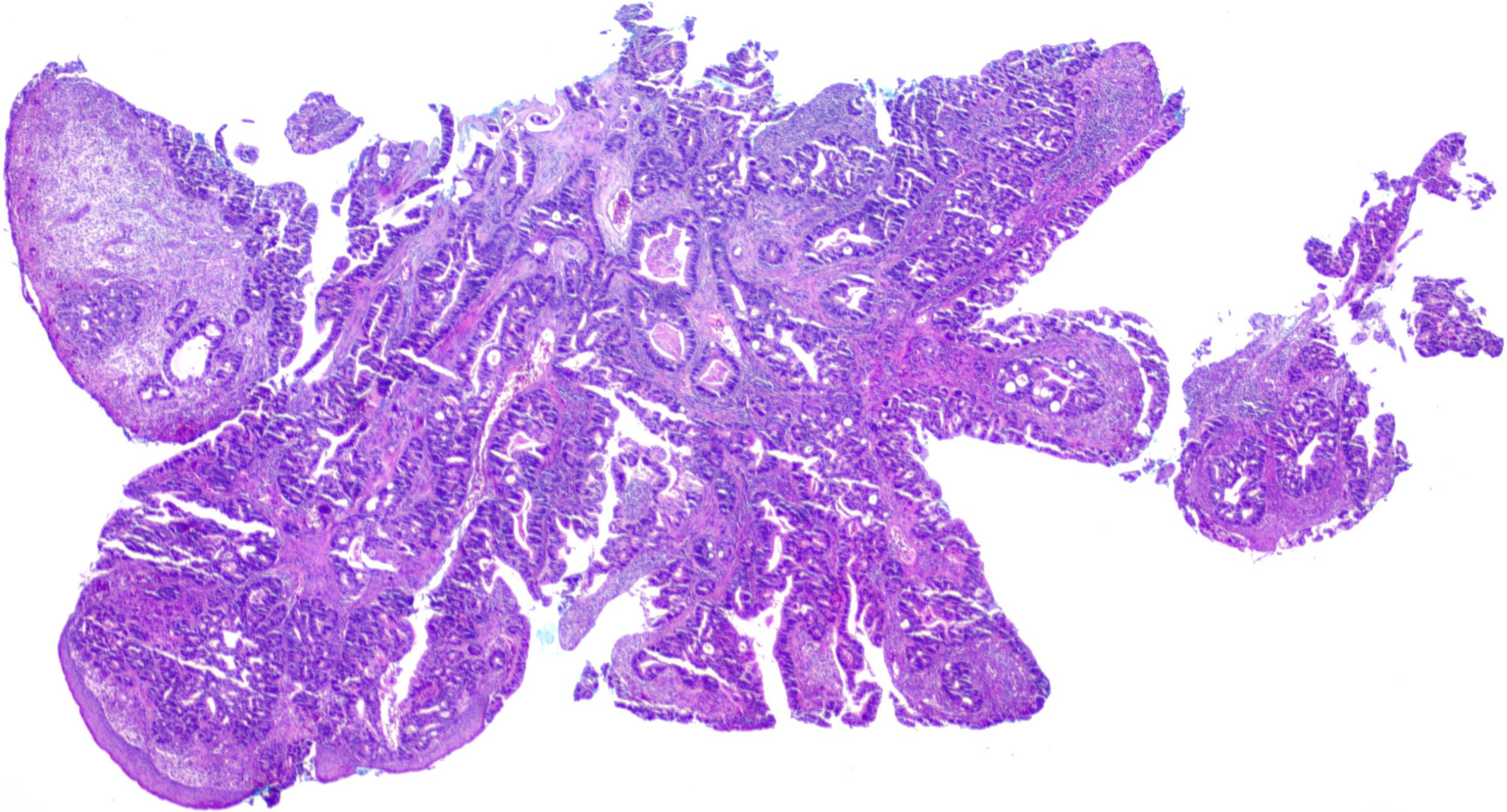
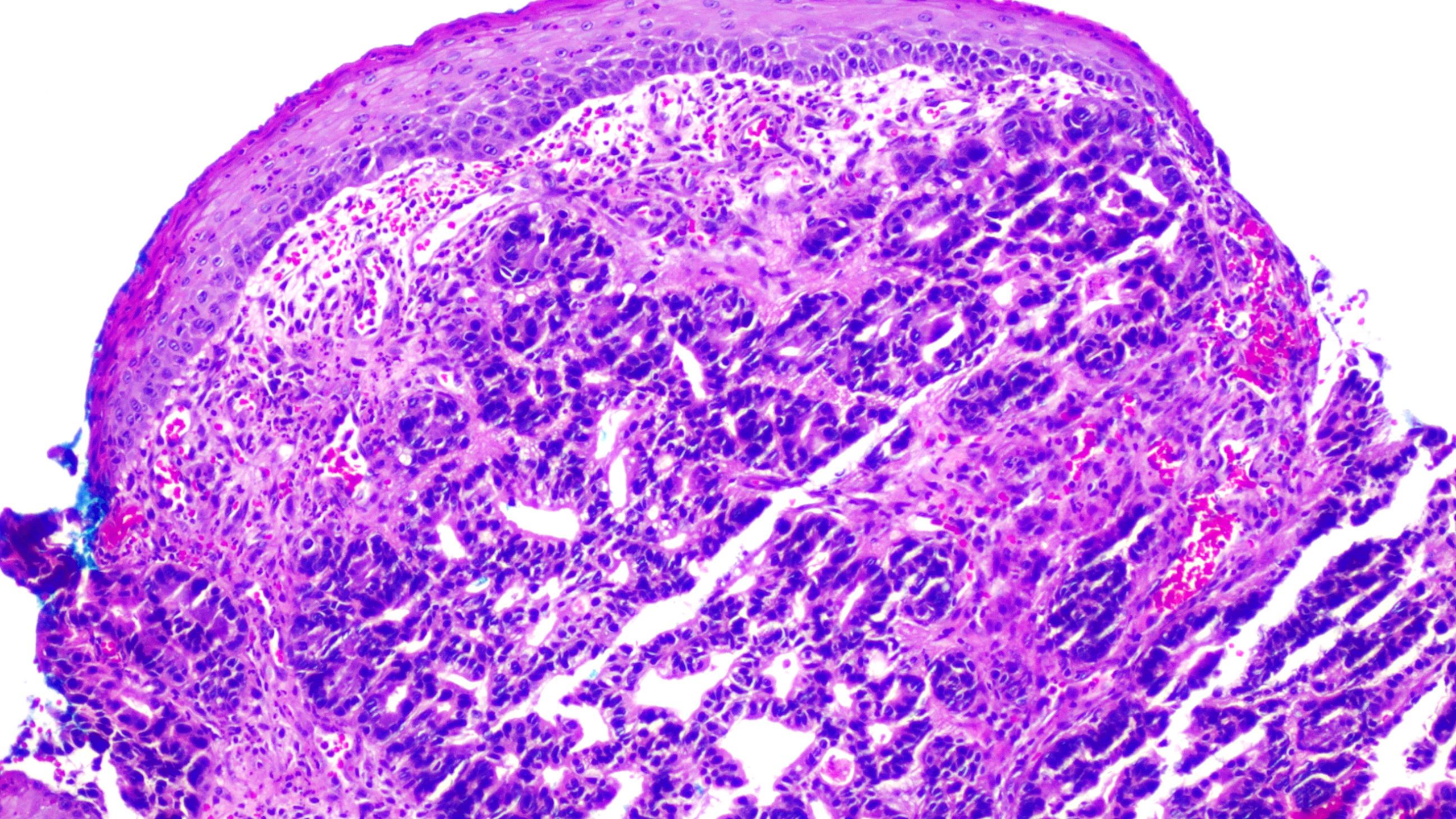
DEMATOPATHOLOGY QUIZ CASES 102-109

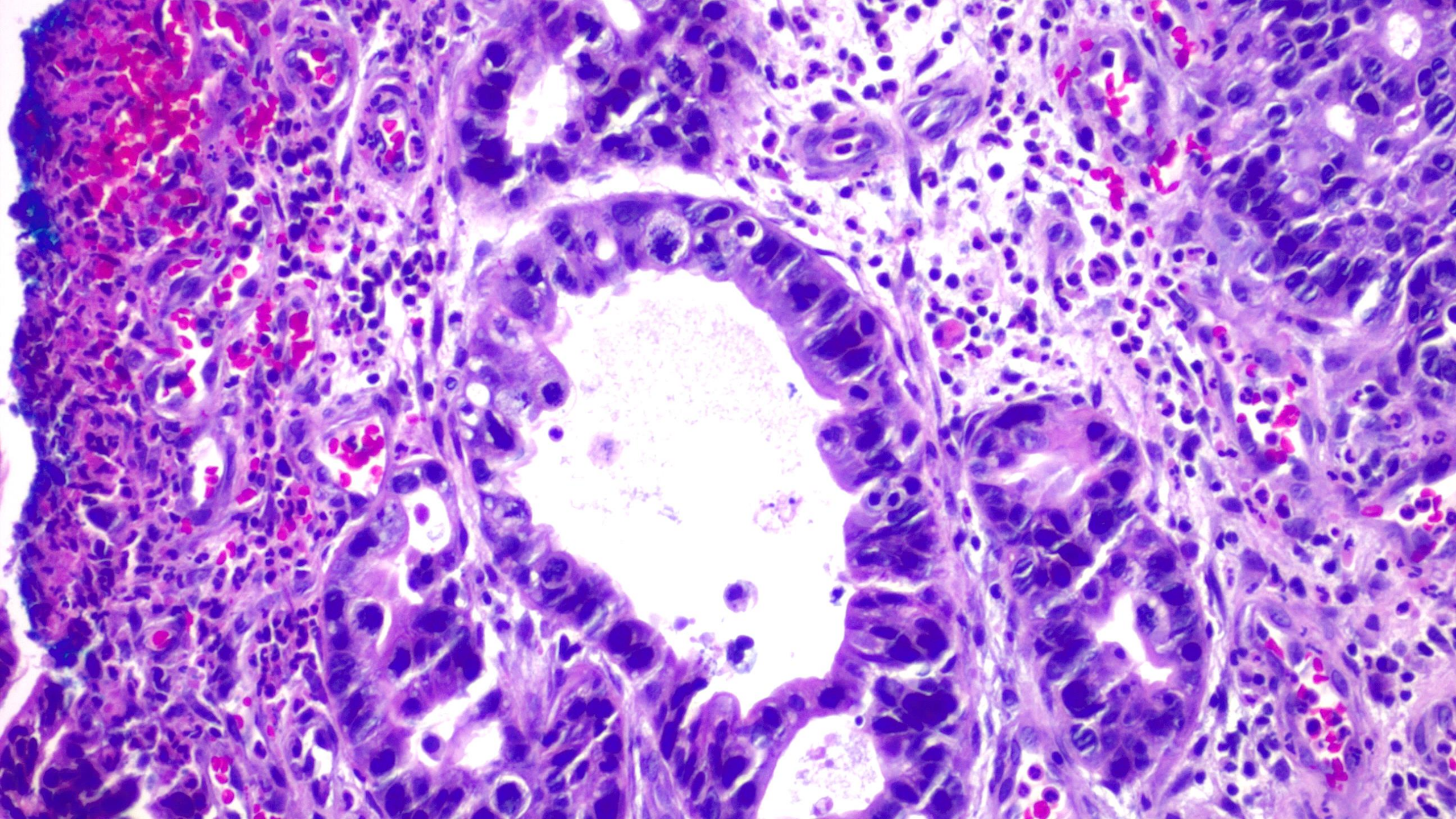
Soheil S. Dadras MD-PhD

Test your knowledge of diagnostic skin pathology

See	• Find 3 image magnifications: low, medium & high
Examine	• Examine the images
Answer	• Answer the questions
Find	• Find the answer key







Case 102. 88F, umbilicus; D48.5.

What is your diagnosis?

A. Endometriosis

B. Primary umbilical (urachal) adenocarcinoma

C. Metastatic adenocarcinoma, gastrointestinal primary

D. Adnexal carcinoma with glandular differentiation

E. Metastatic melanoma with glandular differentiation

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Metastatic carcinoma to the umbilicus: **Sister Mary Joseph nodule**

Named after **Sister Mary Joseph Dempsey** (1856–1939), a surgical assistant to Dr. William Mayo, who first observed the association between umbilical nodules and intra-abdominal cancer

Most Common Primary Sources:

Gastrointestinal (40–50%) – Gastric (most common), colorectal, pancreatic.

Gynecologic (20–30%) – Ovarian, endometrial, cervical.

Other:

Breast cancer (especially lobular carcinoma).

Lung adenocarcinoma.

Rarely: Prostate, bladder, biliary, or unknown primary.

Histopathology: Gland-forming or signet-ring cells.

