors
Yolk sac tumor, solid pattern
Struma ovarii, solid pattern

IHC	
EMA	Negative
CK7, Keratin	Negative
PAX8	Negative
ER	Negative

SALL4	Negative
TTF	Negative

Clear cell rich tumor; solid, nested pattern

Epithelial Tumors
Clear cell carcinoma
Endometrioid adenocarcinoma, clear cell rich
High grade serous carcinoma, clear cell rich

Germ Cell Tumors
Yolk sac tumor, solid pattern
Struma ovarii, solid pattern

Sex Cord-Stromal Tumors
Granulosa cell tumor, luteinized
Sertoli cell tumor, lipid rich
Steroid cell tumor

Other Tumors
PEC-oma
Melanoma

IHC	
EMA	Negative
CK7, Keratin	Negative
PAX8	Negative
ER	Negative

SALL4	Negative
TTF	Negative

Clear cell rich tumor; solid, nested pattern

Epithelial Tumors
Clear cell carcinoma
Endometrioid adenocarcinoma, clear cell rich
High grade serous carcinoma, clear cell rich

Germ Cell Tumors
Yolk sac tumor, solid pattern
Struma ovarii, solid pattern

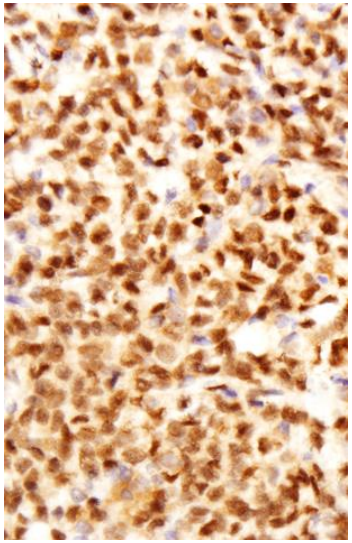
Sex Cord-Stromal Tumors
Granulosa cell tumor, luteinized
Sertoli cell tumor, lipid rich
Steroid cell tumor

Other Tumors
PEC-oma
Melanoma

IHC	
EMA	Negative
CK7, Keratin	Negative
PAX8	Negative
ER	Negative

SALL4	Negative
TTF	Negative

FOXL2	Negative
Inhibin	Positive
Calretinin	Positive
SF-1	Positive



FOXL2 Is a Sensitive and Specific Marker for Sex Cord-Stromal Tumors of the Ovary

Osama M. Al-Agha, MD,† Hassan F. Huwait, MD,‡ Christine Chow, BMLSc,* Winnie Yang, BSc,† Janine Senz, BSc,† Steve E. Kalloger, BSc,*† David G. Huntsman, MD,*† Robert H. Young, MD,§ and C. Blake Gilks, MD*†‡*

(*Am J Surg Pathol* 2011;35:484–494)

Histopathology

Histopathology 2014, **64**, 380–388. DOI: 10.1111/his.12253

A current perspective on the pathological assessment of *FOXL2* in adult-type granulosa cell tumours of the ovary

Stefan Kommoss,[1,2] Cyril Blake Gilks,[2] Roland Penzel,[3] Esther Herpel,[3] Robertson Mackenzie,[4] David Huntsman,[2,4] Peter Schirmacher,[3] Michael Anglesio,[2] Dietmar Schmidt[5] & Friedrich Kommoss[5]

Sex Cord-Stromal Tumors	FOXL2 IHC Positive
Granulosa Cell Tumor	98%
Fibroma, Thecoma	100%
Sclerosing Stromal Tumor	100%
SCTAT	100%
Sertoli-Leydig Cell Tumor	50%
Leydig Cell Tumor	0 %
Stromal Luteoma	0 %
Steroid Cell Tumor, NOS	1/1 (weak)

Table adapted from: (*Am J Surg Pathol* 2011;35:484–494)

1 additonal case of FOXL2 IHC positive steroid cell tumor: *Histopathology* 2014, **64**, 380–388.

Ovarian Steroid Cell Tumor Family is Usually FOXL2 IHC Negative

FOXL2	Negative
Inhibin	Positive
Calretinin	Positive
SF-1	Positive

MelanA	Positive
Androgen R	Positive

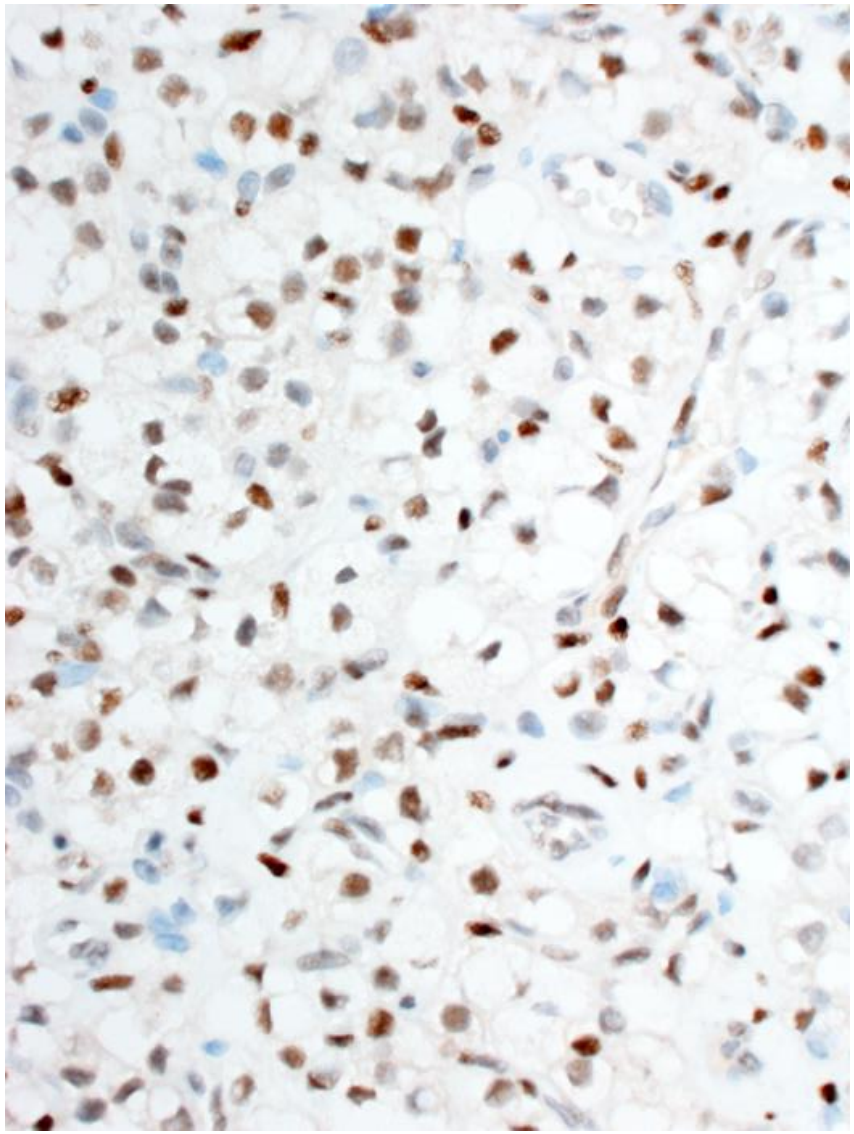
References:

Al-Agha et al. FOXL2 Is a Sensitive and Specific Marker for Sex Cord-Stromal Tumors of the Ovary. Am J Surg Pathol 2011;35:484–494

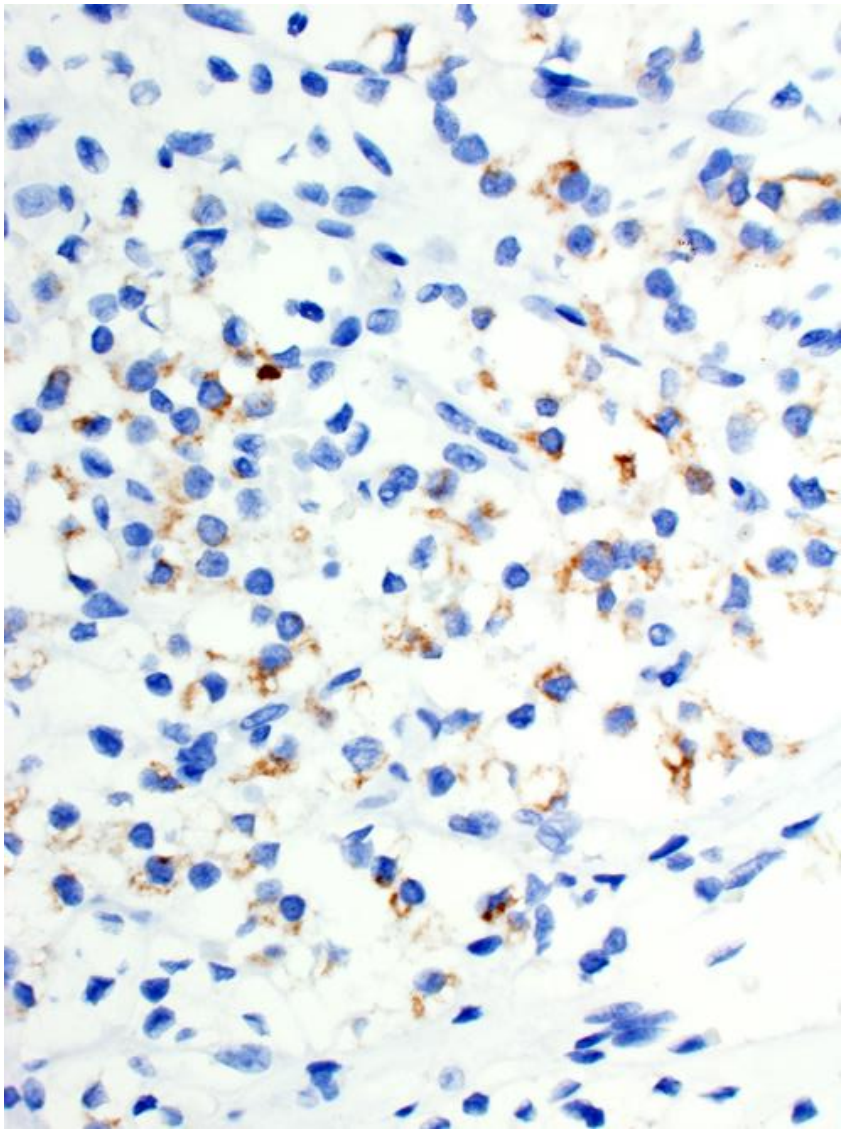
Kommoss et al. A current perspective on the pathological assessment of FOXL2 in adult-type granulosa cell tumours of the ovary. Histopathology 2014, 64, 380–388

Ovarian Steroid Cell Tumor, NOS

Androgen Receptor



Melan A



Adverse Prognostic Findings in Ovarian Steroid Cell Tumor

Accuracy of adverse findings not well studied, but worth documenting them:

Size > 7 cm
Necrosis
Hemorrhage
Significant nuclear atypia
Mitosis >2/10 HPF
Older patient age

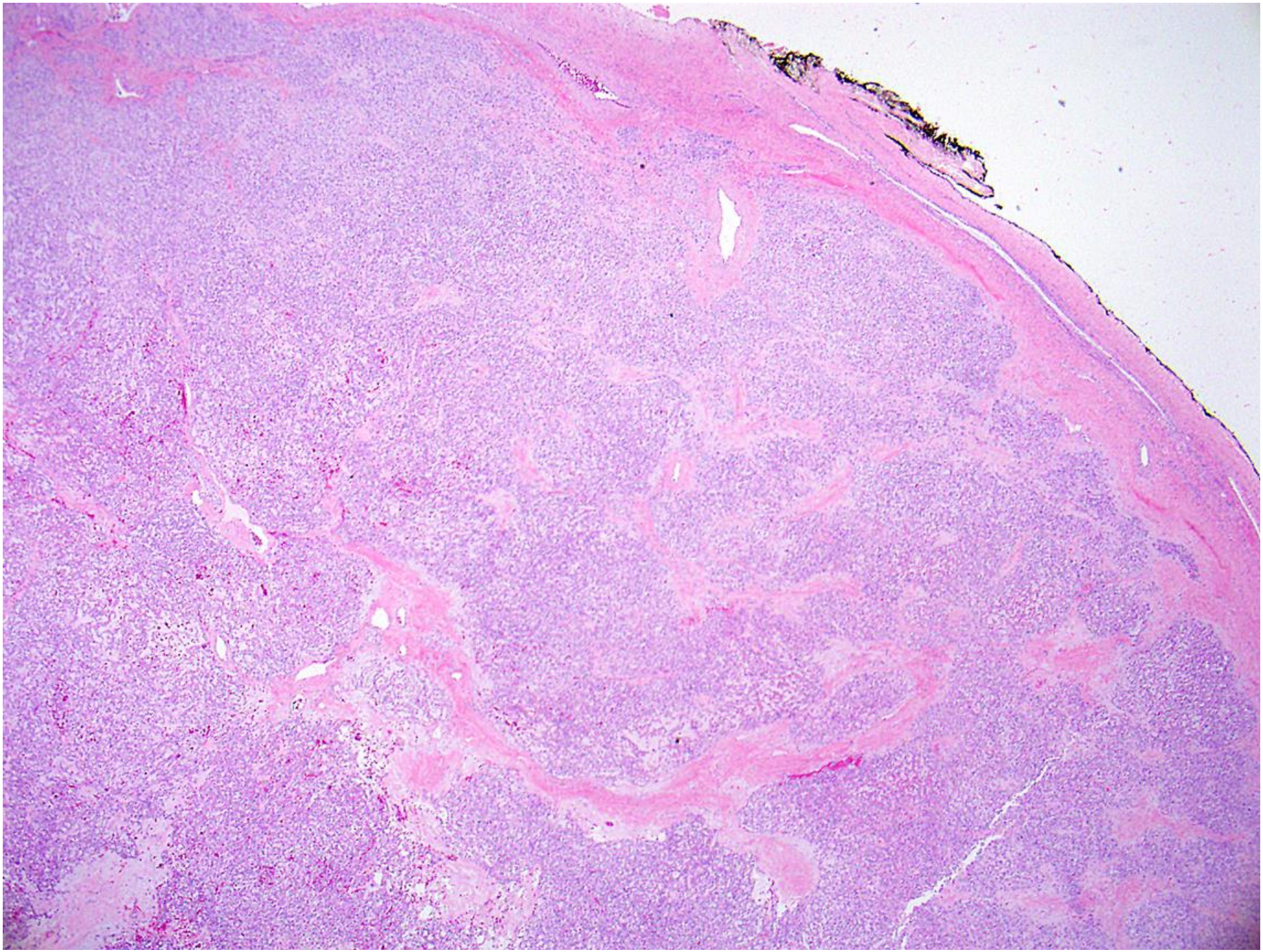
References:

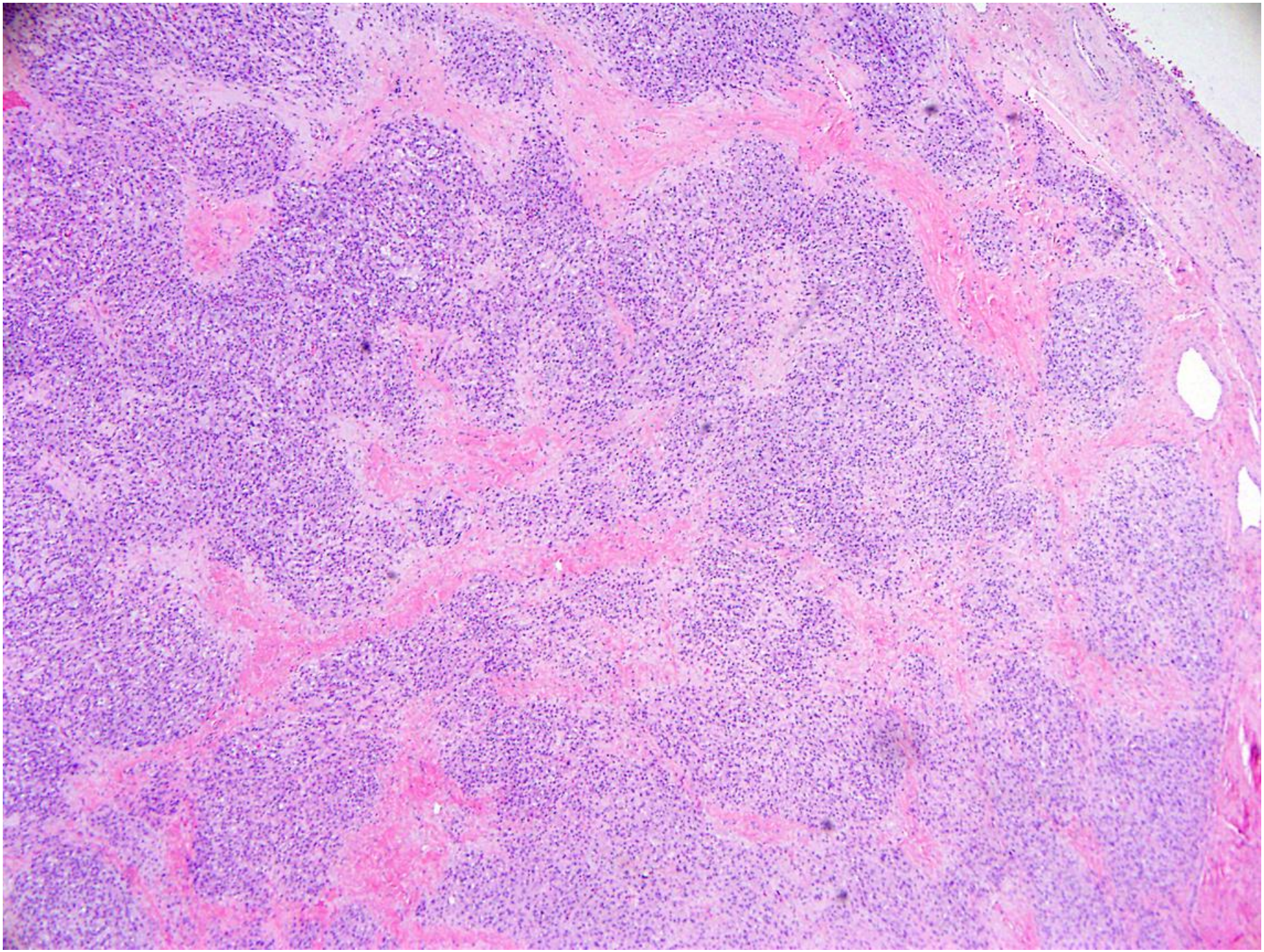
Hayes et al. Ovarian steroid cell tumors NOS: A clinicopathological analysis of 63 cases. Am J Surg Pathol 1987; 11: 835-845.

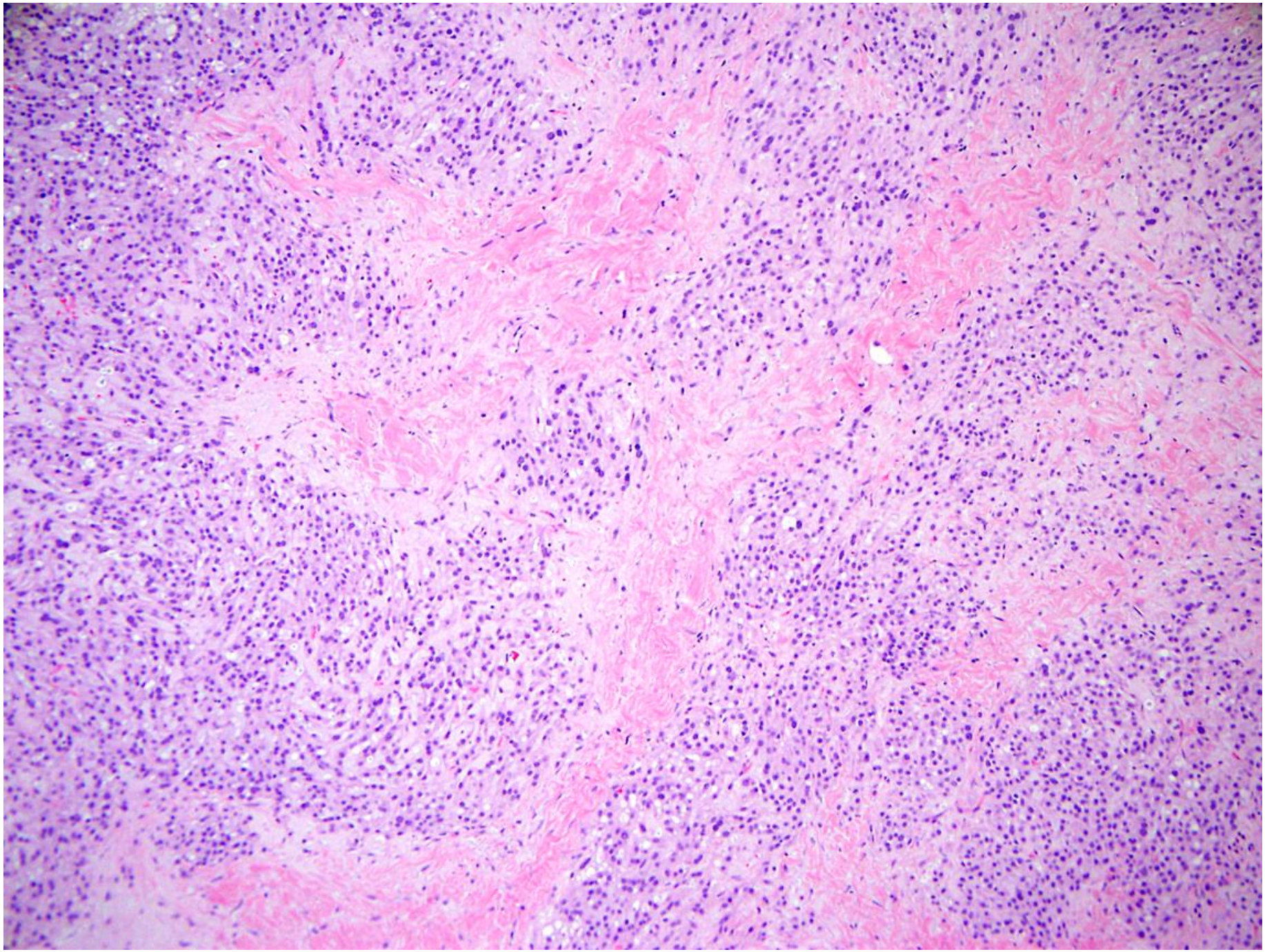
Jones et al. Immunohistochemical profile of steroid cell tumors of the ovary. Int J Gyn Path. 2010; 315-320

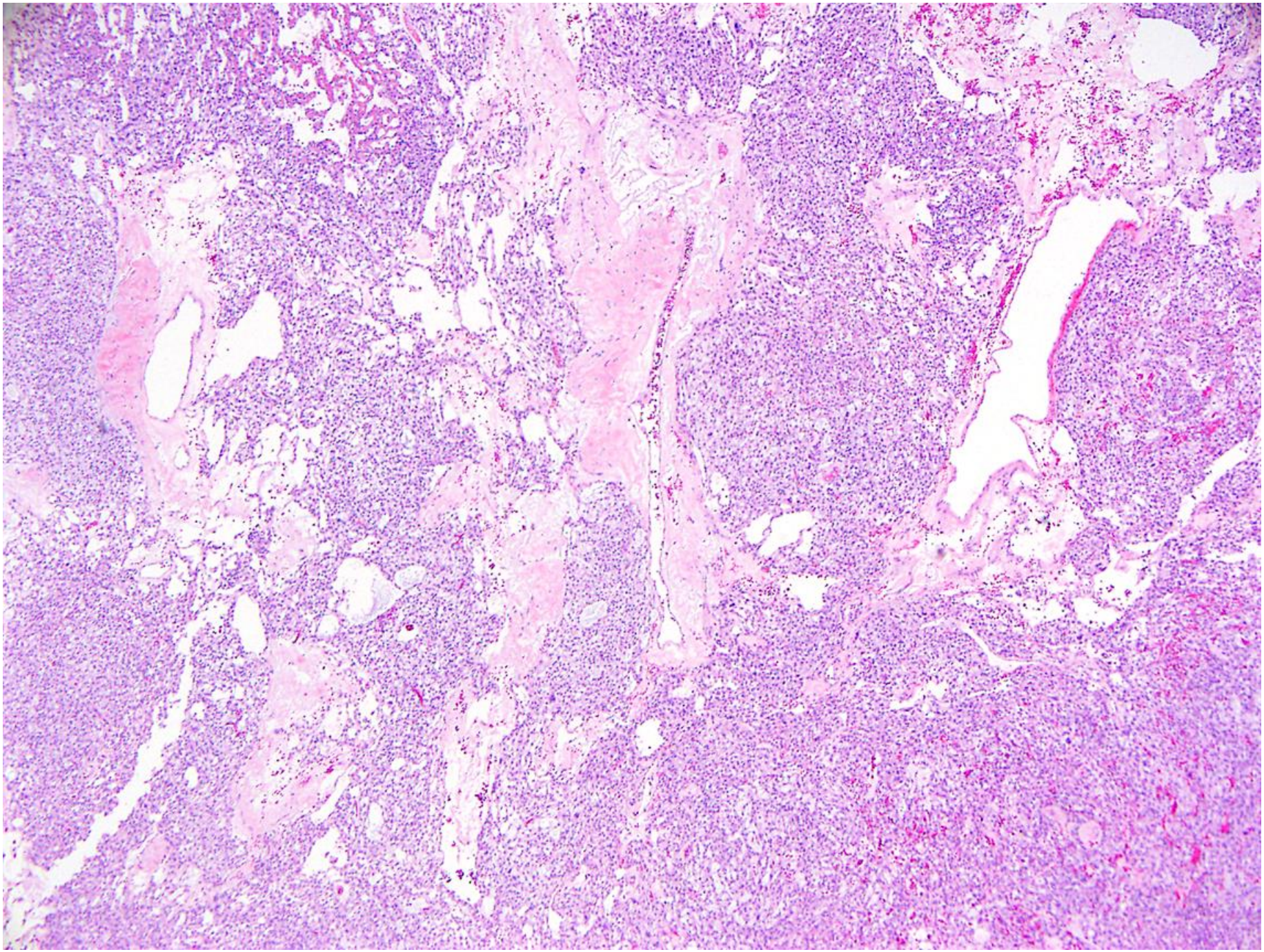
SB 5952
Joe Rabban; UCSF

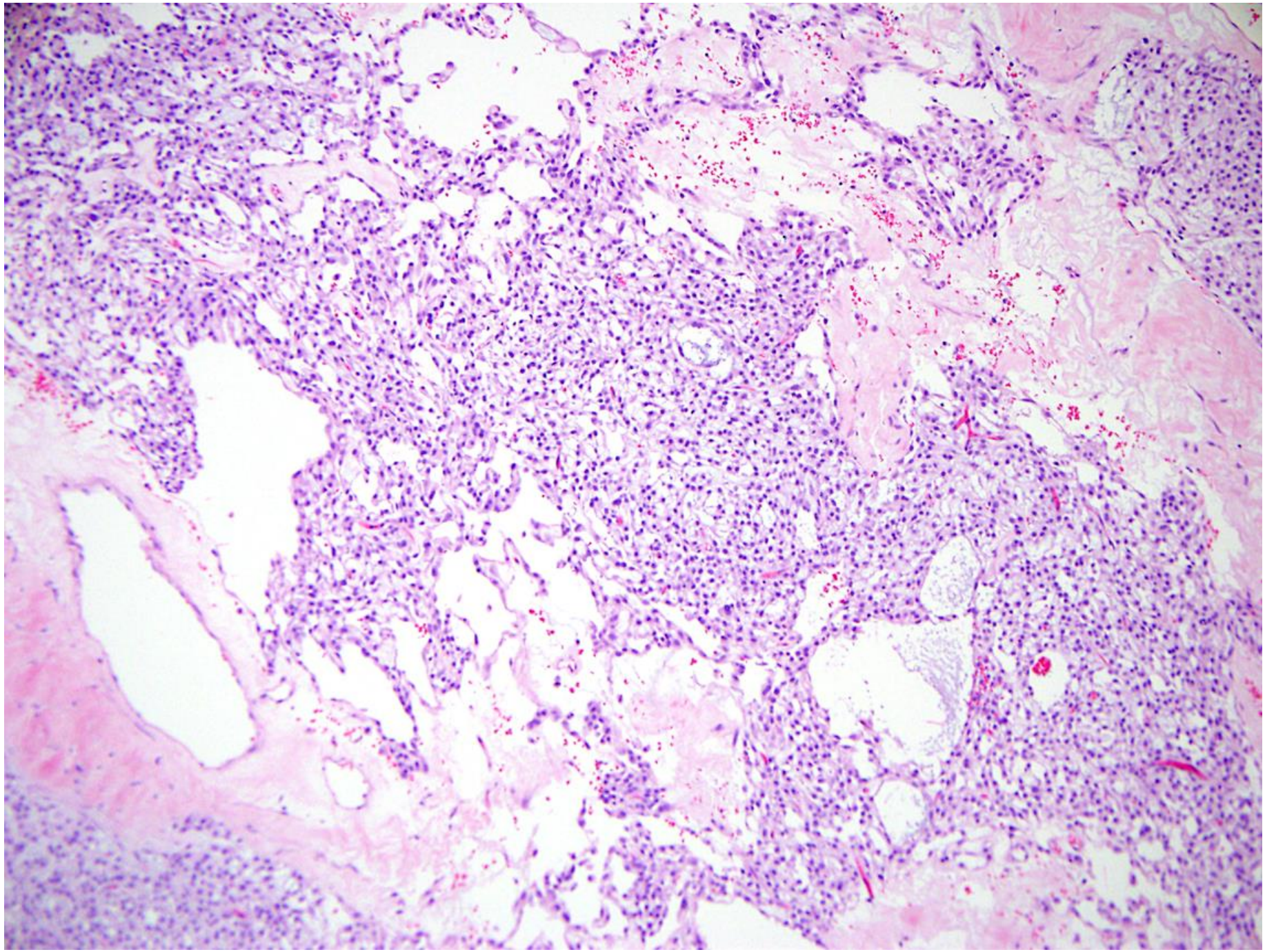
55-year-old woman presented with pelvic pain and a 13 cm ovarian cystic mass was detected on imaging, suspicious for a mucinous tumor. She underwent bilateral salpingo-oophorectomy. Grossly the tumor was 13 cm, cystic / solid, and pink-grey. The cyst contents were clear and straw-colored. There was no hemorrhage or necrosis.

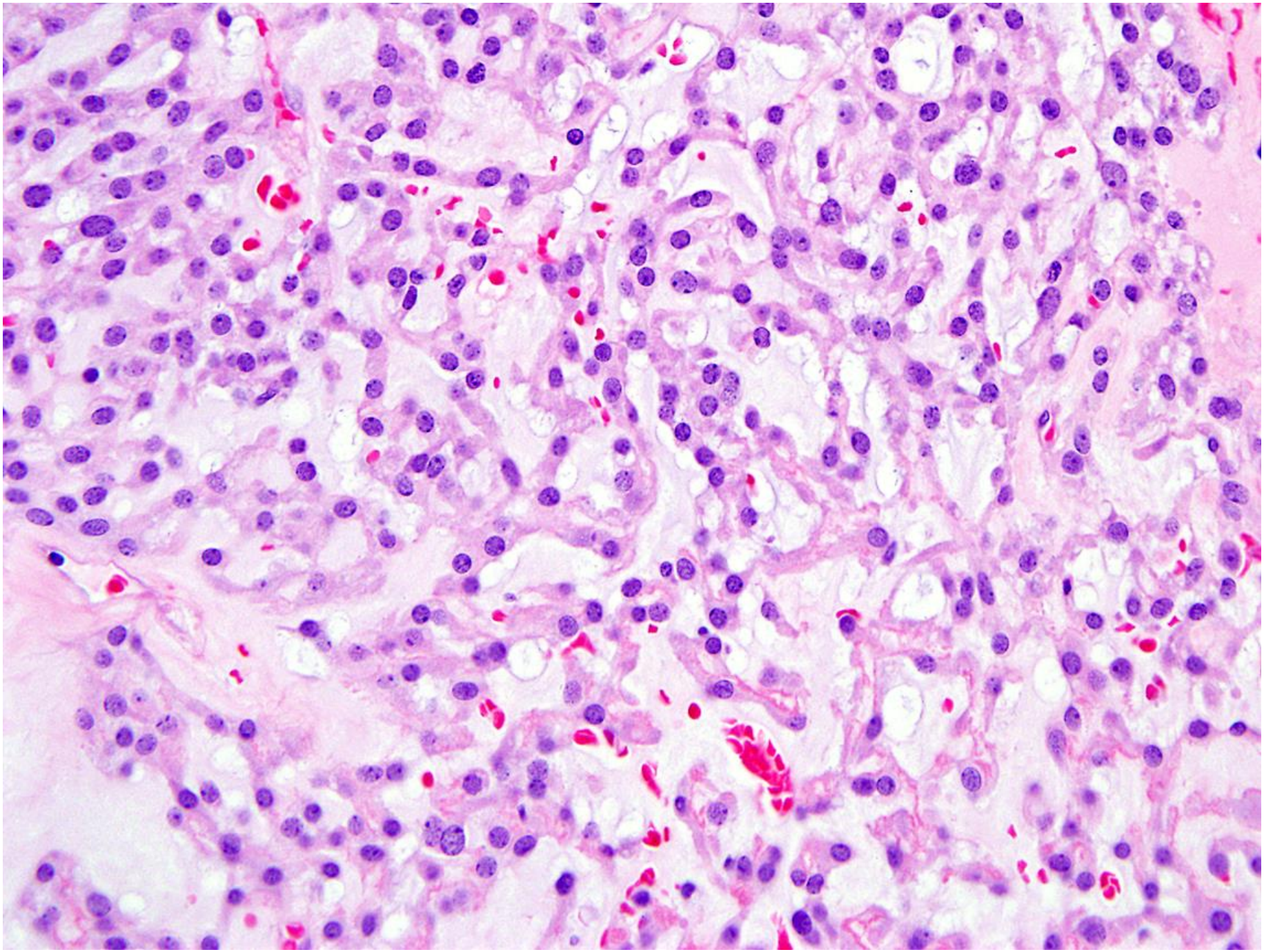


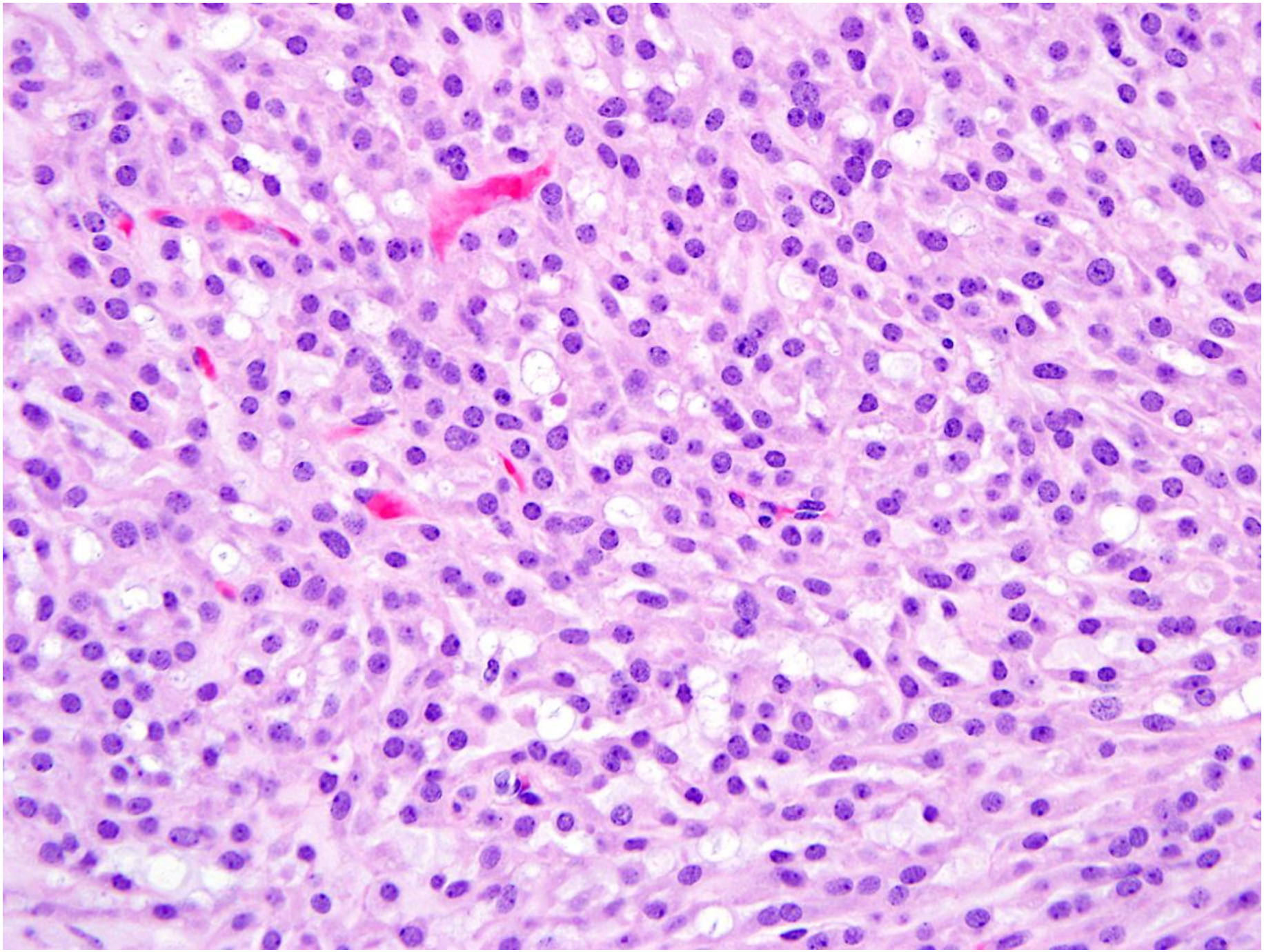


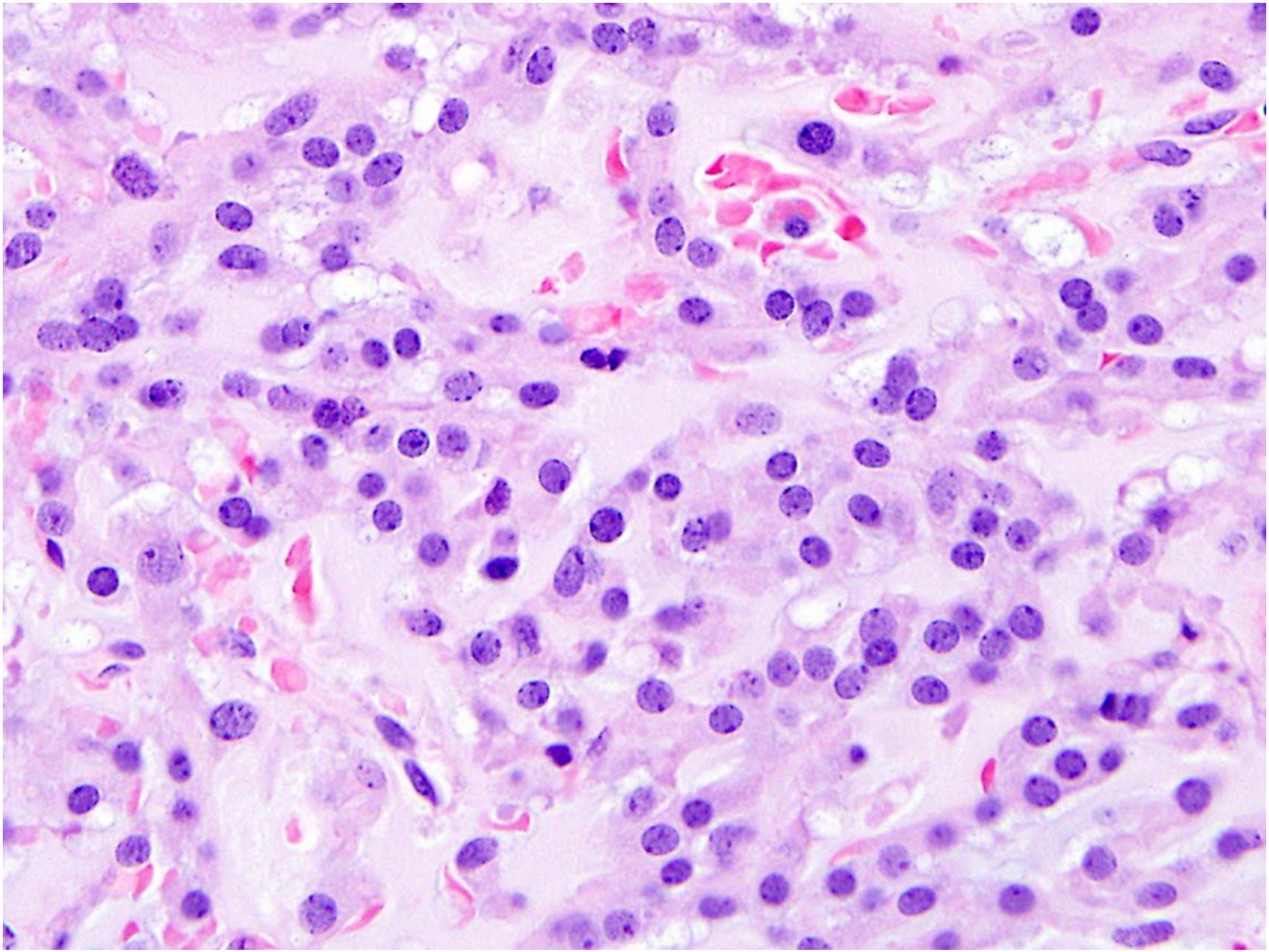






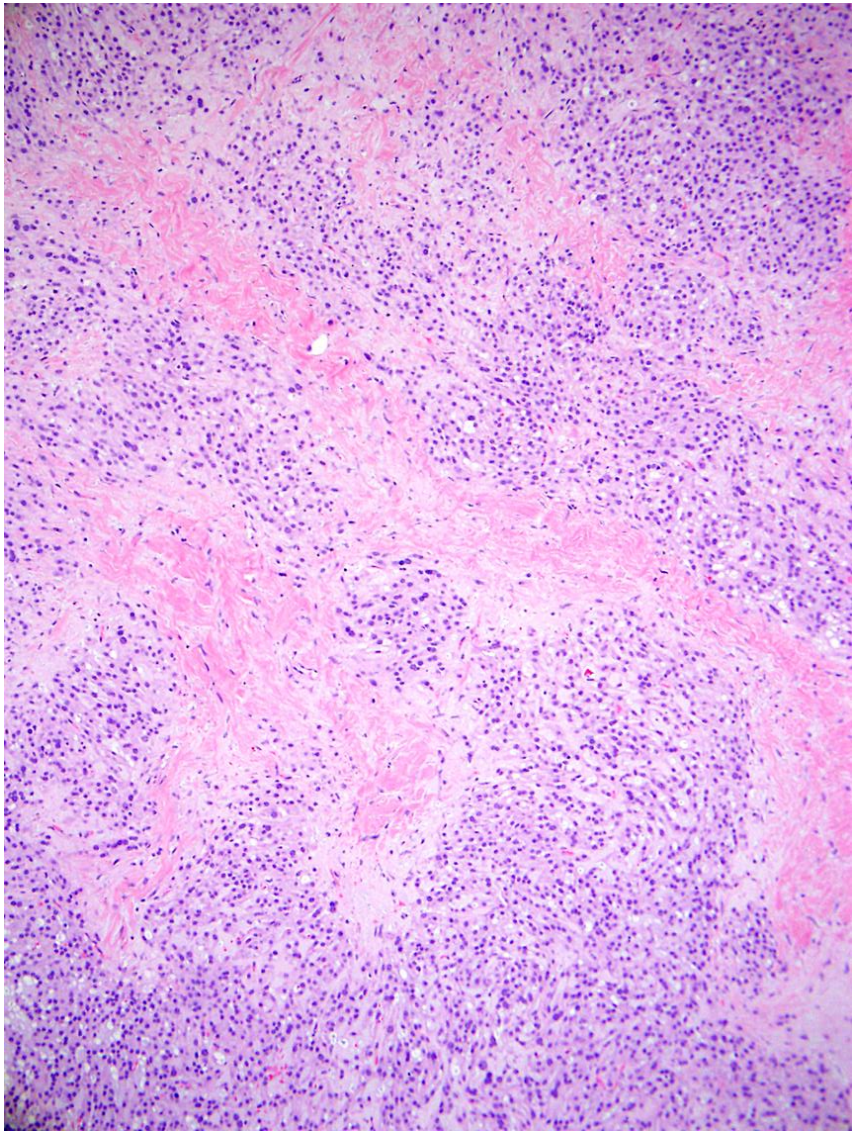




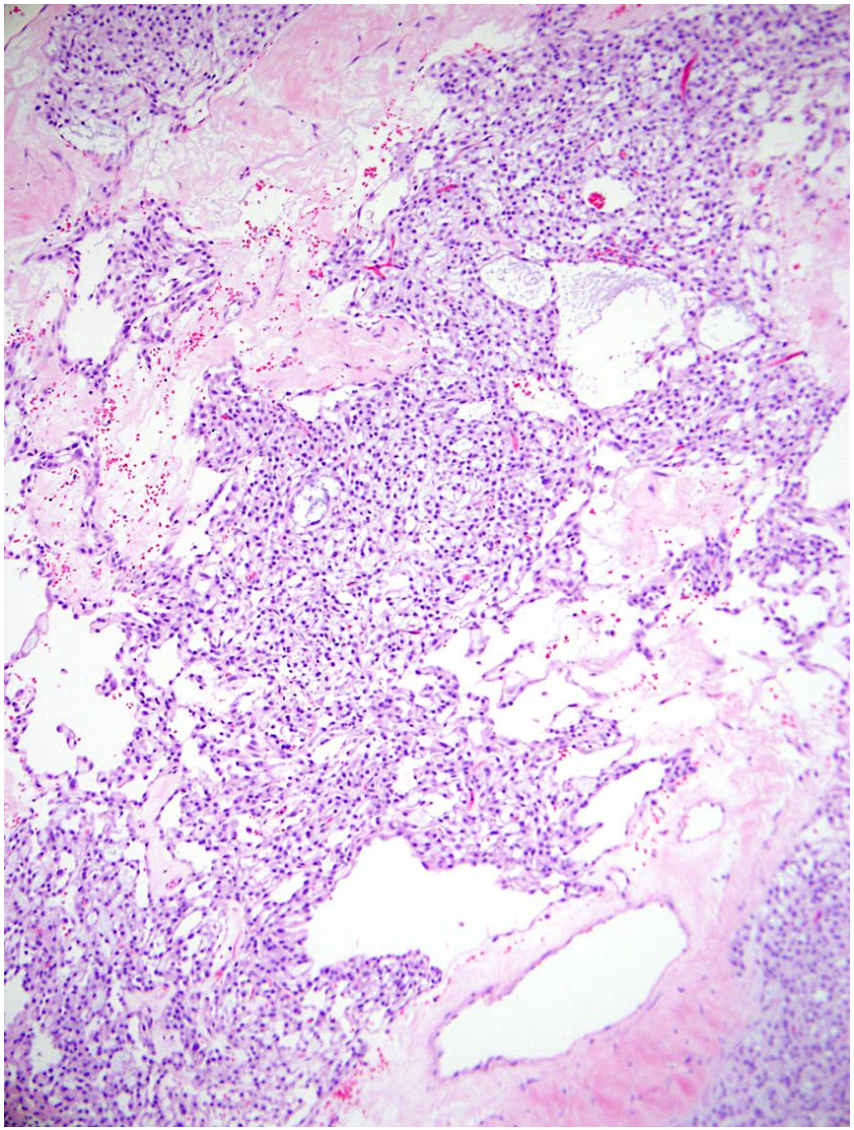



Diagnosis?