Immunohistochemistry (IHC):

Gastric/Colonic: CK20+, CDX2+

Ovarian: PAX8+, WT1+ (serous carcinoma)

Breast: GATA3+, ER/PR+

Pancreatic/Biliary: CK7+, CK19+, SMAD4 loss

Differential Diagnosis (Non-Metastatic Umbilical Lesions):

- Endometriosis (if cyclical pain, ER/PR+)
- Primary umbilical adenocarcinoma (urachal remnant)
- Sebaceous cyst / Epidermal inclusion cyst
- Keloid / Fibroma
- Hernia (omphalocele, umbilical hernia)

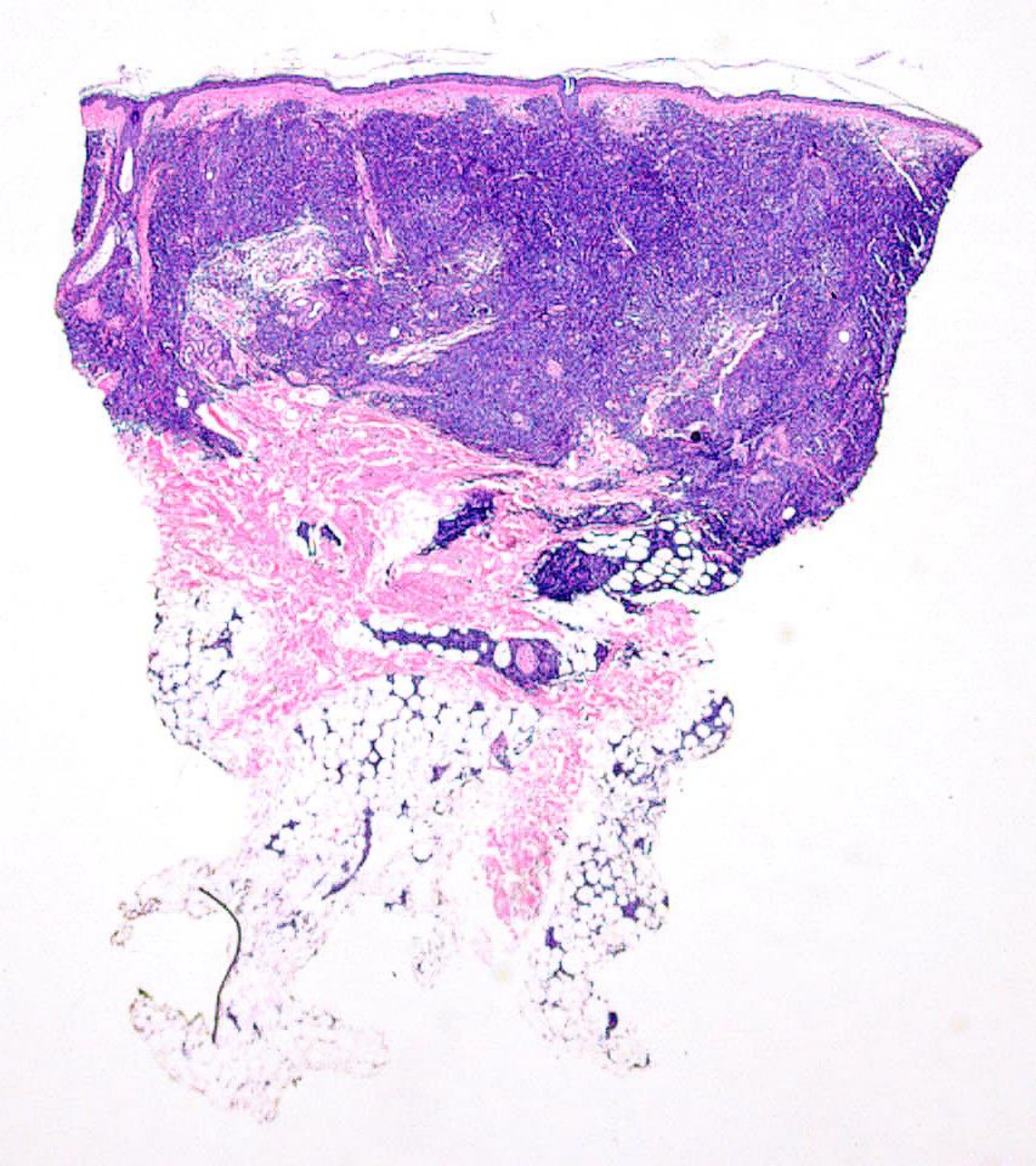
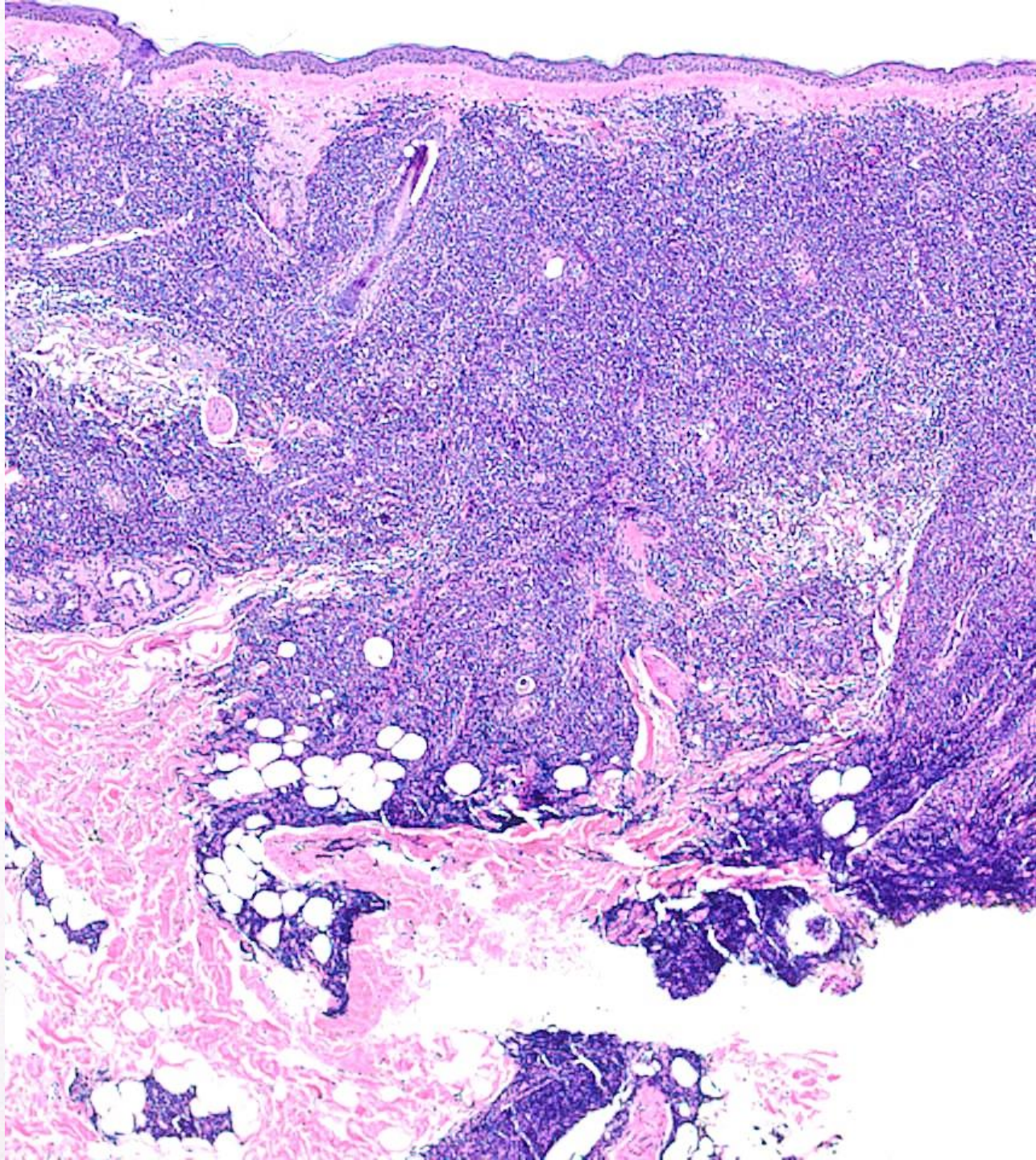
Diagnostic Workup:

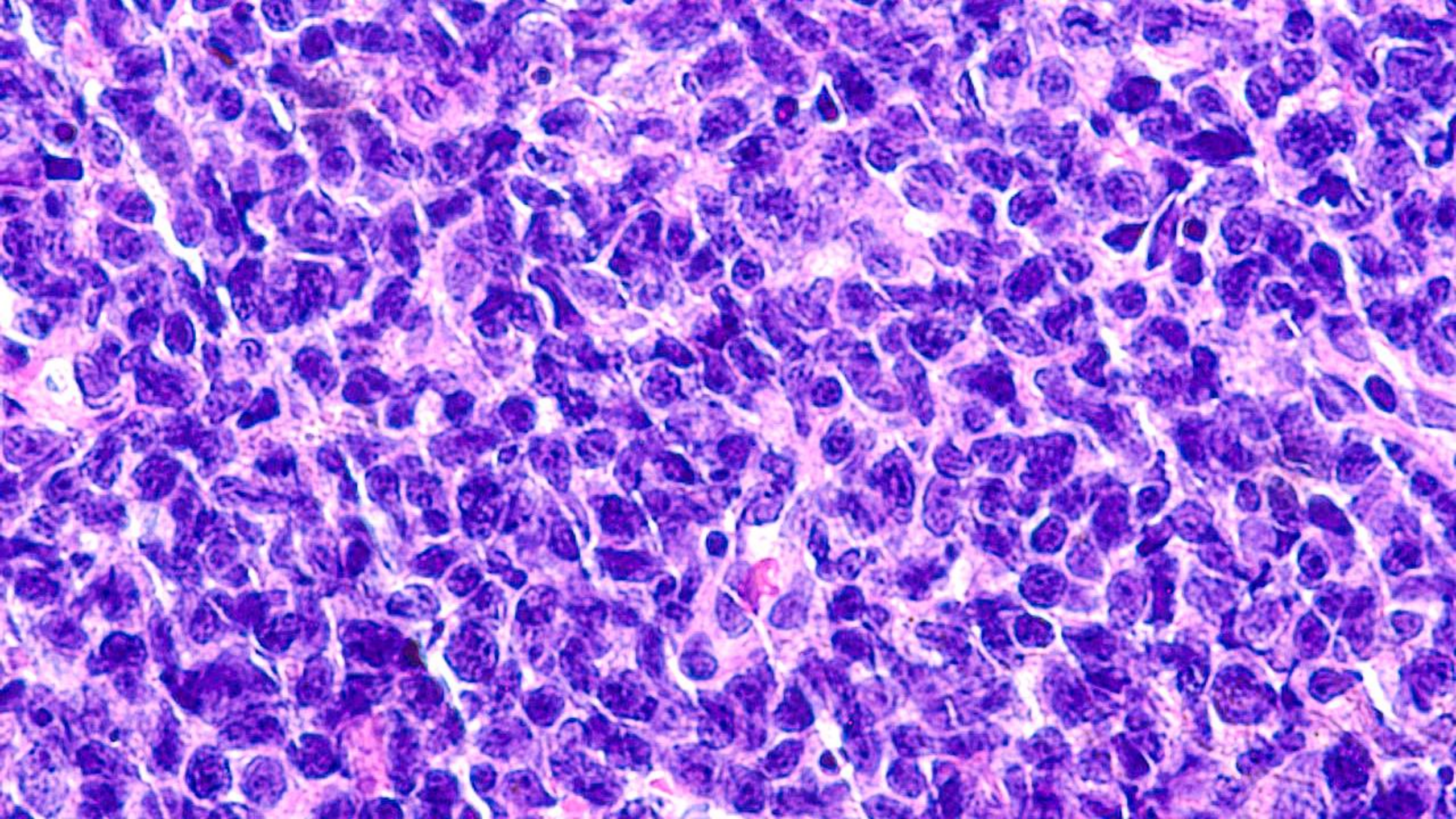
- Biopsy (histology + IHC).
- Imaging (CT/MRI/PET-CT to locate primary tumor).
- Endoscopy (if GI primary suspected).
- Tumor markers (CA-125, CEA, CA19-9, etc.).