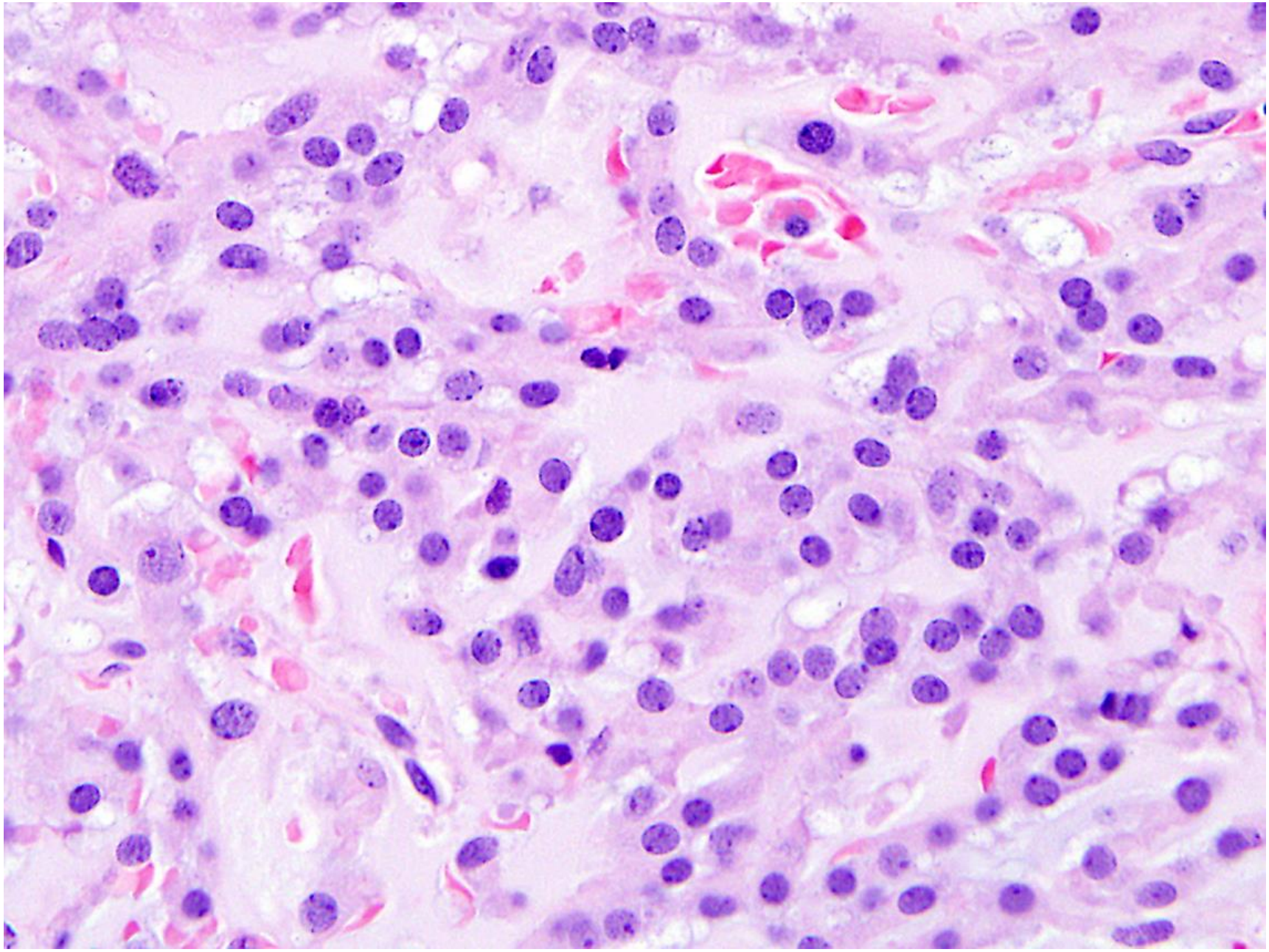
Solid nests
Sclerotic background



Micro-cystic, macro-cystic



Bland nuclei



Epithelial Tumors
Low grade serous carcinoma
Clear cell carcinoma
Metastatic adenocarcinoma (Krukenburg)

Germ Cell Tumors
Yolk sac tumor, solid pattern
Struma ovarii, solid pattern

Sex Cord-Stromal Tumors
Juvenile granulosa cell tumor
Sclerosing stromal tumor
Microcystic stromal tumor

Other Tumors
Small cell carcinoma, hypercalcemic type

IHC	
EMA	Negative
CK7, Keratin	Negative
PAX8	Negative
ER	Negative

SALL4	Negative
TTF	Negative

Inhibin	Negative
Calretinin	Negative
SF-1	Negative
FOXL2	Positive

Microcystic Stromal Tumor of the Ovary

Report of 16 Cases of a Hitherto Uncharacterized Distinctive Ovarian Neoplasm

Julie A. Irving, MD† and Robert H. Young, MD‡§*

(*Am J Surg Pathol* 2009;33:367–375)

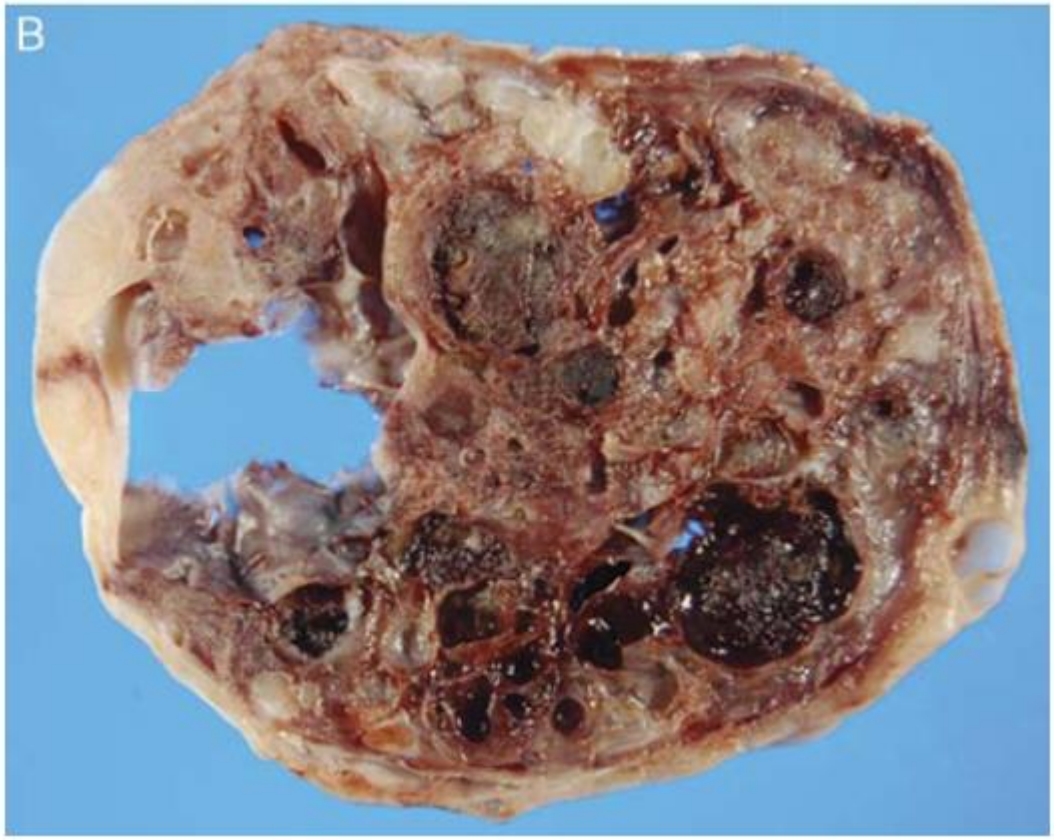
Microcystic Stromal Tumor of Ovary

TABLE 1. Clinicopathologic Features of 16 Microcystic Stromal Tumors

Case	Patient Age (y)	Clinical History	Tumor Side	Tumor Size (cm)	Surgery	Gross Appearance
1	62	Pelvic mass	Left	27	TAH-BSO, LND, omentectomy	Solid-cystic, smooth surface, tan with gelatinous areas, focal hemorrhage, and necrosis
2	45	Abdominal fullness	Left	10	TAH-BSO, peritoneal biopsies	Solid-cystic, smooth surface, tan-white with focally hemorrhagic with myxoid areas
3	51	Adnexal mass	Left	12	TAH-BSO, omentectomy, appendectomy, pelvic washings	Solid-cystic, smooth surface, tan
4	29	Incidental ovarian mass on U/S, 22 wk pregnant	Left	10	LO	Multicystic, smooth surface, tan-white fibrous walls
5	58	Ovarian mass	Right	6.2	TAH-BSO, LND, peritoneal biopsy, pelvic washings	Unilocular cyst up to 1.0 cm thick, smooth surface, tan-pink
6	26	Pelvic pain	NS	8.5	BSO	Solid-cystic, smooth surface, pink-red to yellowish; gritty
7	29	Ovarian mass	Right	6.0	RO	Solid-cystic; smooth surface, tan with focal hemorrhage, and necrosis
8	45	Adnexal mass, menorrhagia, anemia	Left	4.0	LSO, uterine curettings	Solid, tan
9	63	Adnexal mass	Right	4.6	RO	Solid-cystic, smooth surface, tan-gray
10	56	Pelvic mass		4.2	BSO	Solid-cystic, smooth surface, tan with myxoid areas
11	45	Ovarian cyst	Right	4.5	TAH-BSO	Solid-cystic, tan-white
12	55	Ovarian mass	Left	24	TAH-BSO	Solid-cystic, cyst walls smooth and glistening, cystic areas filled with old blood
13	44	Pelvic mass	Left	7.0	TAH-BSO	Solid-cystic, tan-white
14	36	Left ovarian mass	Left	3.0	LSO	Solid-cystic, tan-white
15	37	DUB	Right	2.0	TAH-BSO	Solid, well demarcated, rubbery tan-white
16	39	Pelvic mass	Right	6.4	RSO, pelvic washings	Solid, well demarcated, reddish-gray

(*Am J Surg Pathol* 2009;33:367–375)

Microcystic Stromal Tumor of Ovary



(*Am J Surg Pathol* 2011;35:1429–1440)

Microcystic Stromal Tumor of Ovary

Immunophenotype: ***First report:***

Negative for epithelial markers
Negative for inhibin, calretinin

Positive CD10, WT1

Proposed origin: **Variant of sex cord stromal tumor (thecoma/SST)**

Outcome: **Limited data but appear to all be benign**

(*Am J Surg Pathol* 2009;33:367–375)

β-catenin (*CTNNB1*) S33C Mutation in Ovarian Microcystic Stromal Tumors

Daichi Maeda, MD, PhD, Junji Shibahara, MD, PhD,* Takahiko Sakuma, MD, PhD,† Masanori Isobe, MD,‡ Shinichi Teshima, MD,§ Masaya Mori, MD,‖ Katsutoshi Oda, MD, PhD,¶ Shunsuke Nakagawa, MD, PhD,¶ Yuji Taketani, MD, PhD,¶ Shumpei Ishikawa, MD, PhD,* and Masashi Fukayama, MD, PhD**

(*Am J Surg Pathol* 2011;35:1429–1440)

Also: no mutations in FOXL2 gene were observed

Microcystic Stromal Tumor of Ovary

Immunophenotype: *Current literature:*

Positive FOXL2, CD10, WT1, beta-catenin

Negative for SF1, inhibin, calretinin

Negative for epithelial and germ cell markers

Proposed origin: **? variant of sex cord stromal tumor**

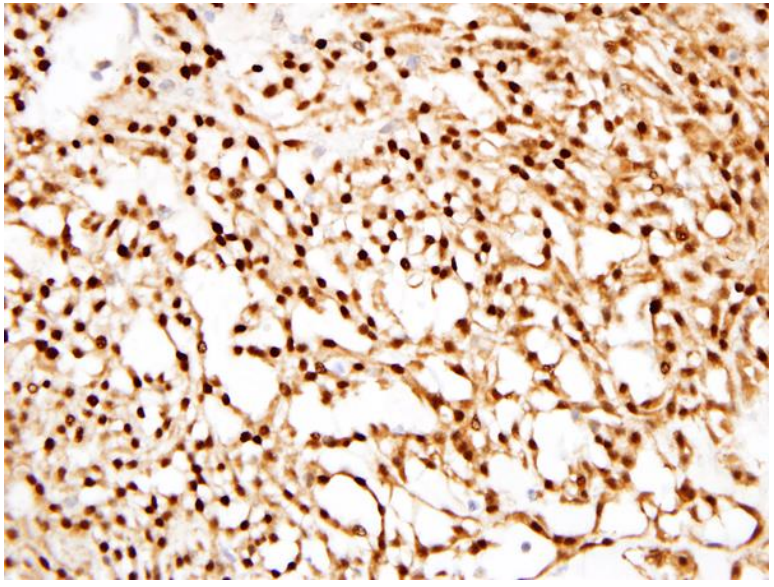
Outcome: **Limited data but appear to all be benign**

Significance: **Avoid over-calling as granulosa cell tumor**

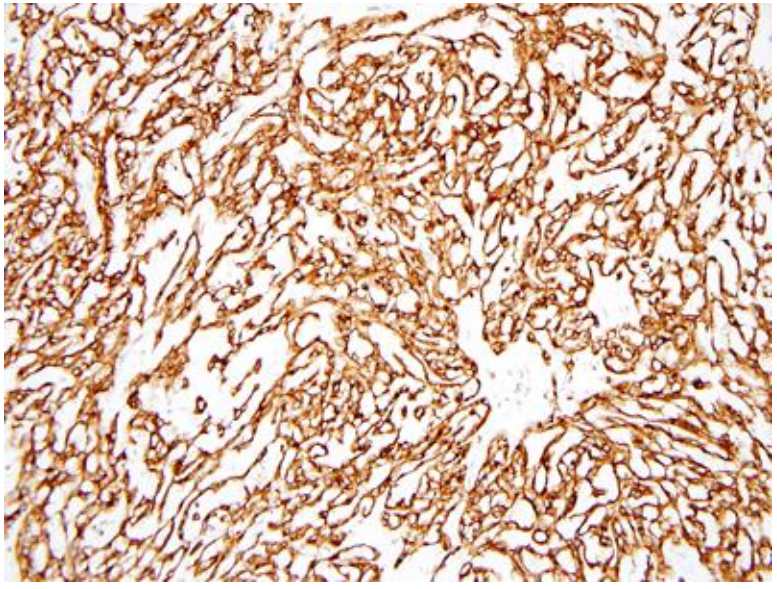
(*Am J Surg Pathol* 2011;35:1429–1440)
(*Am J Surg Pathol* 2009;33:367–375)

Diagnosis: Microcystic Stromal Tumor of Ovary

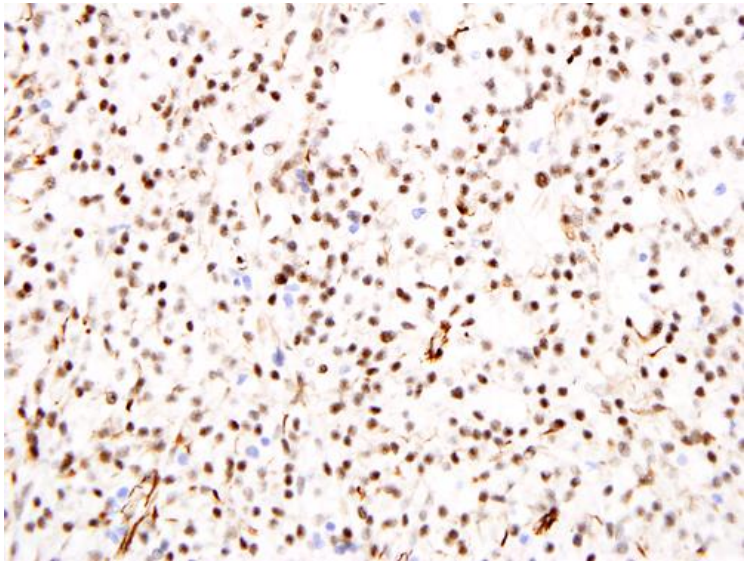
FOXL2



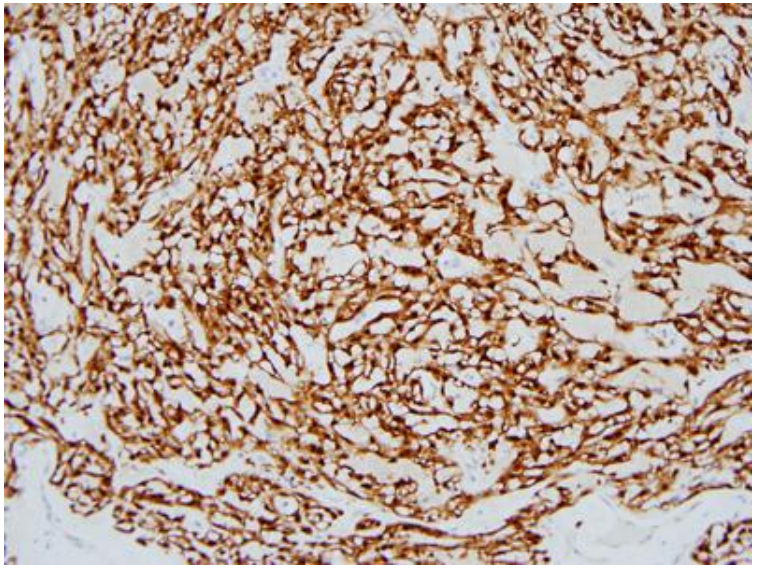
CD10



WT1

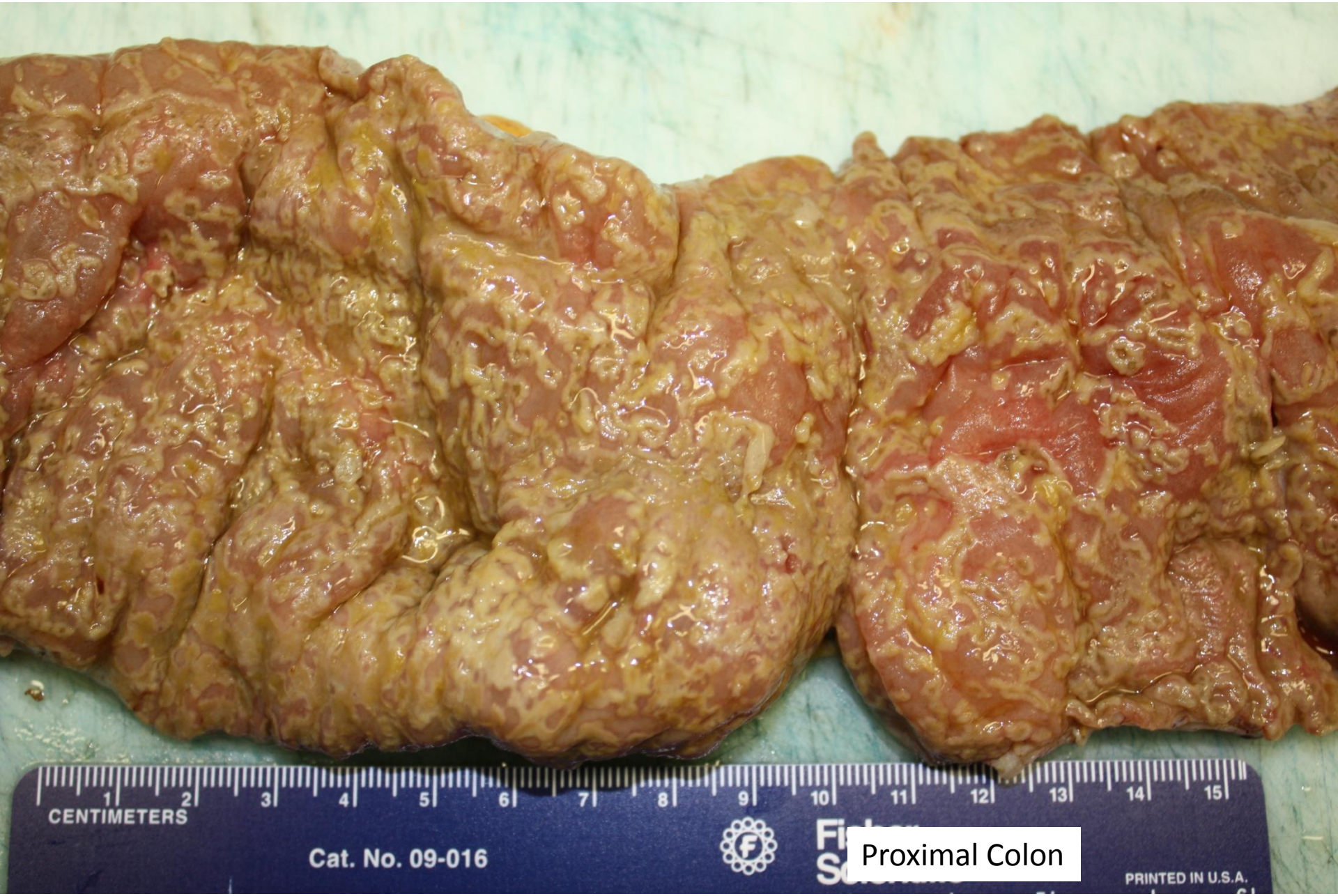


b-catenin



SB 5953
Charles Lombard;
El Camino Hospital

61-year-old woman presenting with total colectomy for sepsis.


CENTIMETERS
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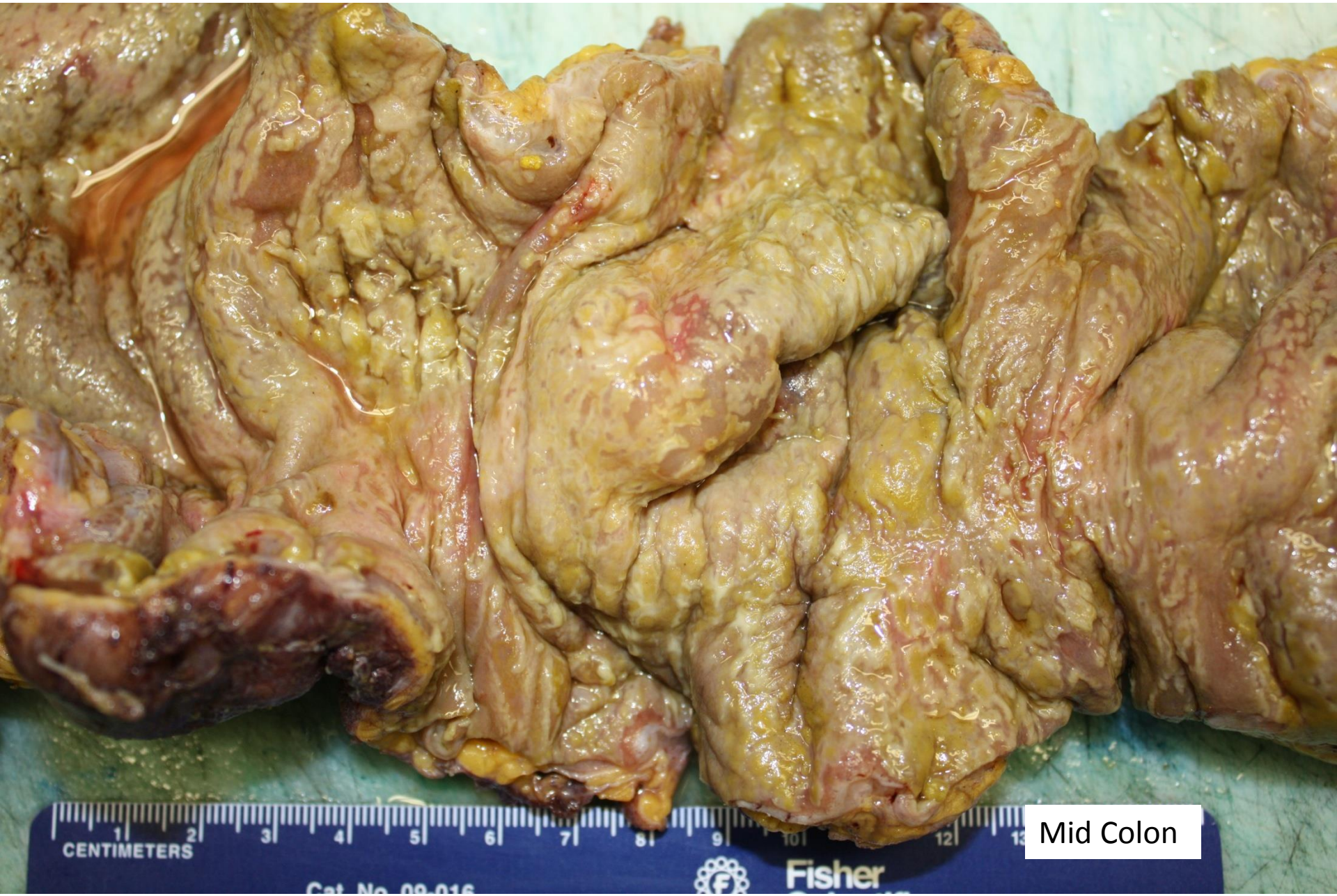
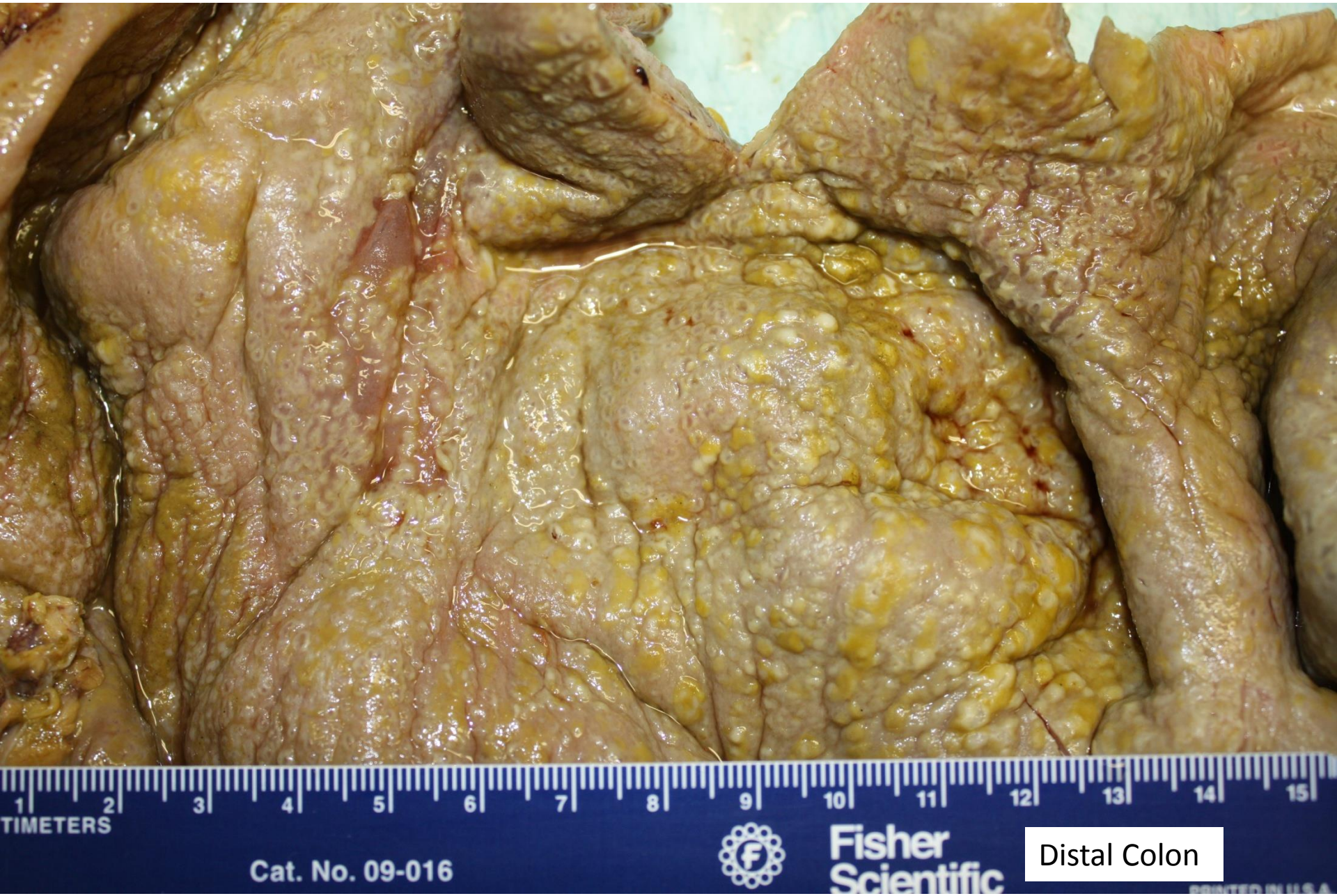
Proximal Colon


CENTIMETERS
Fisher
Mid Colon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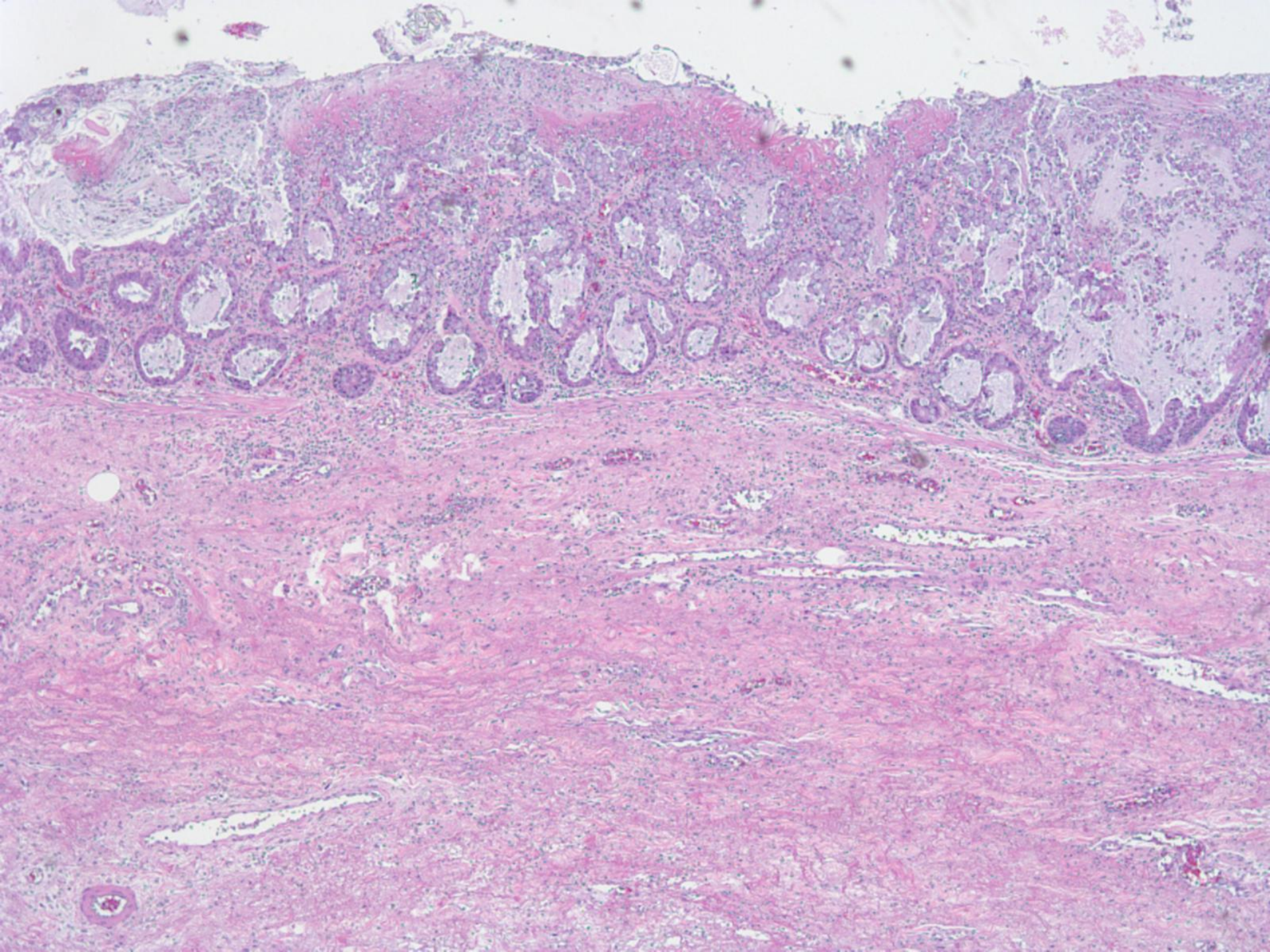
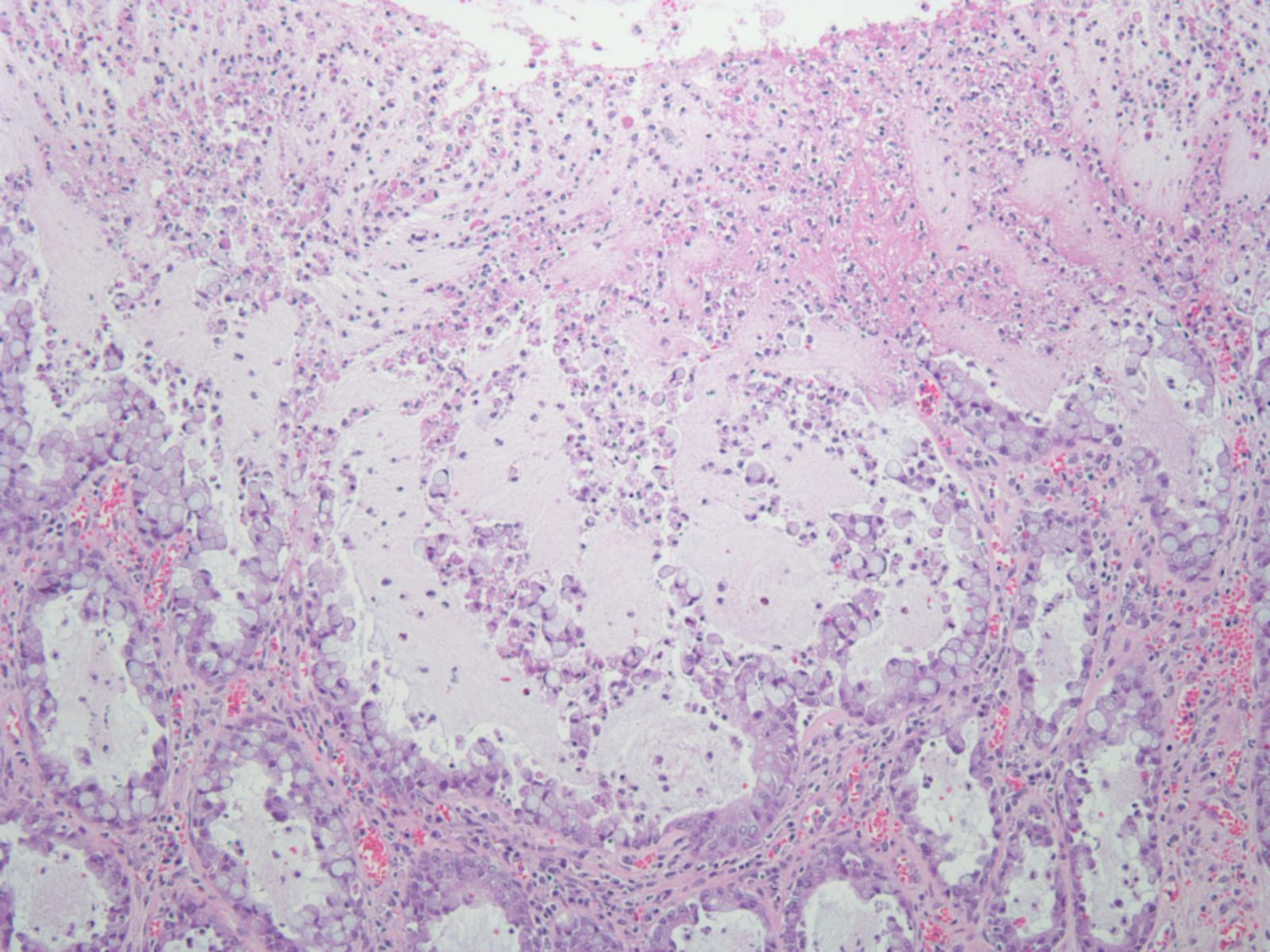
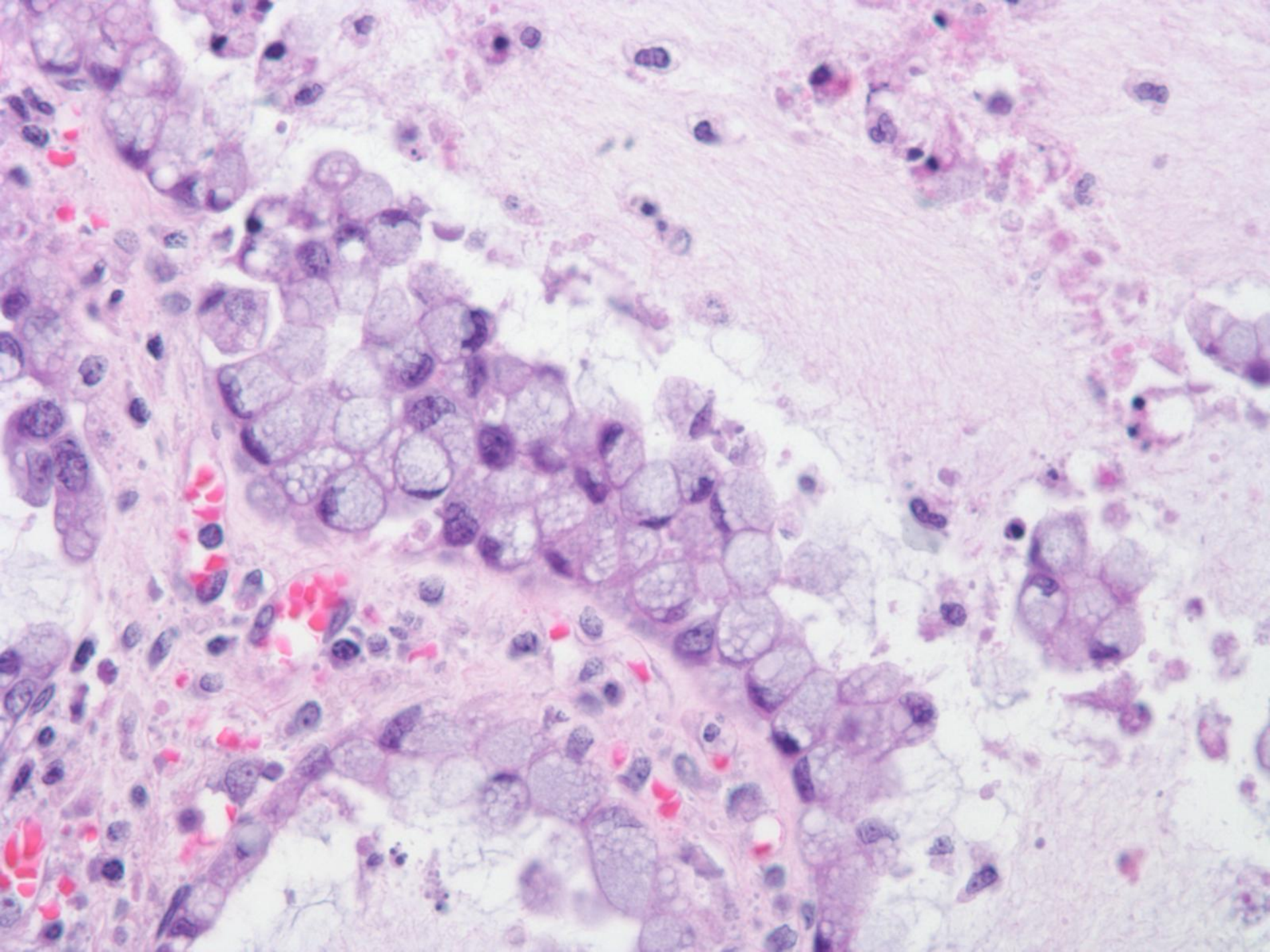
Scientific
Distal Colon








Diagnosis?

C.Difficile-associated colitis

Damage is due to toxin A produced by Clostridium difficile in bowel lumen
Not due to tissue invasion by bacteria

Damage is centered on the crypts

Frequently patchy with abrupt involvement of 2-10 or more crypts surrounded by normal crypts

Entire length of crypt is usually involved

Affected crypts denuded and distended and appear to erupt into the bowel lumen

Resembles an erupting volcano

Lamina propria between involved crypts frequently remains intact

C.Difficile-associated colitis

Pseudomembrane is formed by necrotic epithelial cells, mucus, fibrin and neutrophils

Neutrophils and fibrin frequently appear linear in pseudomembrane

Pseudomembrane may not always be identified on biopsy

Signet ring cells may be seen in rare cases

Confined to crypts and epithelial surface

No infiltration into lamina propria

Cells have small bland nuclei

C.Difficile-associated colitis

Muscularis mucosae, submucosa and muscularis propria are not primarily involved

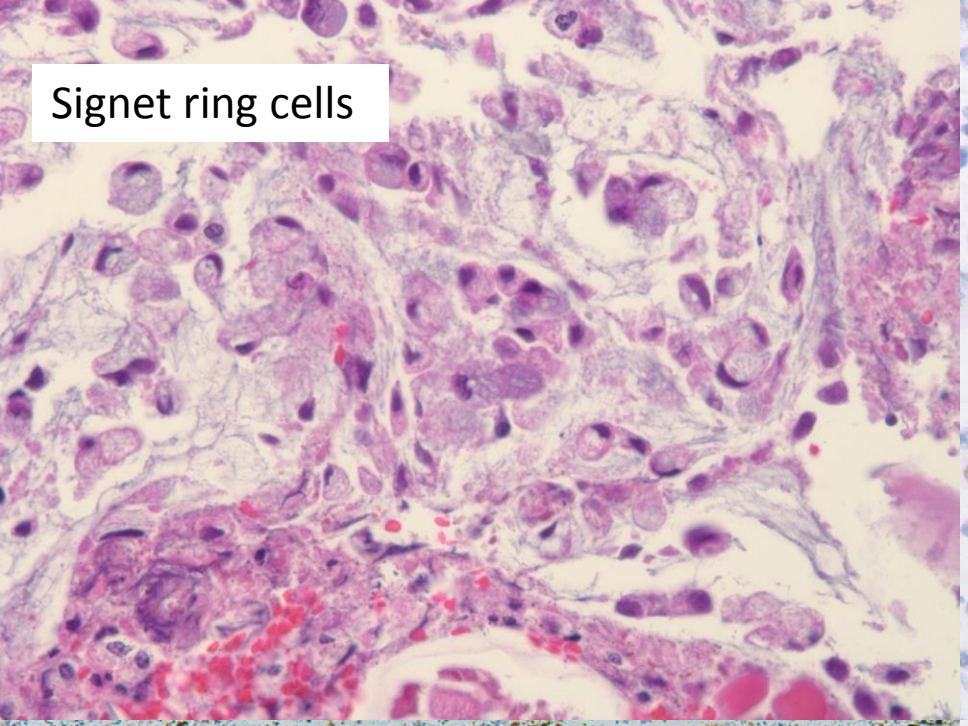
Severe cases may result in complete destruction of mucosa leading to toxic megacolon

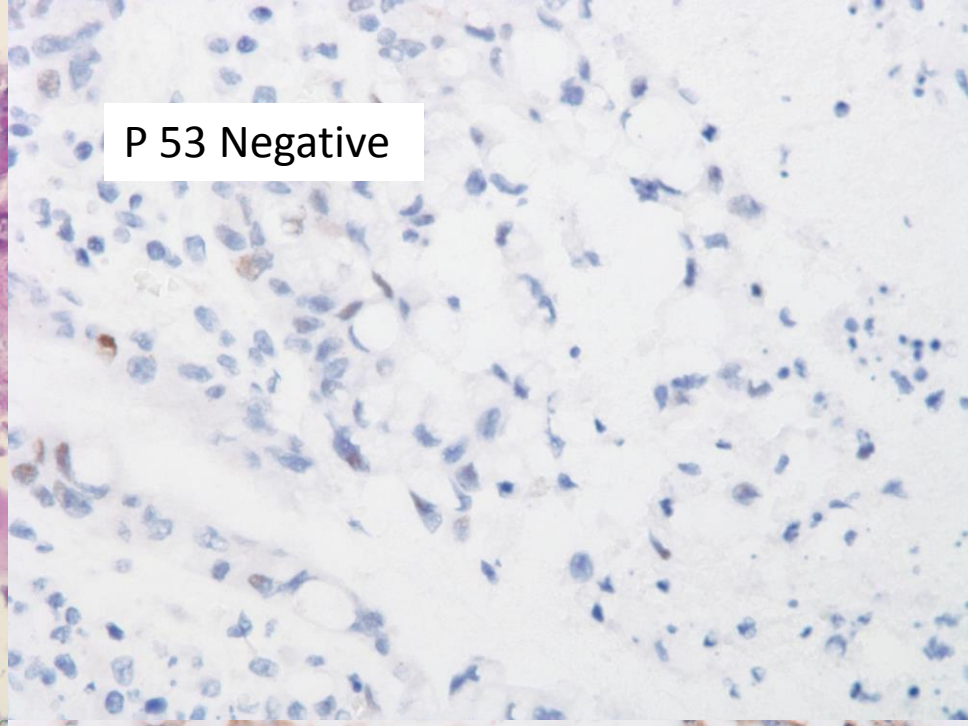
Because of patchy involvement, fragments of pseudomembrane may be present without mucosal changes

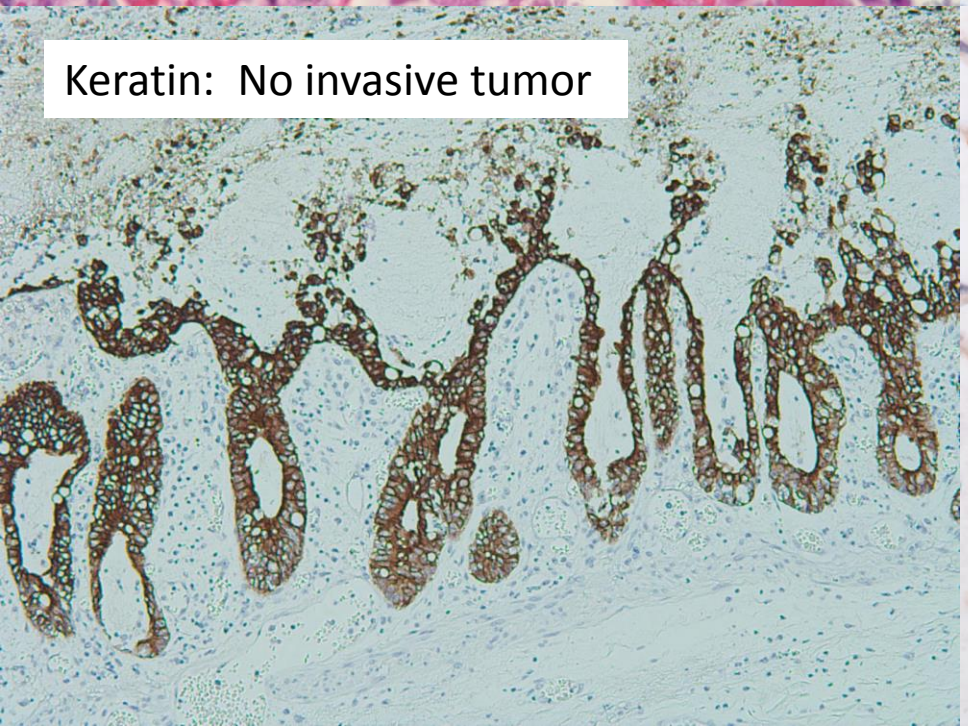
This finding should prompt additional sections and/or clinical correlation

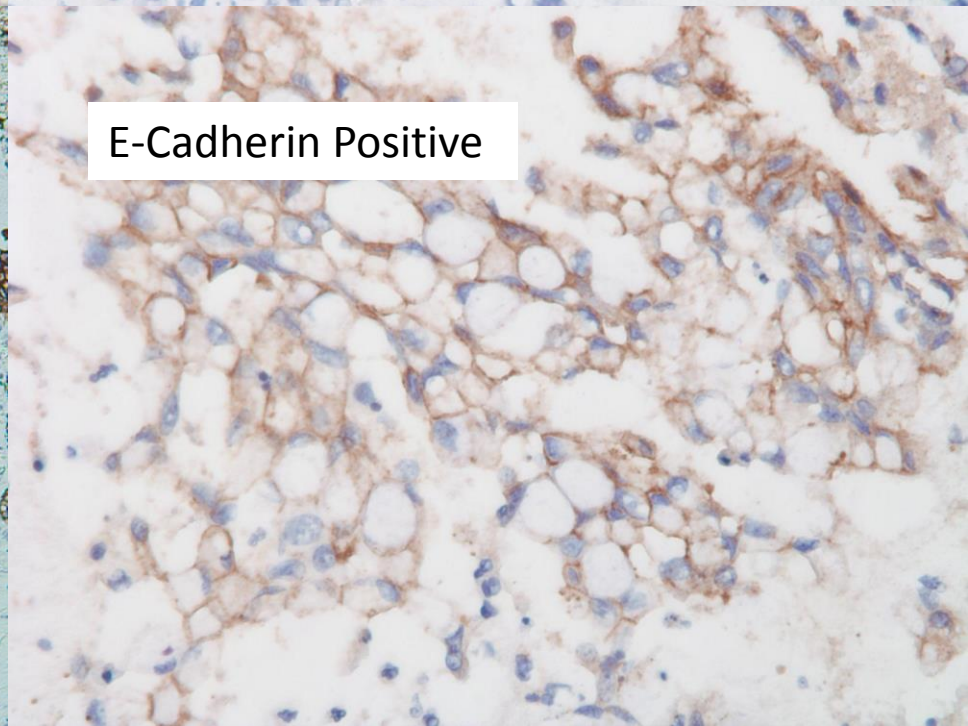
C. Difficile-associated colitis
Signet ring cells

- In setting of colectomy easy to separate from signet ring adenocarcinoma
  - No invasion
  - P53, Ki-67, Keratin
- Potential pitfall in diagnosis on endoscopic biopsy
- Usually seen in fulminant cases


Signet ring cells


P 53 Negative


Keratin: No invasive tumor


E-Cadherin Positive

Other GI sites with benign signet ring cell change

- Stomach
- Small bowel
- Gall Bladder/Biliary tree

- Thought to be related to inflammation and/or ischemia

Hospital acquired C.Difficile Colitis

- Admitted in March for large pleural effusion
- DX: Severe hypothyroidism/myxedema
  - HSV esophagitis
  - Bacteremia with fusobacterium
  - Treated with Unicin x 2 weeks
  - C.Diff toxin studies were negative on admission
- Readmitted 2 days after D/C to SNIF
  - Severe diarrhea
  - C. Difficle screen positive
    - CDG and Toxins A/B
- Reference:
  - Gerding and Lessa: Epidemiology of C Diff Colitis. Infectious Disease Clinics of NA 29 (2015):37-50

The Epidemiology of *Clostridium difficile* Infection Inside and Outside Health Care Institutions

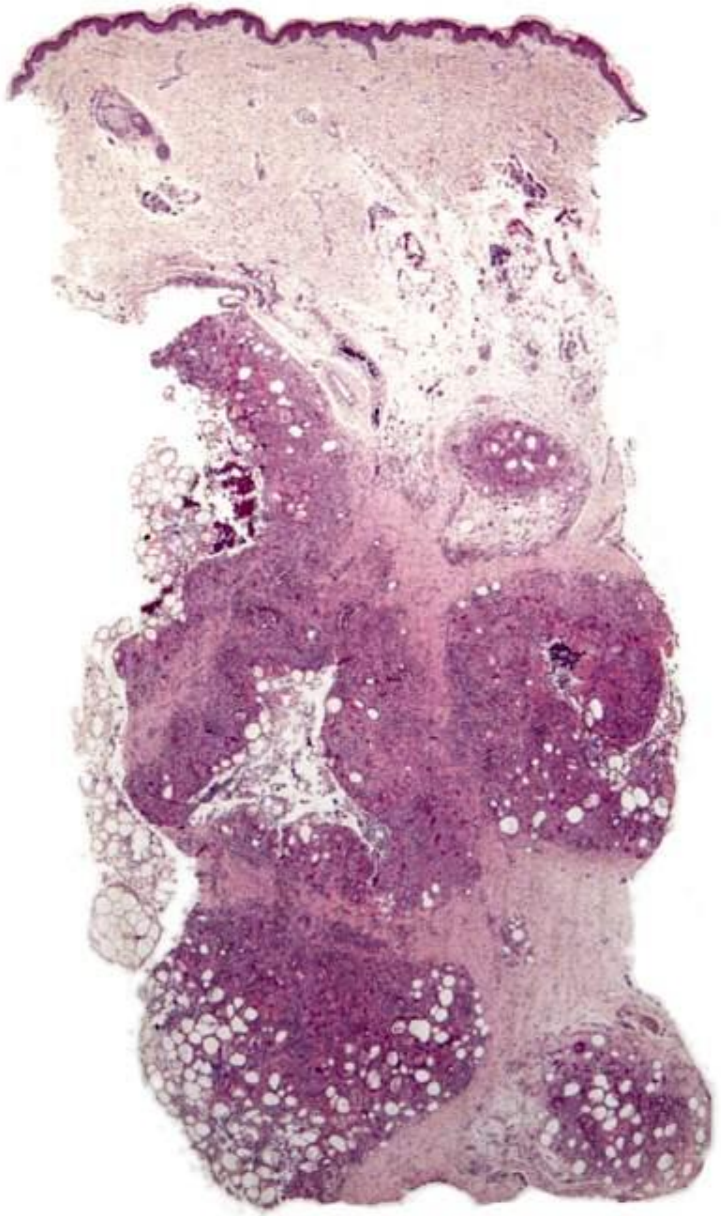
Dale N. Gerding, MD[a,b,*], Fernanda C. Lessa, MD, MPH[c]

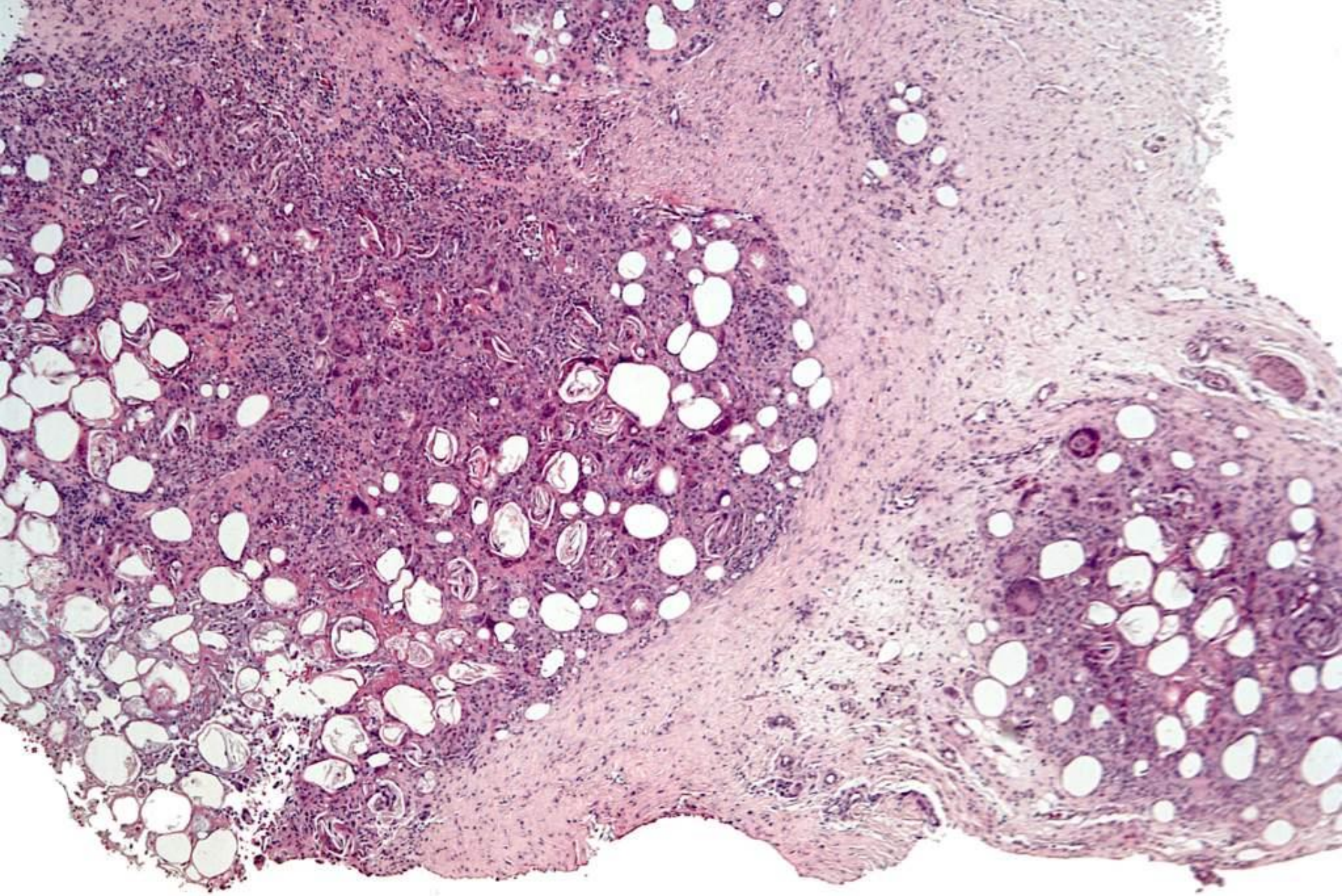
KEY POINTS

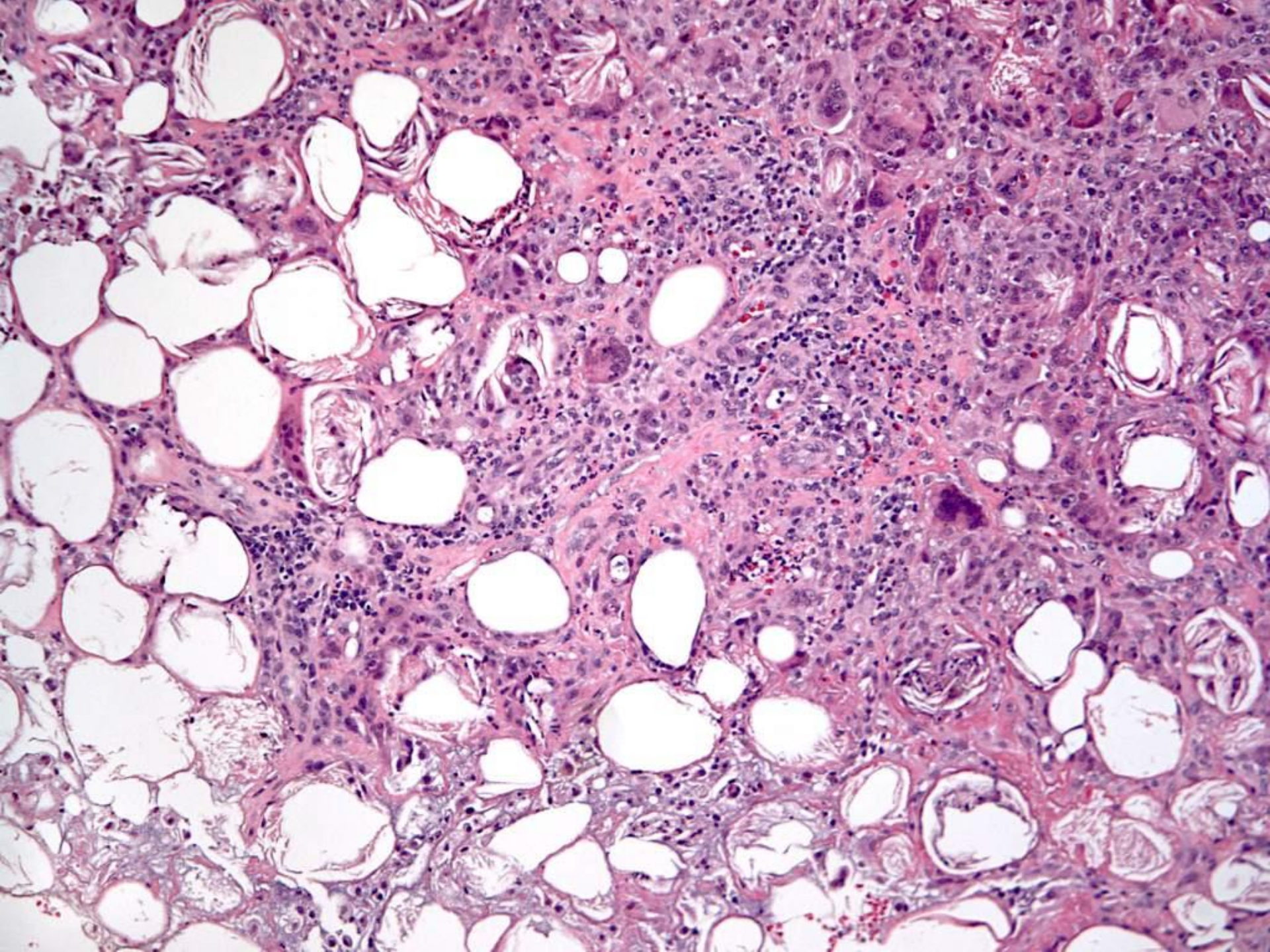
- *Clostridium difficile* has increased in incidence and severity, becoming the most common pathogen of health care–associated infections.
- The epidemiology of *C difficile* is shifting, with most patients having disease onset outside hospital settings.
- Most patients with onset of *C difficile* infection (CDI) in the community either had a recent inpatient or outpatient health care exposure, suggesting that *C difficile* continues to be largely a health care–associated pathogen.
- The molecular epidemiology of CDI is dynamic and other epidemic strains are likely to emerge.

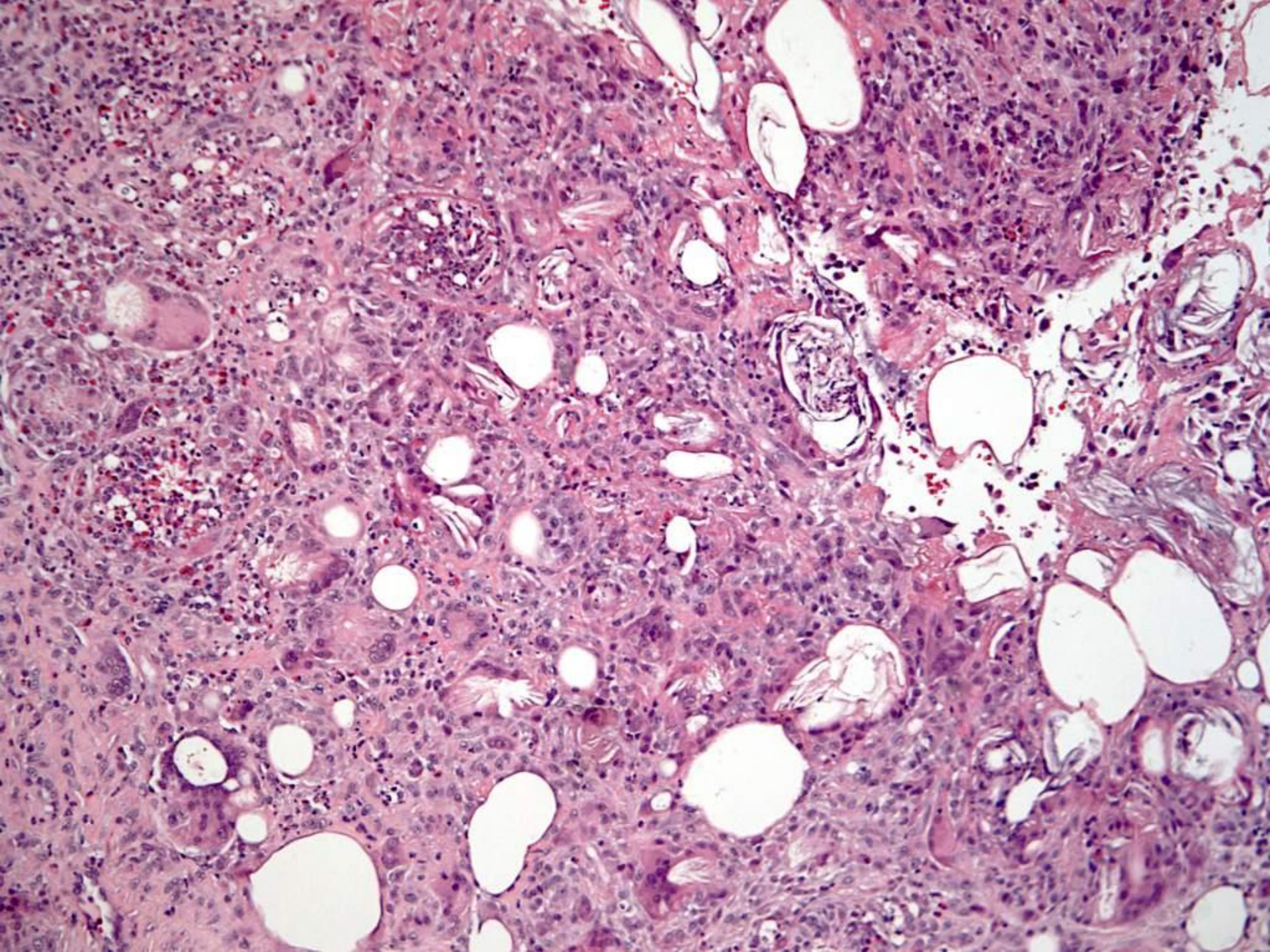
SB 5954
Uma Sundram; APMG

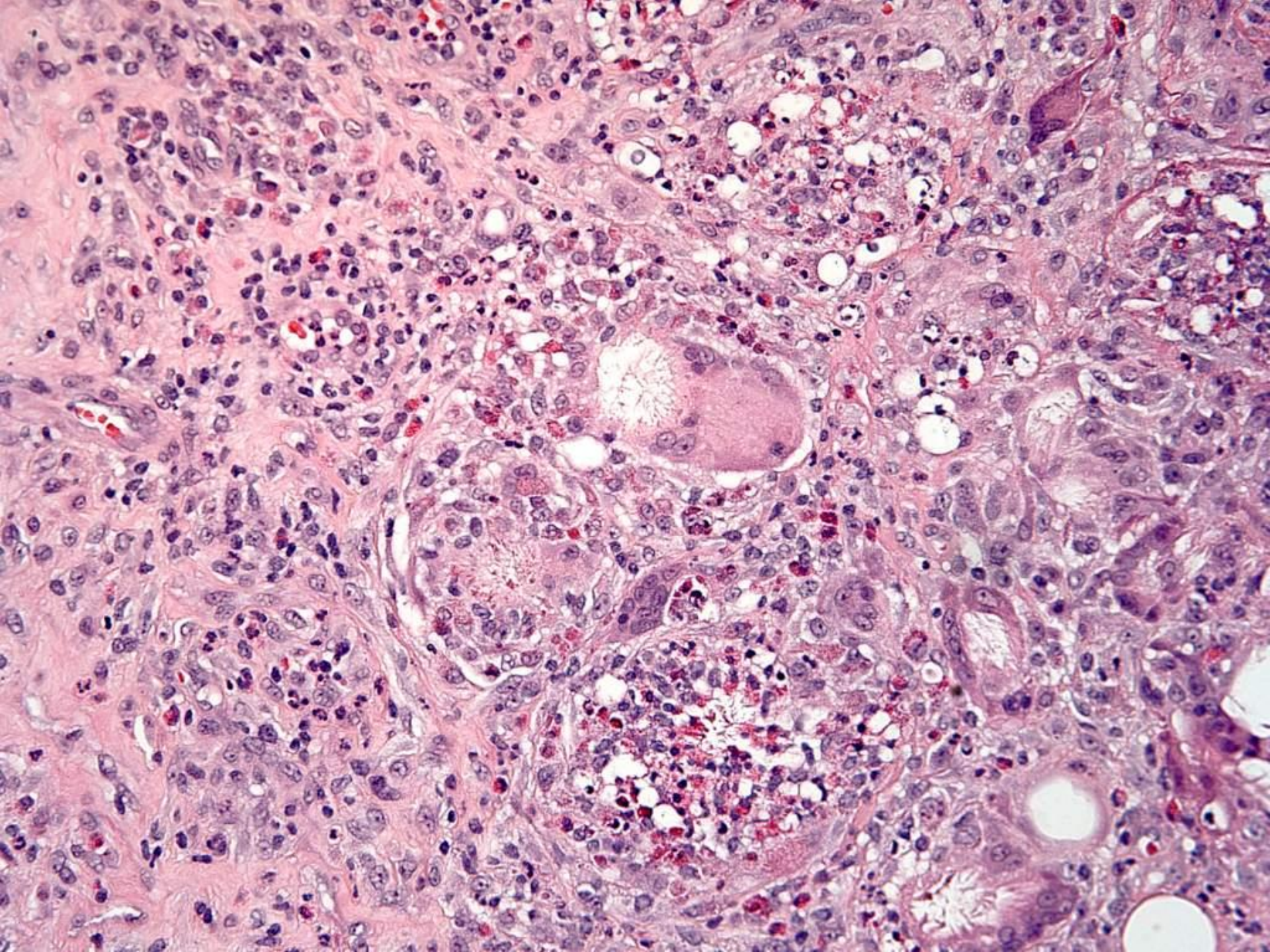
One-month-old female with blue firm nodules on right upper arm and back since 1 week of age. Biopsy of right upper arm lesion performed.

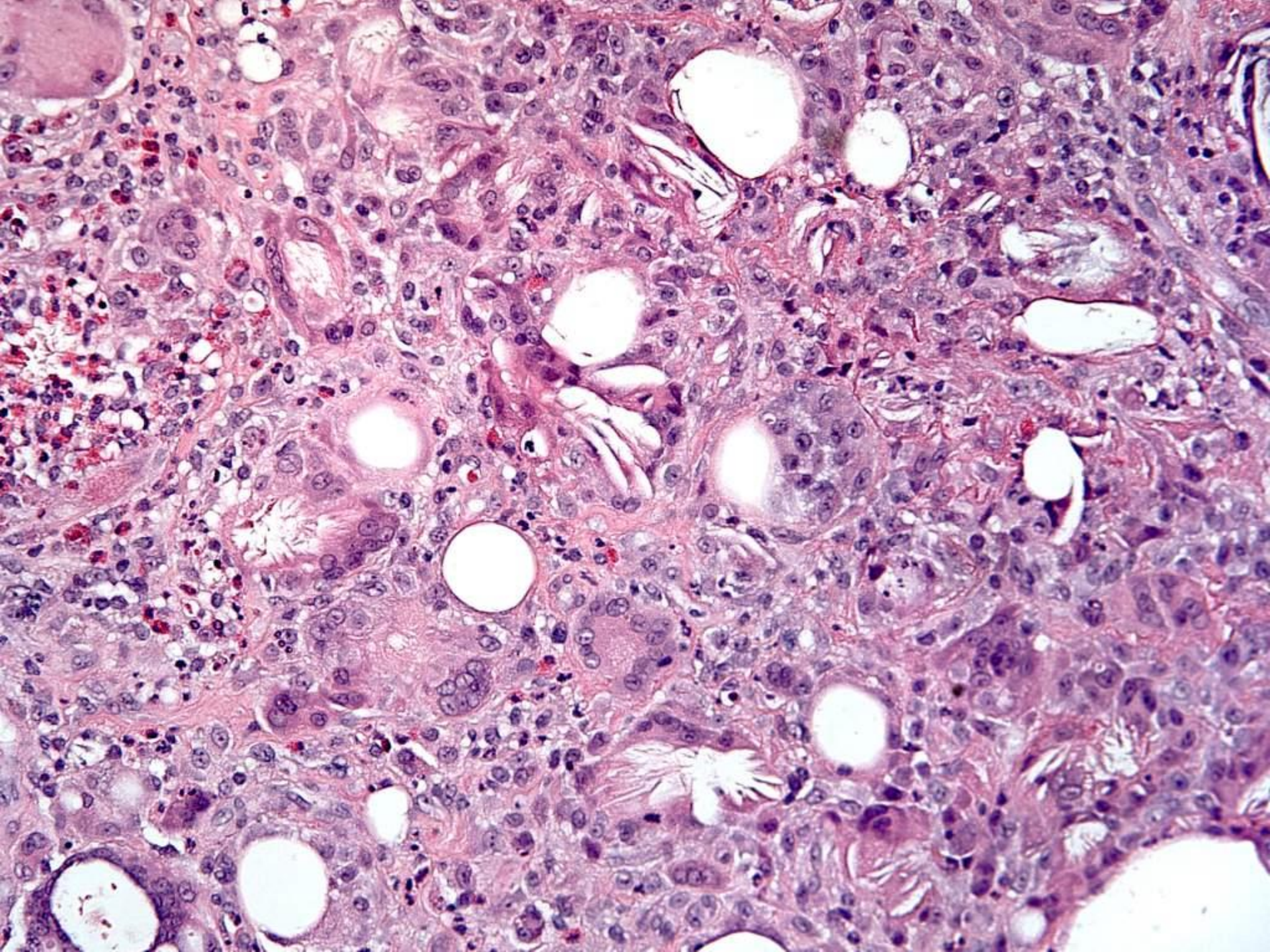


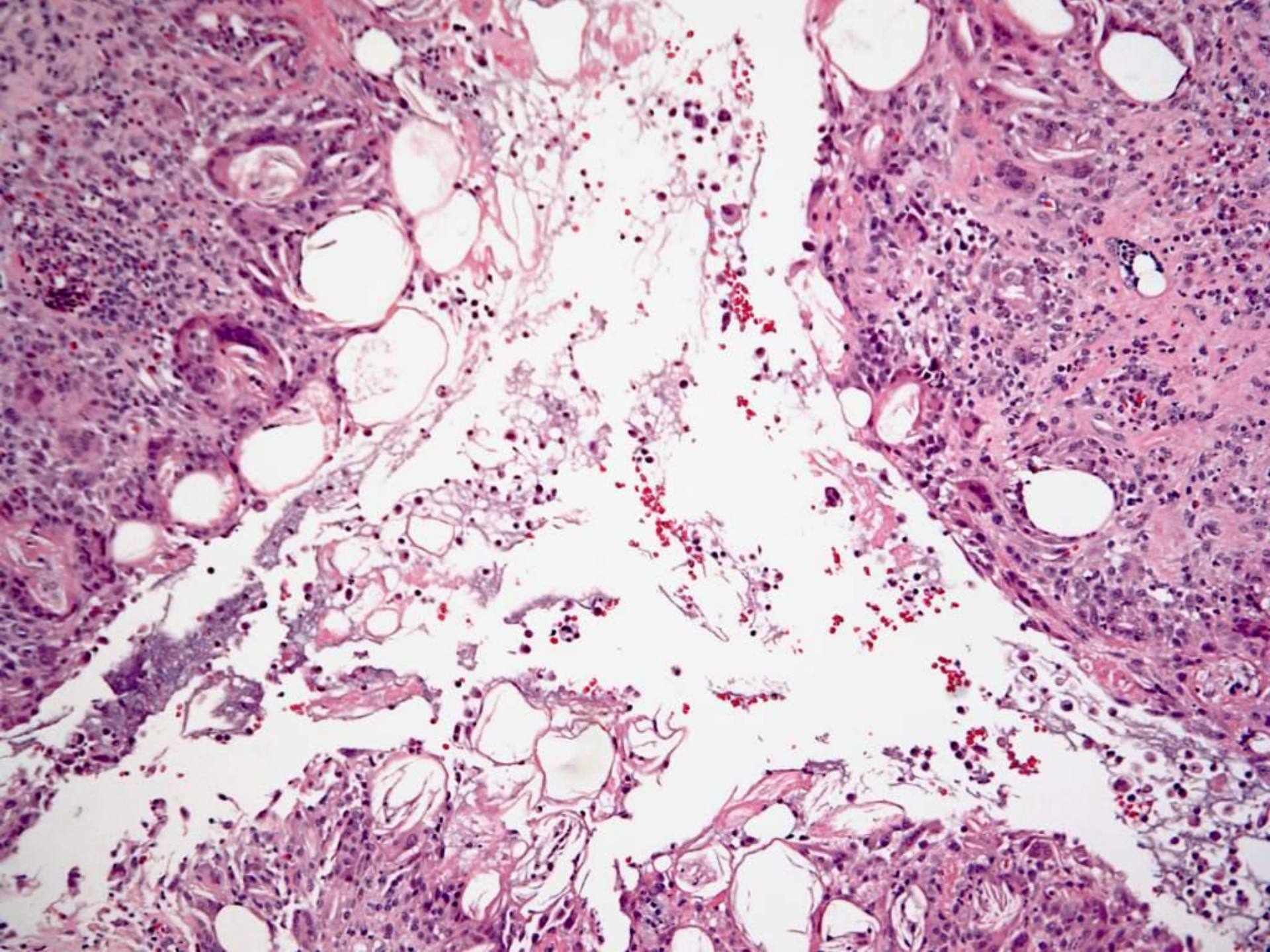













Diagnosis?

Subcutaneous fat necrosis of the new born

Subcutaneous fat necrosis of the new born

- Present at birth or within first few days of life
- Self limited
- Indurated lesions on cheeks, shoulders, buttocks, thighs and calves
- Lesions may be painful

More recent associations

- Risk factors: asphyxia and hypothermia
- Birth asphyxia (risk factor for moderate to severe neonatal encephalopathy) often treated with passive cooling
- Whole body cooling and selective head cooling have both had associations with SCFN

Hypercalcemia

- Hypoxic events thought to lead to granulomatous inflammation of fat followed by necrosis
- Other predisposing events: maternal diabetes, pre eclampsia, drugs
- SCFN can be accompanied by metabolic changes, including hypercalcemia, hypoglycemia, hypertriglyceridemia, thrombocytopenia
- Further complication by nephrocalcinosis can occur

Subcutaneous fat necrosis of the new born

- On histology, primarily a panniculitic process (characterized as a lobular panniculitis)
- Very minimal involvement above the dermal-subcutis interface
- Focal fat necrosis is present, leading to fat cyst formation

Subcutaneous fat necrosis of the new born

- An infiltrate composed of lymphocytes, histiocytes and multinucleated giant cells
- Eosinophils can be seen but neutrophils are uncommon
- Spiky crystal like material within fat cells
- In older lesions, fibrosis and calcification can be seen

Differential diagnosis: Sclerema neonatorum

- Also seen in newborns, but clinical lesions are wax like, hard, cold, and dry
- These patients tend to be far more ill (preterm, septic, jaundiced, poor nutrition)
- Common in developing countries (ie, Bangladesh)
- 50-100% fatality rate

Sclerema neonatorum

- On histology, also see fine needle like crystals within fat cells
- However, very little inflammation and rare giant cells

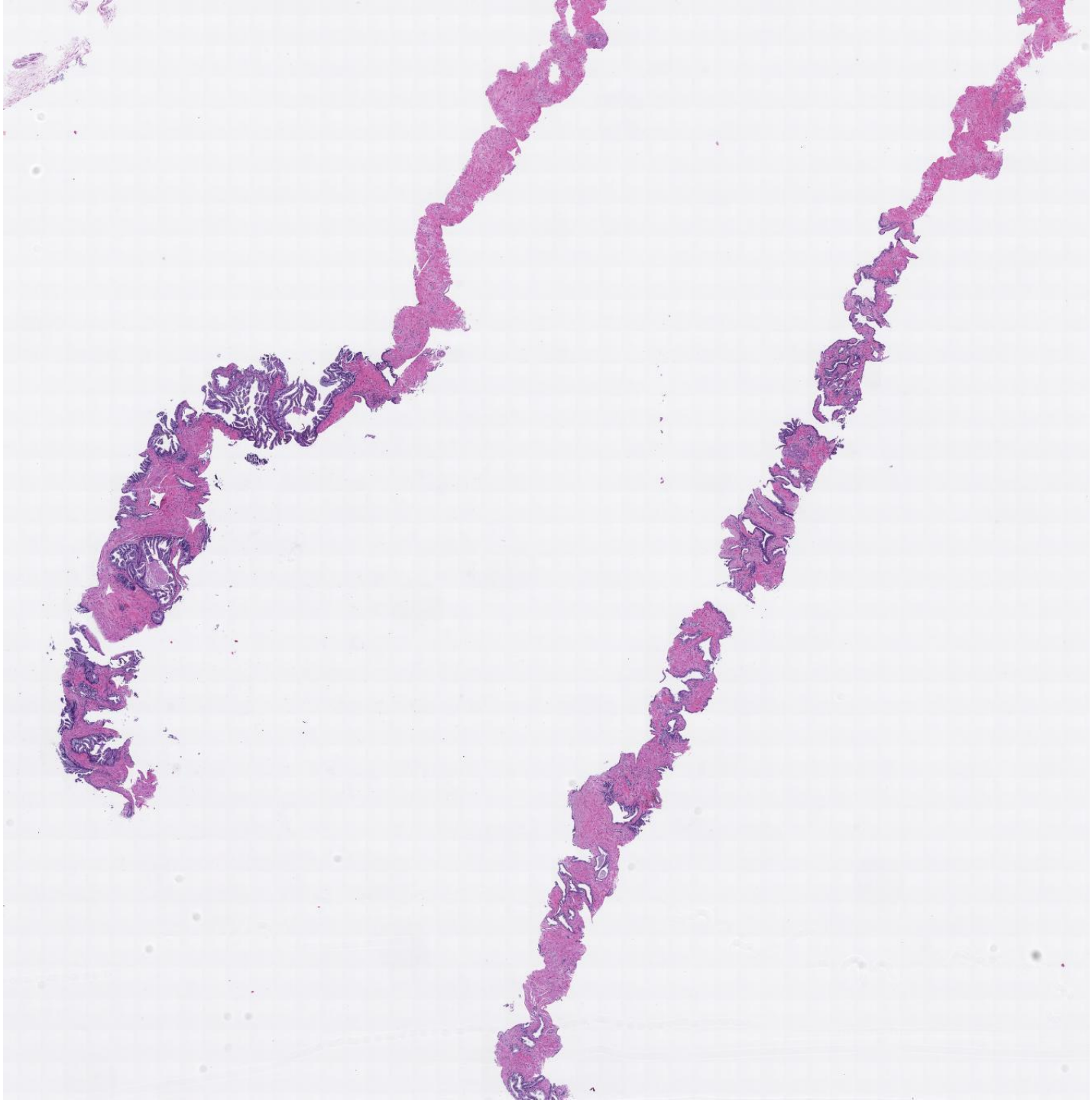
References

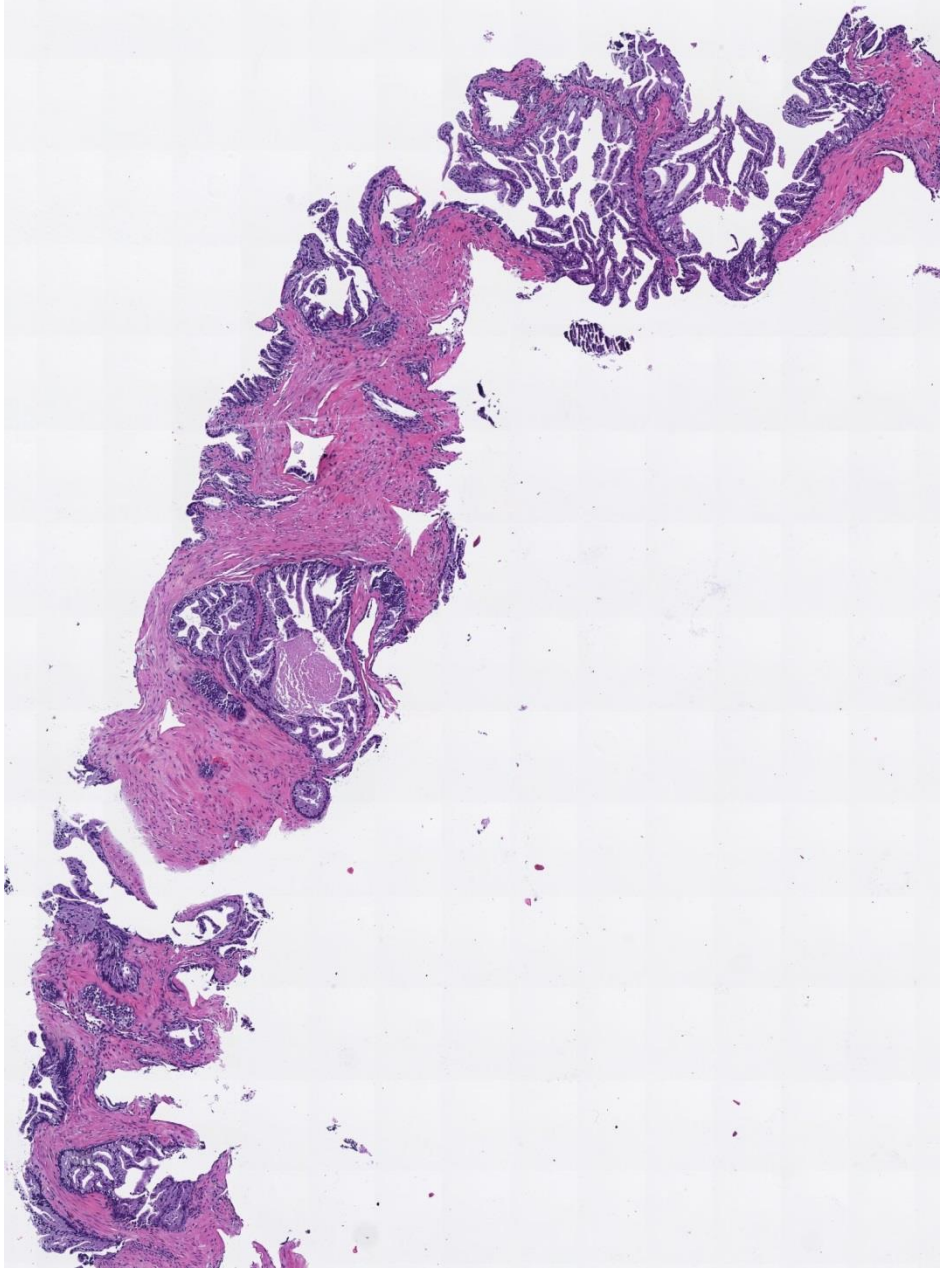
- Mitra S et al. Subcutaneous fat necrosis in newborn-an unusual case and review of literature. Eur j Pediatr 2011 170:1107-1110.
- Scheans P. Subcutaneous fat necrosis: a complication of neuroprotective cooling. Neonatal Netw 2012 Nov-Dec; 31(6):409-12.
- Zeb A et al. Risk factors for sclerema neonatorum in preterm neonates in Bangladesh. Pediatr Infect Dis J. 2009 May;28(5):435-8.