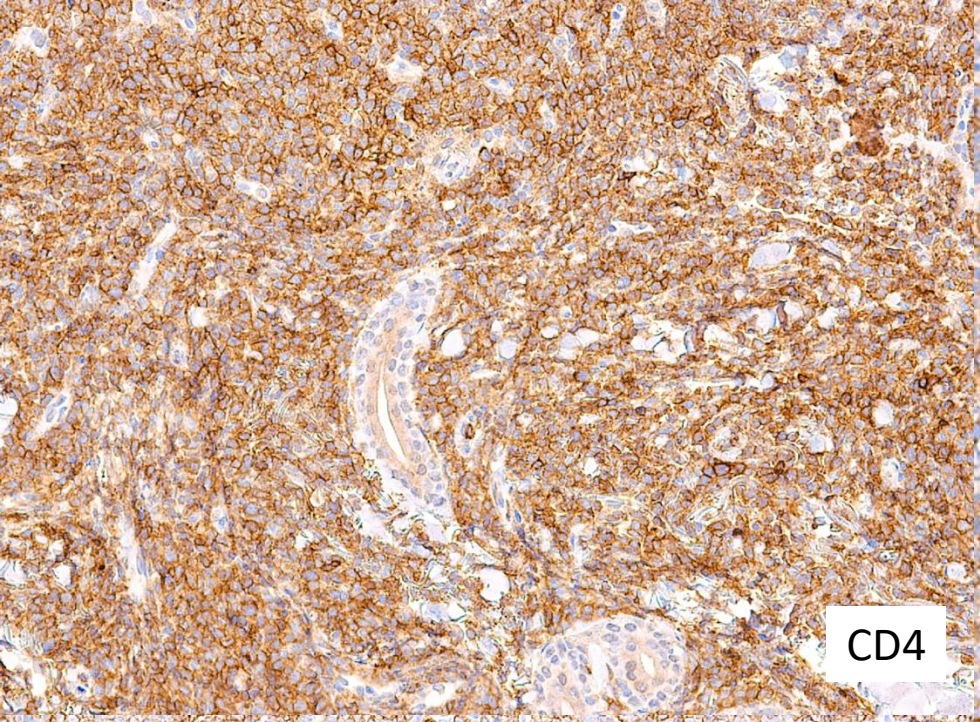
Patient's IHC Profile

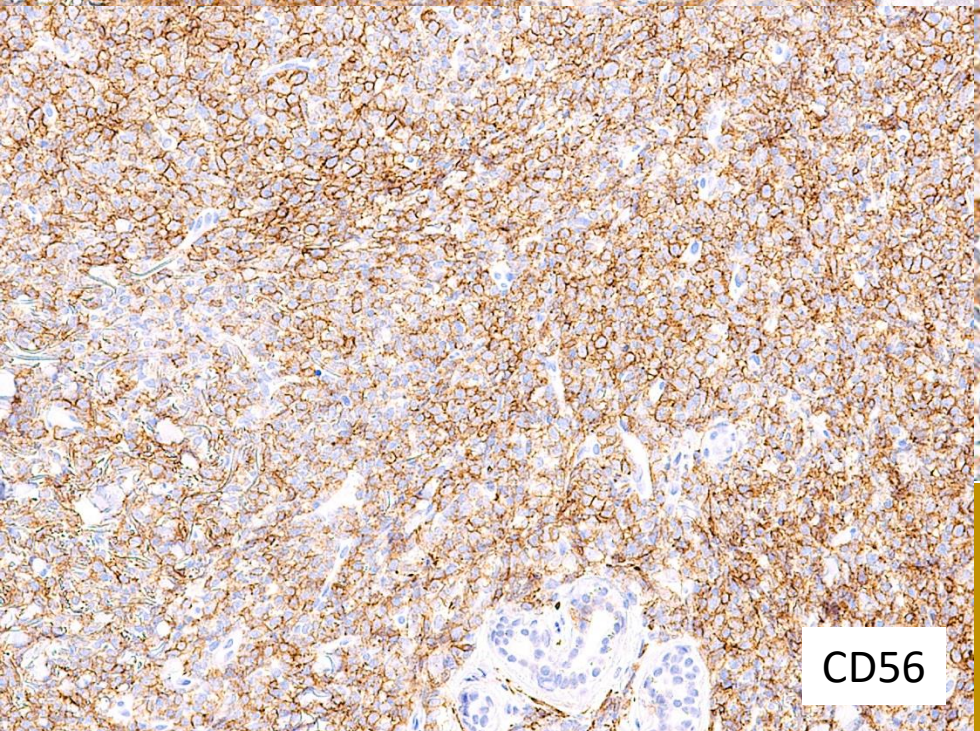
Positive	Negative
CK20	CK7, GATA3, PAX8
CDX2	WT1, ER, PR
SATB2	Beta-catenin
	CK903

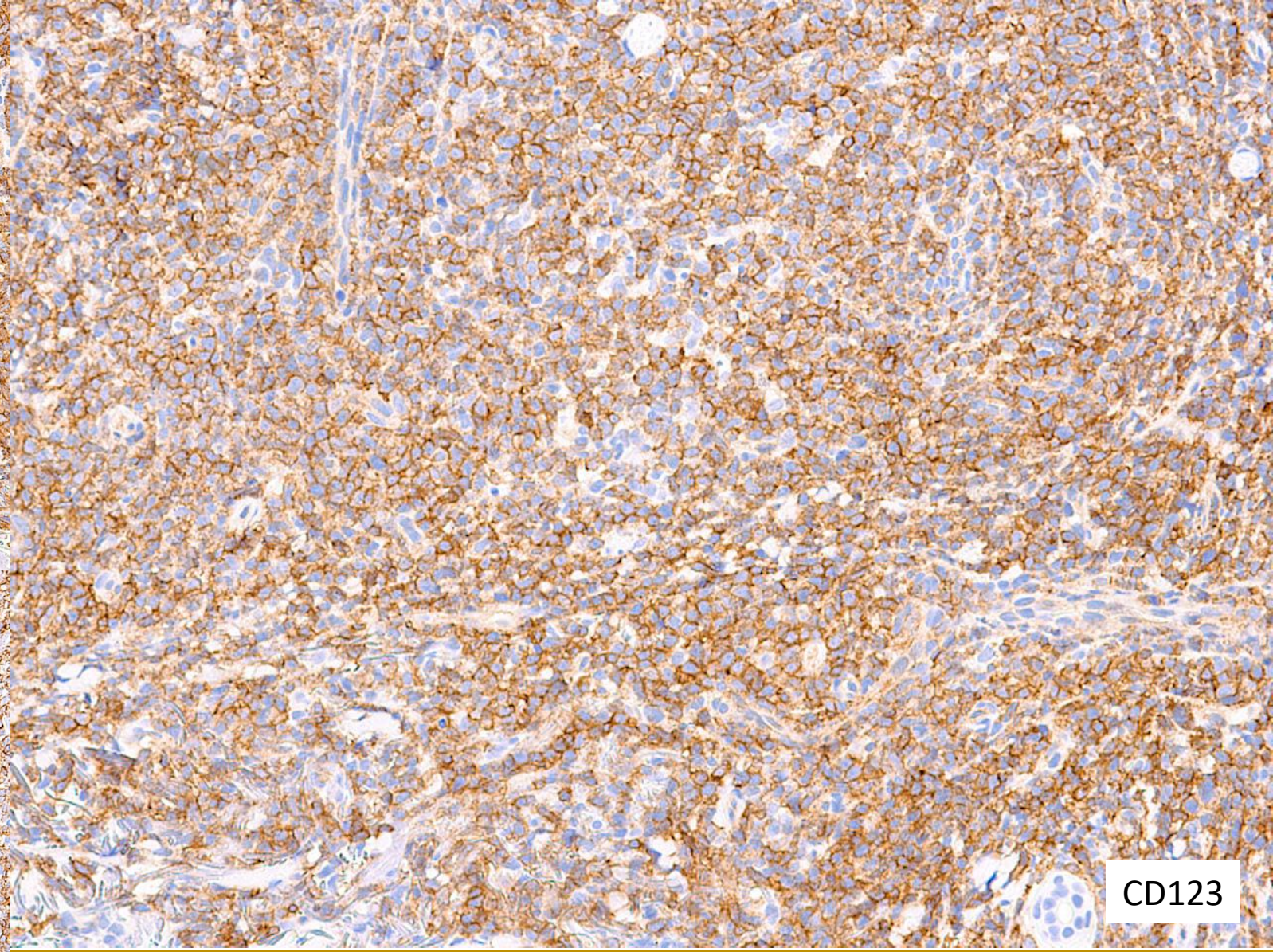
Lower GI profile









IHC Results

Positive: CD43, CD45, CD5 (weak), CD43, CD4, TdT, CD68, CD123, and CD56.
Negative: CD34, CD3, CD8, TIA-1, ALK-1, EBER, CD30, CD20 and PAX-5.

Case 103. 79M, right temple, r/o SCC.

What is your diagnosis?

A. Merkel cell carcinoma

B. NK/T-cell leukemia

C. Anaplastic large cell lymphoma

D. Acute myelogenous leukemia

E. Blastic plasmacytoid dendritic cell neoplasm (BPCDN)

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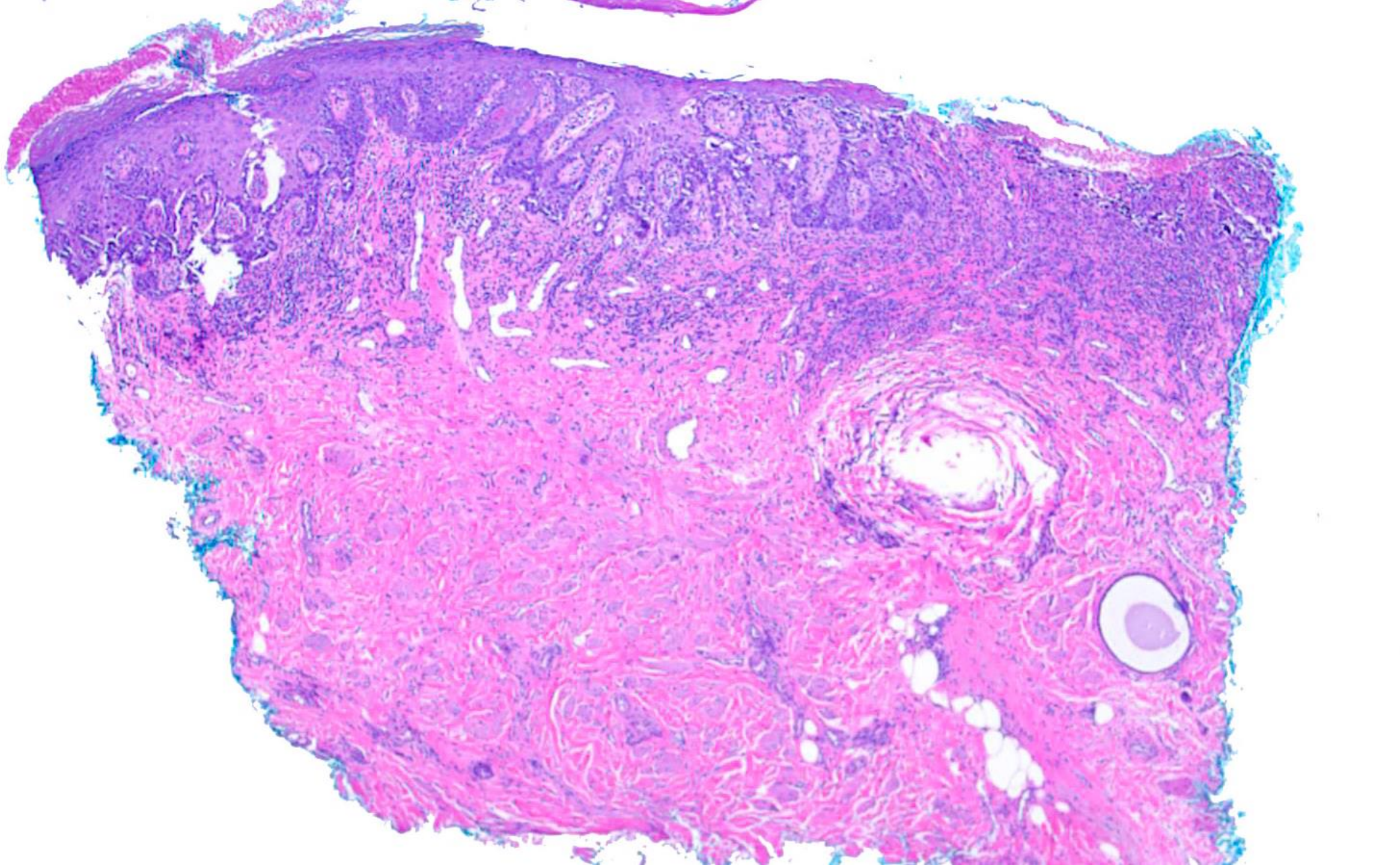
Blastic plasmacytoid dendritic cell neoplasm (BPCDN)