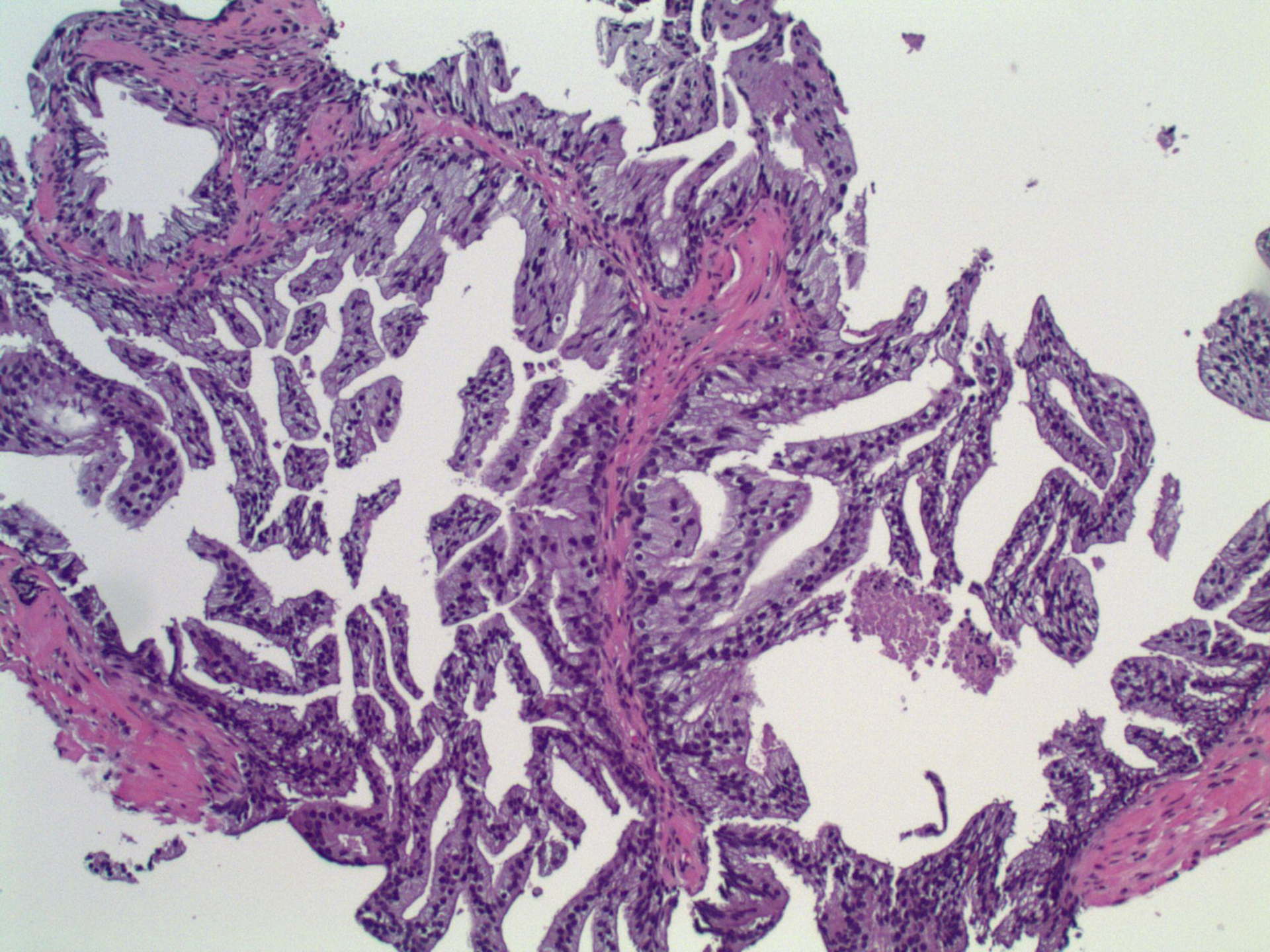
SB 5955

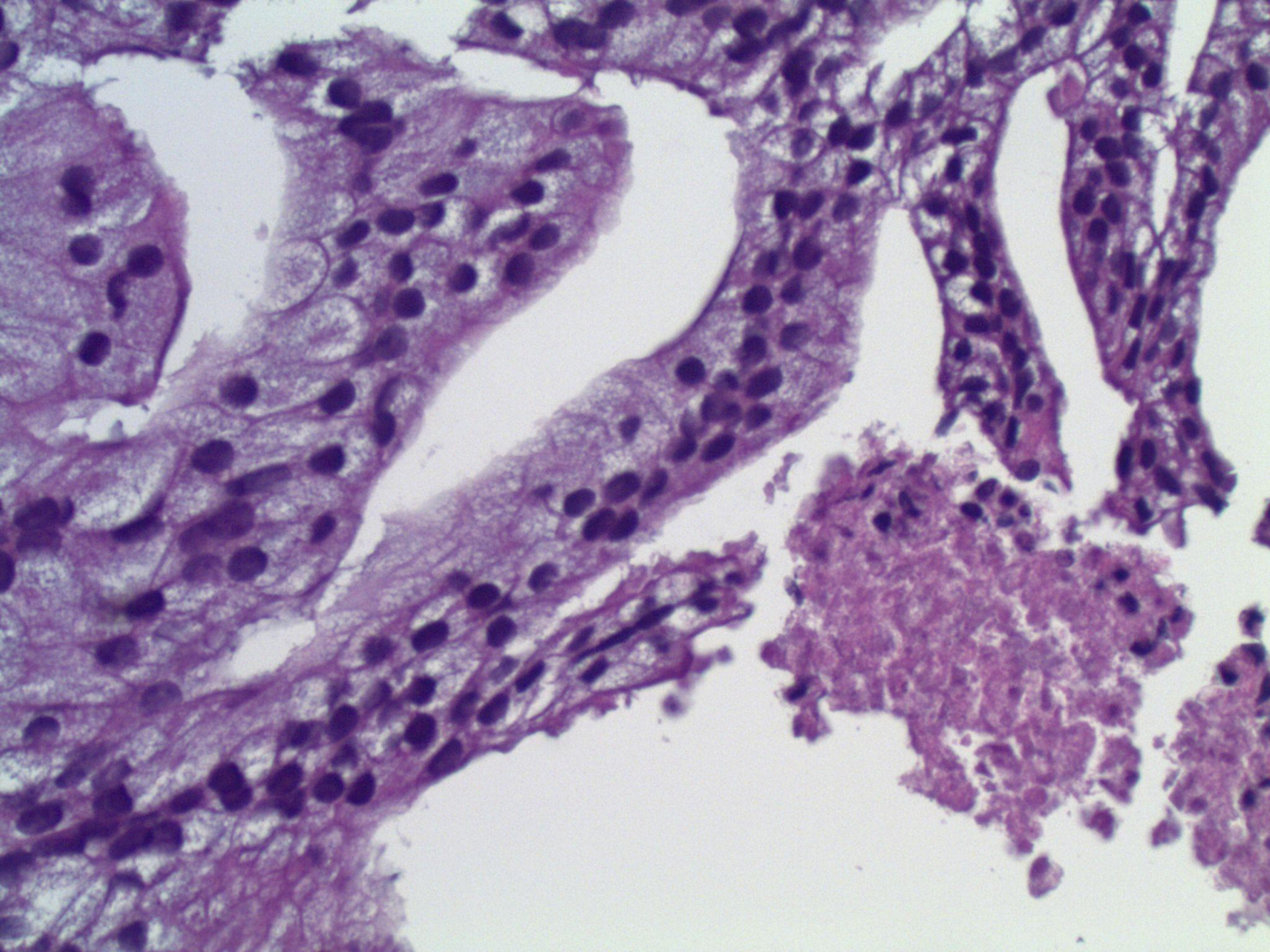
Ankur Sangoi;
El Camino Hospital

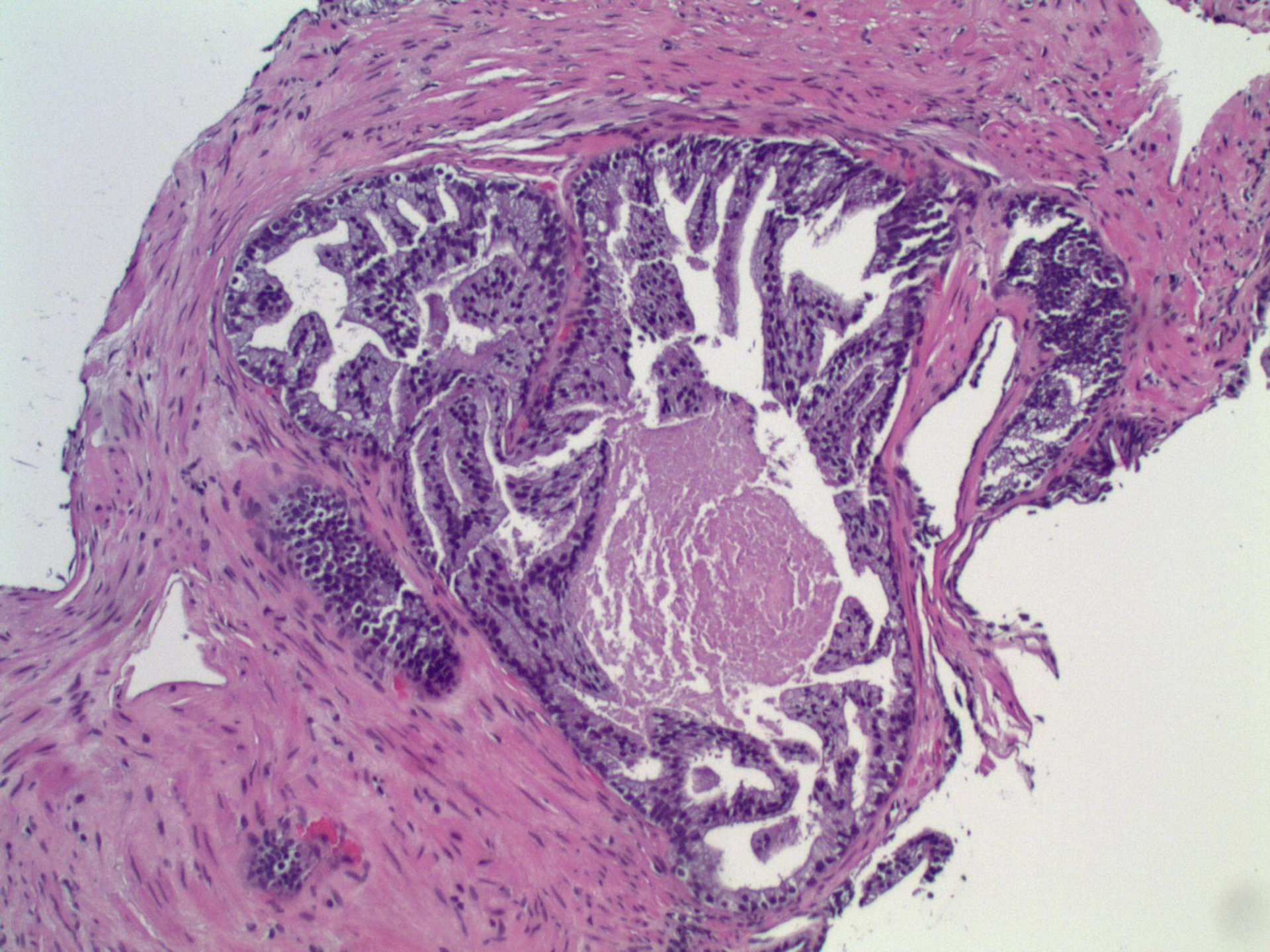
79-year-old male presenting with prostate biopsy.

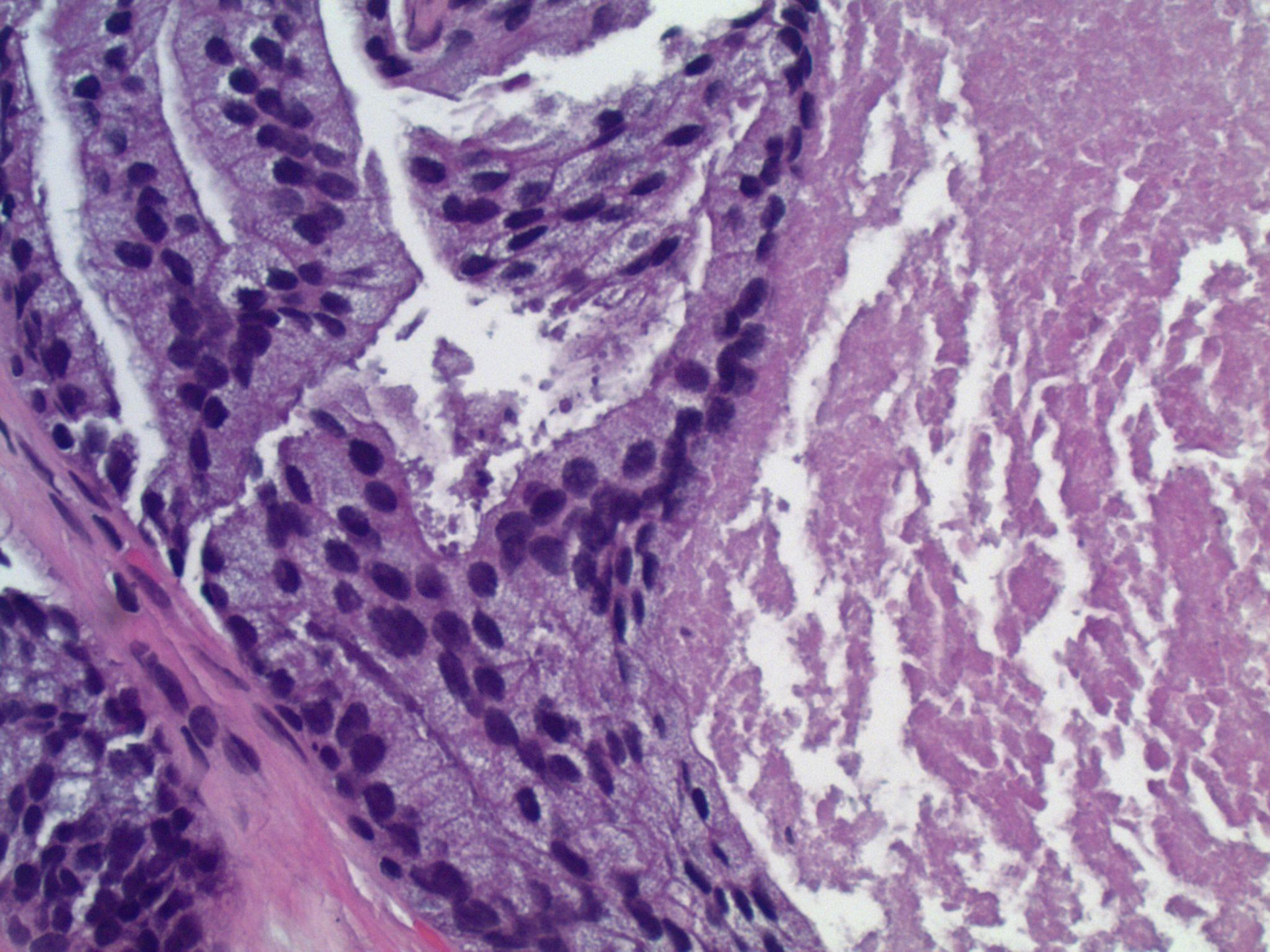




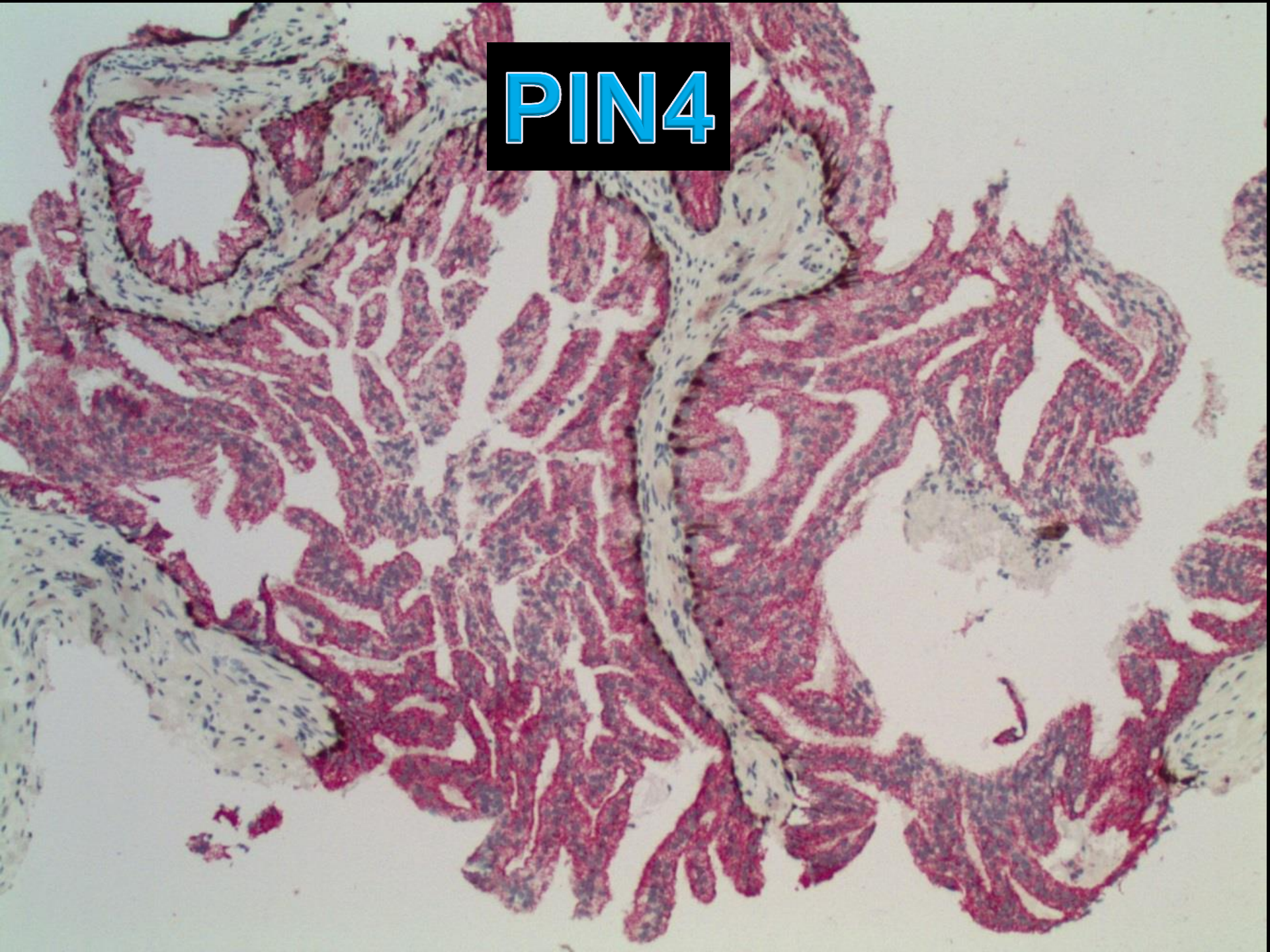









Diagnosis?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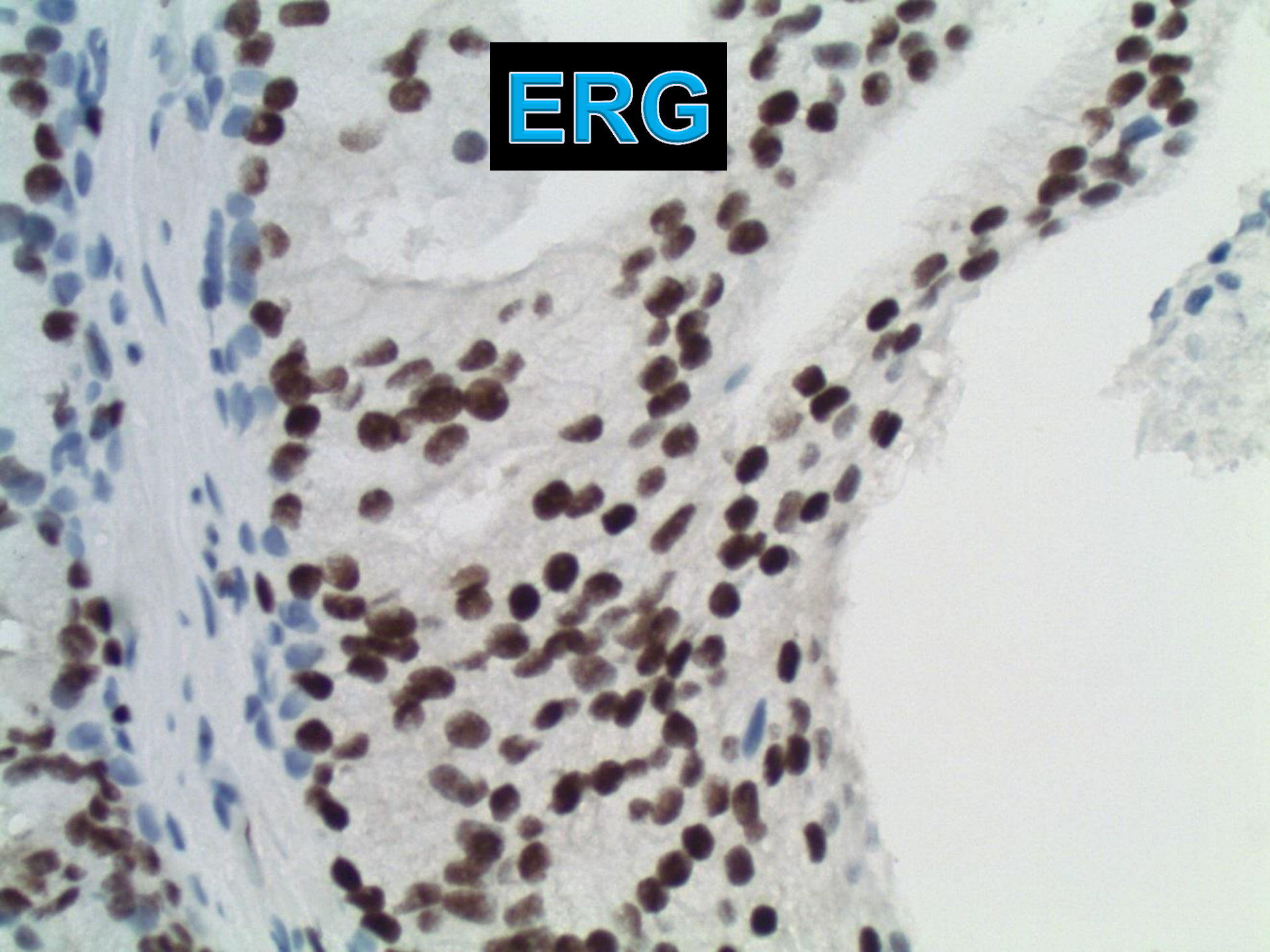

ERG

DIAGNOSIS

- **Atypical large cribriform proliferation**
  - Suspicious for prostatic intraductal carcinoma (recommend immediate re-biopsy)

FOLLOW-UP

- **Patient eventually biopsied again (after few years)**
  - Reportedly Gleason 4+4 cancer
- **Clinically metastatic disease**

Intraductal carcinoma of the prostate on needle biopsy: histologic features and clinical significance

Charles C Guo[1] and Jonathan I Epstein[1,2,3]

[1]*Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA;*
[2]*Department of Urology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA and*
[3]*Department of Oncology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA*

Modern Pathology (2006) 19, 1528–1535

Table 1 Definition of IDC-P

Malignant epithelial cells filling large acini and prostatic ducts, with preservation of basal cells and:

- Solid or dense cribriform pattern

or

- Loose cribriform or micropapillary pattern with either
  - Marked nuclear atypia: nuclear size 6 × normal or larger
  - Non-focal comedonecrosis

ETS Gene Aberrations in Atypical Cribriform Lesions of the Prostate

Implications for the Distinction Between Intraductal Carcinoma of the Prostate and Cribriform High-grade Prostatic Intraepithelial Neoplasia

Bo Han, MD, PhD,† Khalid Suleman, MD,*† Lei Wang, MD,*† Javed Siddiqui, MS,*† Linda Sercia, MS,‡ Cristina Magi-Galluzzi, MD,‡ Nallasivam Palanisamy, PhD,*† Arul M. Chinnaiyan, MD, PhD,*†§‖¶ Ming Zhou, MD, PhD,‡ and Rajal B. Shah, MD*†‖¶*

Am J Surg Pathol • Volume 34, Number 4, April 2010

Utility of PTEN and ERG Immunostaining for Distinguishing High-grade PIN From Intraductal Carcinoma of the Prostate on Needle Biopsy

Carlos L. Morais, MD, Jeong S. Han, MD,* Jennifer Gordetsky, MD,* Michael S. Nagar, MD,† Ann E. Anderson, MD,† Stephen Lee, MD,* Jessica L. Hicks,* Ming Zhou, MD, PhD,‡ Cristina Magi-Galluzzi, MD, PhD,‡ Rajal B. Shah, MD,§ Jonathan I. Epstein, MD,*‖¶ Angelo M. De Marzo, MD, PhD,*‖¶ and Tamara L. Lotan, MD*‖*

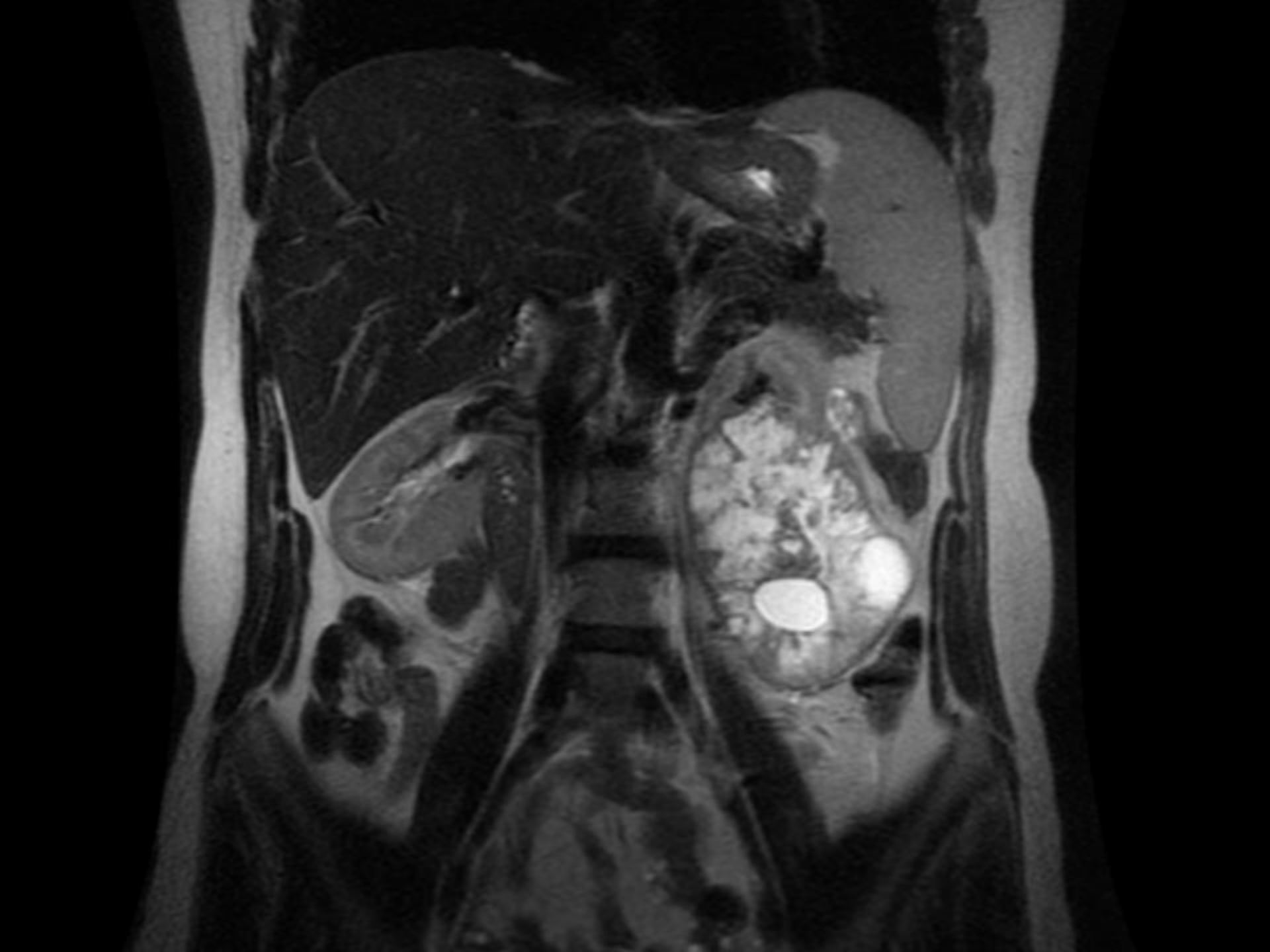
Am J Surg Pathol • Volume 39, Number 2, February 2015

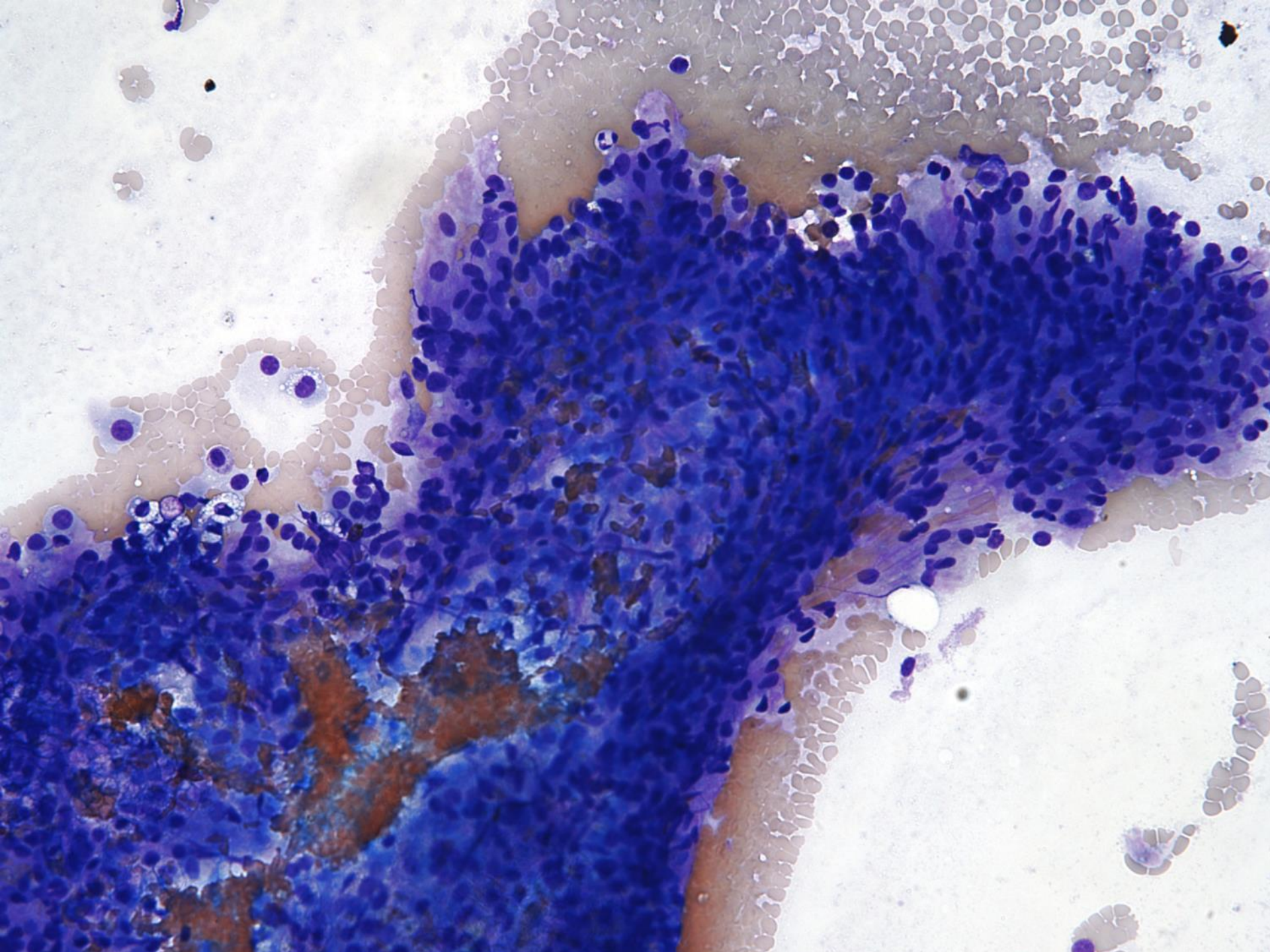
TABLE 1. Rate of PTEN Loss and ERG Expression in a Spectrum of Intraepithelial Prostate Proliferations

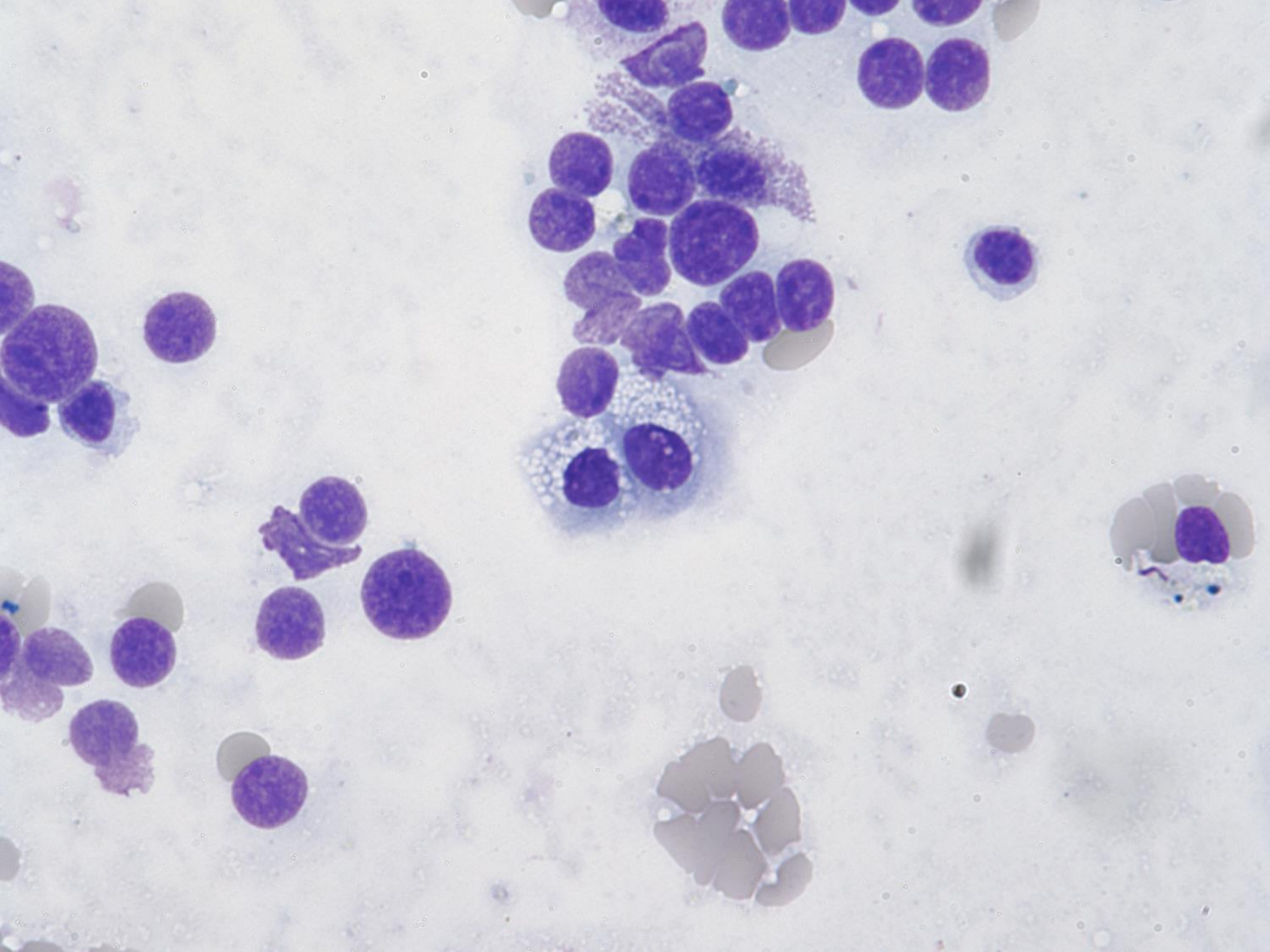
Intraepithelial Lesion	PTEN Loss (n [%])	ERG Expression (n [%])
Intraductal carcinoma with concurrently sampled invasive carcinoma	38/50 (76)	29/50 (58)
Isolated intraductal carcinoma	20/33 (61)	10/33 (30)
Borderline intraductal proliferations	11/21 (52)	4/15 (27)
PIN with concurrently sampled invasive carcinoma	0/7 (0)	0/7 (0)
Isolated PIN	0/12 (0)	0/12 (0)

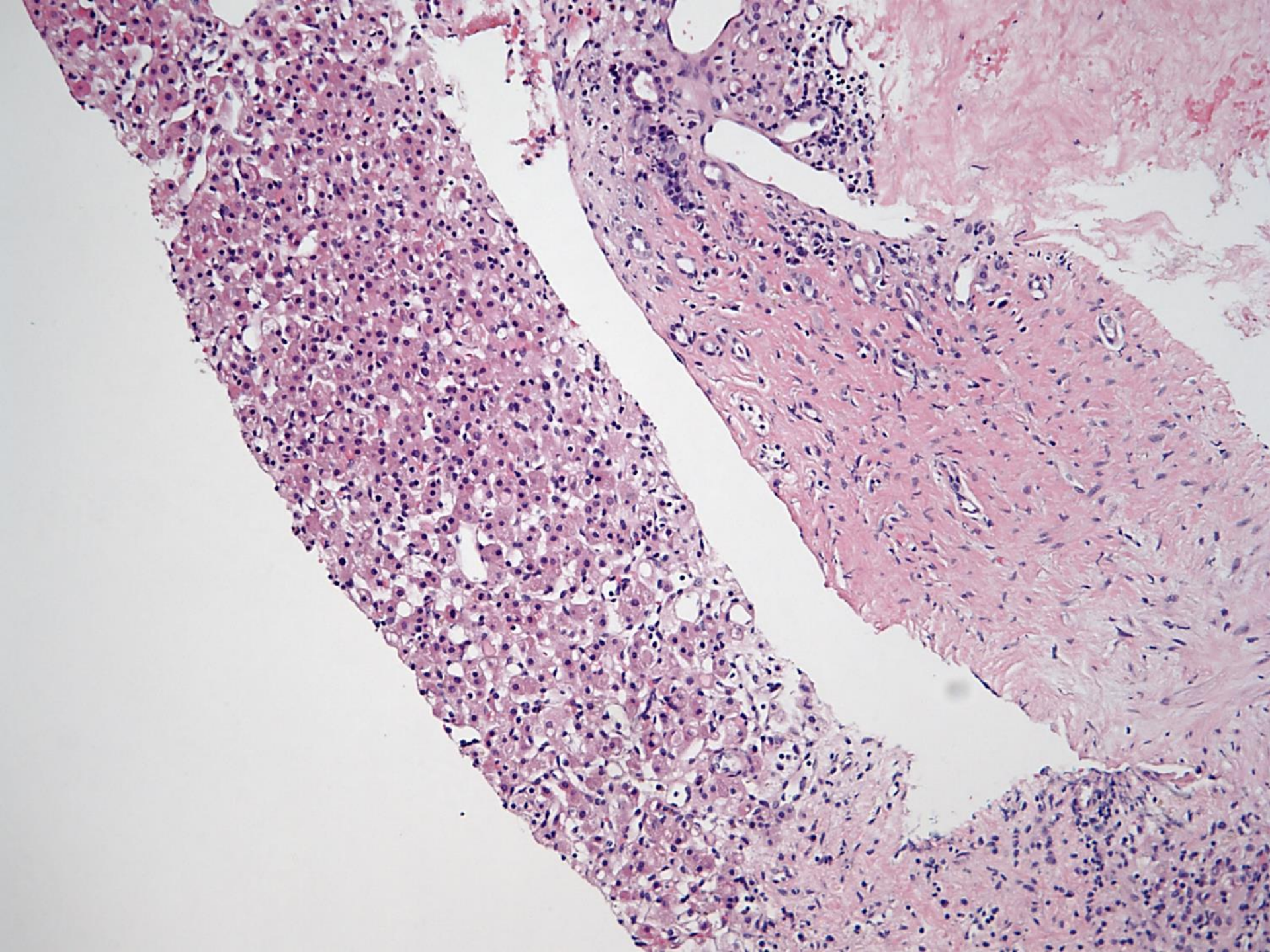
SB 5956
Allison Zemek/John Higgins; Stanford

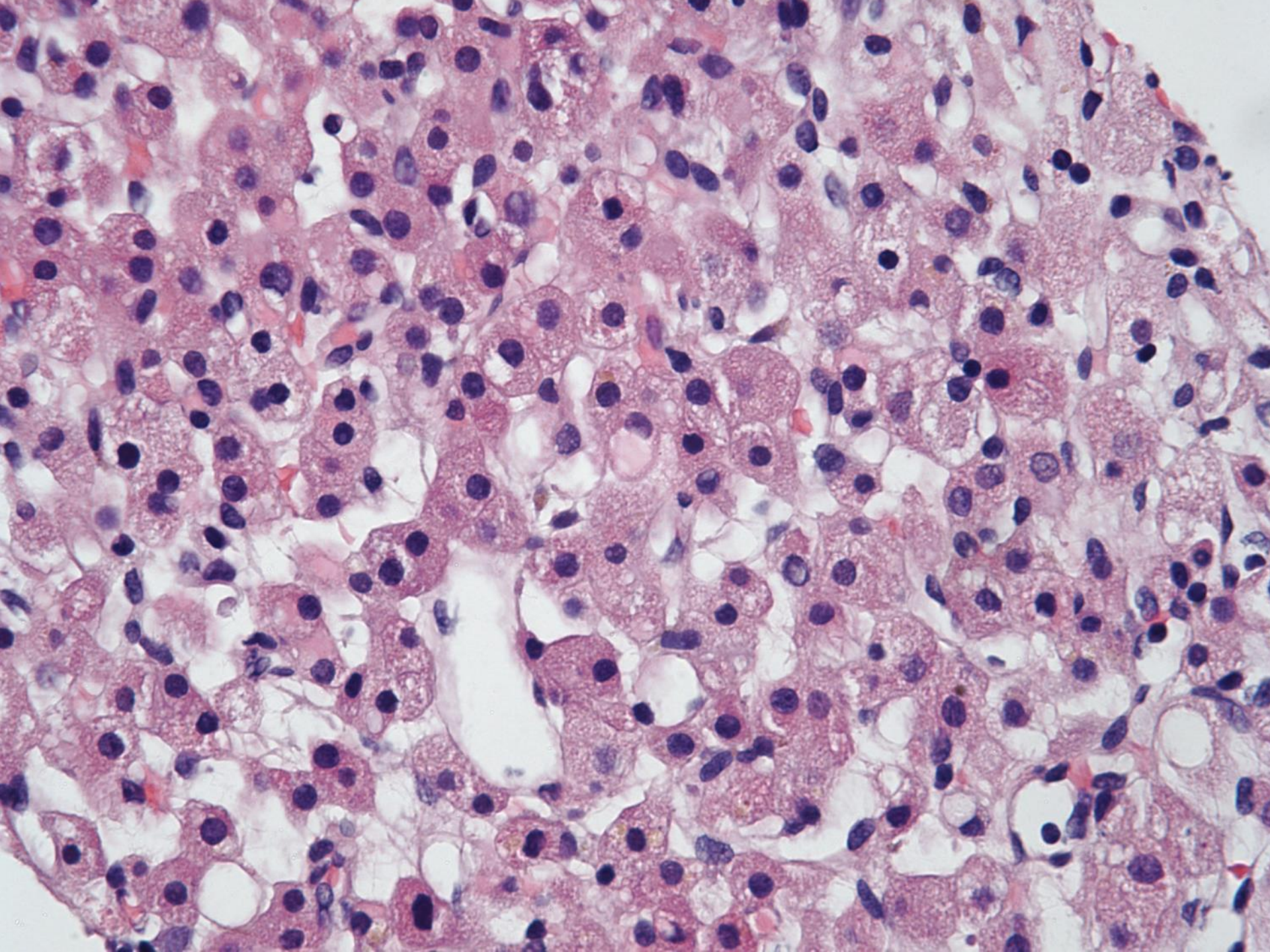
47-year-old female with bilateral kidney masses.

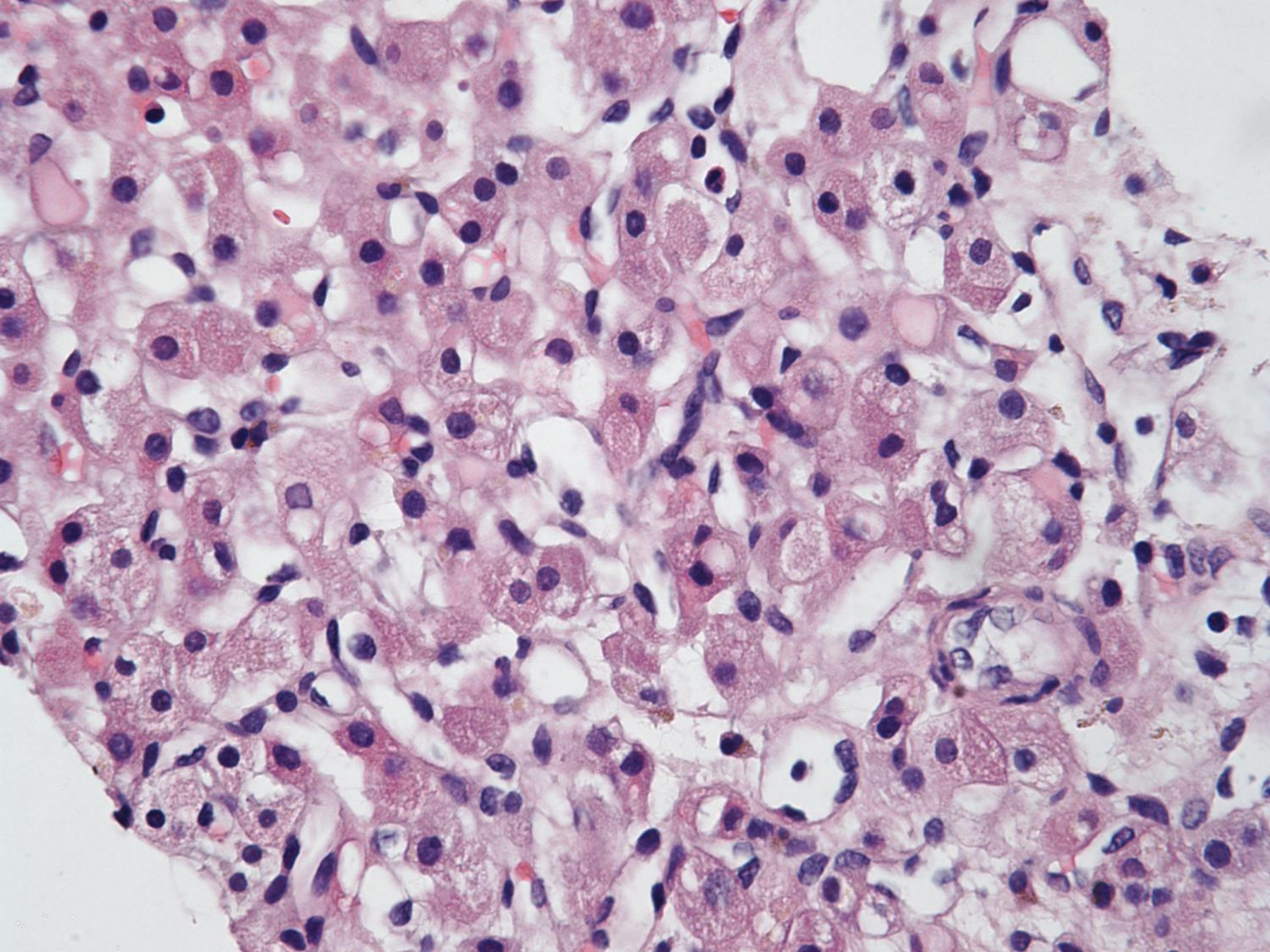




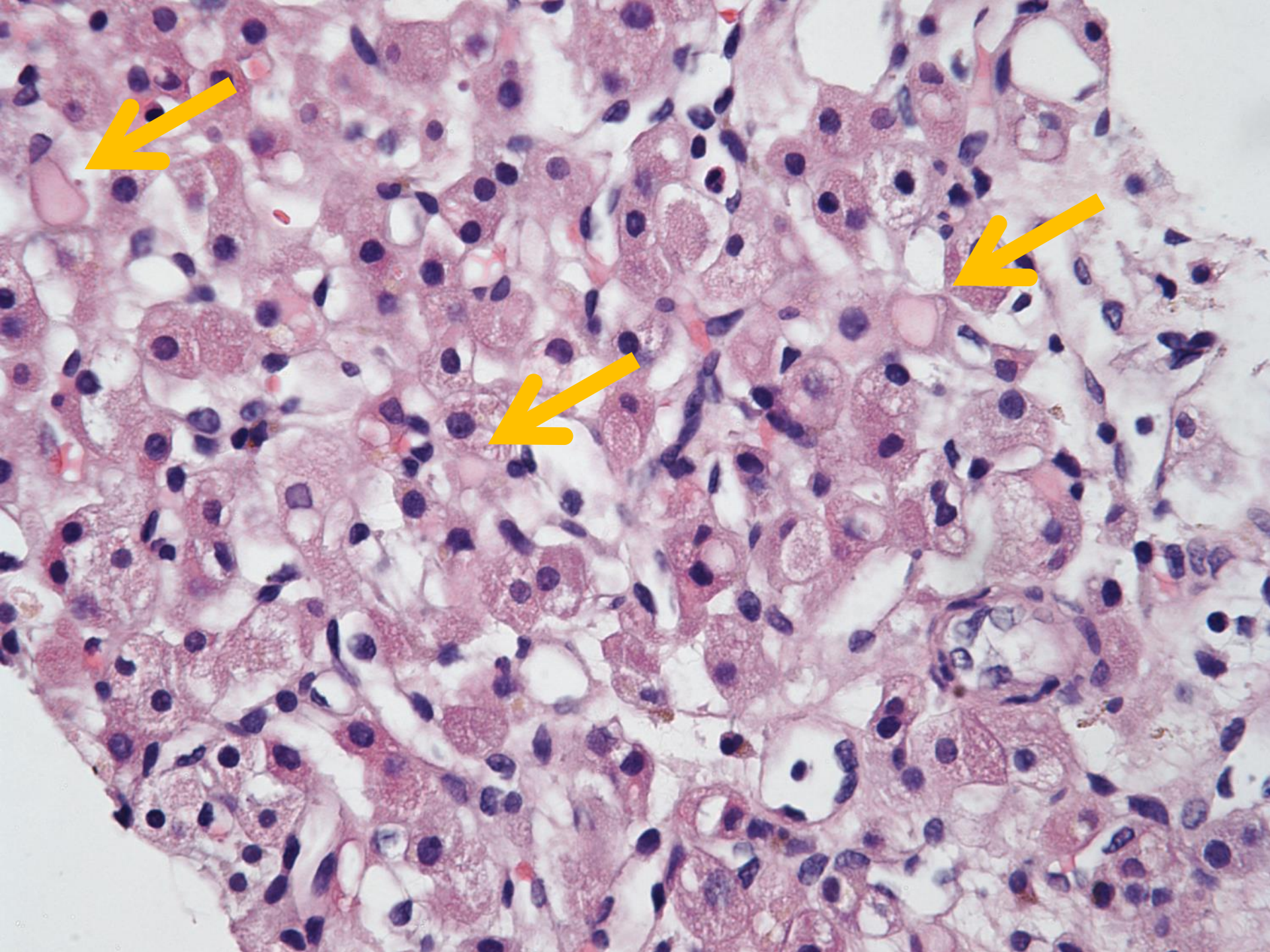









Diagnosis?



Additional clinical history

47 Y female with hereditary paraganglioma syndrome with **SDHB mutation** (confirmed: Exon 8 deletion), with incidental findings of bilateral renal masses on **screening MRI** 2014 based upon an affected son and a presumed affected 1st degree relative. She underwent an open right partial nephrectomy in 2014 and three left partial nephrectomies in 2015.

Succinate dehydrogenase deficient Renal cell carcinoma

Ref: Gill, AJSP Dec 2014, SDH-B deficient RCC

Clinical features:

- Strong syndromic and hereditary nature
  - 15% with SDH-def GIST
  - 15% with paragangliomas
- Rare (53 RCCs reported in setting of SDH def, 2014)
- Mean age 39.8 yo, M:F = 1.7:1
- Bilateral in 26%

Pathogenesis:

- SDH subunits of Krebs cycle enzyme
- Oxidative phosphorylation (↓) aerobic glycolysis (↑)

SDH deficient renal cell carcinoma

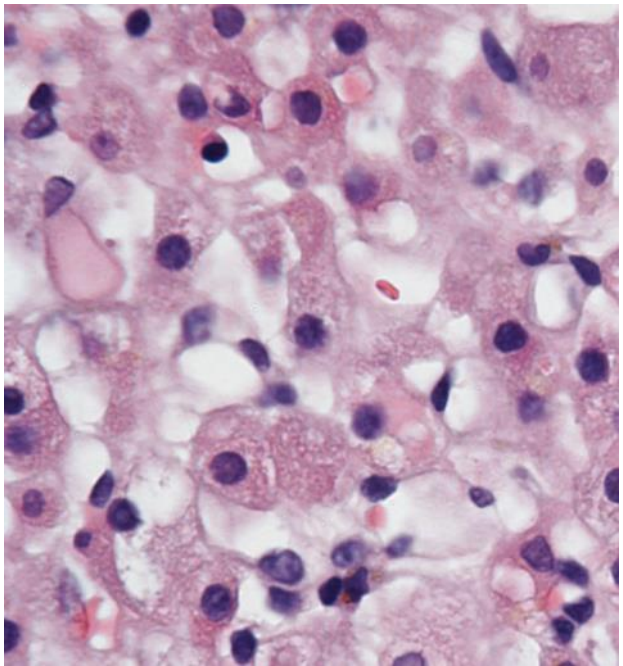
Histopathologic features:

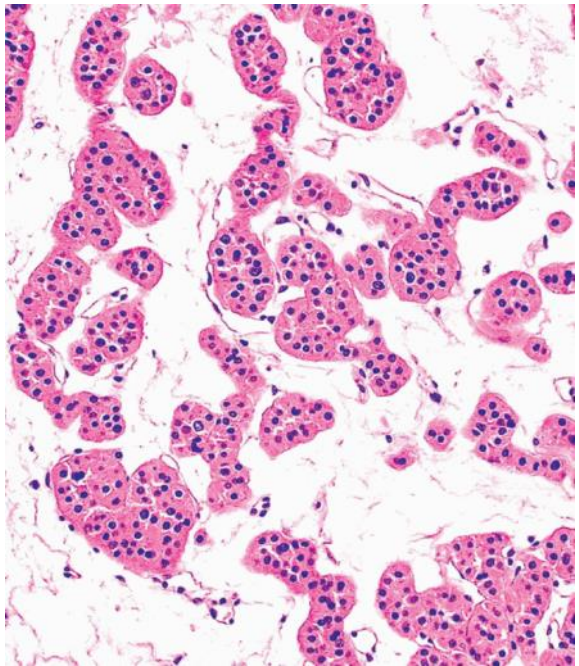
- Solid or focally cystic growth
- Uniform with eosinophilic flocculent cytoplasm
- Intracytoplasmic vacuolations and inclusions
- Round to oval low grade nuclei
- 2/36 (6%) without typical features
    - clear cell and papillary morphology

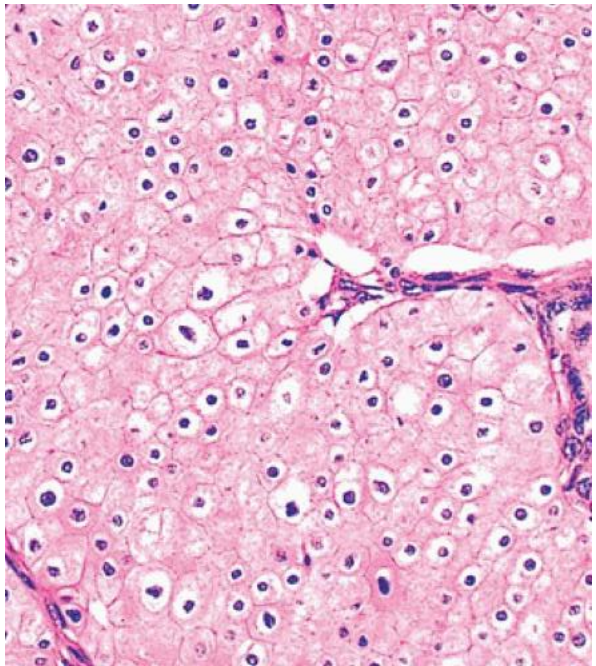
Immunohistochemical features:

- Loss of staining for SDHB
- **PAX8+ CD10+/- AMACR +/- CD117- CK7-**
- CD117 important for ddx of oncocytoma

Features	SDH-def RCC	Oncocytoma	Chromophobe
Cytoplasmic vacuoles	+	-	-
Nested growth in hyaline stroma	-	+	+/-
Large nuclei with degen atypia	-	+/-	+/-
Perinuclear clearing	-	-	+
Colloidal iron	-	-	+
CD117	-	+	+
CK7	-	-	+







SDH deficient Renal cell carcinoma

Ref: Ricketts, J Urology, Dec 2012, SDH Kidney Cancer

Treatment:

- Early identification with prompt surgical intervention
- Following tumors not recommended
- Wide surgical excision

Prognosis:

- 2/17 (12%) metastasized with low grade nuclei
- 7/10 (70%) metastasized with high grade nuclei
- 4/4 (100%) metastasized with coagulative necrosis

Take home points:

- Morphology and clinical features → IHC screening
- High grade (ISUP 3-4) or necrosis → metastases

References

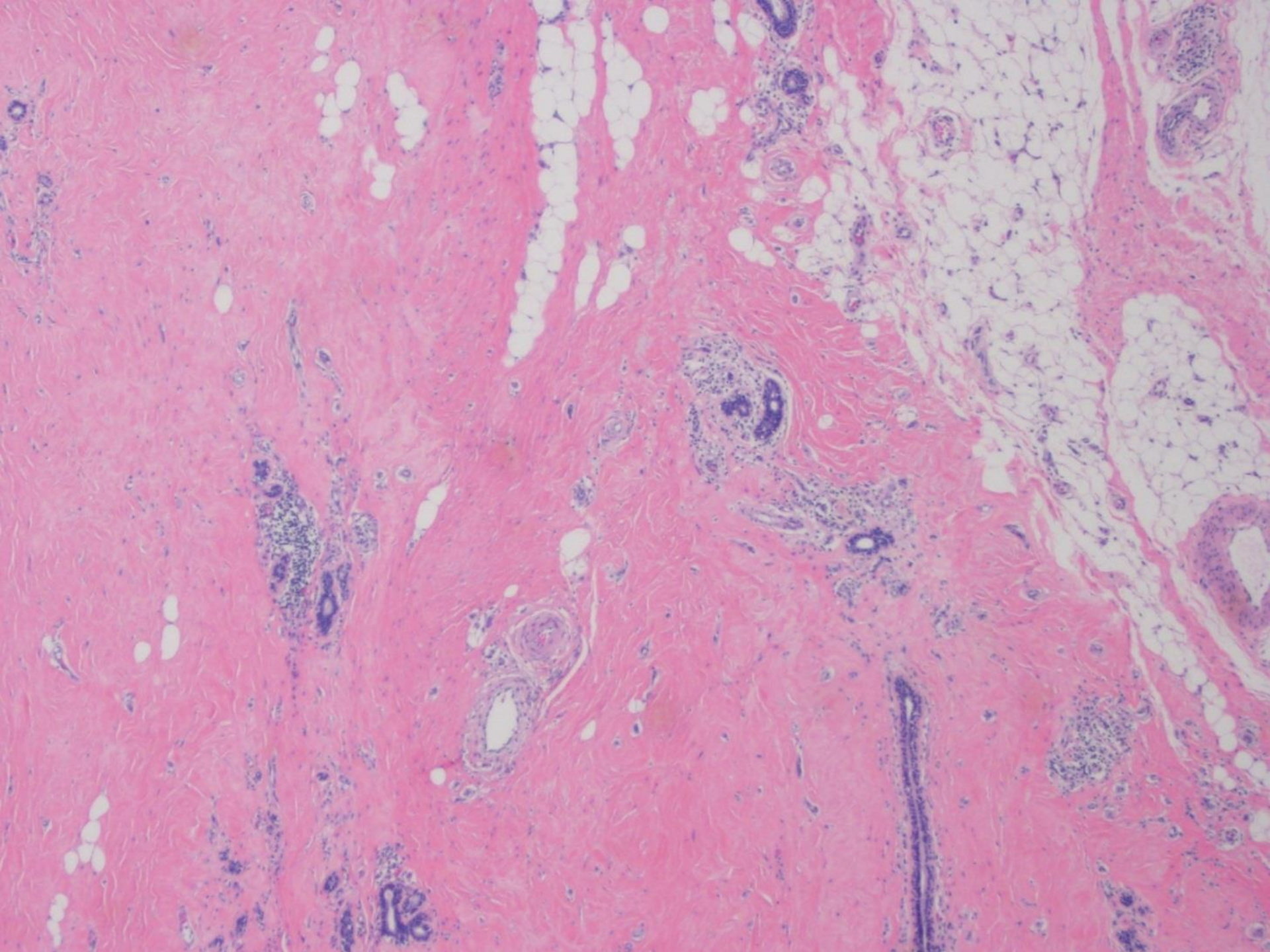
Gill, Anthony J., et al. "**Succinate dehydrogenase (SDH)-deficient renal carcinoma: a morphologically distinct entity: a clinicopathologic series of 36 tumors from 27 patients**." *The American journal of surgical pathology* 38.12 (2014): 1588.

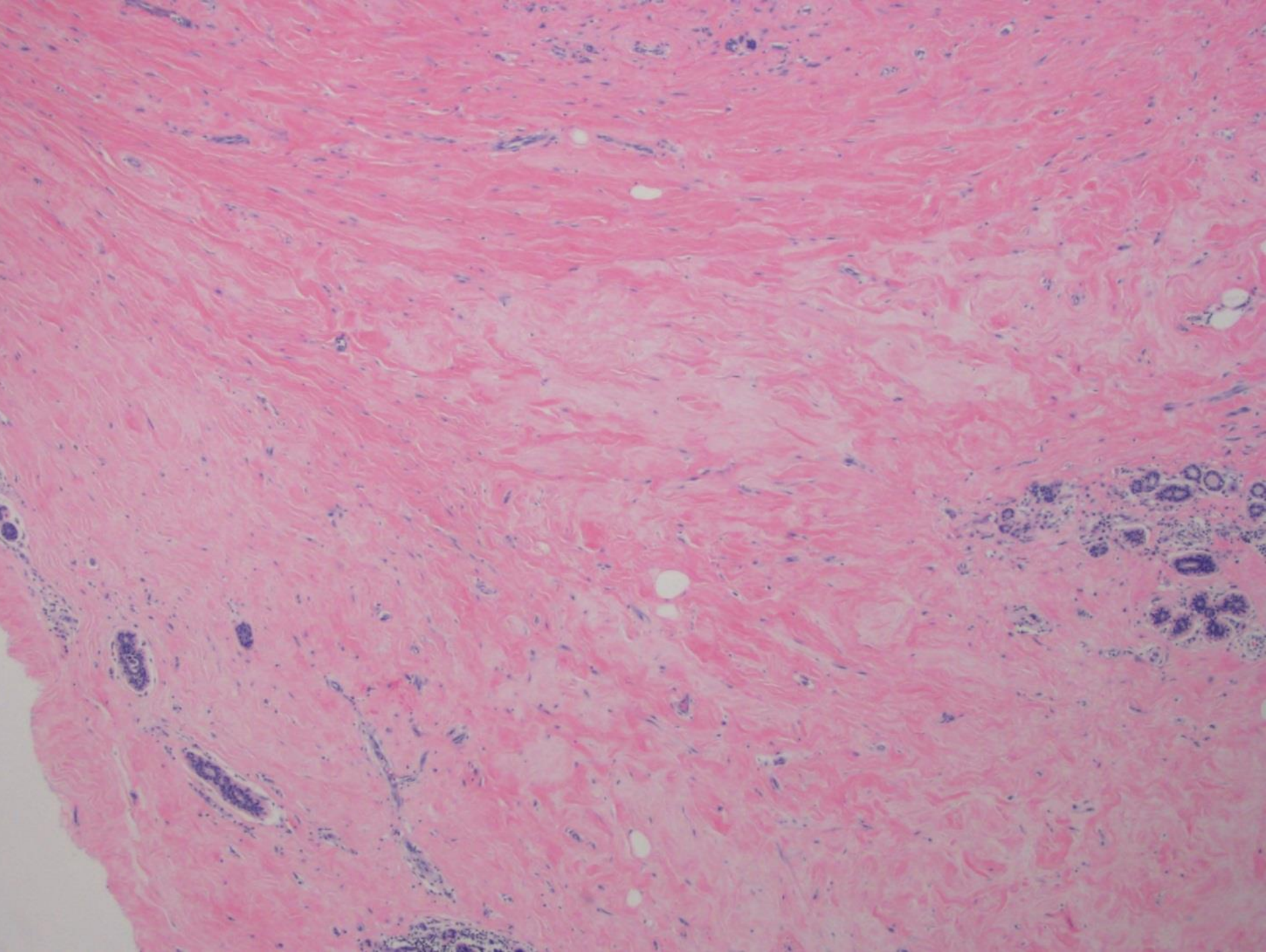
Williamson, Sean R., et al. "**Succinate dehydrogenase-deficient renal cell carcinoma: detailed characterization of 11 tumors defining a unique subtype of renal cell carcinoma**." *Modern Pathology* 28.1 (2015): 80-94.

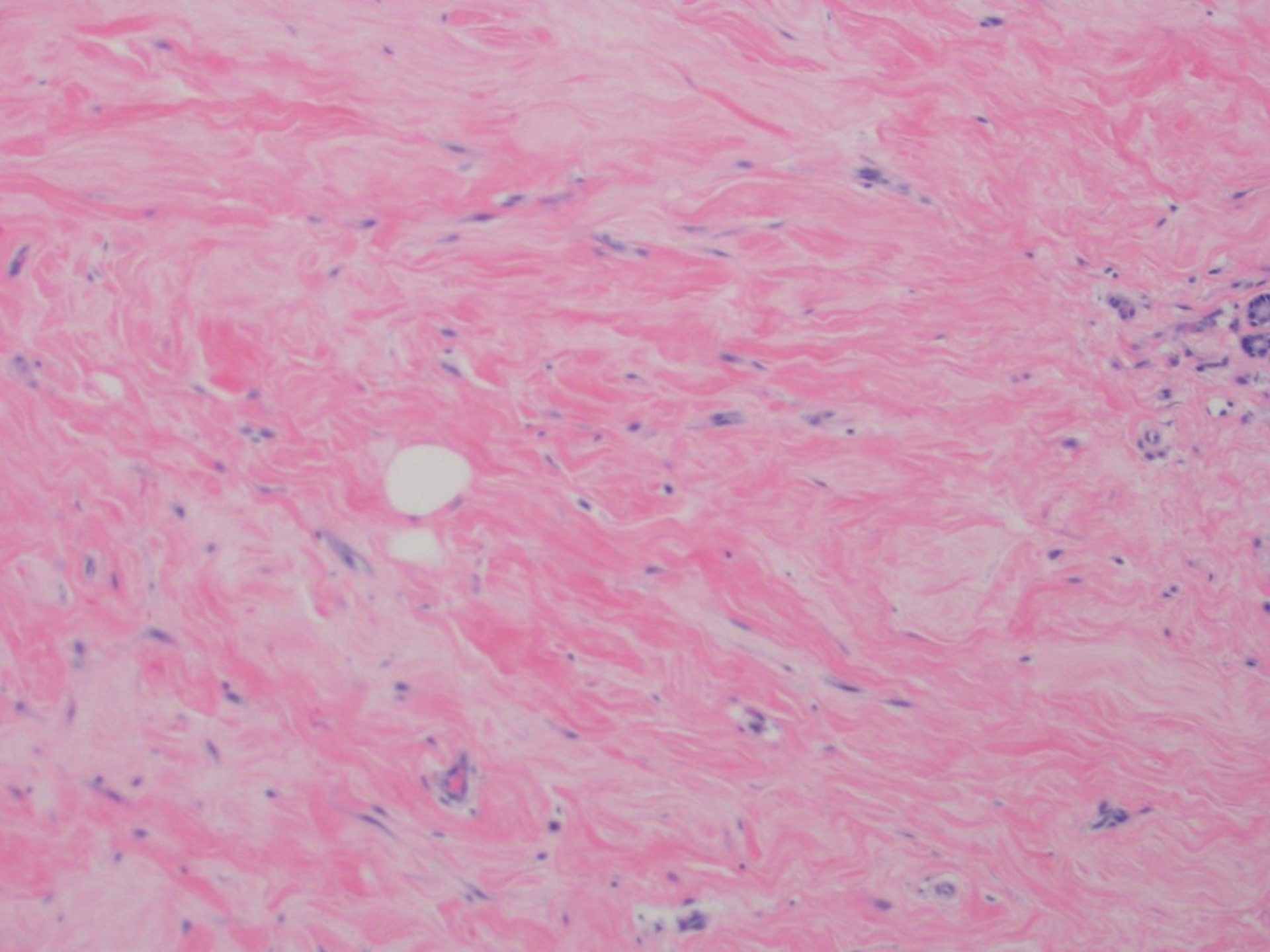
Ricketts, Christopher J., et al. "**Succinate dehydrogenase kidney cancer: an aggressive example of the Warburg effect in cancer**." The Journal of urology188.6 (2012): 2063-2071.

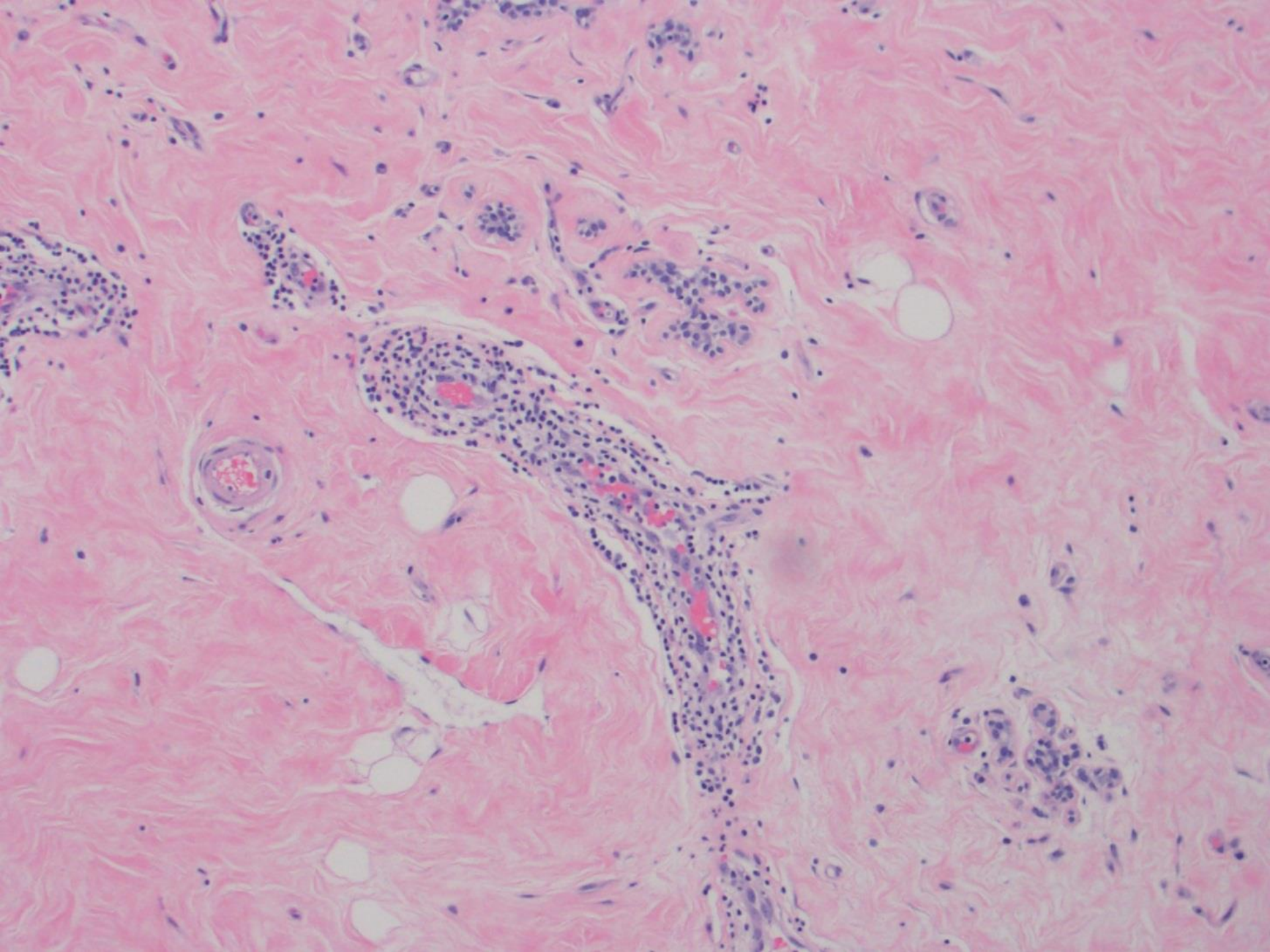
SB 5957
Gregg Manson;
Kaiser Walnut Creek

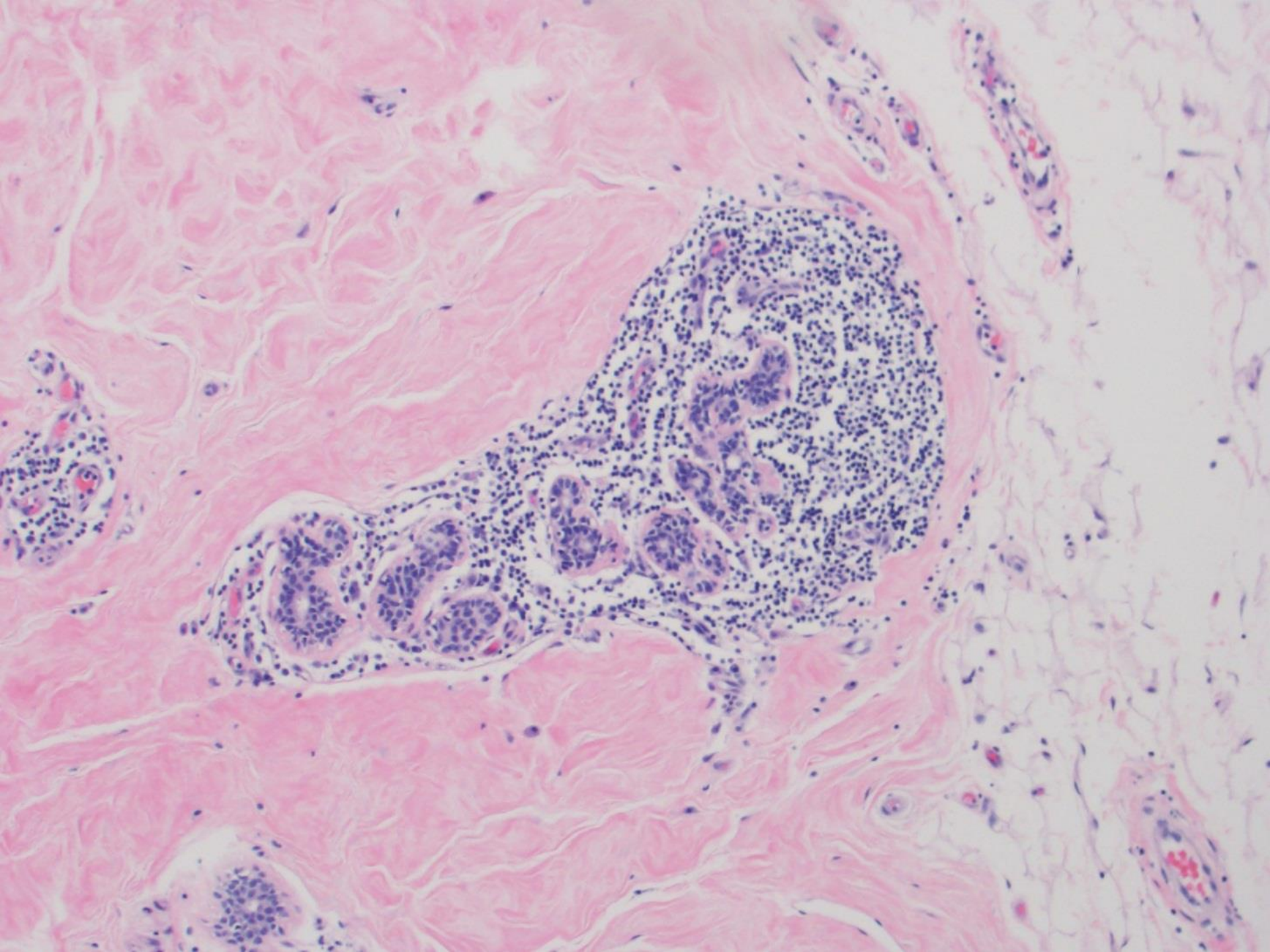
56-year-old woman with 2.7cm mass in subareaolar region of breast. There is no history of DM, thyroid disease, or auto-immune disease. No recurrence since surgery (12/12) including unremarkable mammo (6/14).

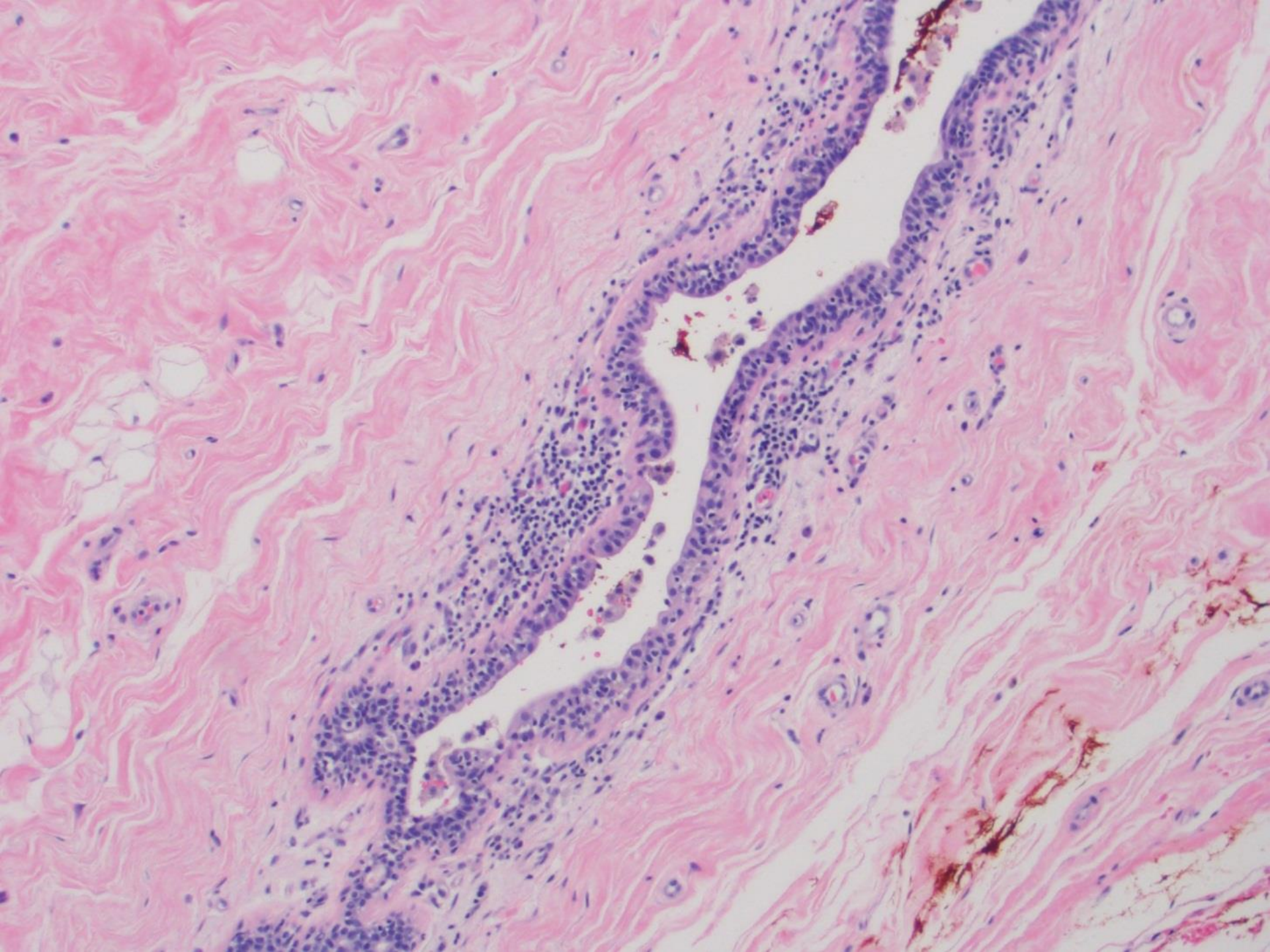


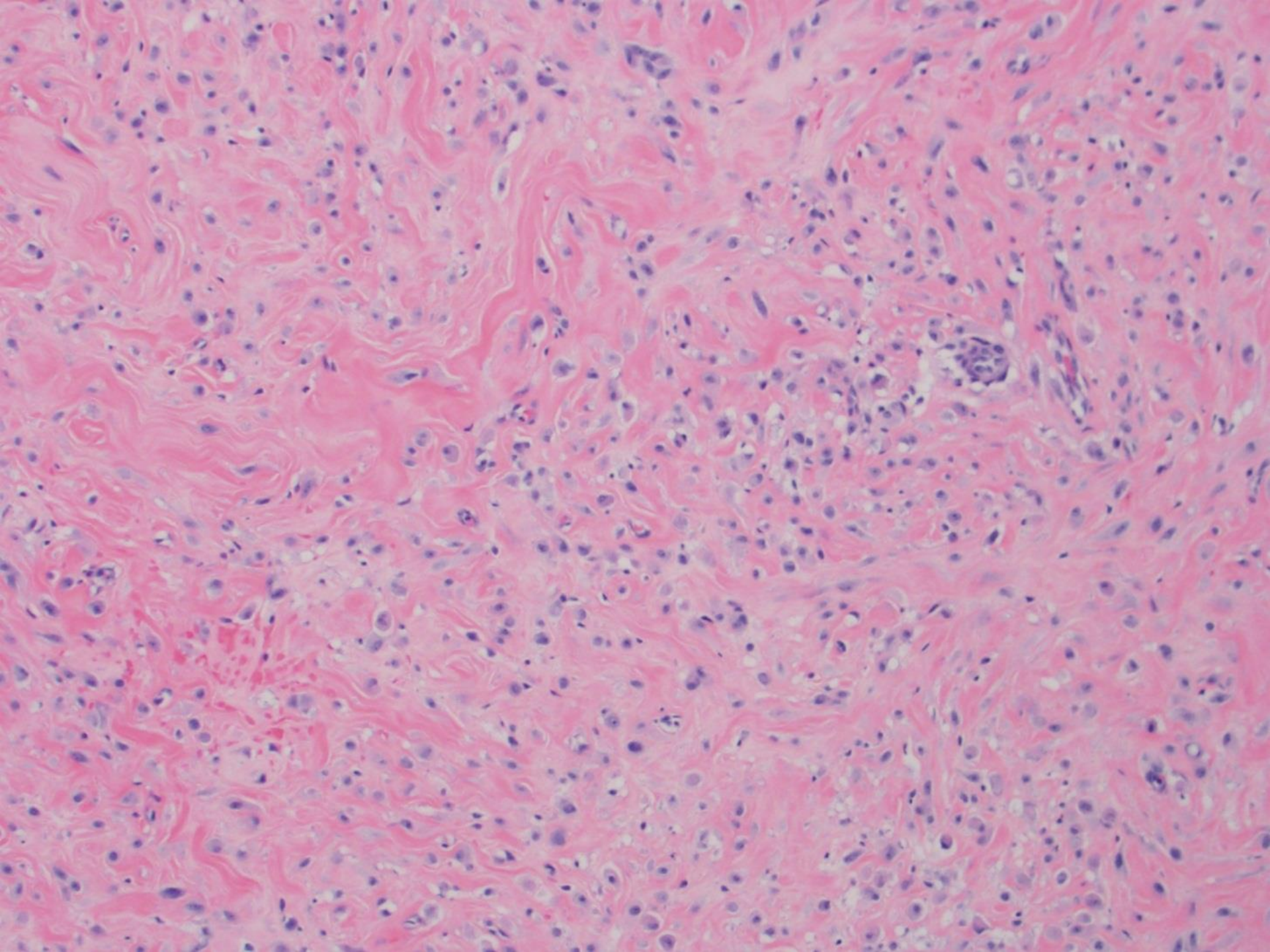


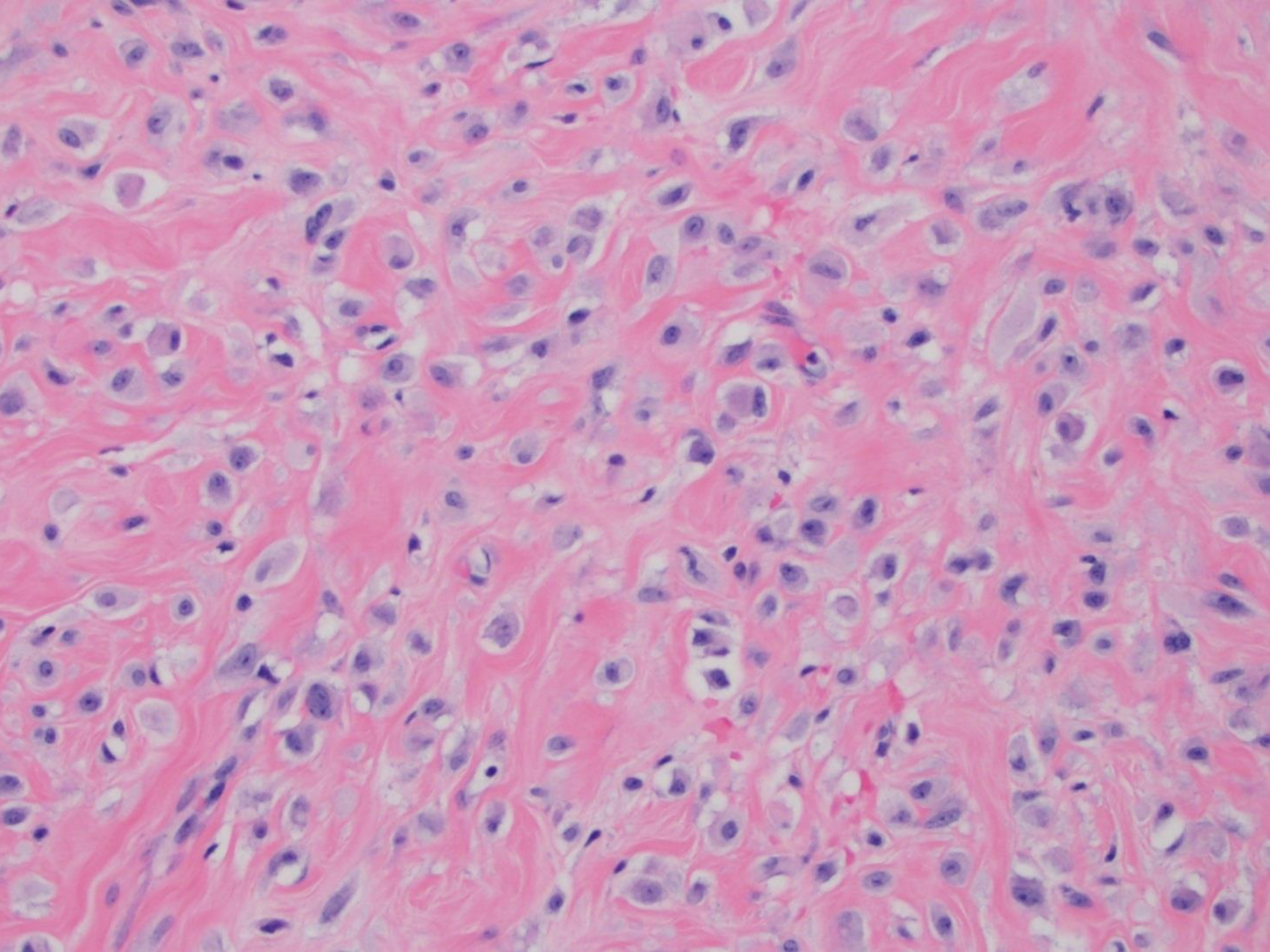


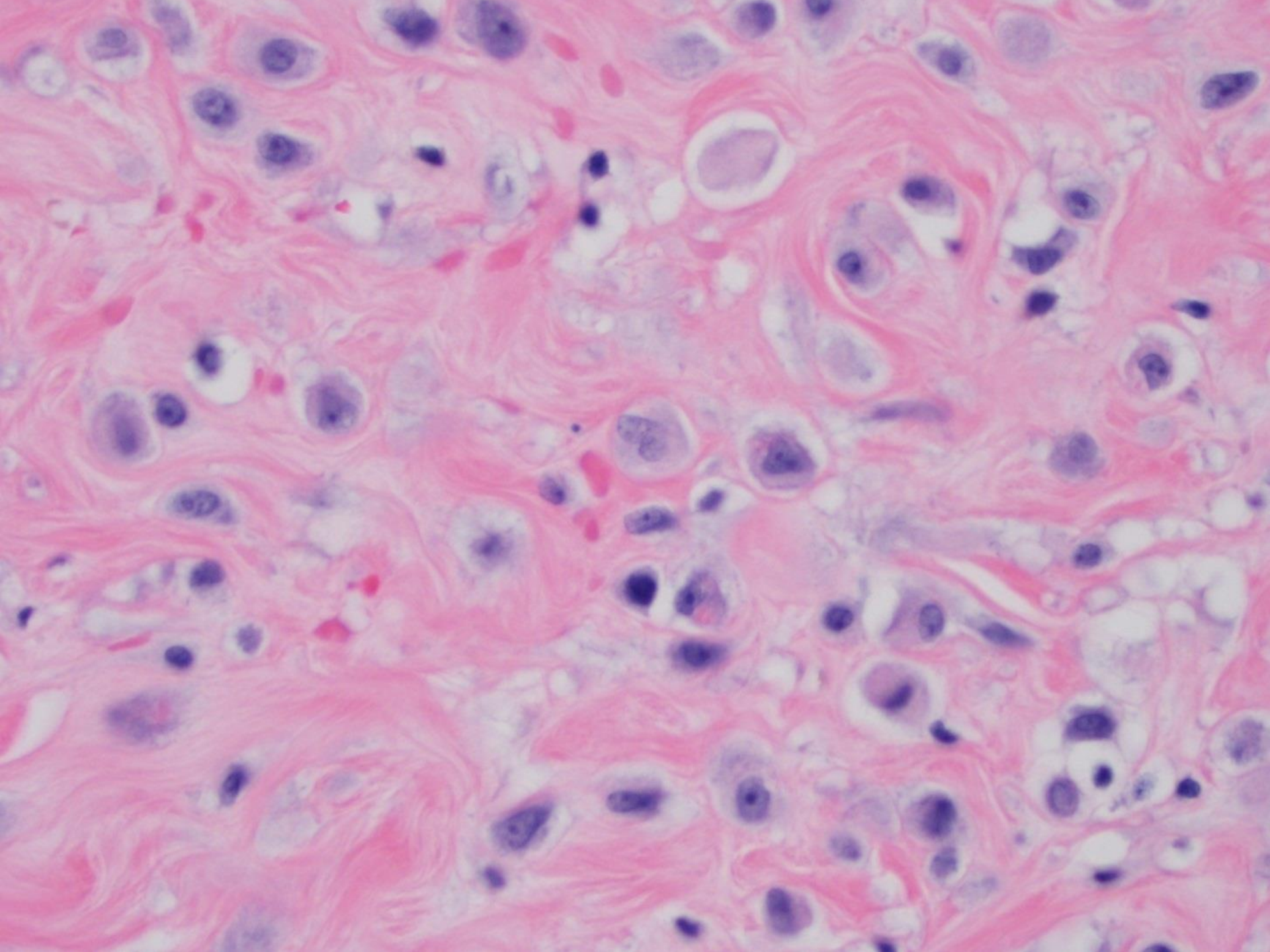













Diagnosis?