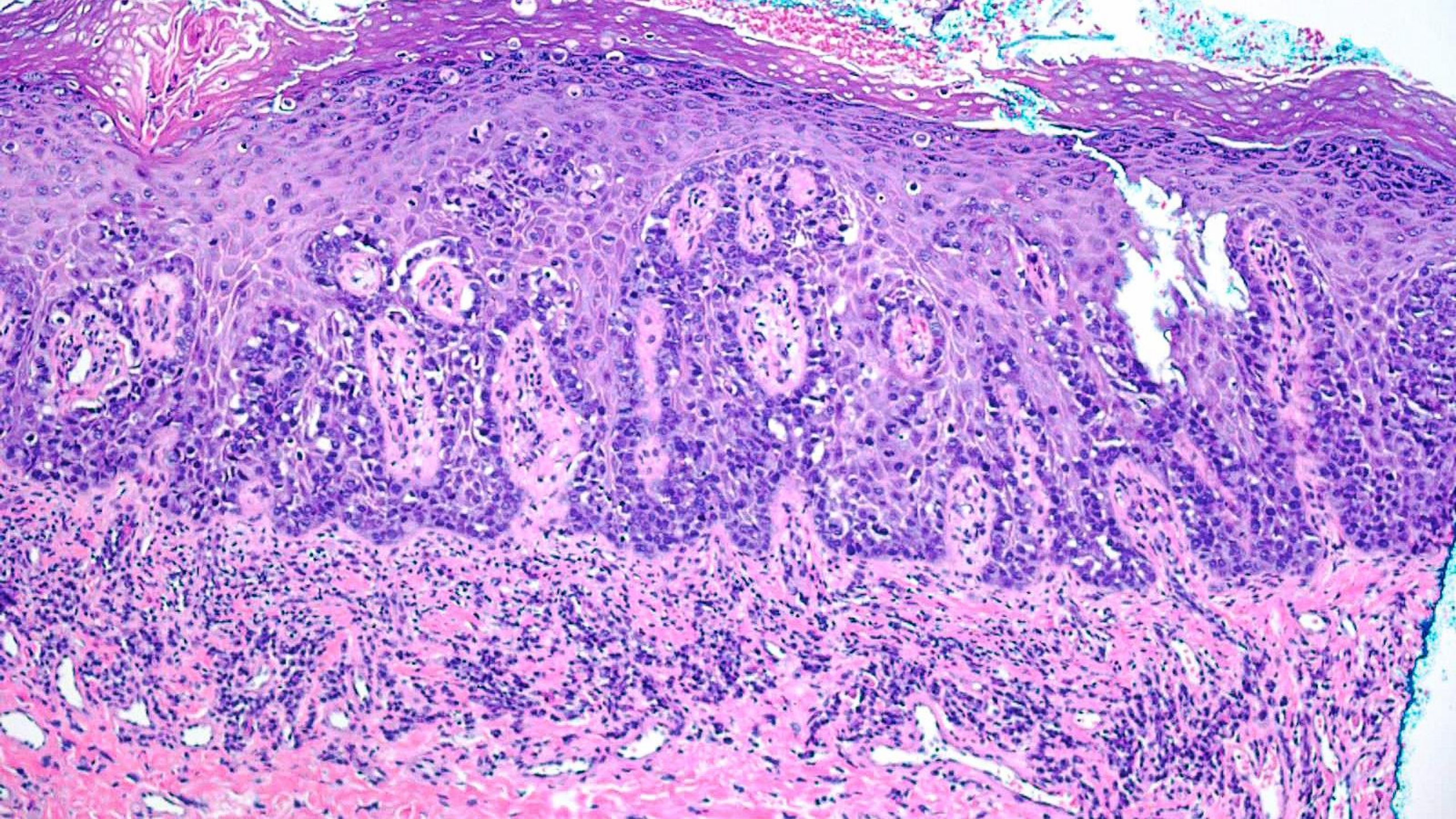
Histologic Features

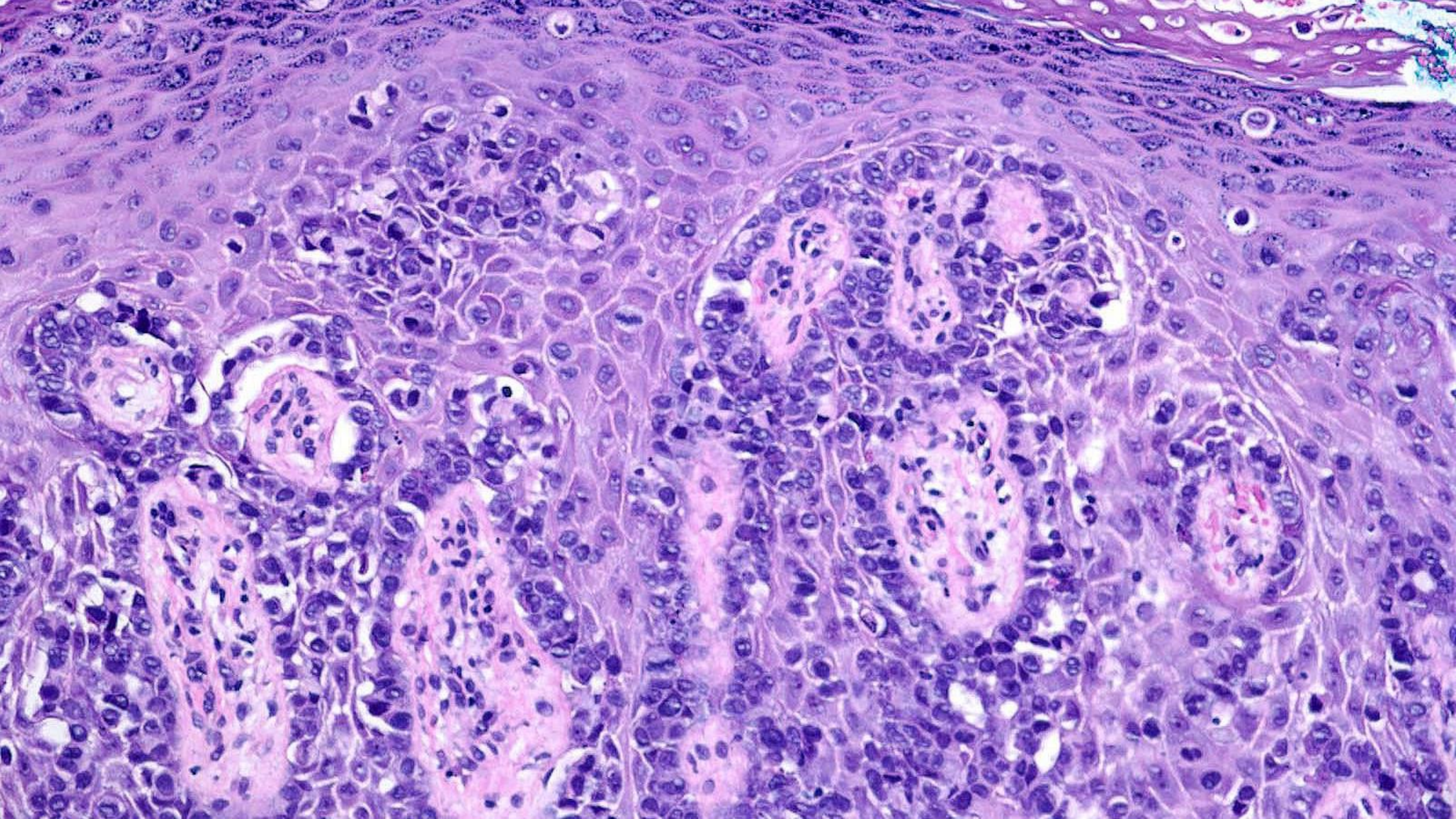
- **Architecture**:
  - **Diffuse** or **nodular** dermal infiltrate, often with **subcutaneous extension**.
  - Epidermis is typically spared (**Grenz zone**).
- **Cell Morphology**:
  - **Medium-sized blasts** with **blast-like appearance** (high N:C ratio).
  - **Round to irregular nuclei** with **fine chromatin** and **prominent nucleoli**.
  - **Scant to moderate cytoplasm** (may appear plasmacytoid).
- **Mimics**:
  - **AML** (myeloid blasts), **lymphoblastic lymphoma**, **aggressive NK-cell leukemia**.

Summary Table: BPDCN IHC Profile

Highly Positive	Variable/Negative	Exclusion Markers
CD123, CD4, CD56, TCF4, TCL1	CD68 (weak/focal), CD7 (rare)	MPO, CD3, CD20, CD34







Case 104. 77F, right labia, erosion.

What is your diagnosis?

A. Squamous cell carcinoma in situ, eroded

B. Melanoma in situ, eroded

C. Extramammary Paget disease

D. Pagetoid reticulosis

E. High-grade intraepithelial lesion (VIN 3)

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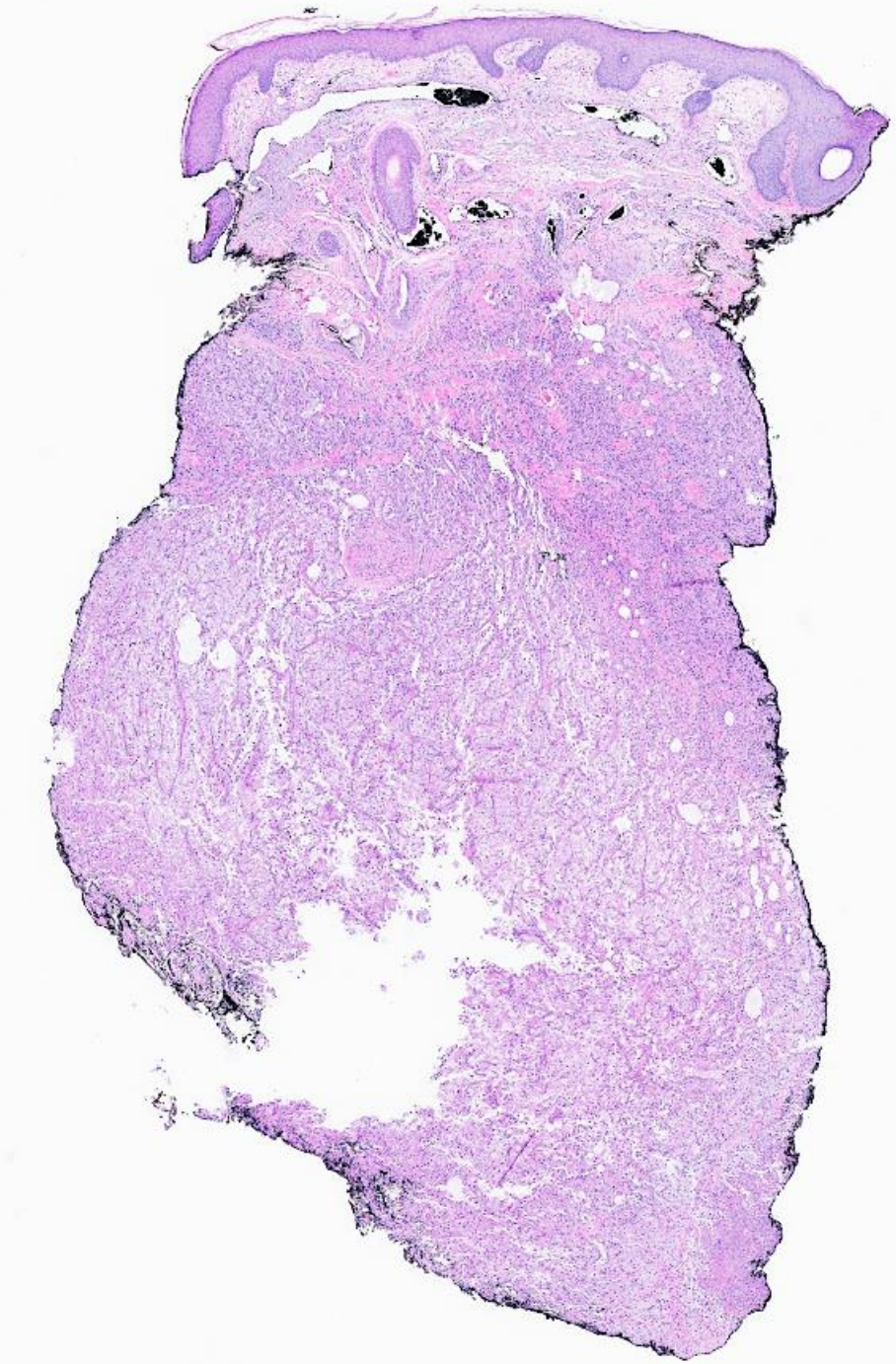
C. Extramammary Paget disease

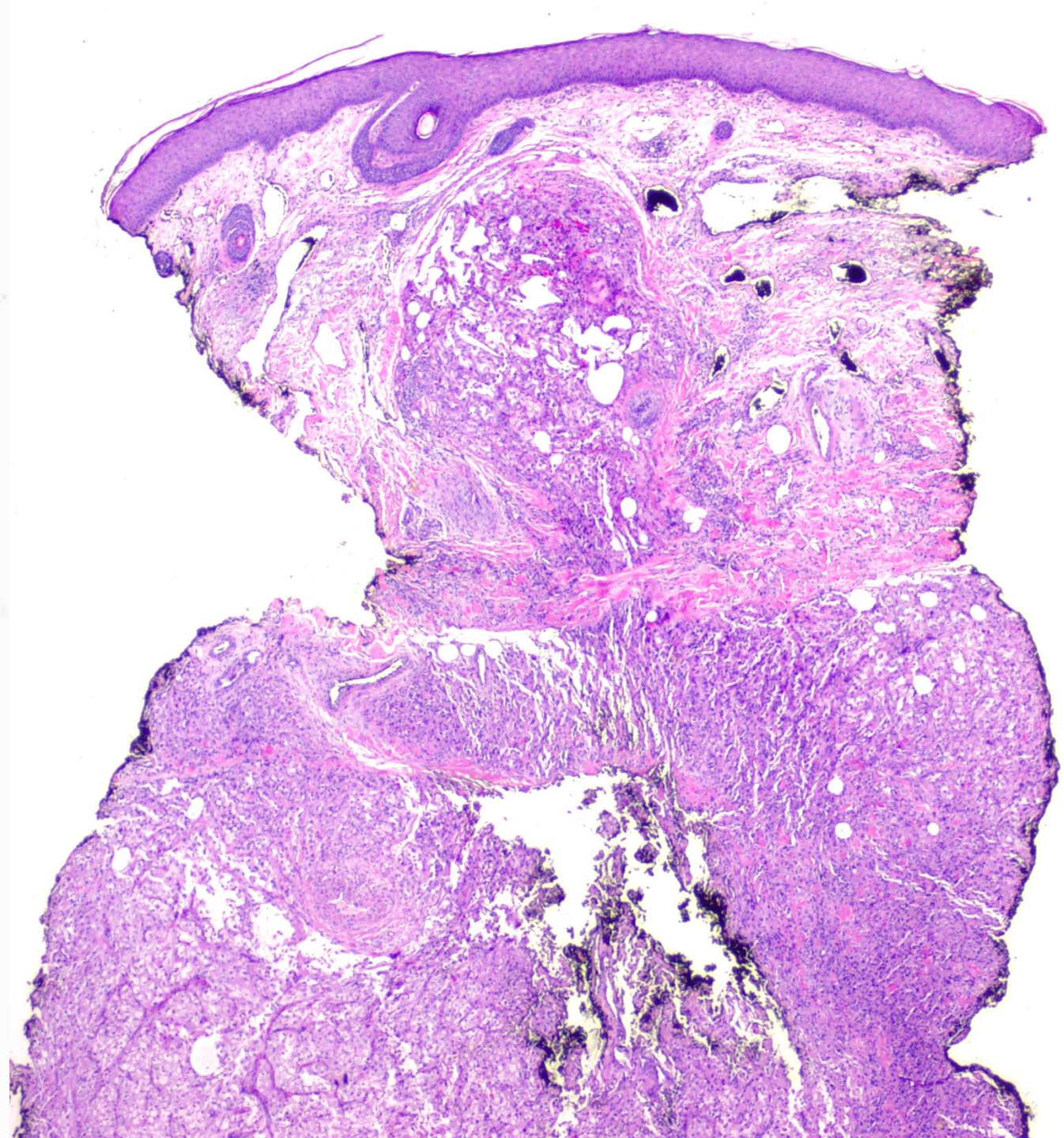
D. Pagetoid reticulosis

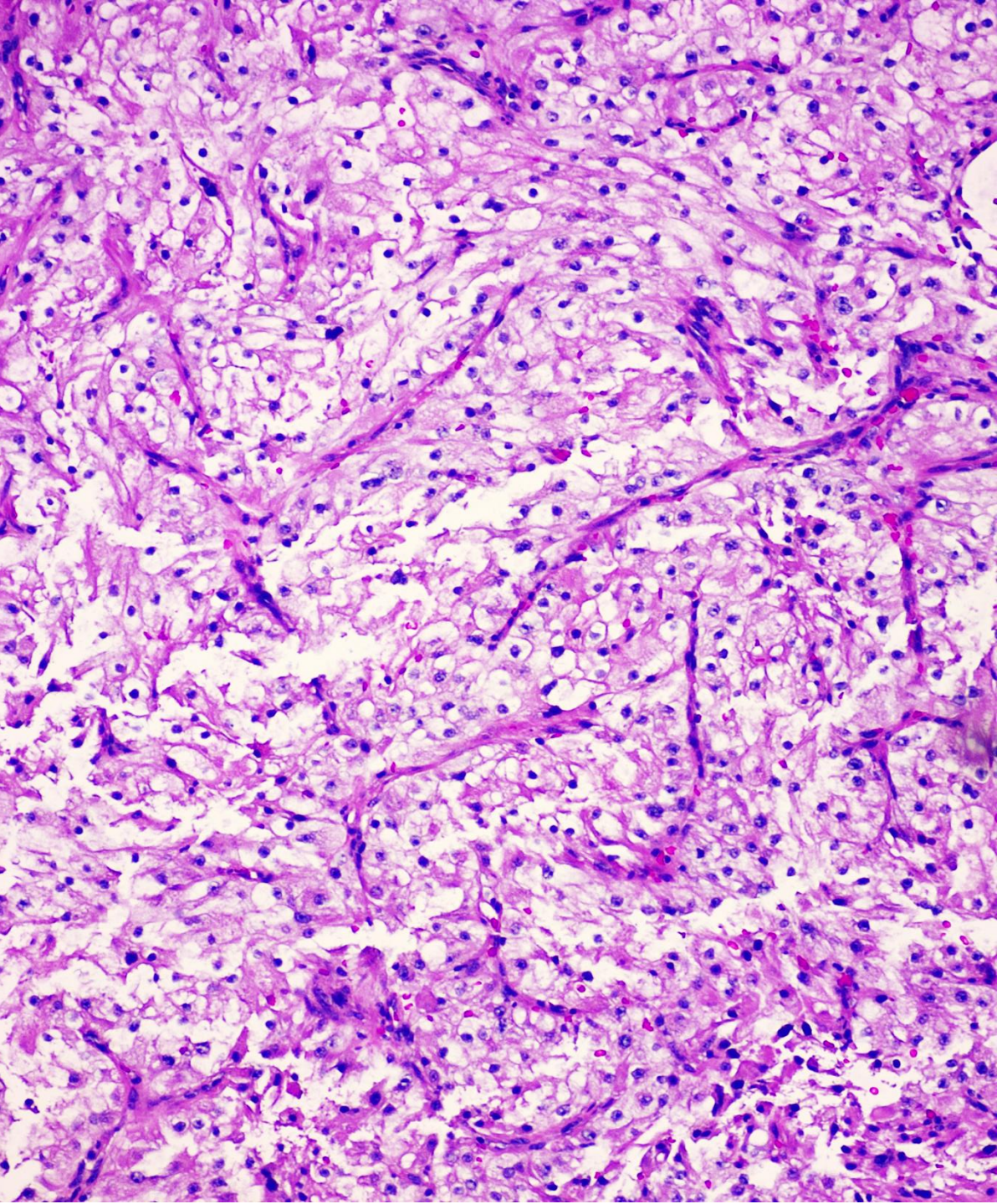
E. High-grade intraepithelial lesion (VIN 3)

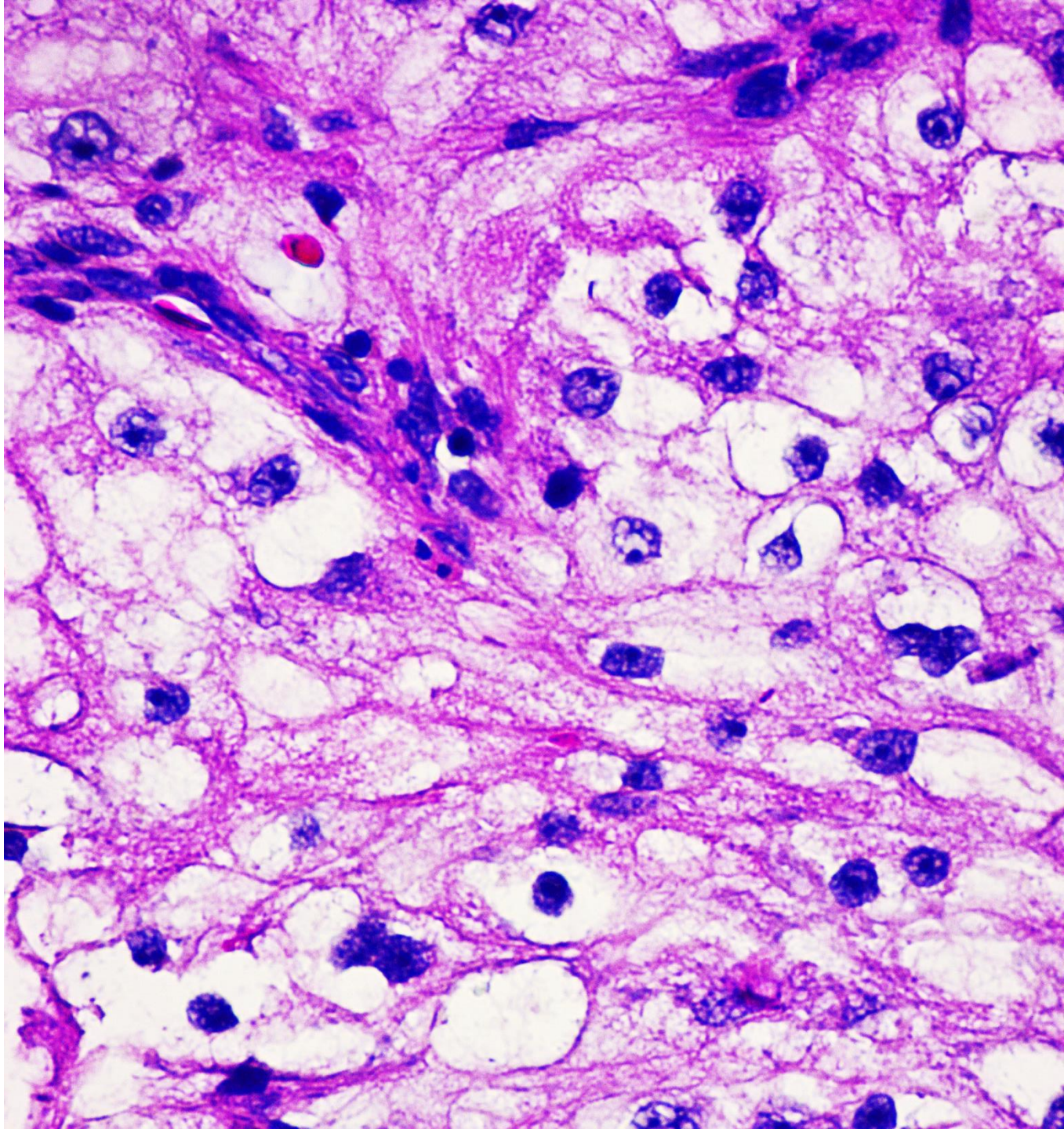
Extramammary Paget Disease (EMPD) vs. Mimics

Condition	Key Distinguishing Features	IHC Markers
Vulvar/Perianal SCC	Keratin pearls, intercellular bridges	p40+, p63+, CK7-
Bowen's Disease (SCC in situ)	Full-thickness epidermal atypia	p16+ (if HPV-related), CK7-
Melanoma	Junctional nests, melanin pigment	S100+, Melan-A+, CK7-
Seborrheic Dermatitis/Psoriasis	No atypical cells, spongiosis	CK7-, PAS-
Pagetoid Dyskeratosis (Benign)	Small, scattered keratinocytes	CK5/6+, CK7-









Case 105. 72M, Chin lesion, no history provided. What is your diagnosis?

A. Sebaceous carcinoma

B. Metastatic clear cell carcinoma, lung primary

C. Metastatic melanoma (clear cell variant)

D. Adrenal cortical carcinoma

E. Metastatic renal cell carcinoma

Case 105. 72M, Chin lesion, no history provided. What is your diagnosis?

A. Sebaceous carcinoma

B. Metastatic clear cell carcinoma, lung primary

C. Metastatic melanoma (clear cell variant)

D. Adrenal cortical carcinoma

E. Metastatic renal cell carcinoma

Case 106. 72M, Chin lesion (same case 105). What are the immunohistochemical markers to confirm your diagnosis?