Lymphocytic/Diabetic Mastopathy

History

- 56 yo with 2.7 cm mass in subareolar region of breast
- No h/o DM, thyroid dz or autoimmune dz
- No recurrence since surgery (12/12) including unremarkable mammo (6/14)

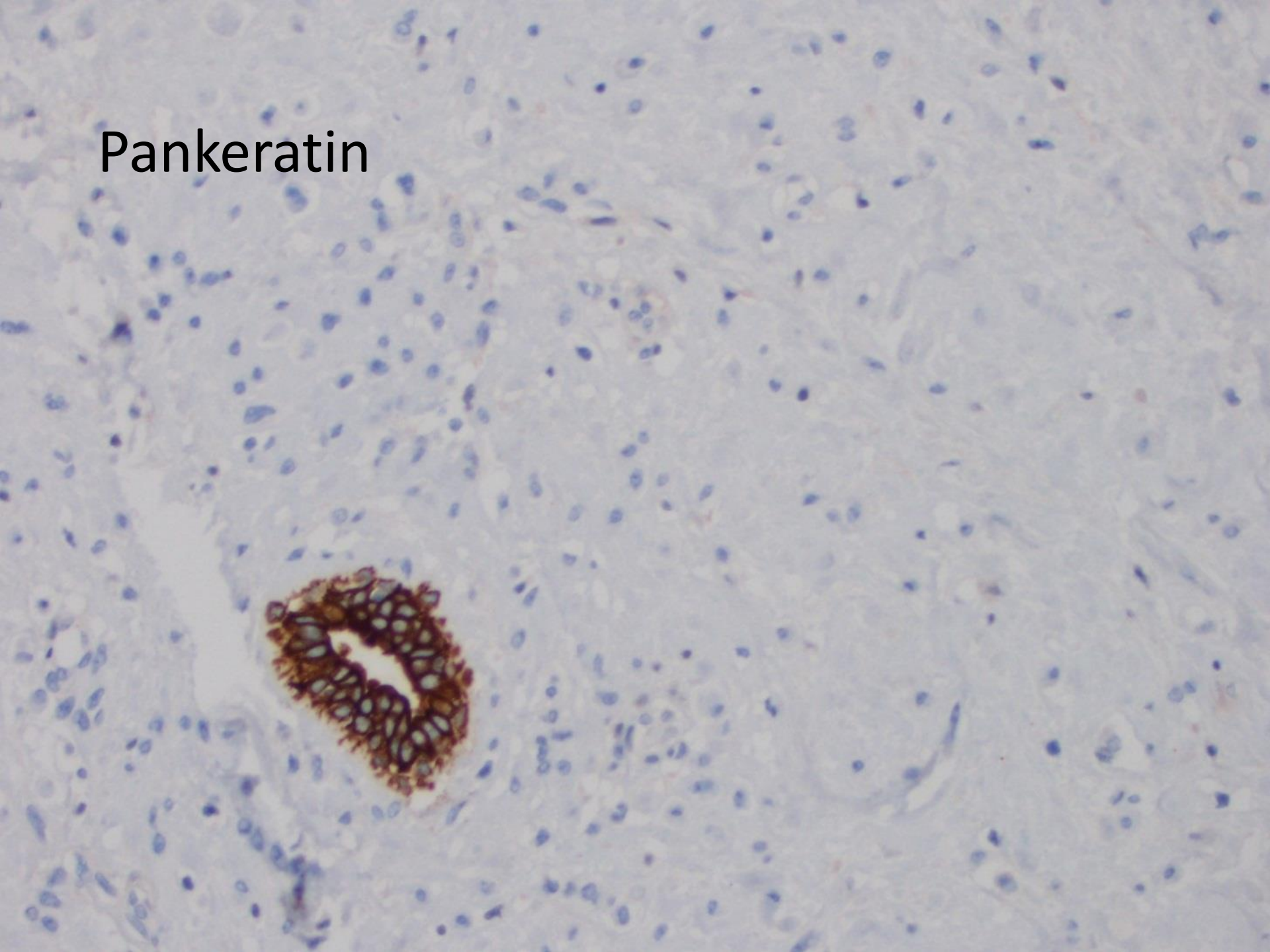
Gross

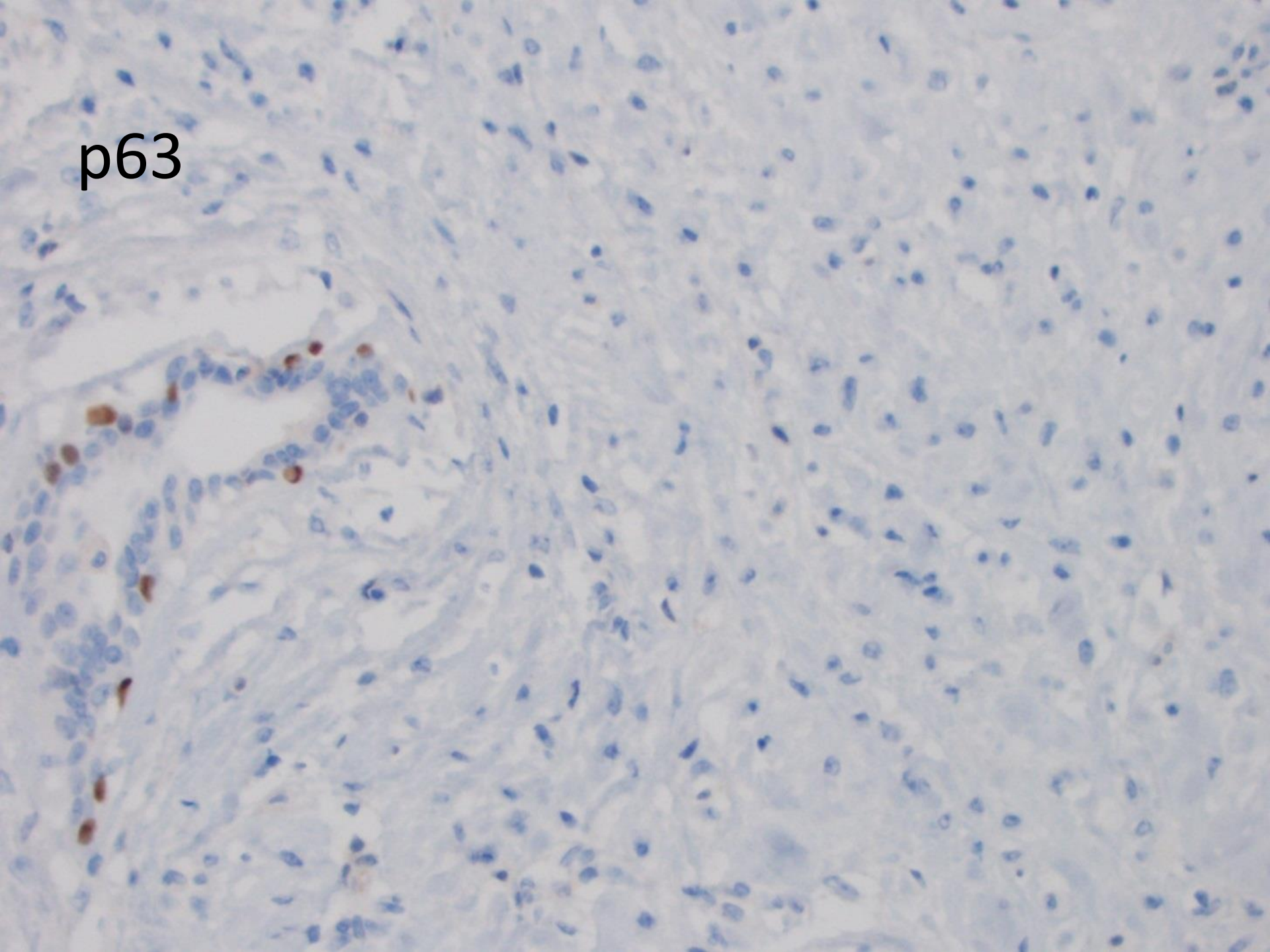
- 2.5 cm ill defined 2.5 cm. firm grey-tan mass

Histology

- Expanded collagen stroma with keloidal features
- Lymphocytic vasculitis/lobulitis/ductitis
- Polygonal epithelioid myofibroblasts

Pankeratin

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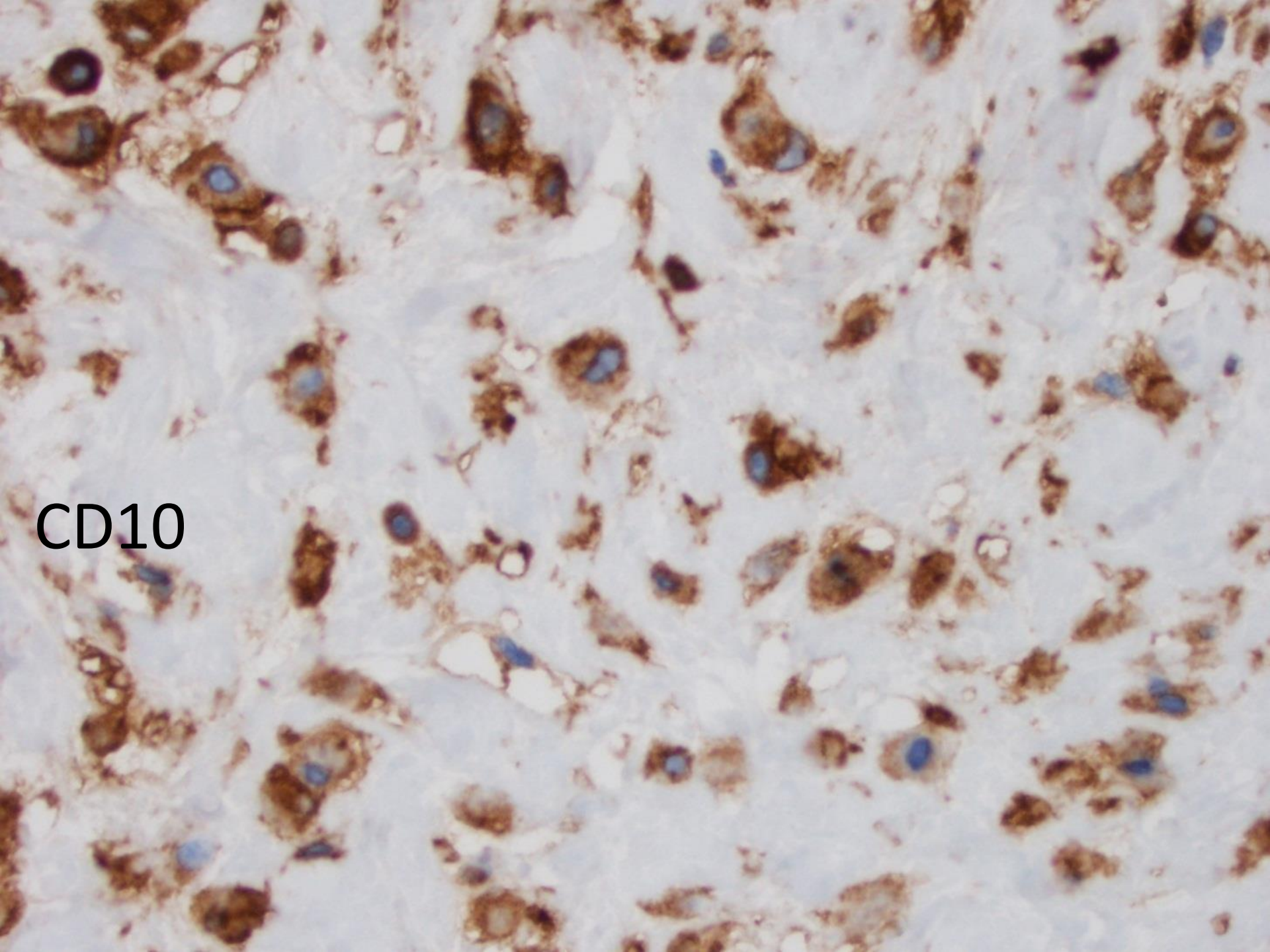
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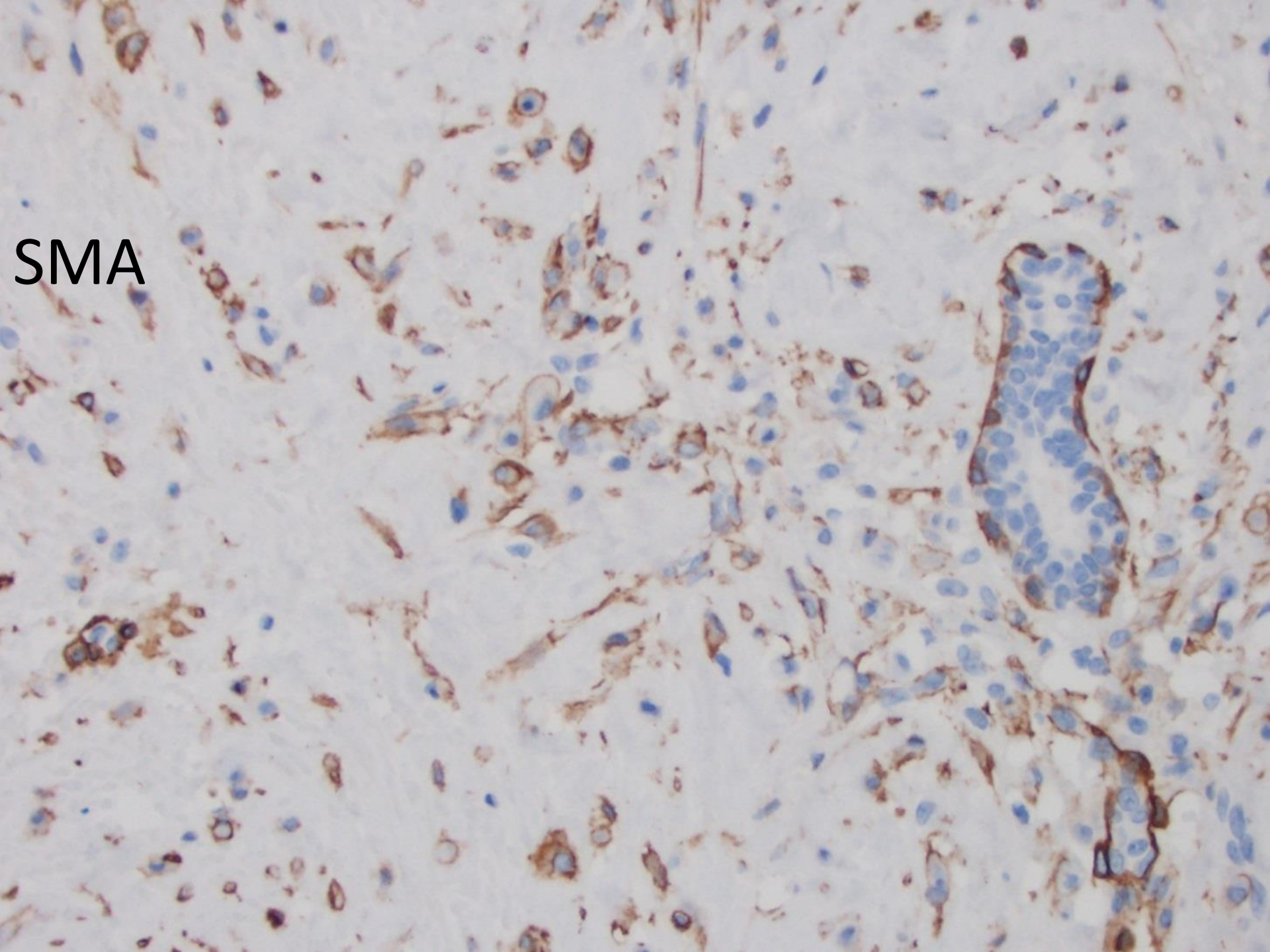
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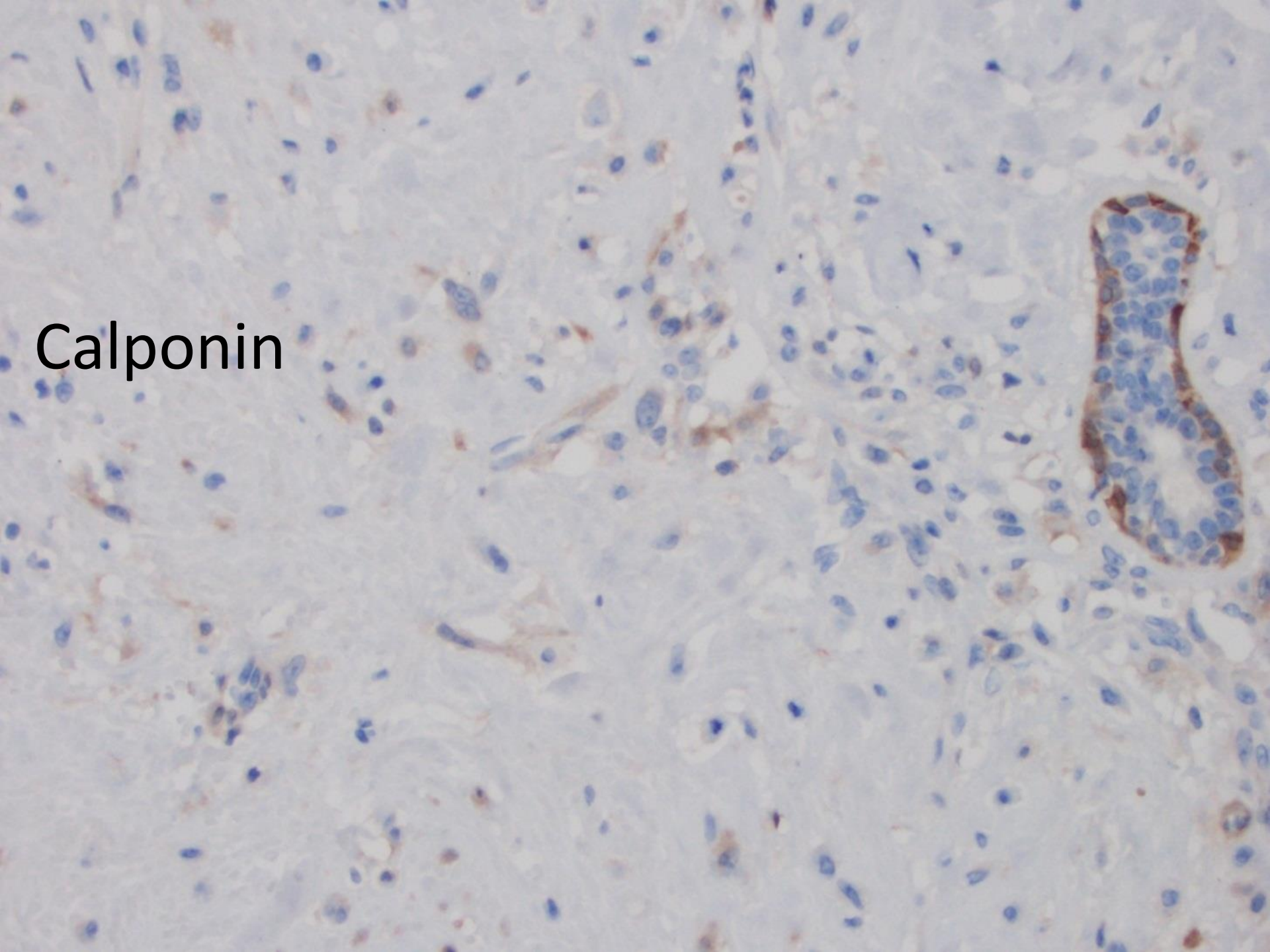

Calponin

Feature

- Most young (<30 yrs) females
- Most have DM – other associations thyroid dz and autoimmune dz – 3/19 w/o any association (Page, et al AJCP 2000)
- Palpable firm mass – suspicious
- Mammo – non-specific

Prognosis

- Self-limited
- Recurrences (6/19) may be ipsilateral, bilateral, contralateral, multiple
- No evidence of predisposition to neoplasia

Path DDX

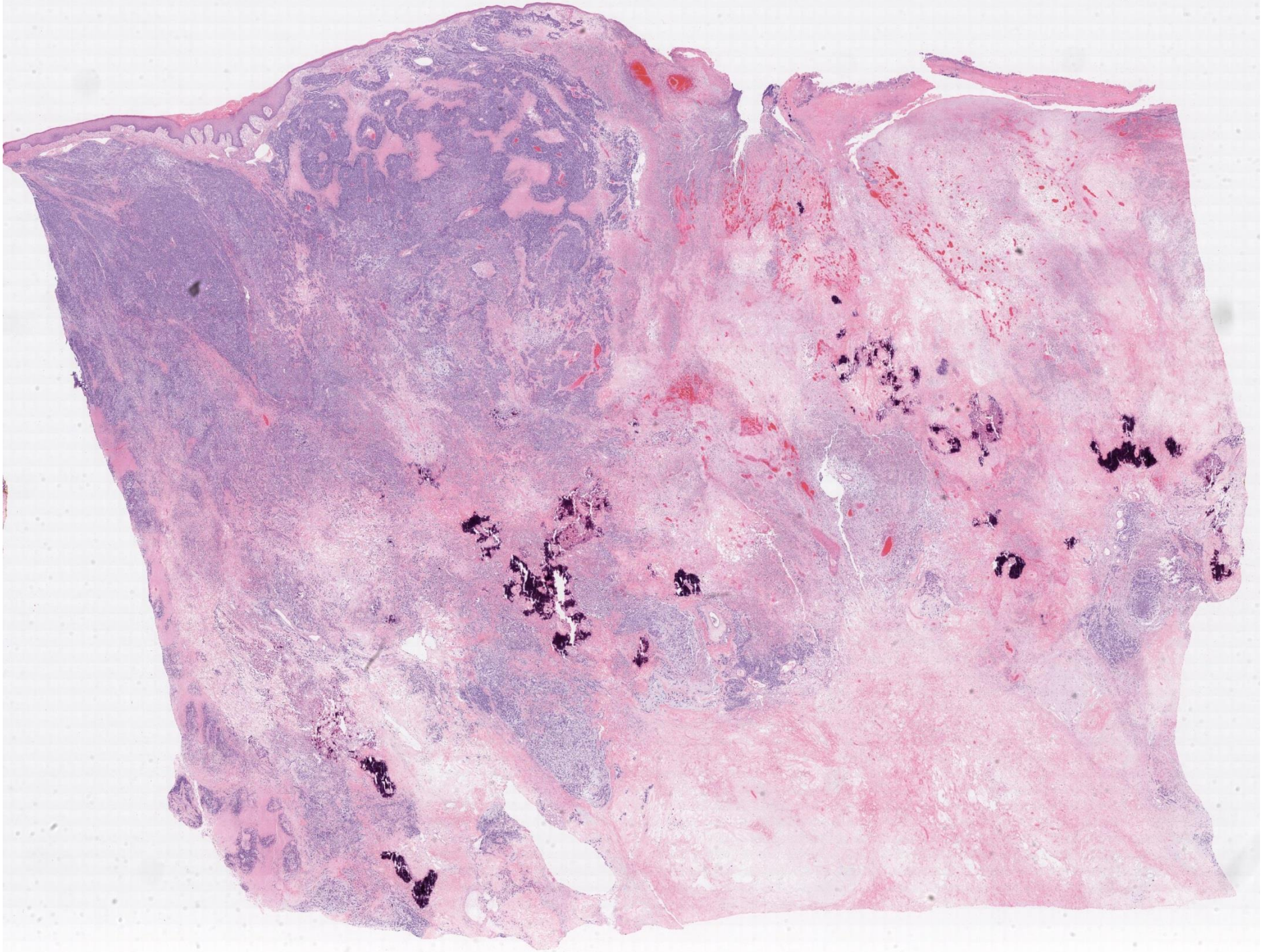
- Invasive carcinoma
- Granular cell tumor

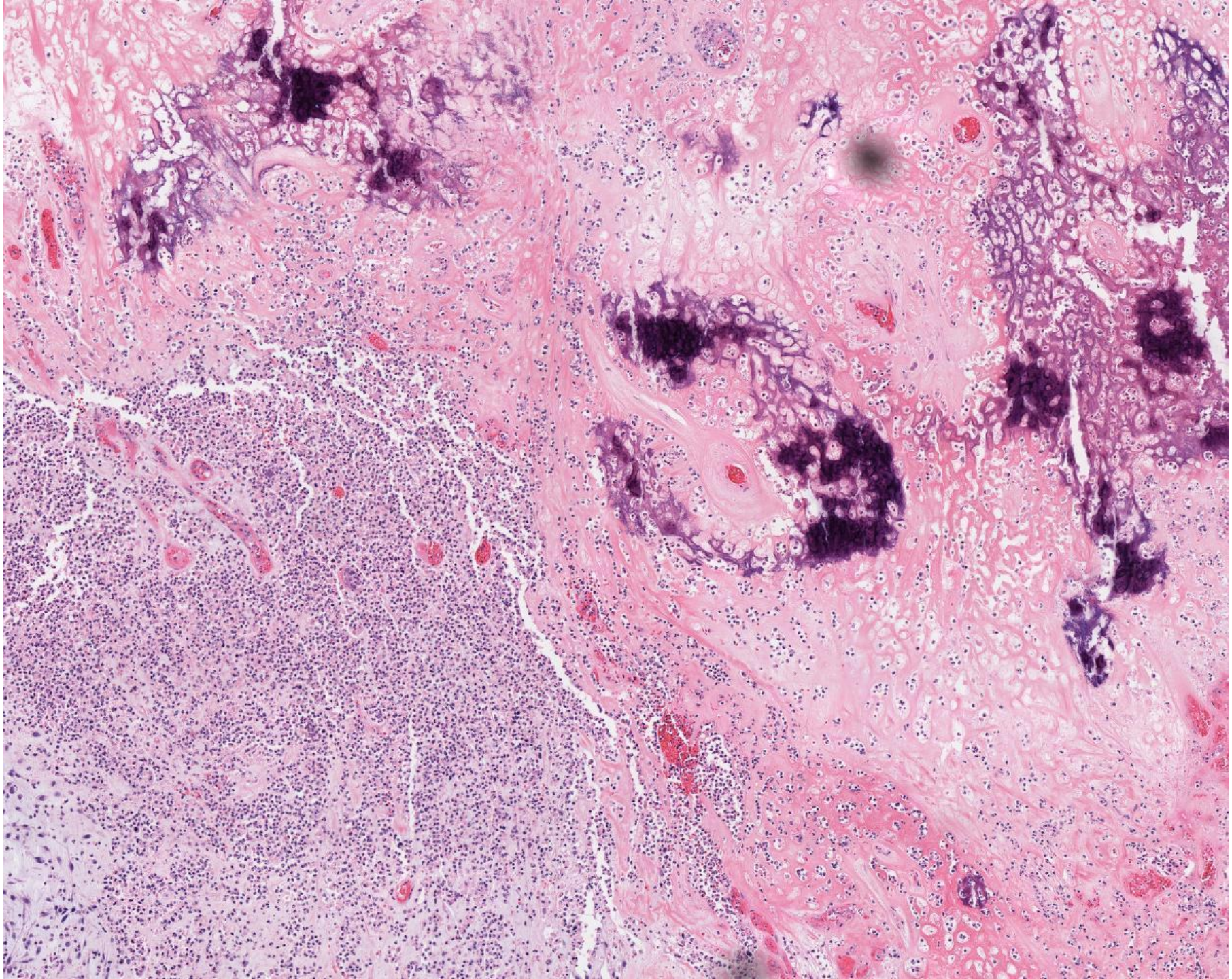
Pathogenesis

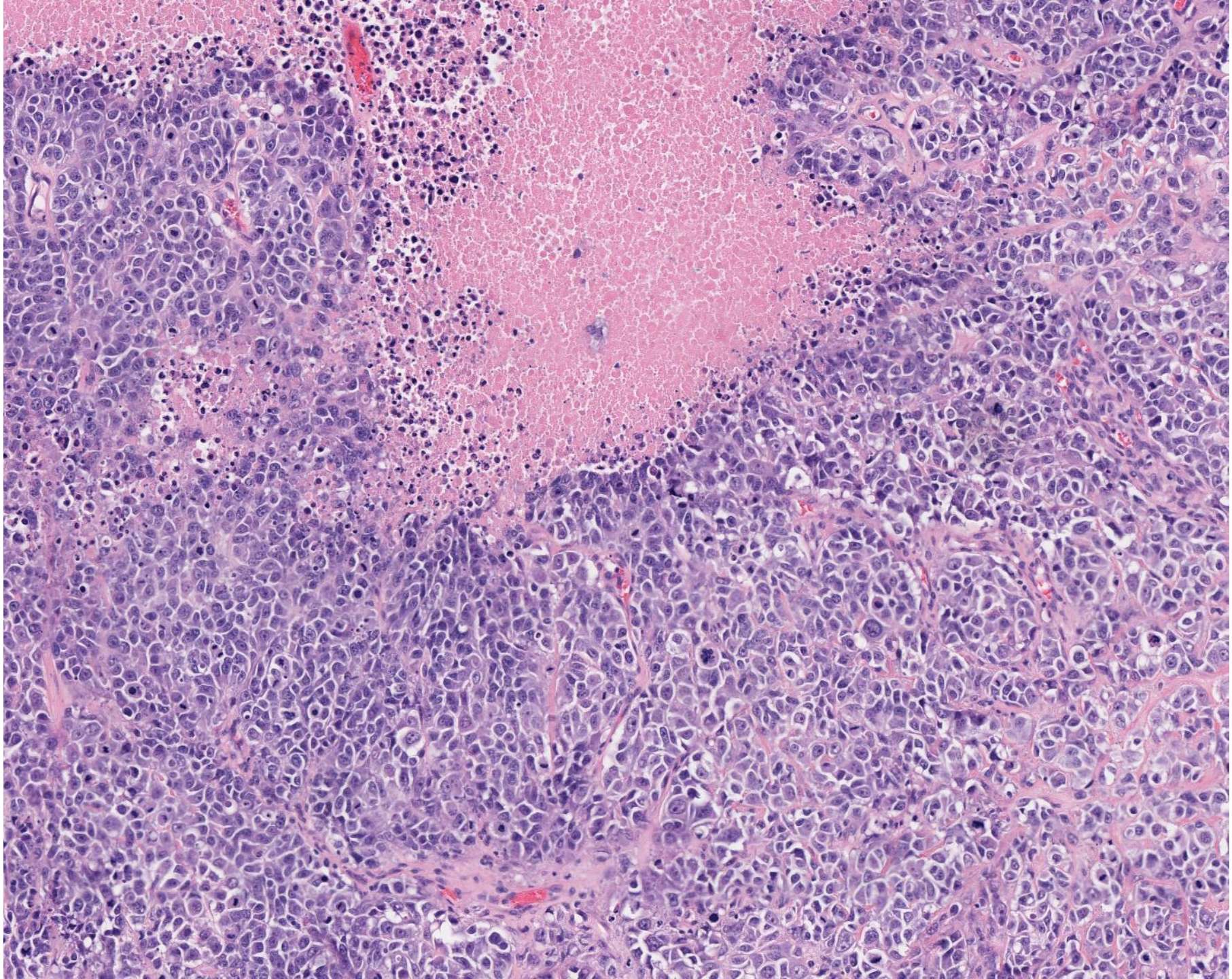
- Hyperglycemia-glycosylated extracellular matrix form neoantigen-autoimmune response with B-cell proliferation/autoab production-cytokines-matrix expansion
- Also association with certain HLA types suggesting autoimmune etiology

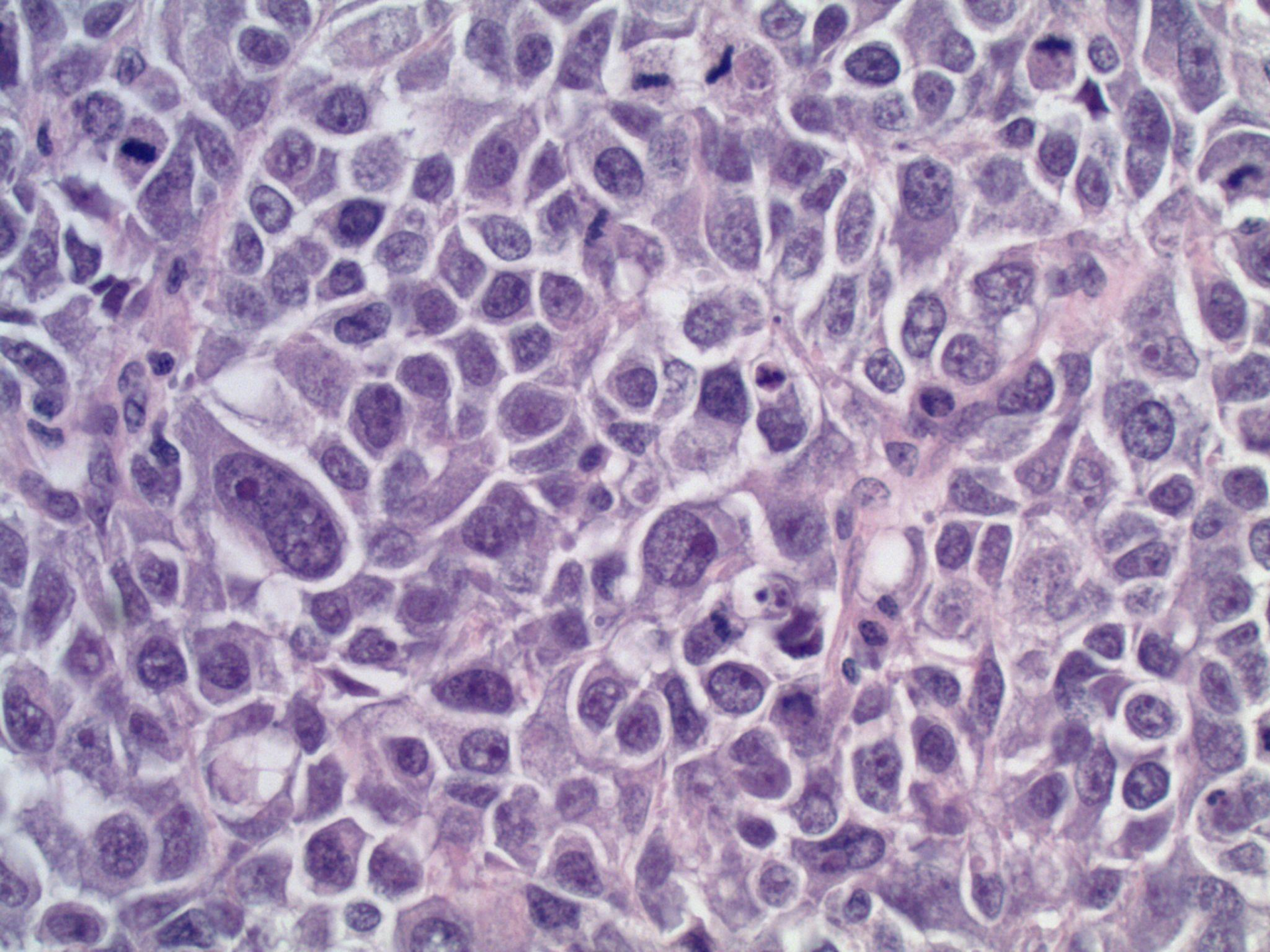
SB 5958
Dana Balitzer/Charles Zaloudek; UCSF

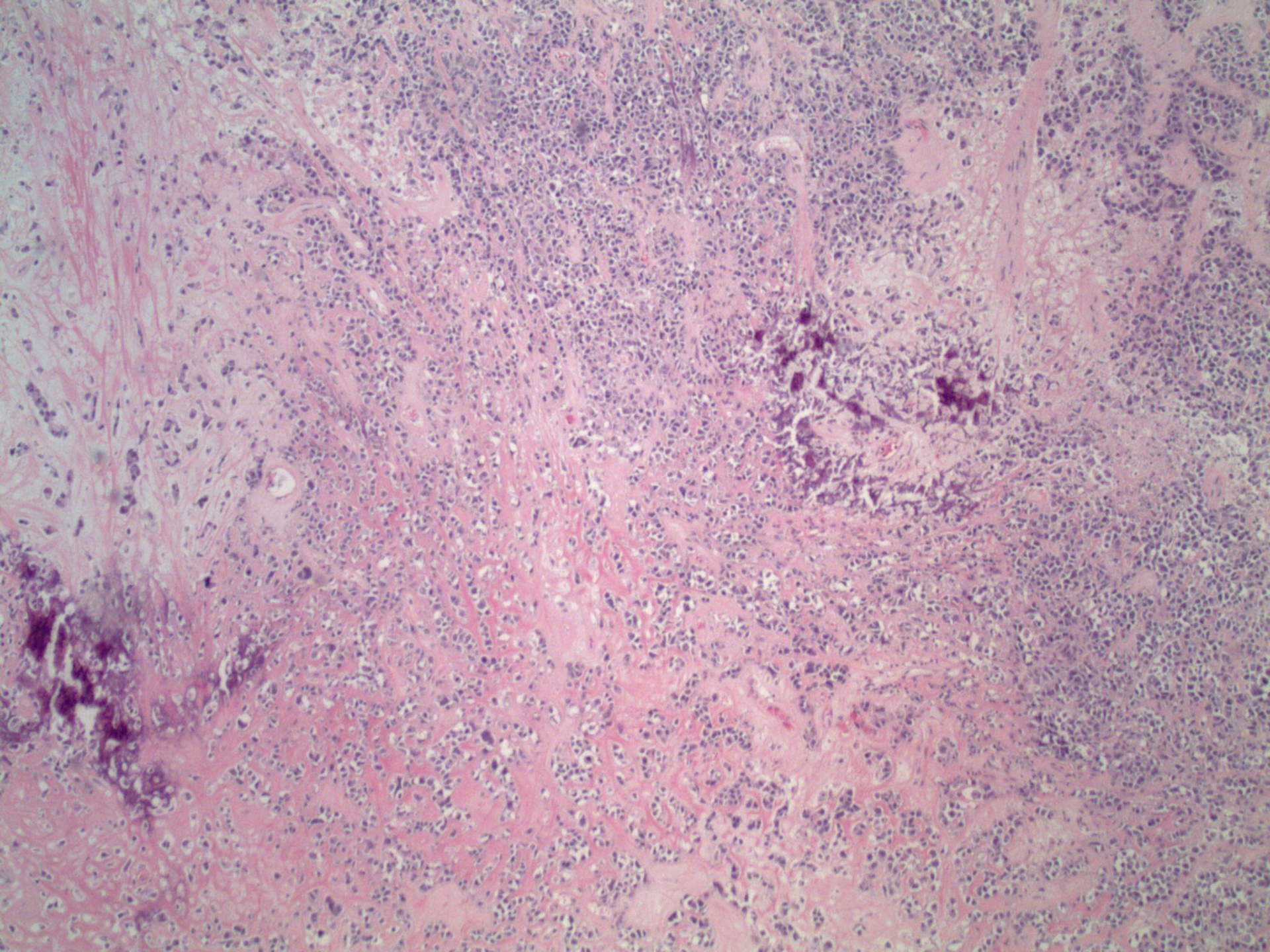
46-year-old female presented with 10-month history of left breast mass that grew to ulcerate through the skin. A core needle biopsy was performed at another hospital and the patient was subsequently referred to UCSF for therapy.

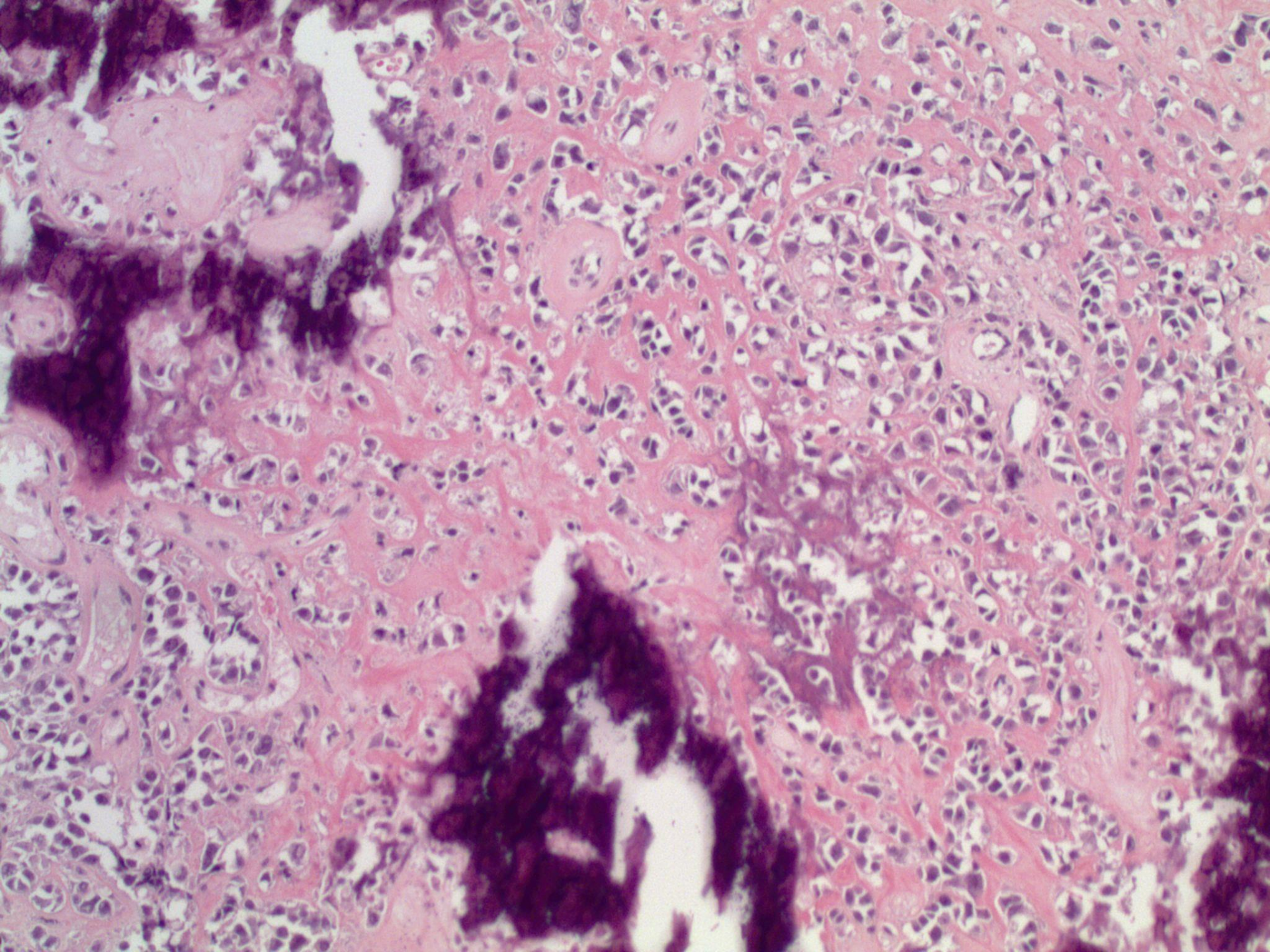


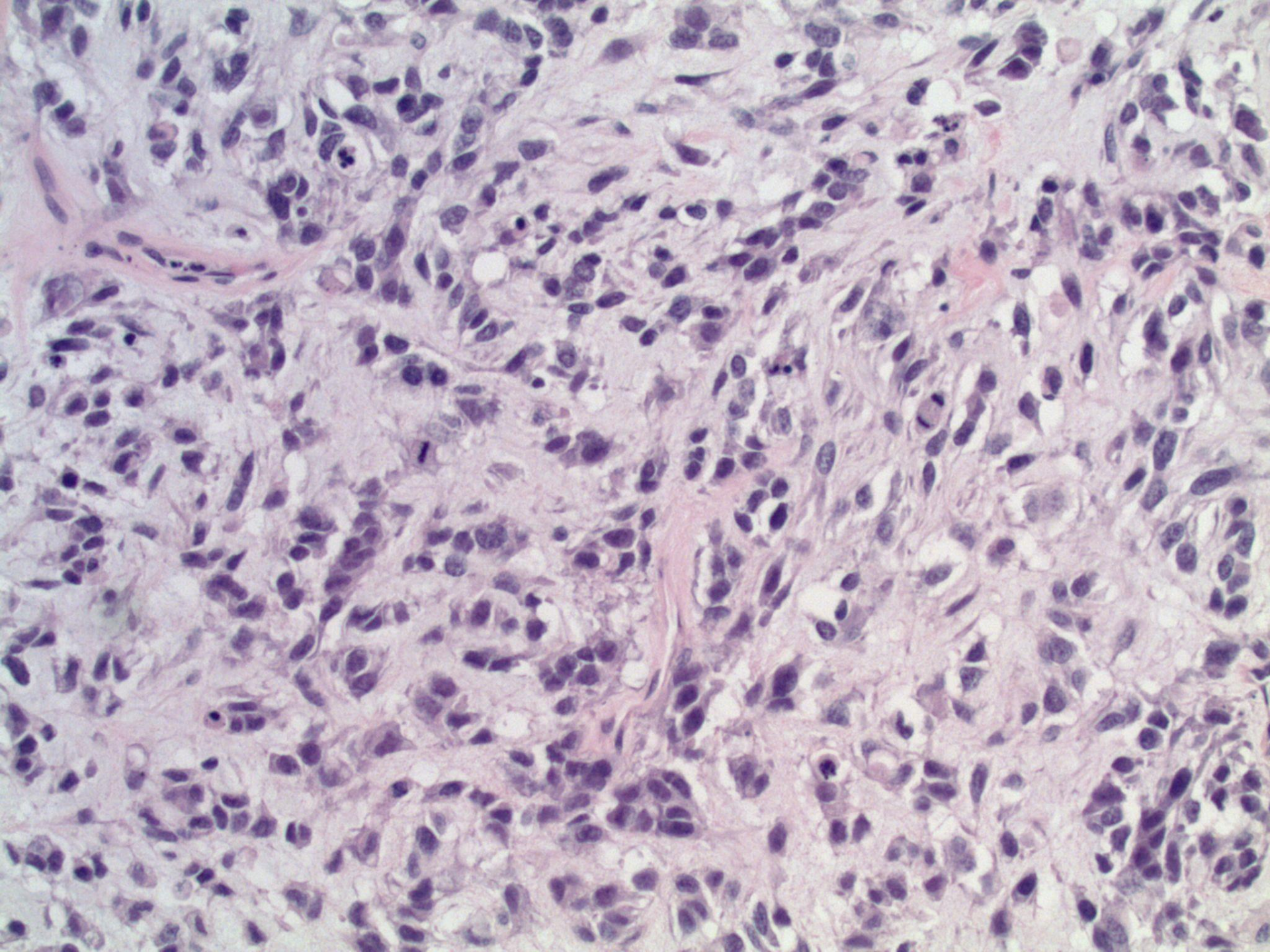













Diagnosis?