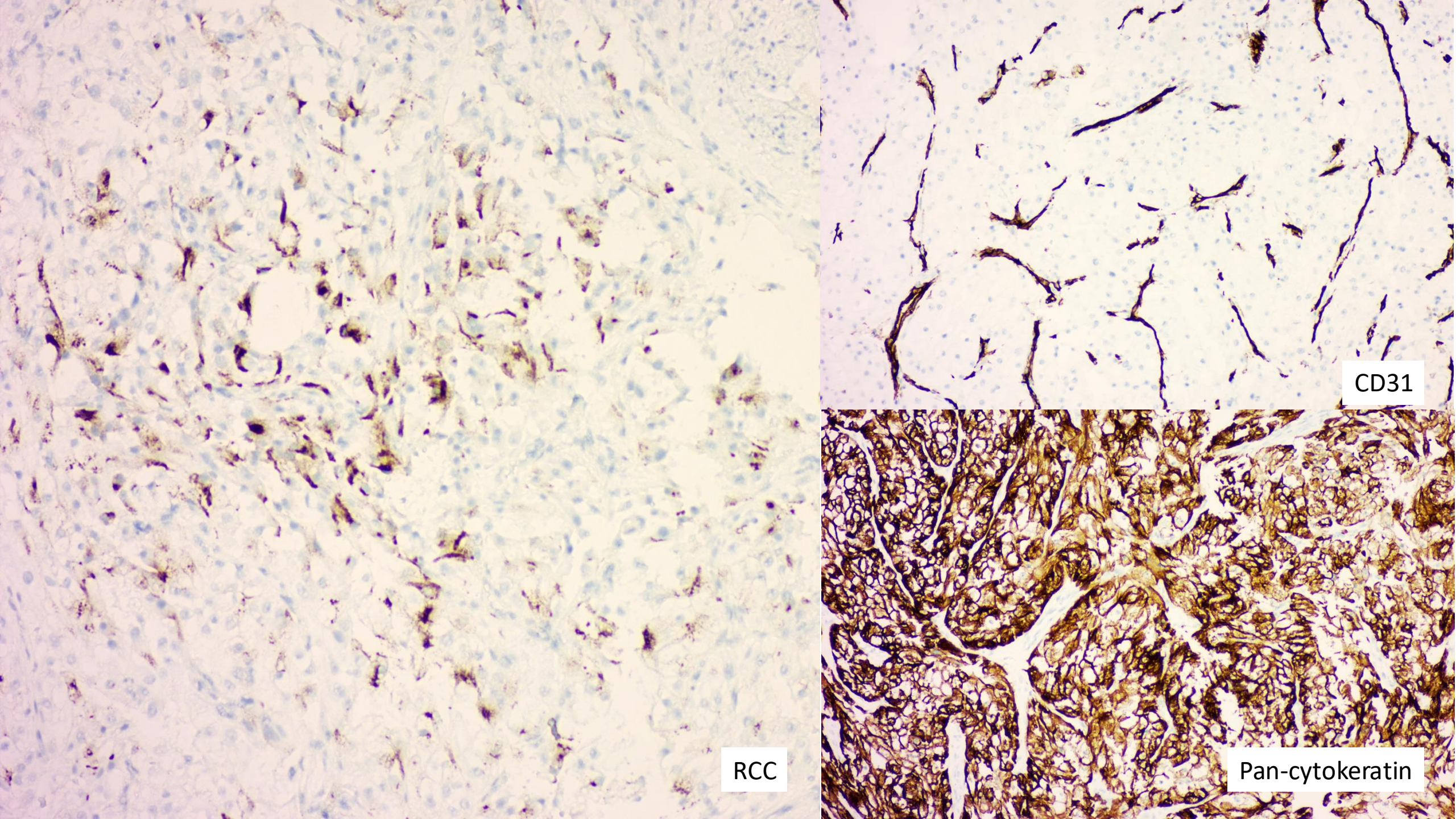
A. EMA+, BerEP4+, Adipophilin+, PAX8-

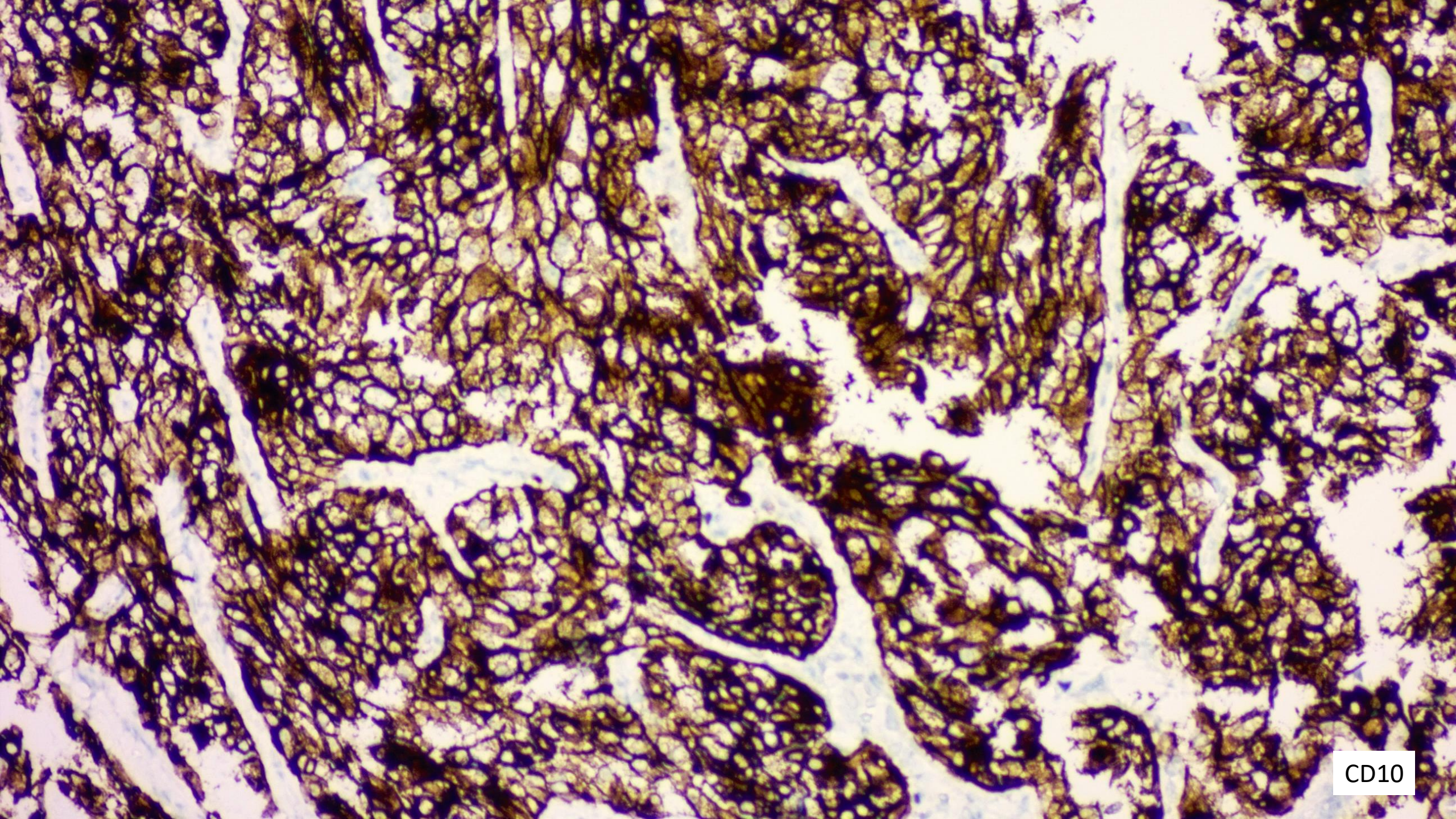
B. TTF1+, Napsin A+

C. S100+, SOX10+, HMB45+, PAX8-

D. Inhibin+, Melan-A+, SF1+, PAX8-

E. CD10+, RCC Ma+, EMA+, Vimentin+, CAIX (Carbonic Anhydrase IX)+, PAX8+


RCC
CD31
Pan-cytokeratin


CD10

Case 106. 72M, Chin lesion (same case 103). What are the immunohistochemical markers to confirm your diagnosis?

A. EMA+, BerEP4+, Adipophilin+, PAX8-

B. TTF1+, Napsin A+

C. S100+, SOX10+, HMB45+, PAX8-

D. Inhibin+, Melan-A+, SF1+, PAX8-

E. CD10+, RCC Ma+, EMA+, Vimentin+, CAIX (Carbonic Anhydrase IX)+, PAX8+

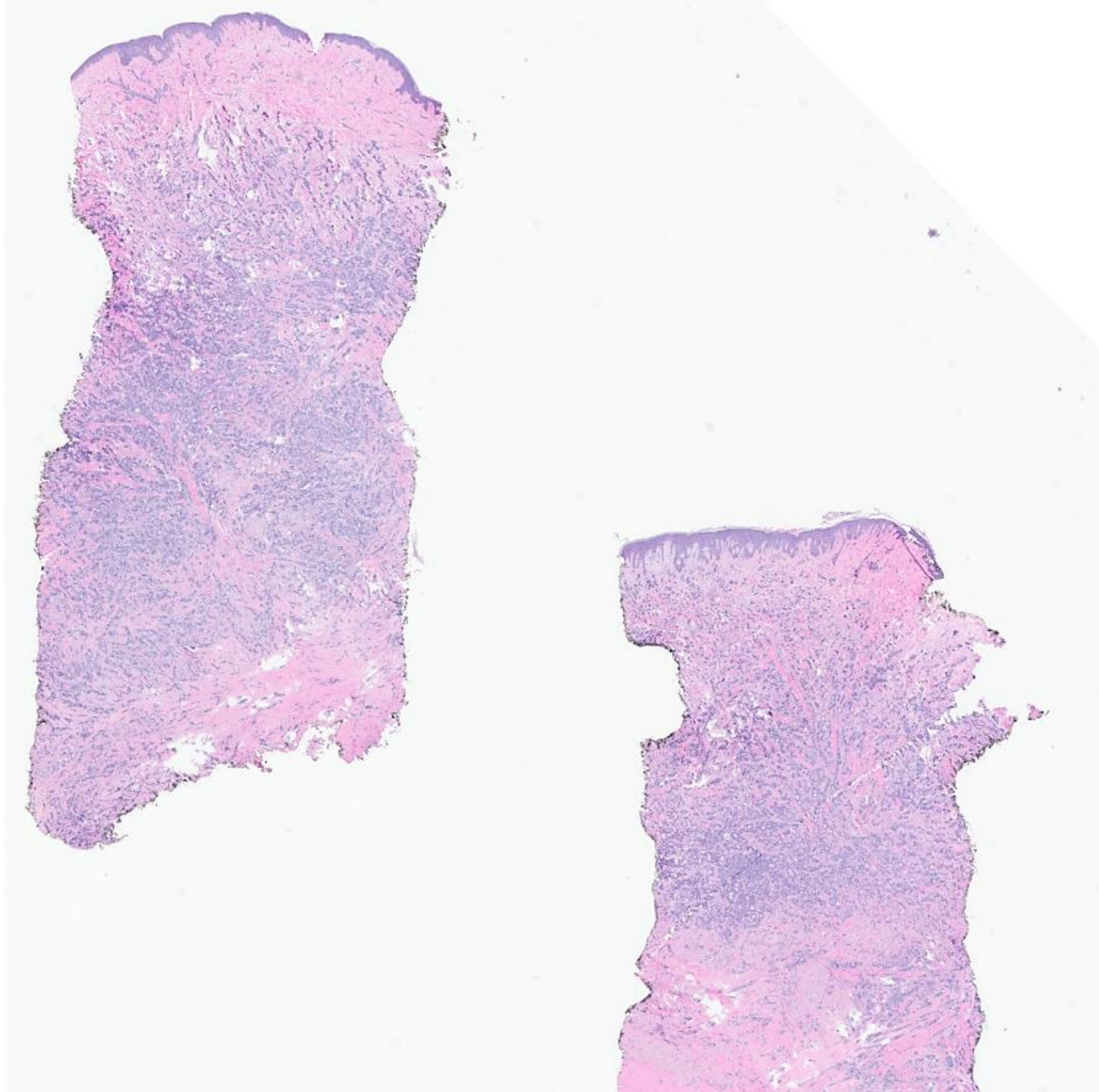
METASTATIC RENAL CELL CARCINOMA

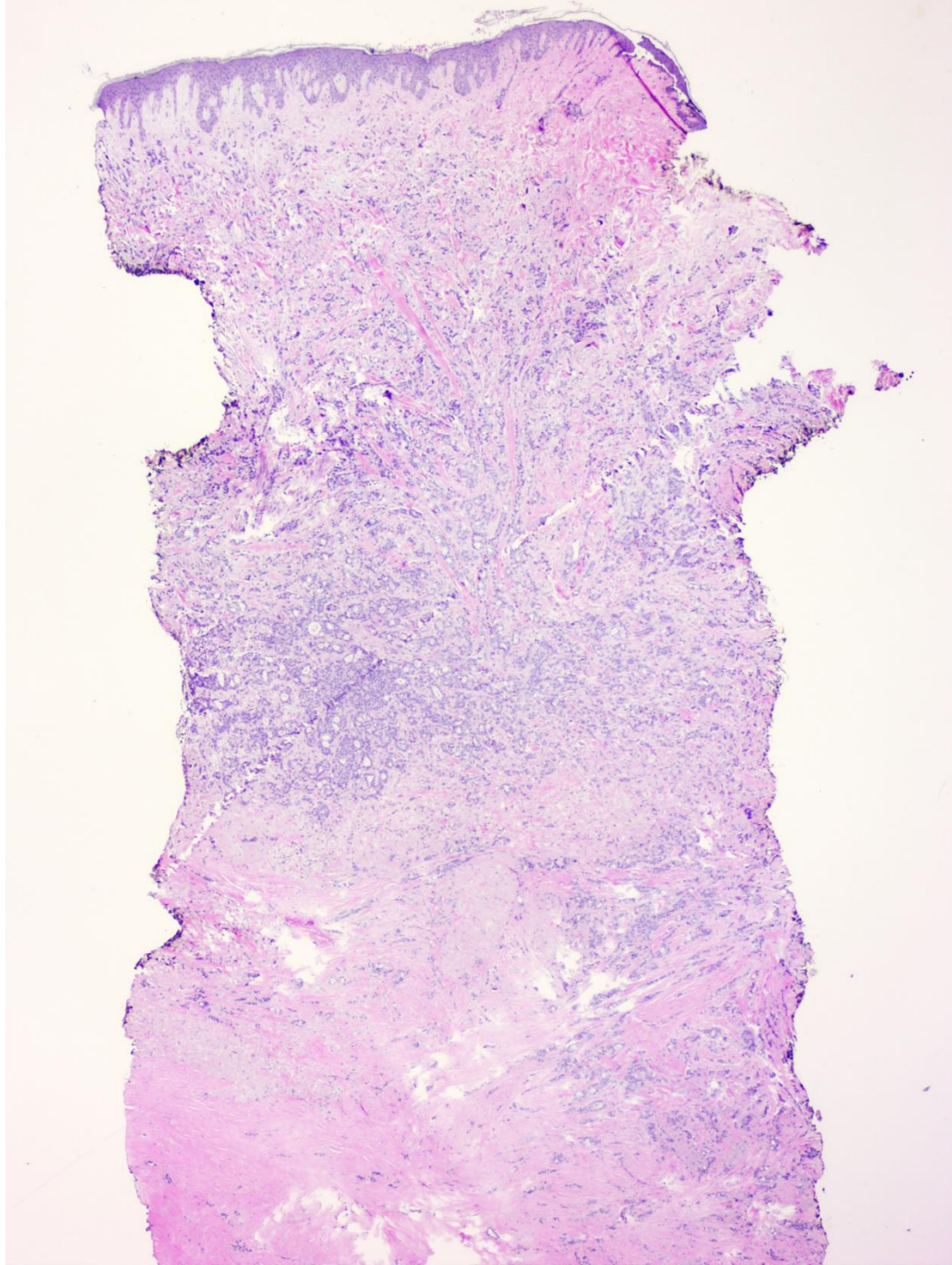
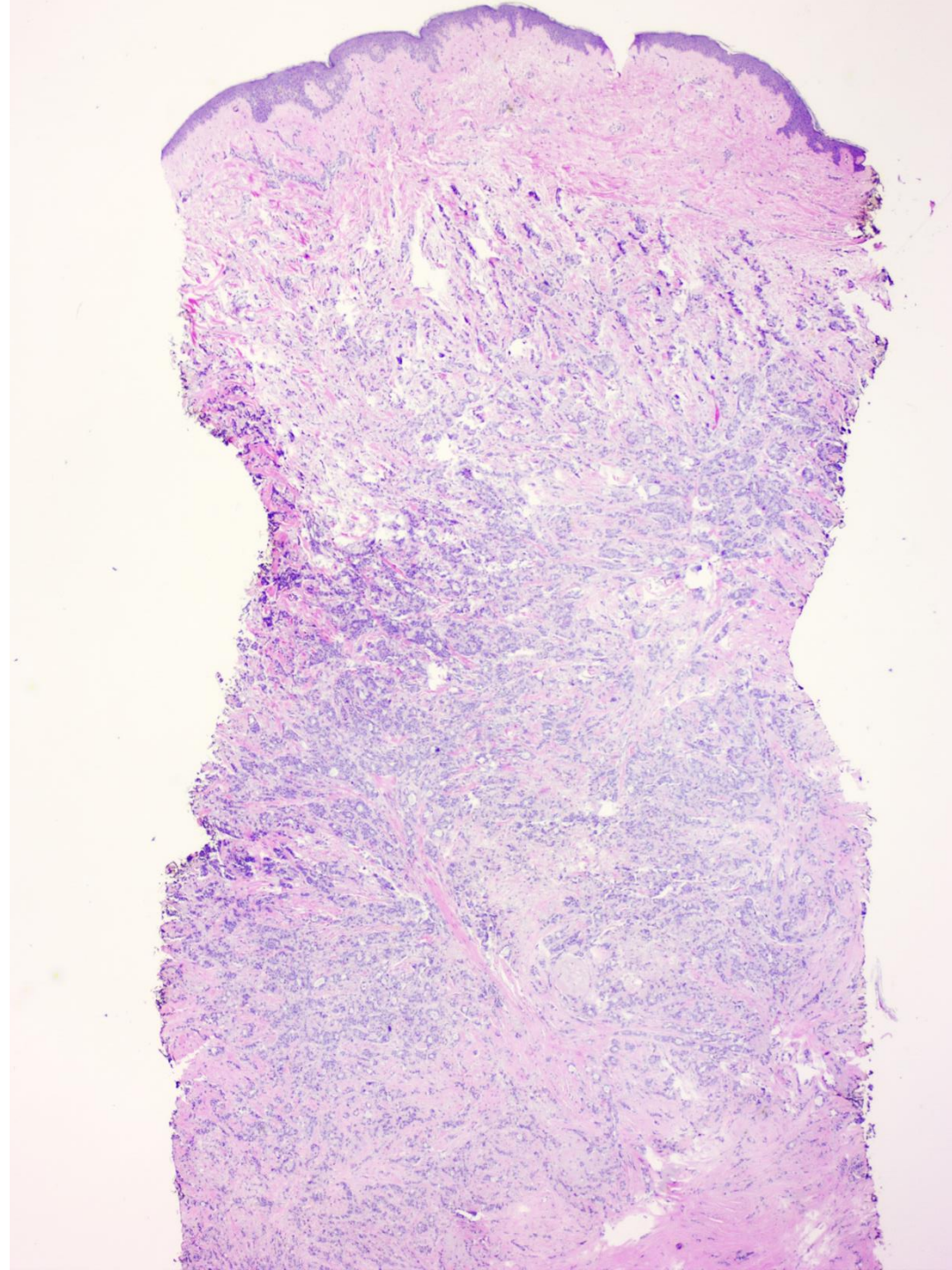
Patient's review of history:

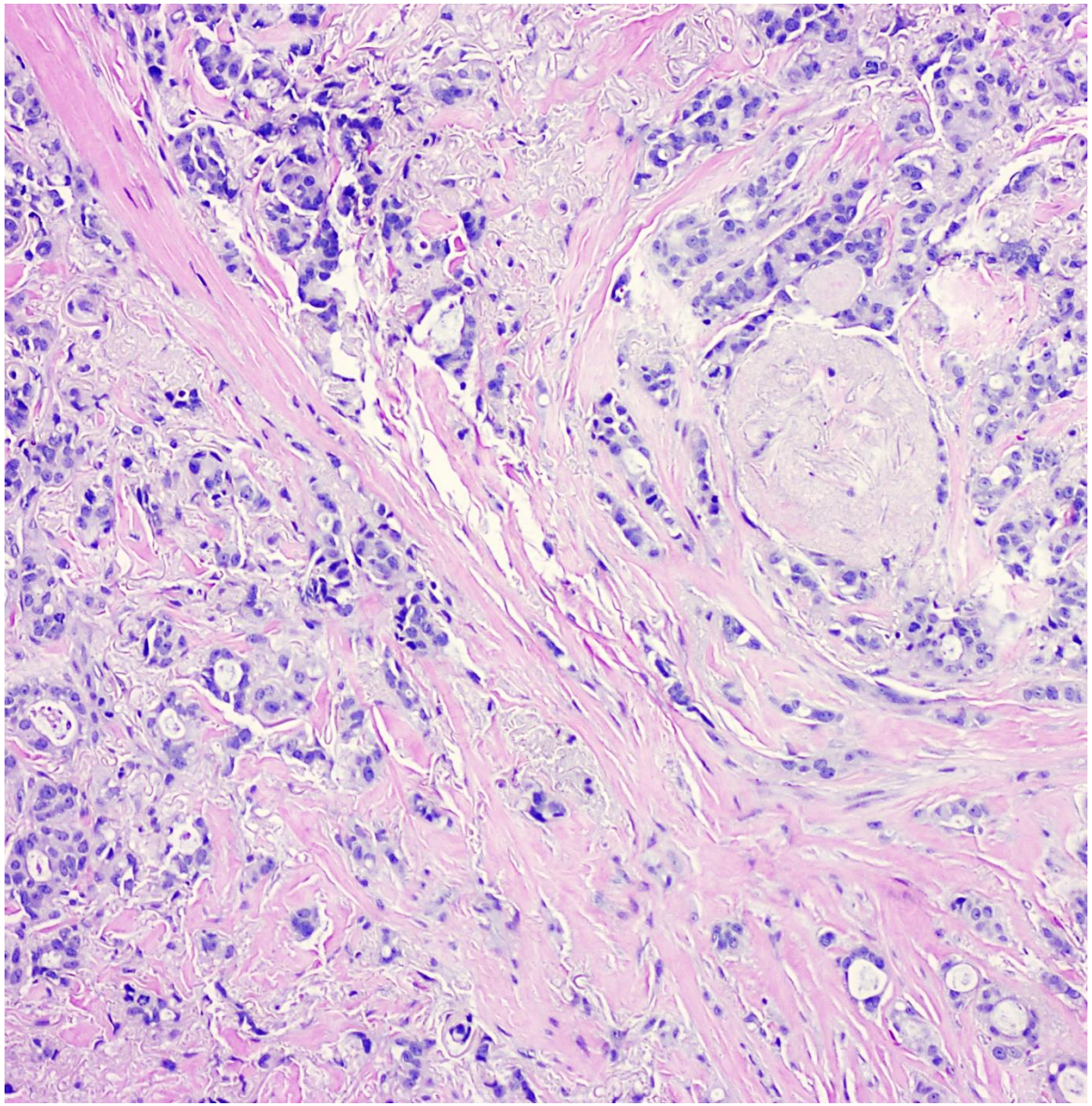
2019: right kidney renal cell carcinoma conventional type (IMP3 negative=less aggressive)

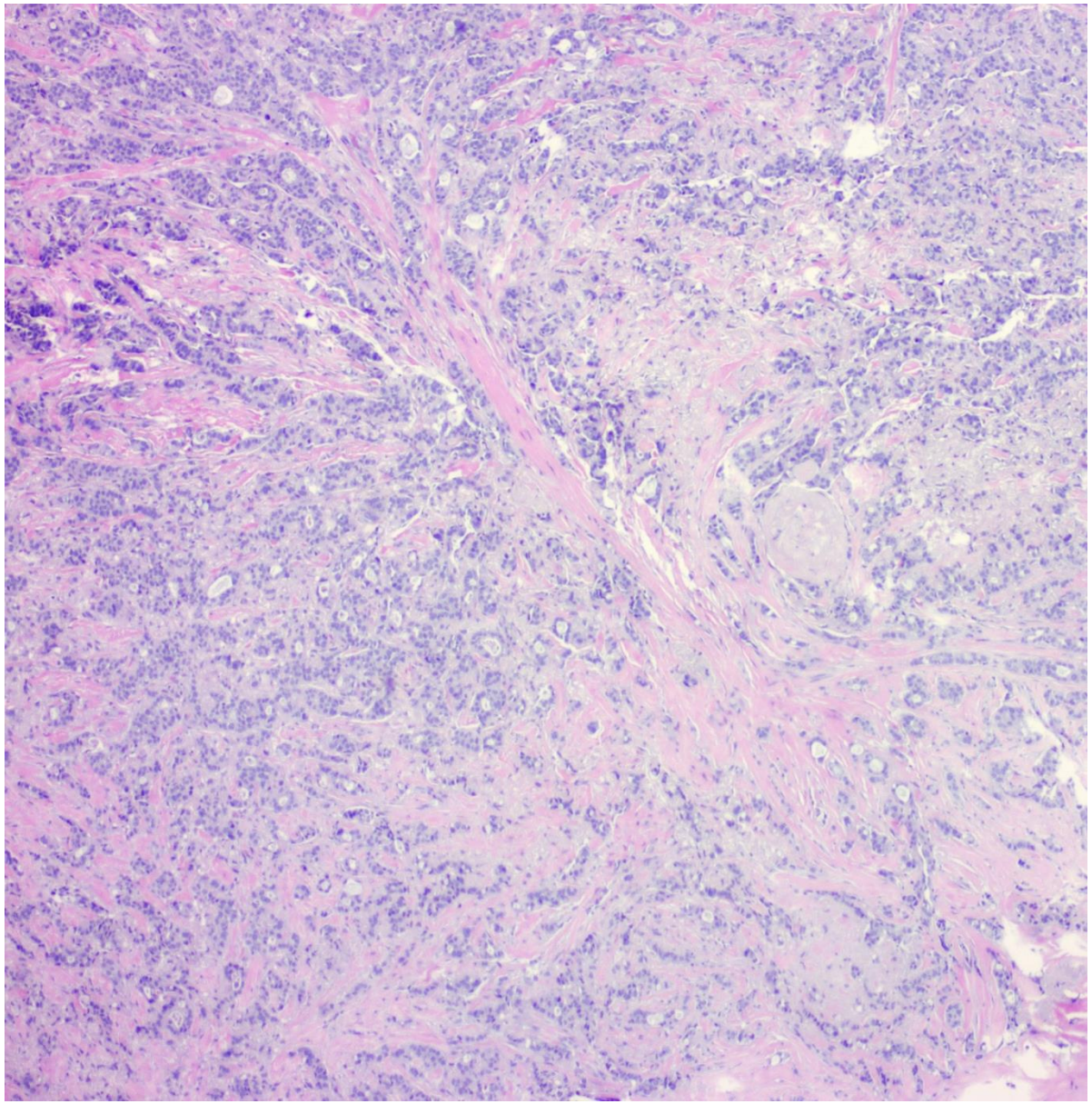
2024: metastasis to lung

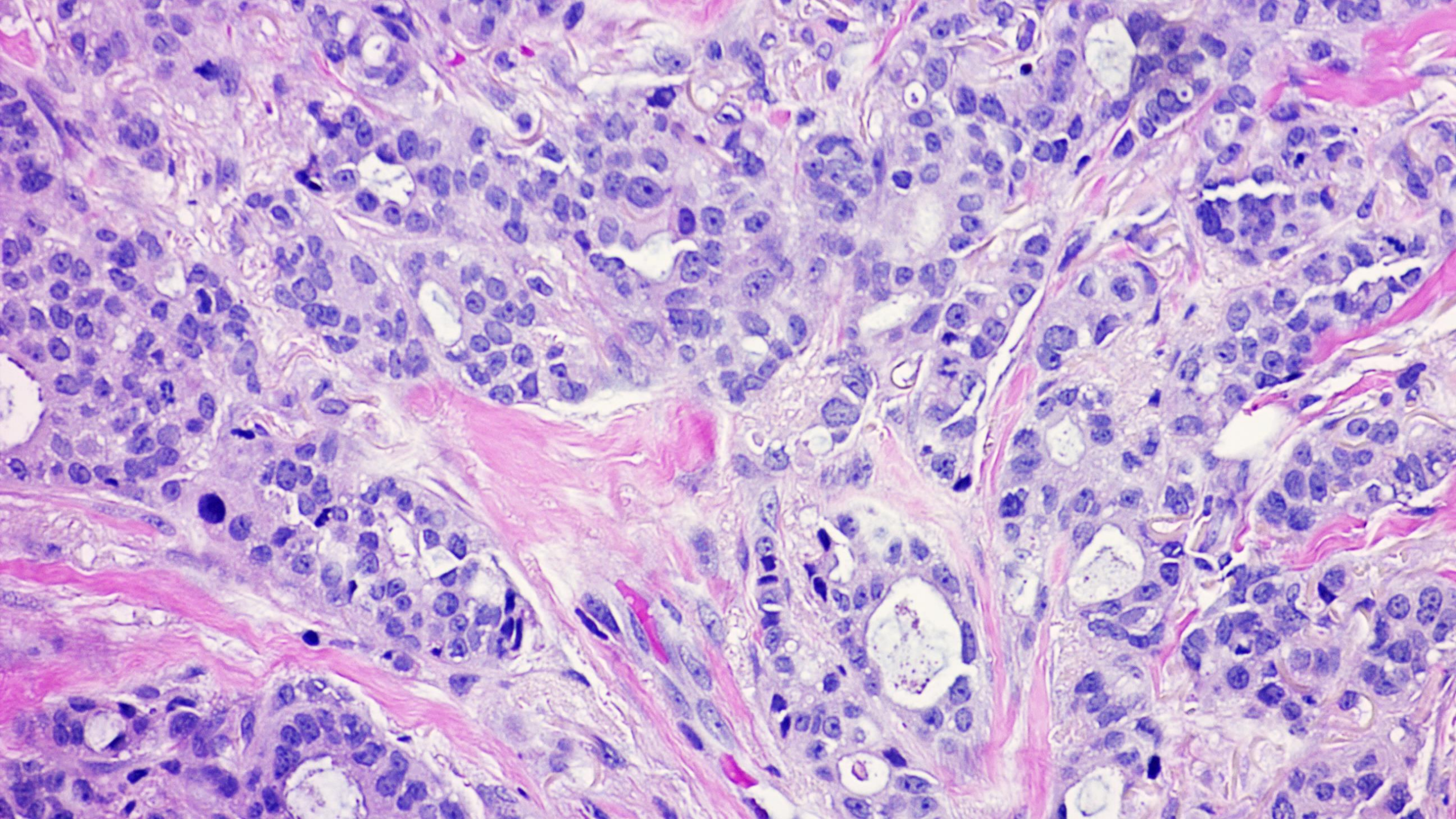
Feature	Findings
Histology	Clear cells, nested/tubular growth, vascular stroma
IHC+	PAX8, CAIX, CD10, EMA, Vimentin
IHC-	CK7, CK20, TTF-1, GATA3, Melanoma markers