AN UNUSUAL BREAST TUMOR

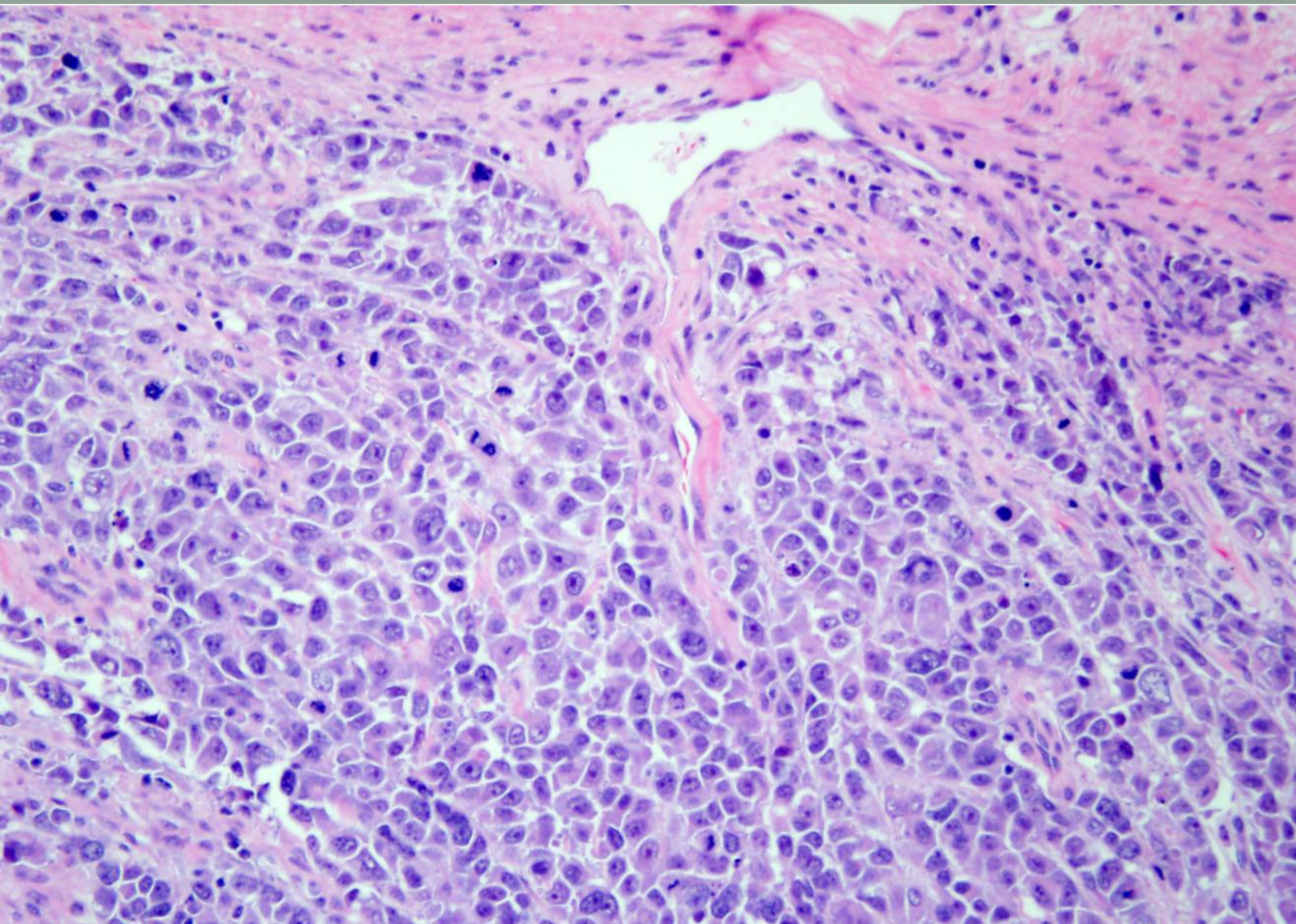
Dana Balitzer, M.D.

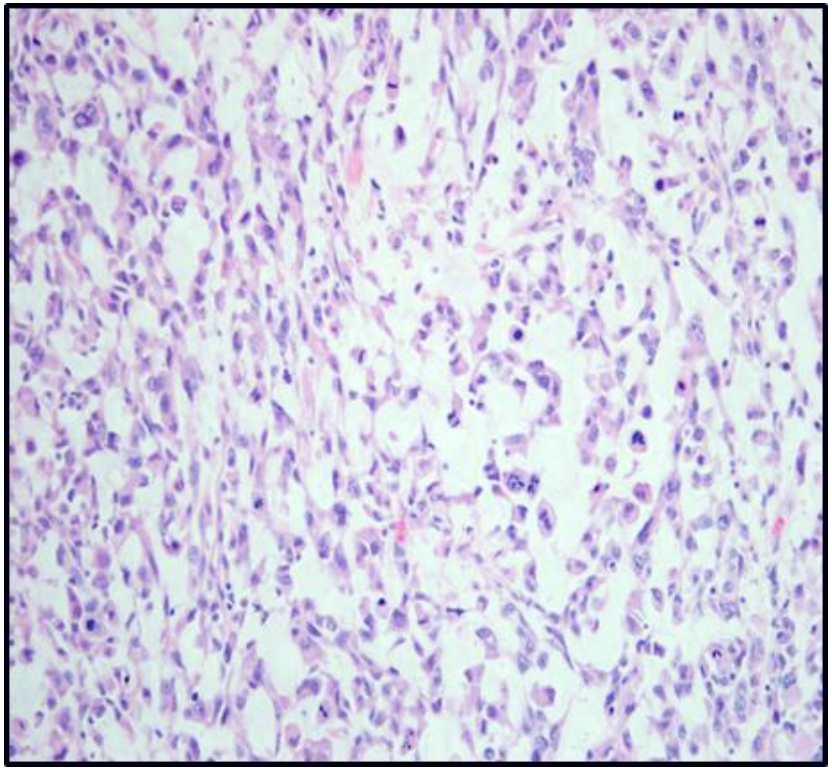
University of California San Francisco PGY-3

Case

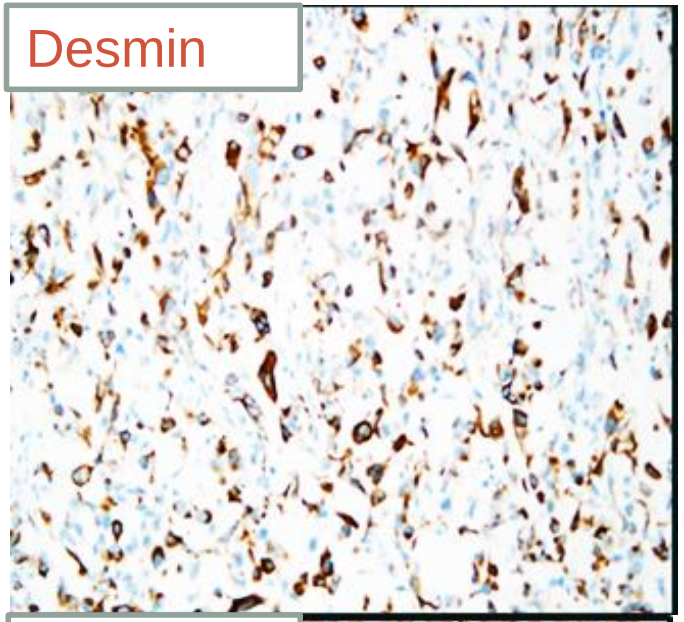
46-year-old woman presenting with 10 months of a large breast mass fungating through the skin

The patient received pre-operative chemotherapy and undergoes radical mastectomy

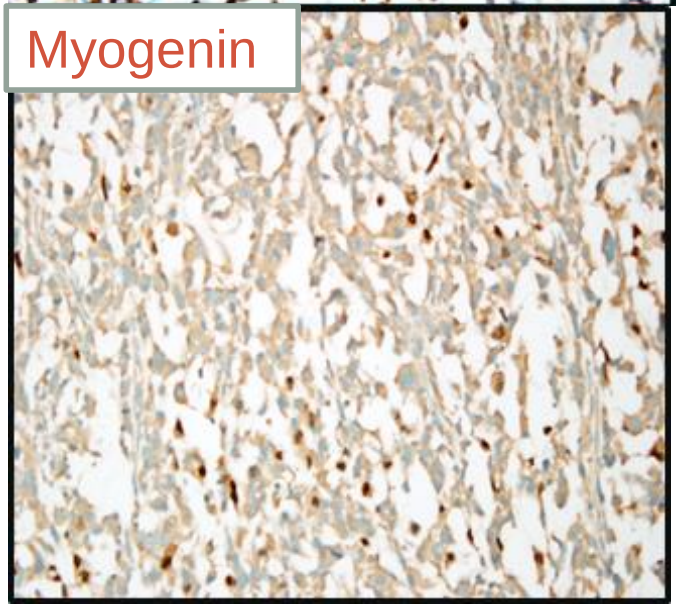


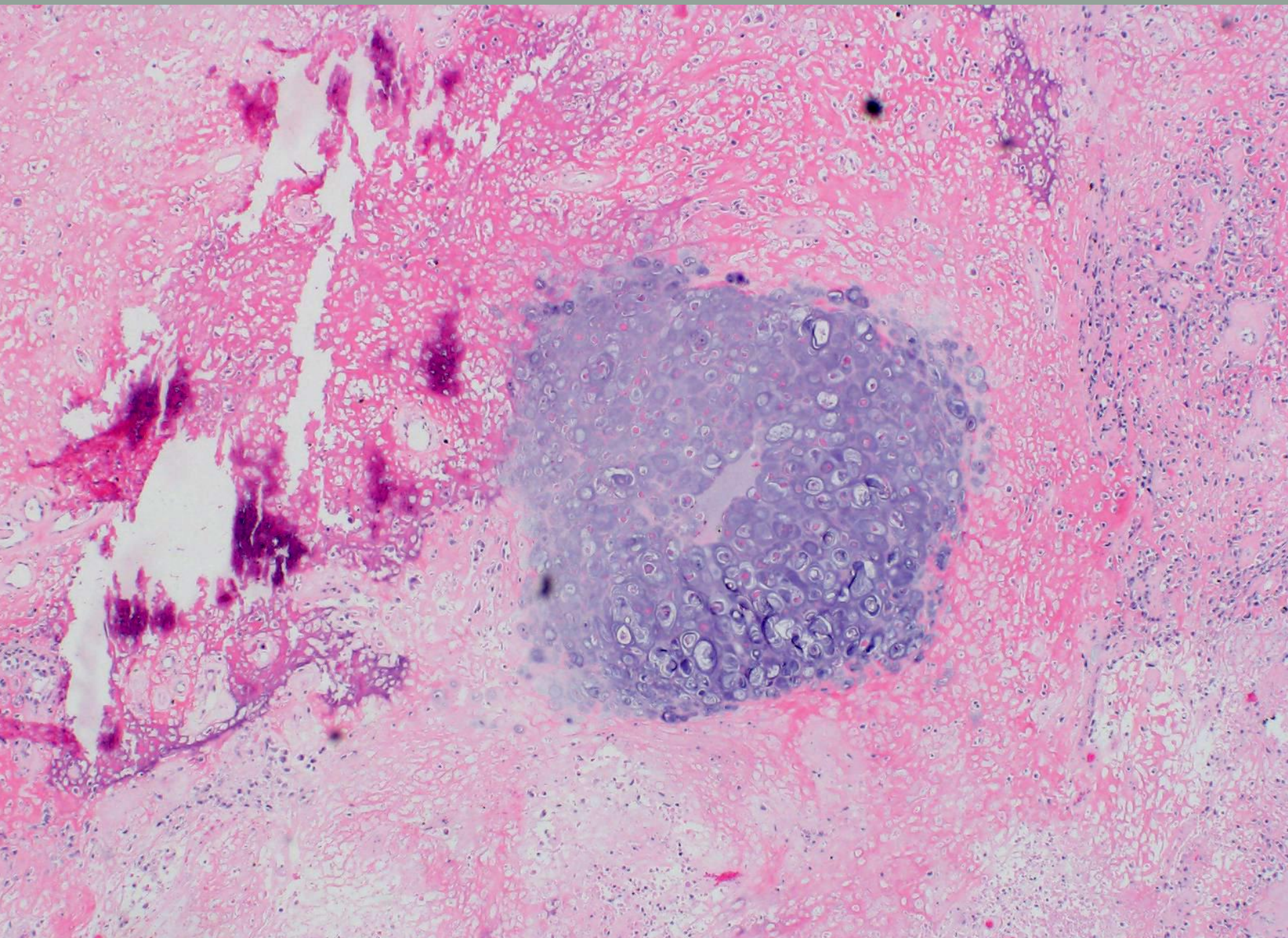


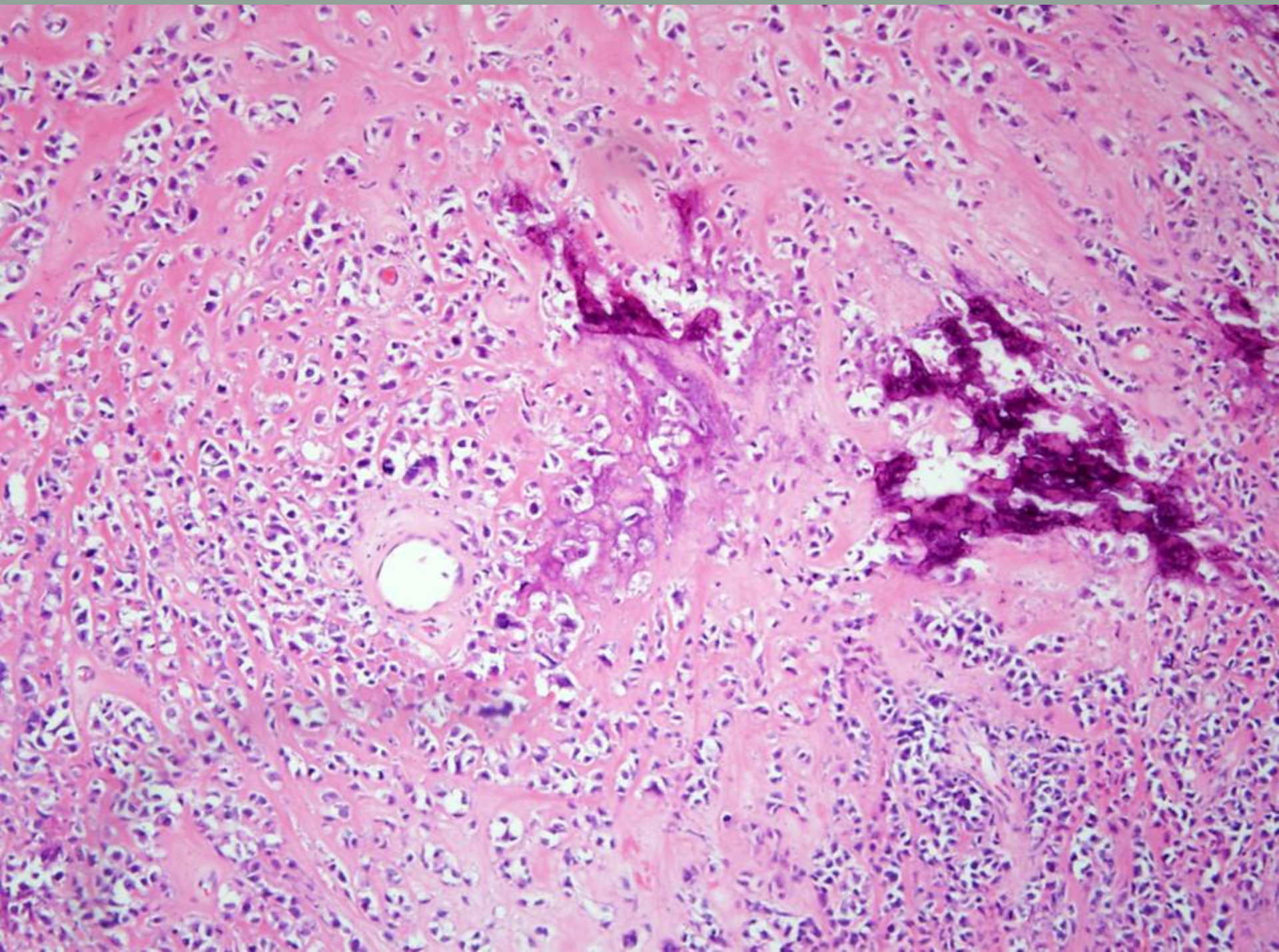
Desmin



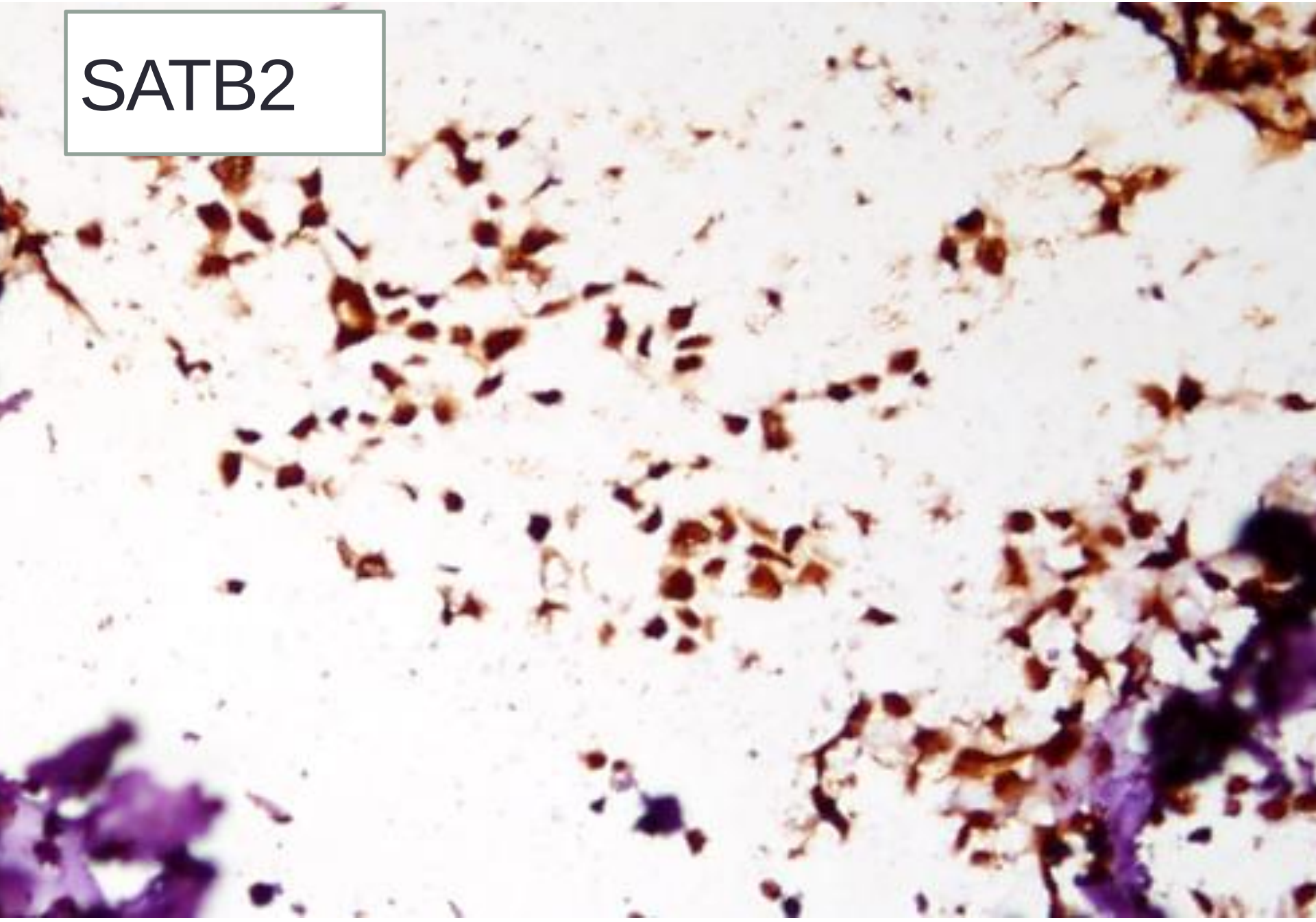
Myogenin







SATB2



Metaplastic Carcinoma

Carcinoma with non-epithelial cellular elements

- Heterogeneous group
- Rare < 1% of all invasive mammary carcinomas
- Poorer outcome when compared with high-grade invasive ductal carcinoma and poor response to chemotherapy
- >90% are triple-negative
- >90% have p63 positivity

Diagn Pathol. 2014 Jul 16;9:139.

J Clin Pathol. 2013 Jun;66(6):522-8.

Special AT-rich sequence-binding protein (SATB2)

- Nuclear matrix-associated transcription factor and epigenetic regulator
- Marker of osteoblastic differentiation in benign and malignant mesenchymal tumors.
- Expressed in the glandular epithelial cells of the lower gastrointestinal tract
  - High sensitivity (93%) and specificity (77%) to determine a cancer of colorectal origin

Adv Anat Pathol. 2014 Jan;21(1):63-7. Histopathology. 2013 Jul;63(1):36-49. doi:

197 SATB2 Expression in Metaplastic Carcinoma of the Breast (MCB) With Osseous Differentiation (OD)

Gregor Krings, Yunn-Yi Chen. University of California, San Francisco, CA.

- 30 cases of metaplastic carcinoma were immunostained with SATB2
  - SATB2 was positive in all 8 (100%) of metaplastic carcinoma with osteoblastic differentiation, and negative in all cases without osteoblastic differentiation.
- SATB2 is **more sensitive than keratin or GATA3** for metaplastic carcinoma with osteoblastic differentiation
- Expression is also diffusely **positive in epithelioid and spindled cells** without histologic features of osteoblastic differentiation, including metastases.

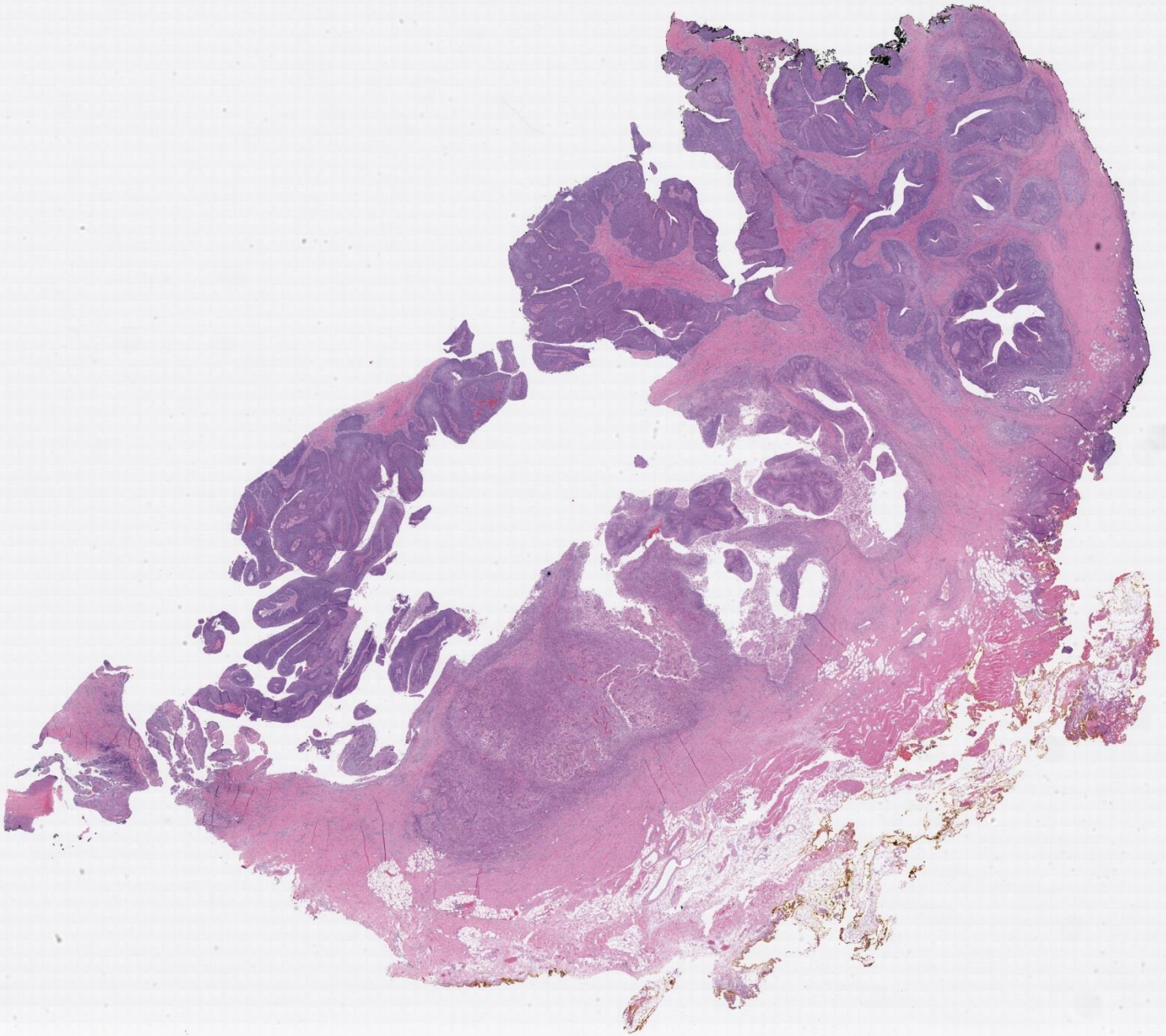
Case Follow-up

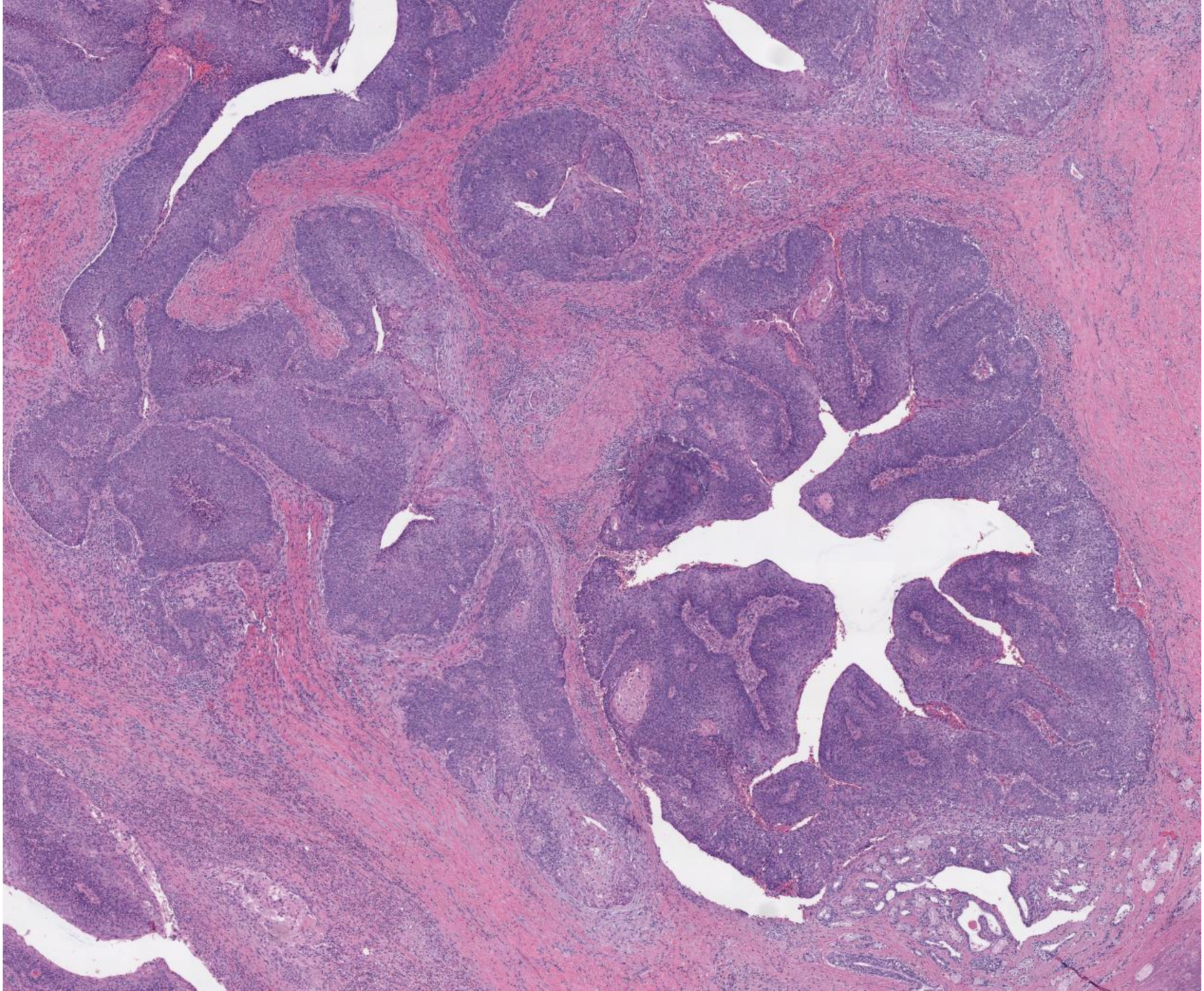
- Completion mastectomy with numerous foci of metaplastic carcinoma, up to 2 cm each and spanning at least 8 cm, with extensive lymphovascular invasion and infiltration of skeletal muscle

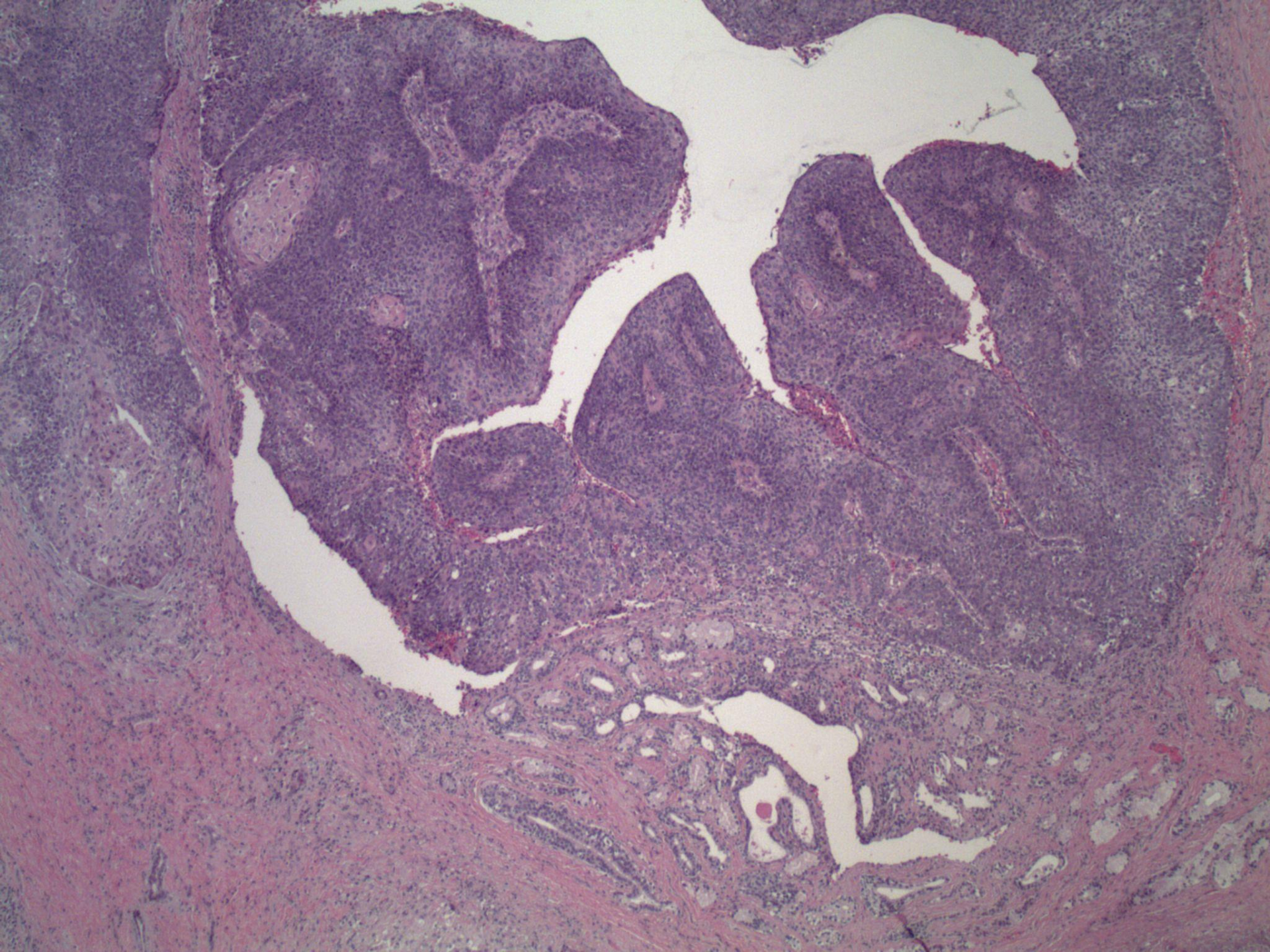
Questions

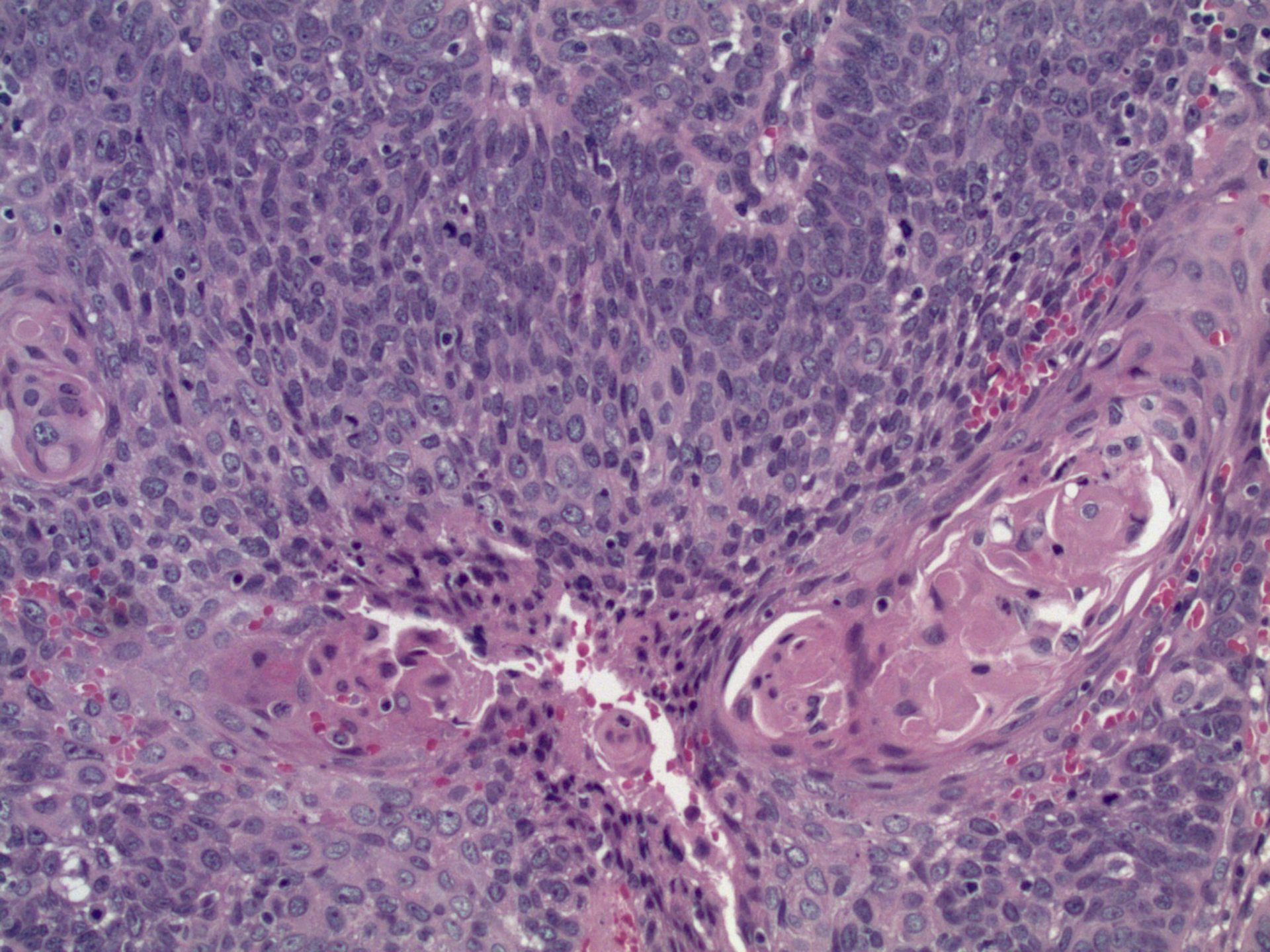
SB 5959
Vanessa Ma/John Bishop; UC Davis

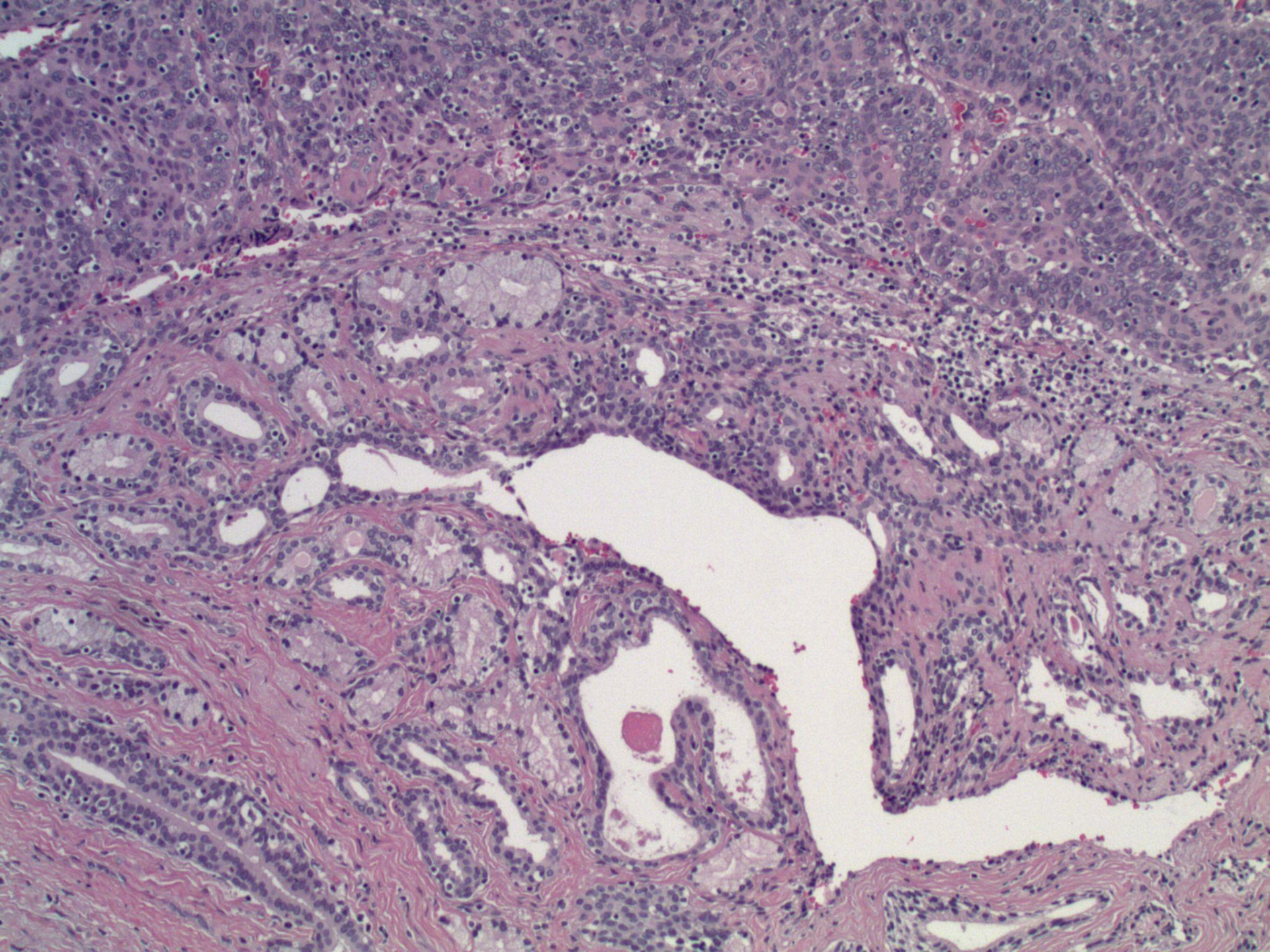
76-year-old woman with new vulvar tender lesion with no change in size. Antiobiotics did not improve symptoms. Vulvar biopsy shows VIN3.

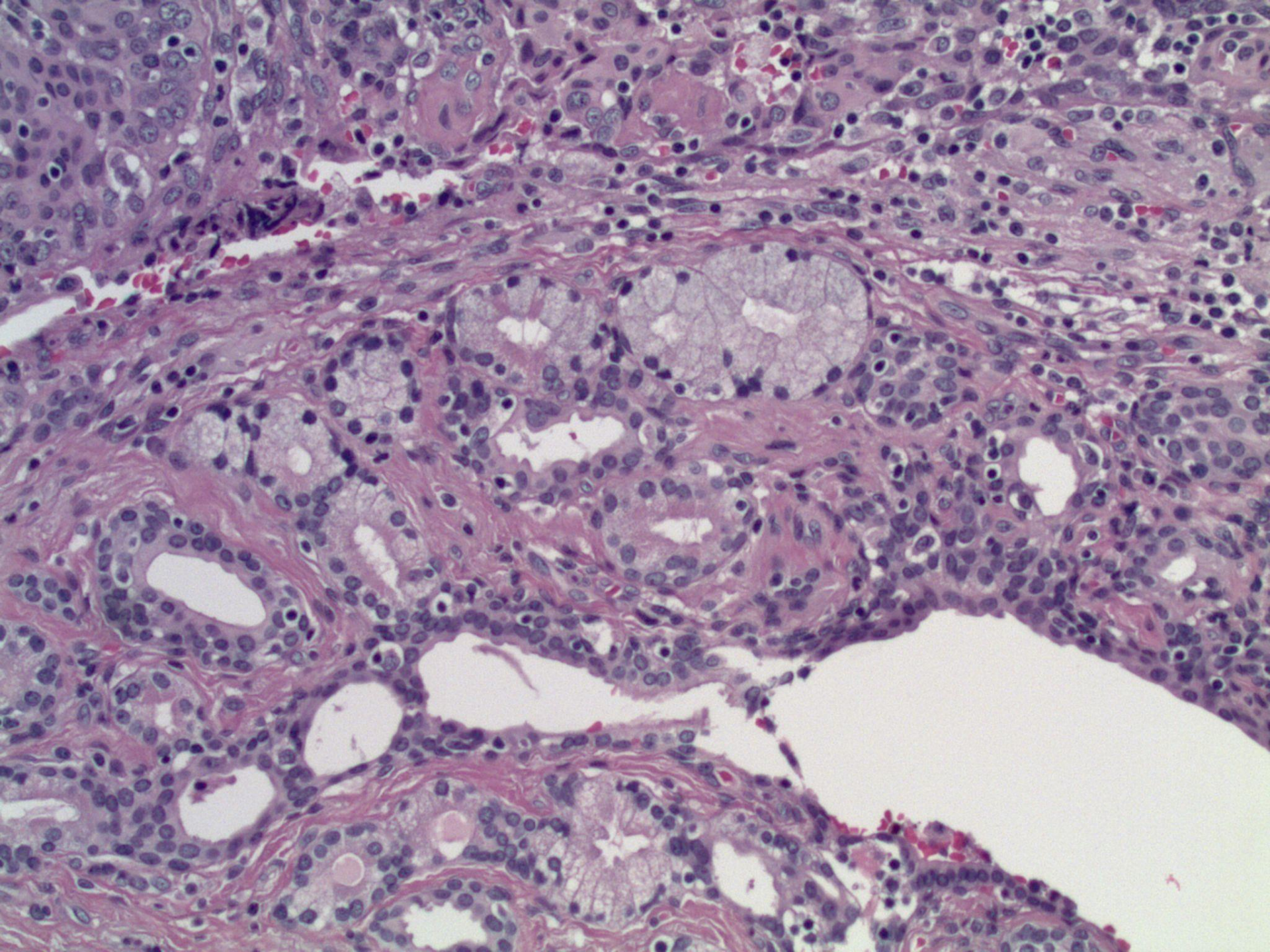













Diagnosis?

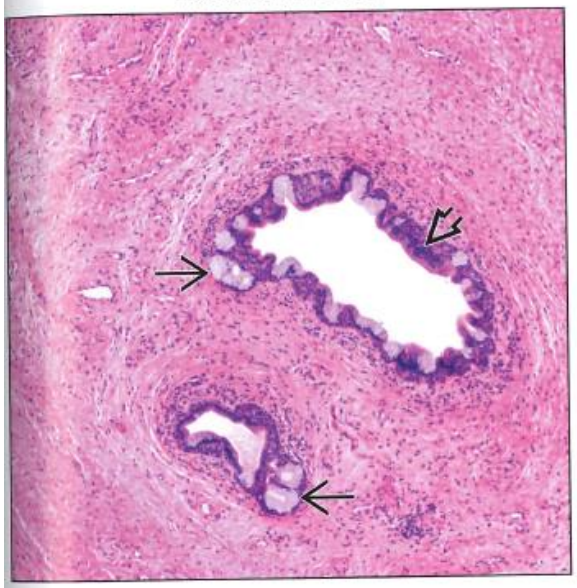
Bartholin gland carcinoma

- Poorly differentiated squamous cell carcinoma type
- Tumor size: 3.0 cm
- Depth of invasion: 19 mm
- Lymphovascular invasion present
- The tumor extended to the distal vaginal and rectovaginal margins
- AJCC staging: pT2NxMx

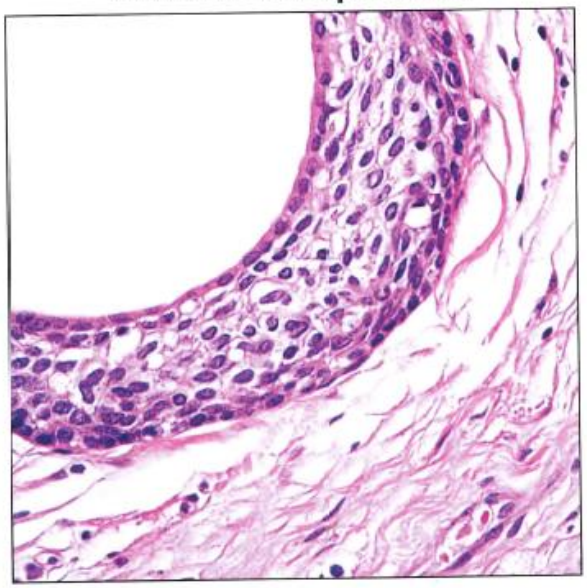
Bartholin gland carcinoma (BGC)

- Primary carcinoma of diverse cells types located in the site of the Bartholin's glands
  - From the mucin-secreting columnar epithelial cells of the acini (40%)
  - From the squamous epithelium at the vestibular orifice of the duct (40%)
- Uncommon
  - In women over 50 years of age
- Nonspecific symptoms and signs
  - Painless lump, bleeding, swelling and pruritus
  - May resemble a Batholin duct cyst/abscess

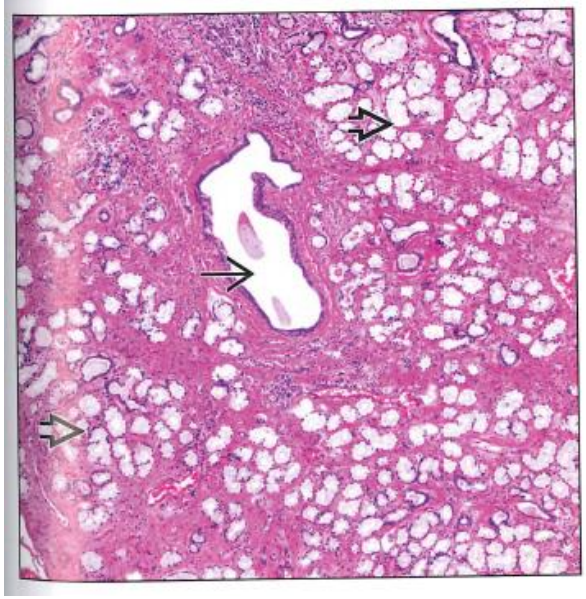
Bartholin Duct



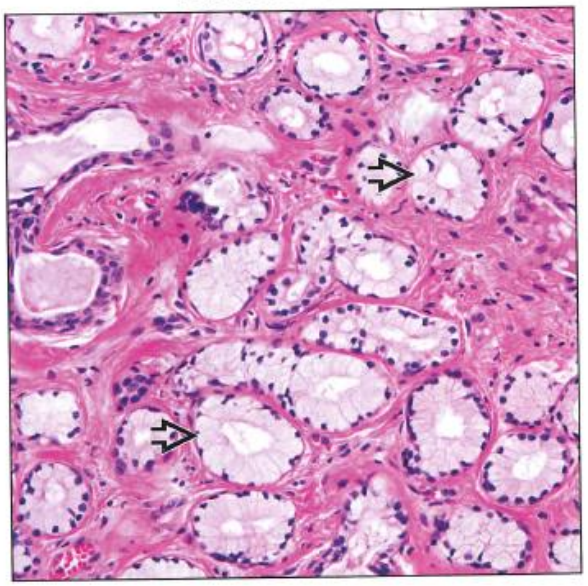
Bartholin Duct Epithelium



Bartholin Gland



Bartholin Gland



Bartholin gland carcinoma

- Typically solid and deeply infiltrative tumor
- Squamous cells carcinoma (40%)
- Adenocarcinoma (40%)
  - Mucinous, papillary, clear cell
- Adenoid cystic carcinoma (15%)
- Adenosquamous carcinoma (5%)
- Transitional cell carcinomas (rare)
- Small cell carcinomas, Merkel cell carcinoma, myoepithelial carcinoma etc.

Table 1. Diagnostic criteria for Bartholin's gland carcinoma.

Anatomical position of tumour located in Bartholin's gland region
Overlying skin intact
Tumour location deep in the labia majora
Normal glandular elements present on histology
Areas of apparent transition from normal to neoplastic elements
Histological tumour type consistent with a Bartholin's gland origin
No evidence of a concurrent primary tumour elsewhere

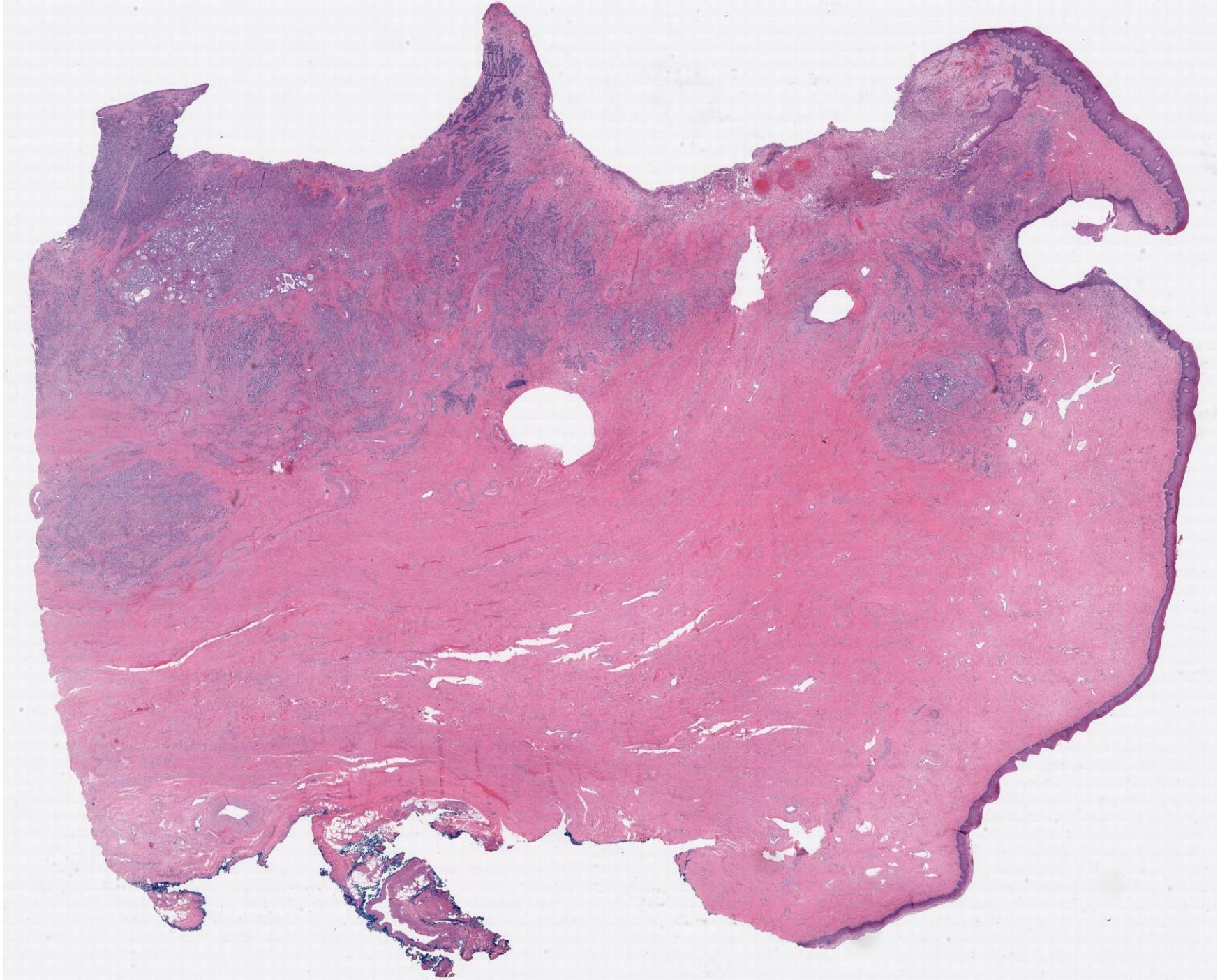
Reproduced from Copeland LJ et al, (1986, *Obstetrics and Gynecology* **67**: 794–801) with permission.

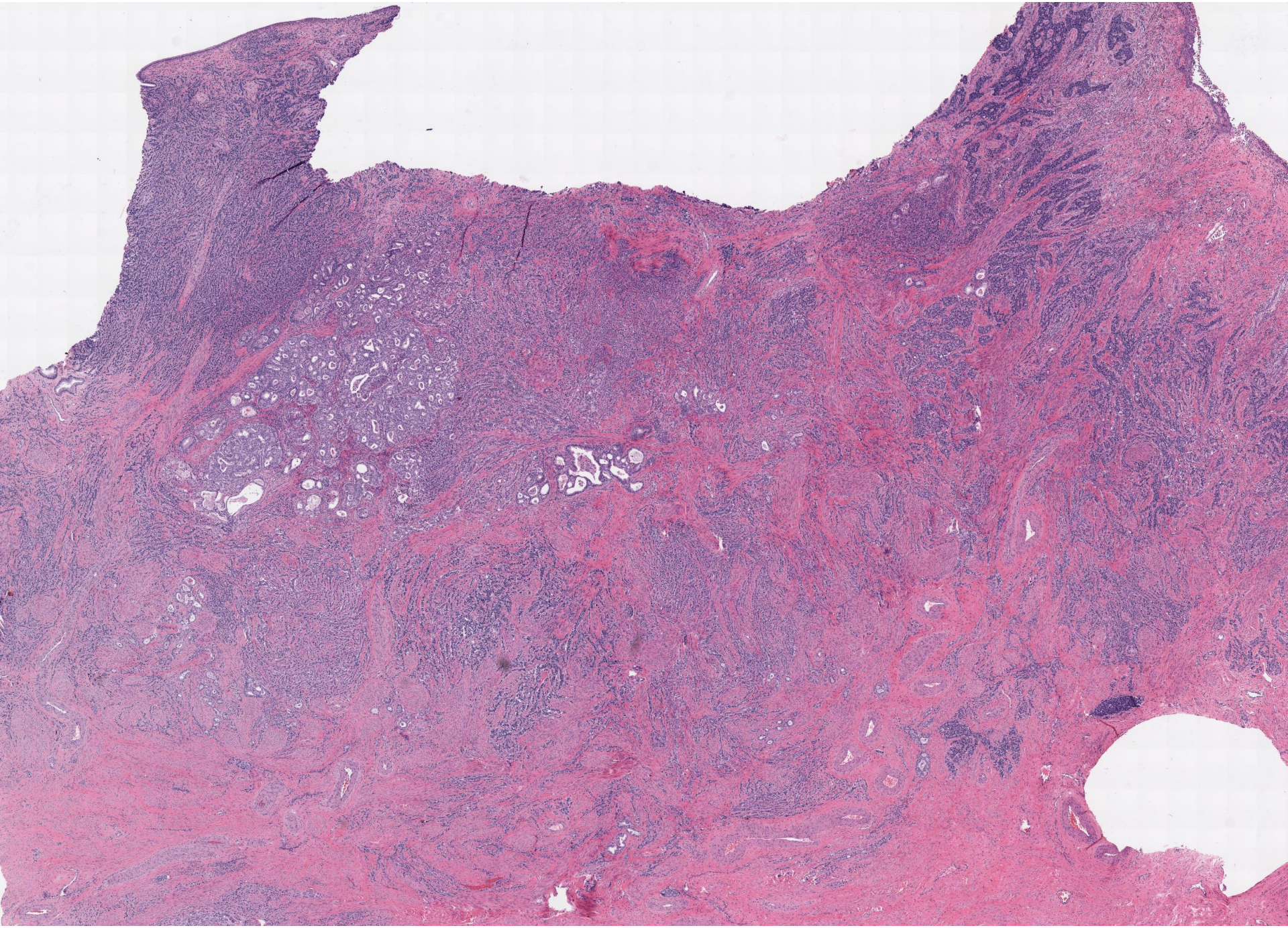
Treatment and prognosis

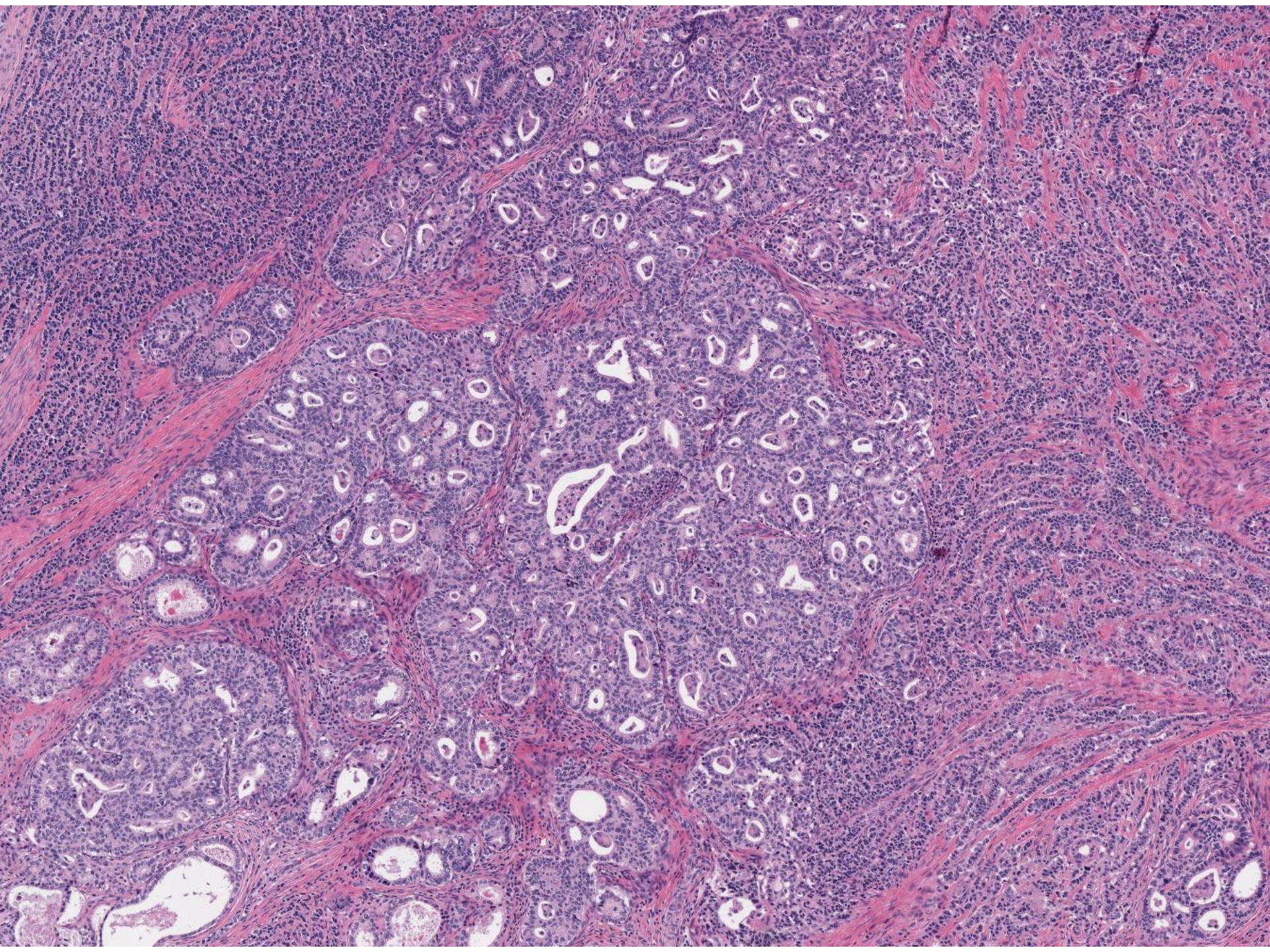
- Surgery
  - Wide local excision
  - Radical local excision
  - Vulvectomy
  - Ipsilateral/bilateral inguinofemoral lymphadenectomy
- Radiation
  - Positive or close margins (≤8 mm), metastatic disease involving the inguinal femoral lymph nodes
  - 45–50 Gy
- Chemotherapy
  - Cisplatin based
- 5-year survival
  - 67% (52-89%) with negative nodes
  - 18–20% with positive nodes

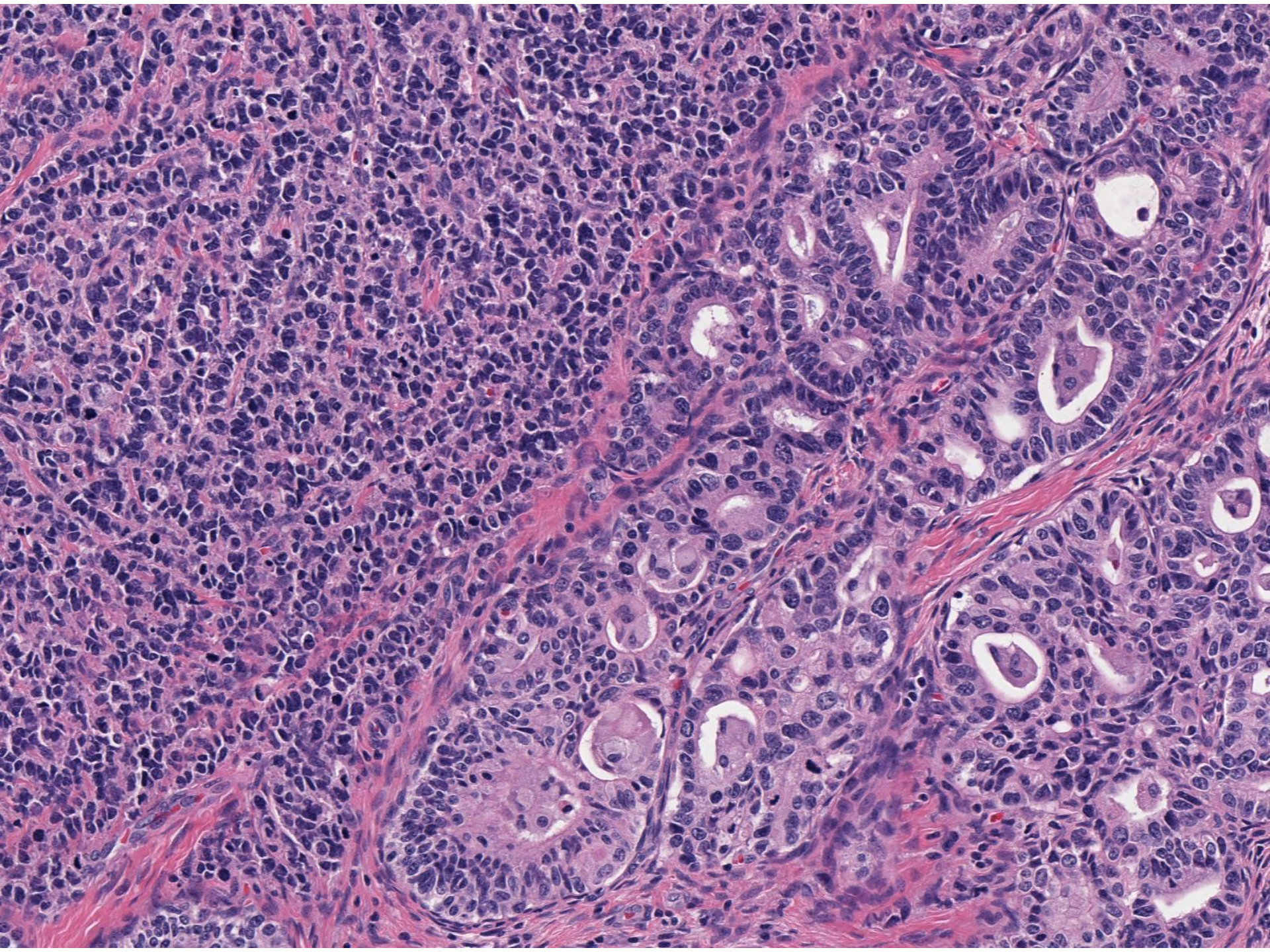
SB 5960
Vanessa Ma/Eric Huang; UC Davis

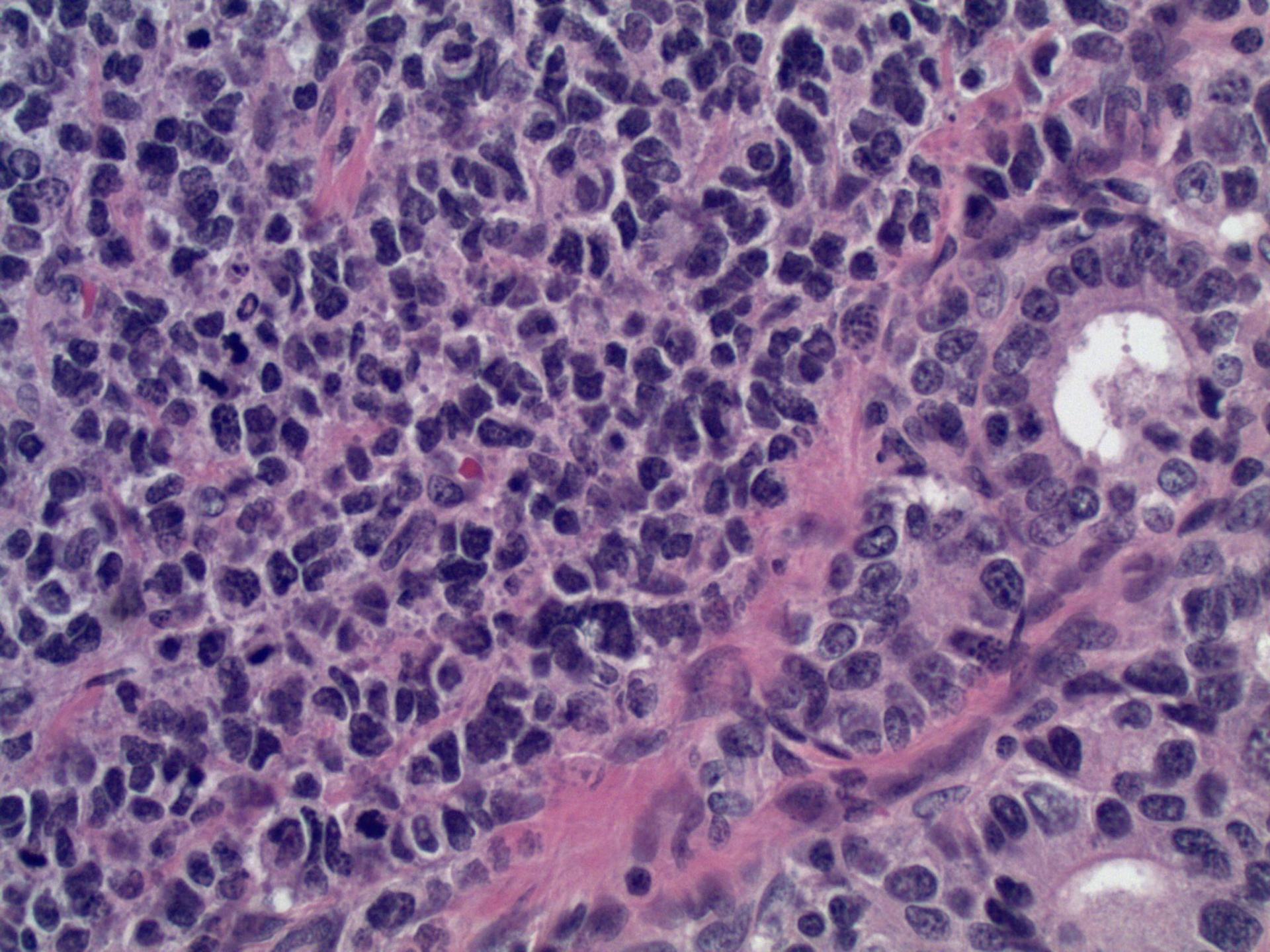
36-year-old woman presented with intermittent post-coital bleeding 4 months ago. Initial work-up showed BV viral infection which was treated with Flagyl. Pap and HPV are all negative.



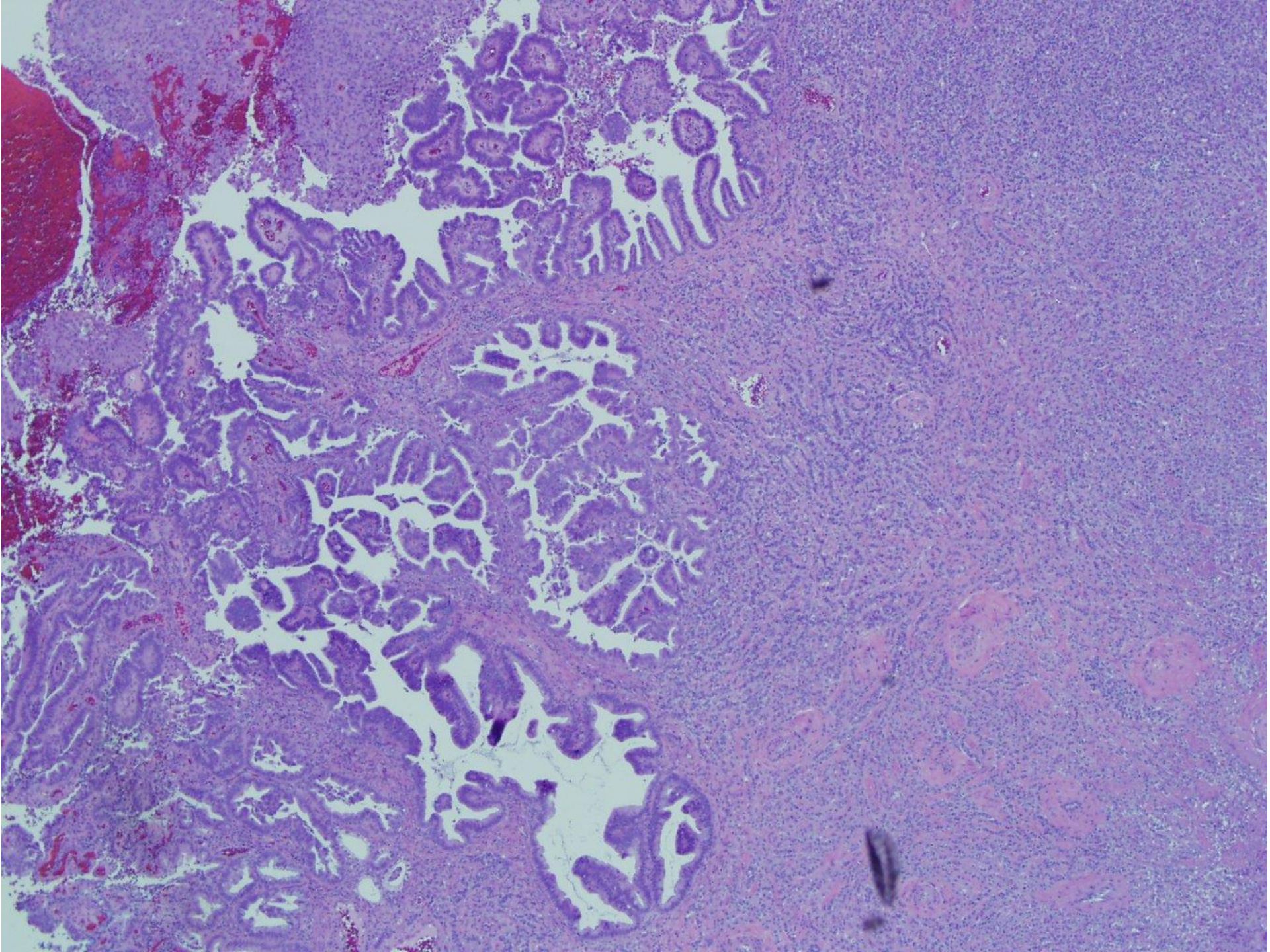


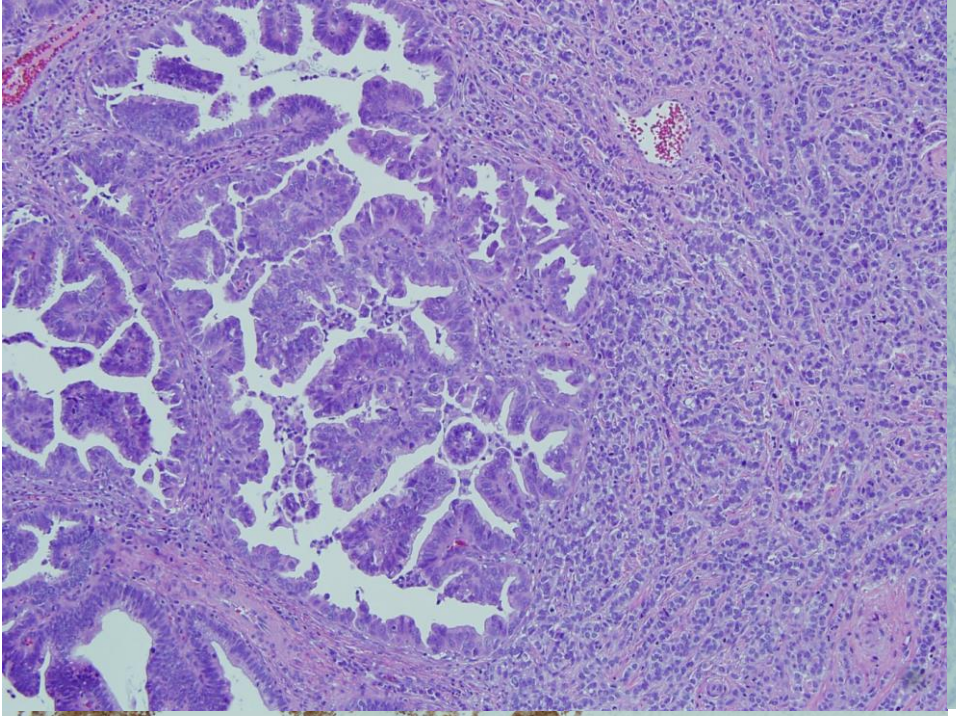


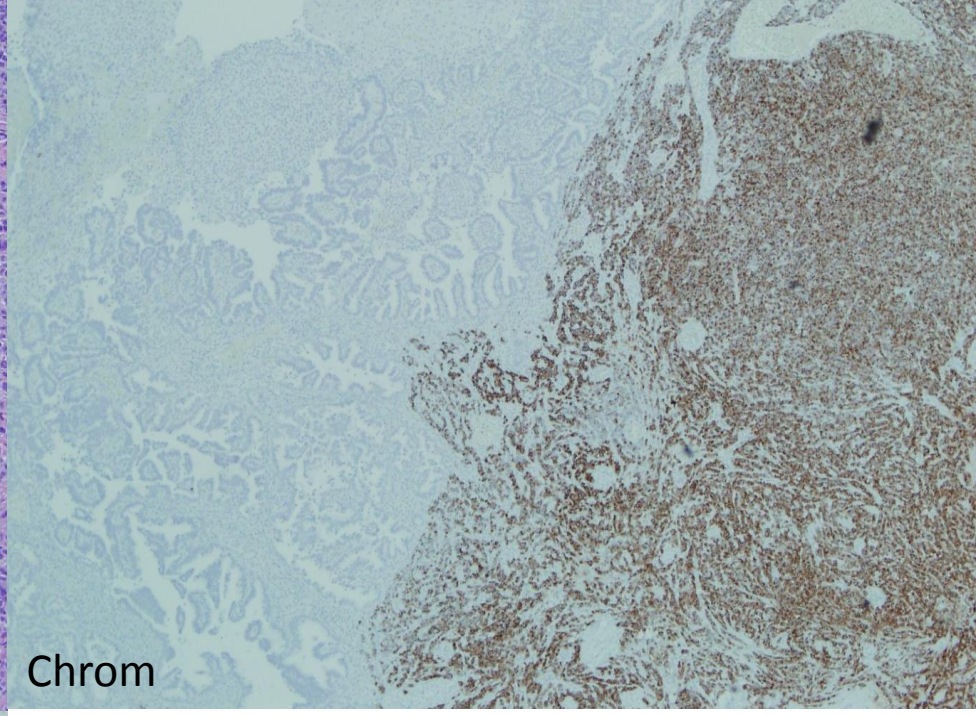





Diagnosis?



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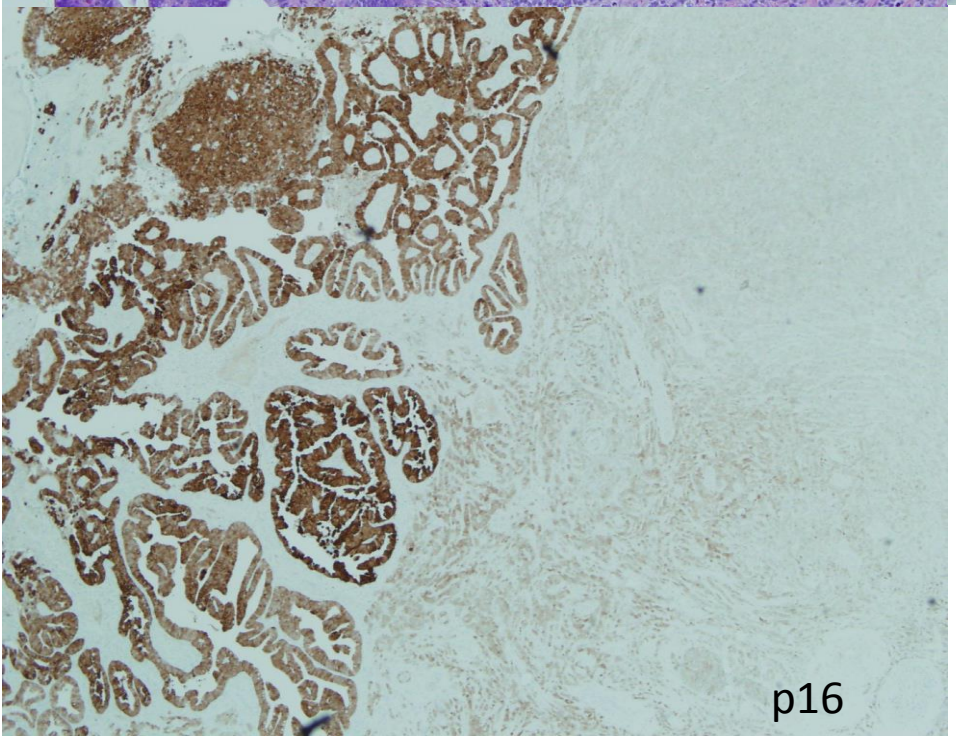
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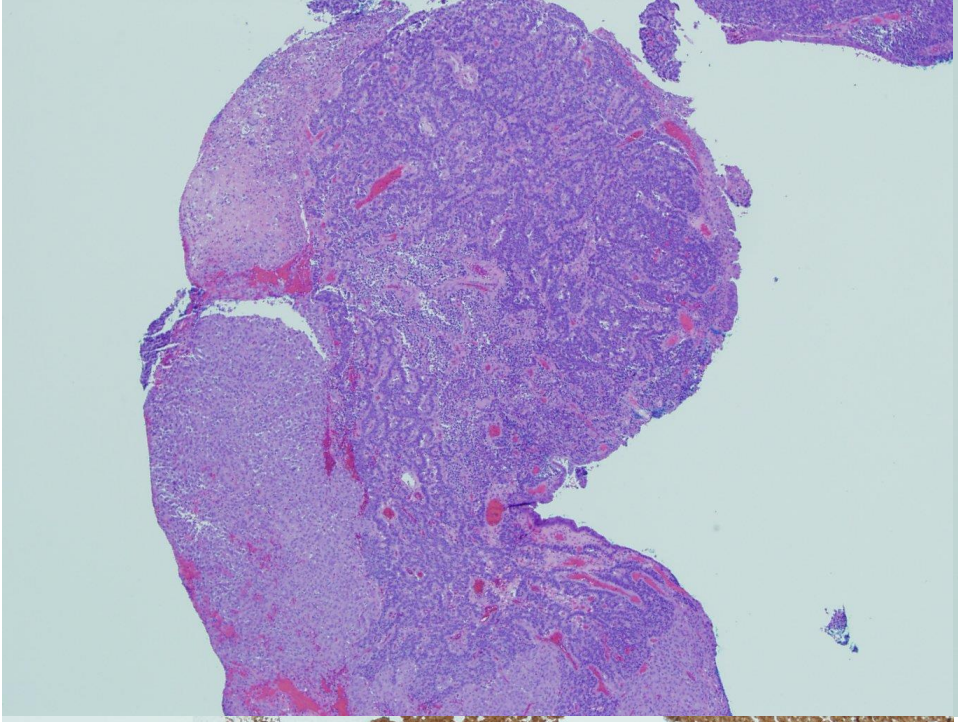

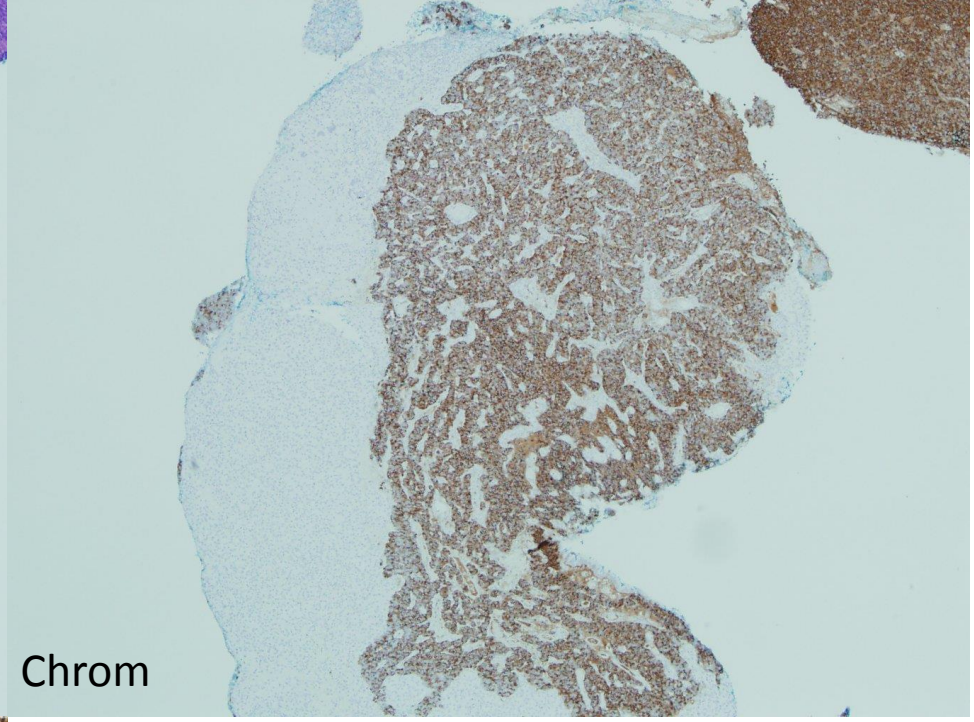
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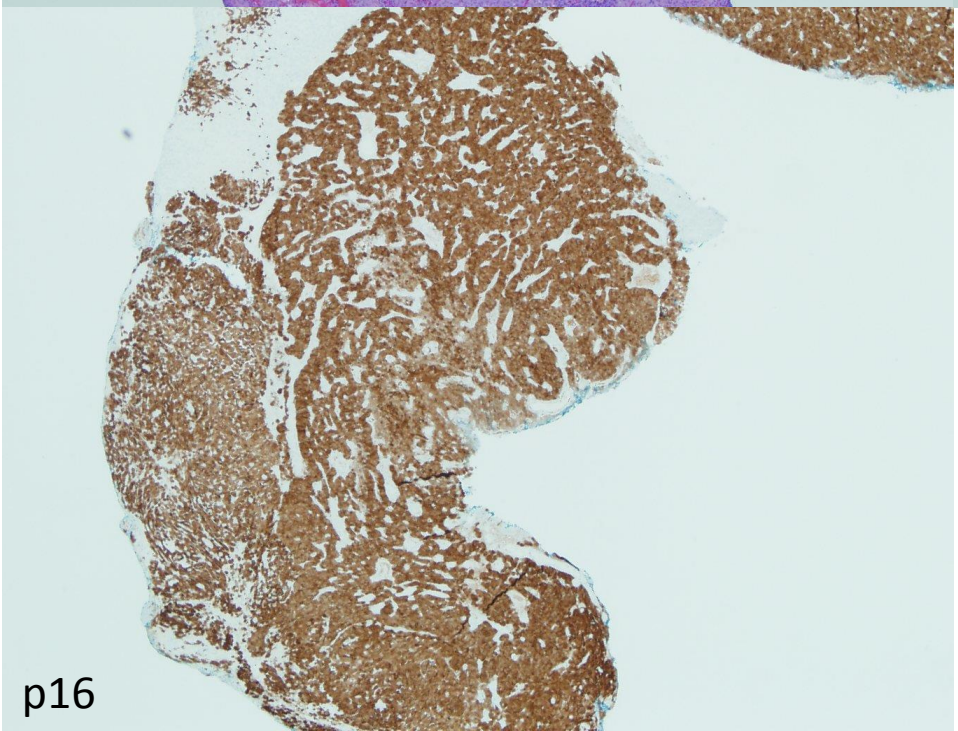
p16

Neuroendocrine carcinoma

- Cervical large cell neuroendocrine carcinoma
- At least 1.8 cm in width and invades at least 0.9 cm in depth
- Extensive lymphovascular invasion identified
- One pelvic lymph node involved by carcinoma (1/6)
- AJCC: pT1b1N1Mx

- Biopsy
  - Adenocarcinoma component: CK7 (+), p16 (+), vim (+), and negative for syn, chrom, CD56, ER and p53.
  - Neuroendocrine component: chrom (+), syn (+), CD56 (+), and negative for CK7, p16, vim, ER and p53.
  - No squamous cell carcinoma is identified (p63 is negative on both components).

Neuroendocrine carcinoma

- Small cell neuroendocrine carcinoma
  - Most common
  - May accompanied by in situ and invasive squamous or adenocarcinoma
  - Reliable asso w HPV-18
- Large cell neuroendocrine carcinoma
- Typical carcinoid tumor
- Atypical carcinoid tumor

Neuroendocrine carcinoma

- Pelvic mass
- Paraneoplastic syndrome
  - Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
  - Cushing syndrome
  - Hypercalcemia
  - A neurologic disorder

Differential diagnosis

- Squamous cell carcinoma
- Undifferentiated carcinomas of lower uterine segment
- Adenocarcinoma
- Embryonal rhabdomyosarcoma
- Lymphoma
- Metastatic disease
  - TTF-1

Treatment and prognosis

- Surgery
- Chemotherapy
  - Cisplatin on D1 and Etoposide on D1, 2 and 3 (3 cycle)
  - Radiation therapy: D1 and D22
  - 4 cycles
- External beam radiation
- Aggressive tumor
  - 5 year survival: 14-39%