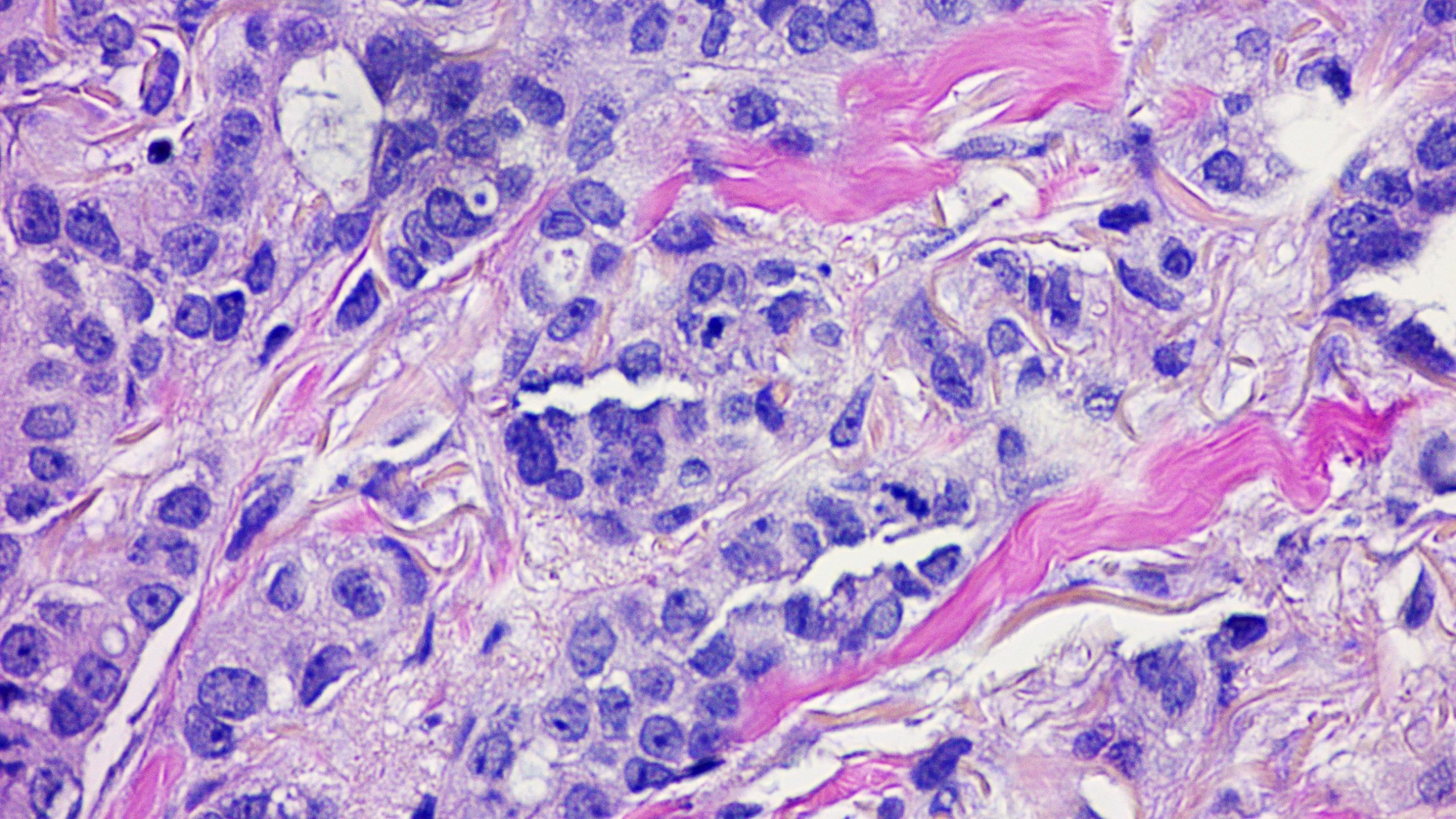










Case 107. 72F, chest; nodule on scar. What is your diagnosis?

A. Infiltrating ductal carcinoma

B. Metastatic ductal carcinoma, breast primary

C. Invasive eccrine carcinoma with ductal differentiation

D. Metastatic lung adenocarcinoma

E. Metastatic gastric/colorectal adenocarcinoma

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METASTATIC DUCTAL CARCINOMA, BREAST PRIMARY

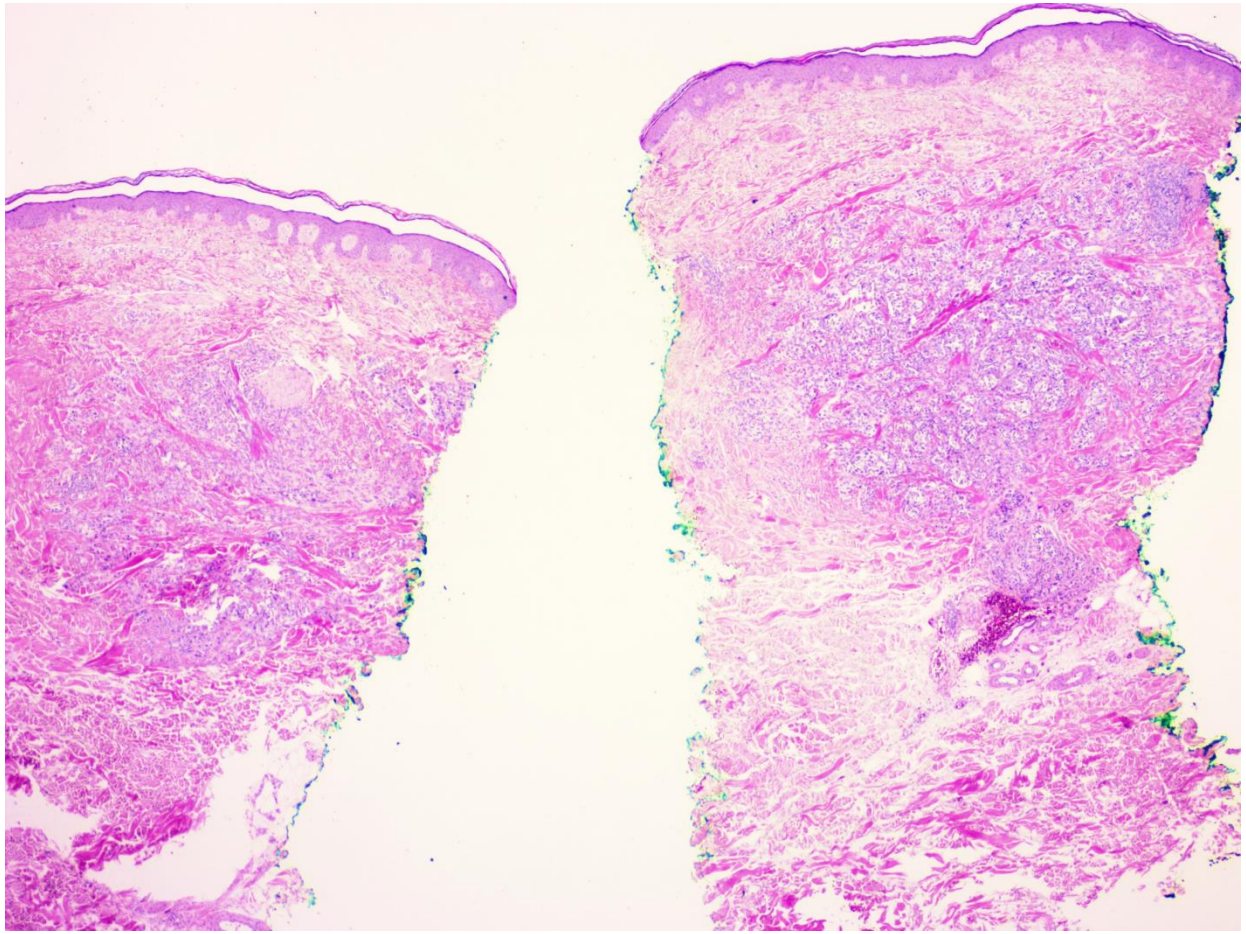
- Patient's history of breast cancer
- Punch biopsy of nodule in left mastectomy incision
- IHC: CK7+, GATA3+, GCDFP-15-
- **Architectural Patterns:**
  - **Nests, cords, or single-file infiltrates** (resembling primary breast carcinoma).
  - **Dermal/subcutaneous involvement** (epidermis is often spared, unlike Paget disease).
  - **Desmoplastic stroma** (common in invasive ductal carcinoma).
  - **Lymphovascular invasion** may be present.
- **Cytologic Features:**
  - **Ductal carcinoma:** Gland formation, nuclear pleomorphism.
  - **Lobular carcinoma:** Small, uniform cells with **single-file (Indian file) pattern**, signet-ring cells possible.
  - **Poorly differentiated carcinoma:** High-grade nuclei, necrosis.

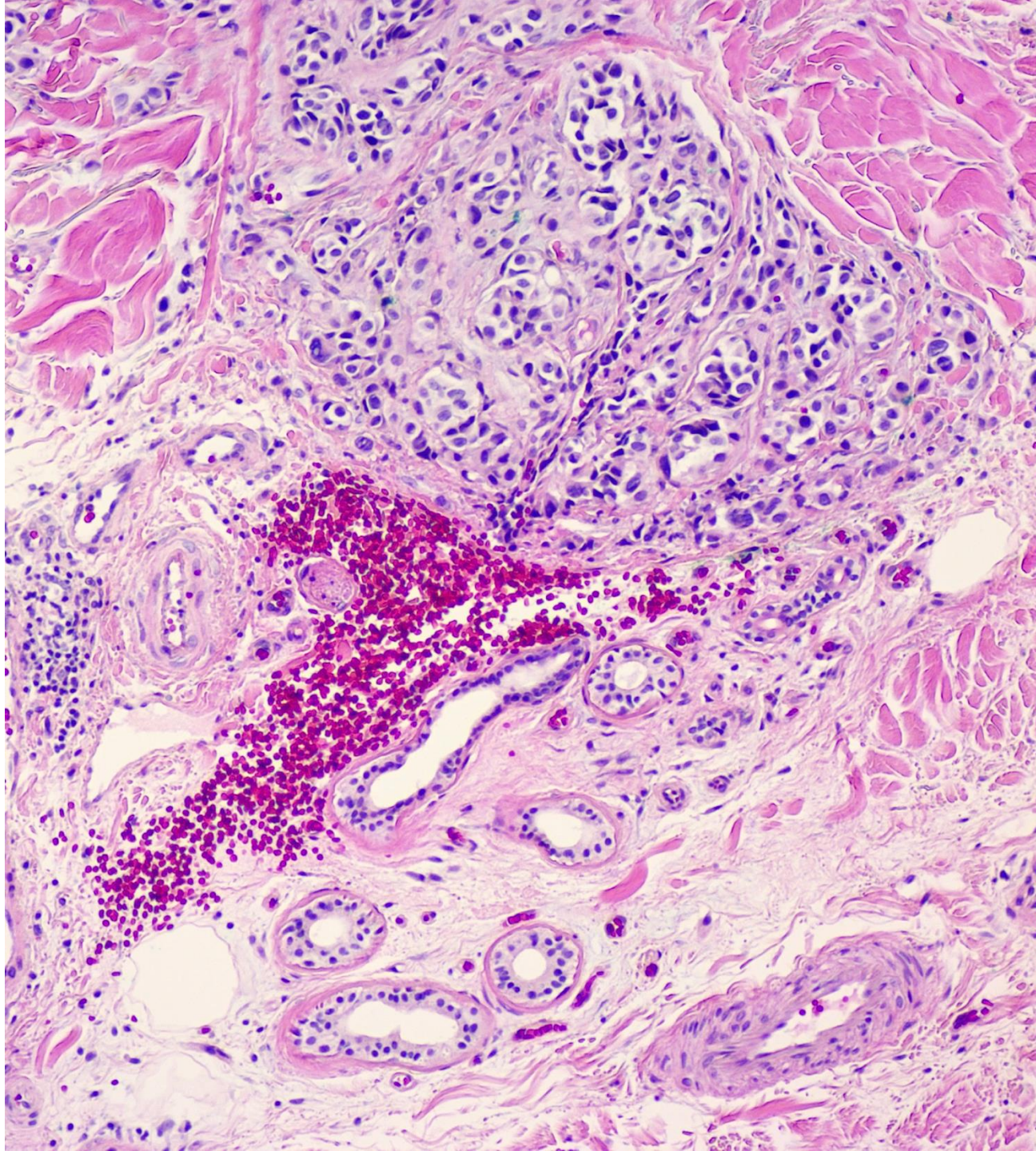
Histologic Differential Diagnosis & Confirmatory Markers

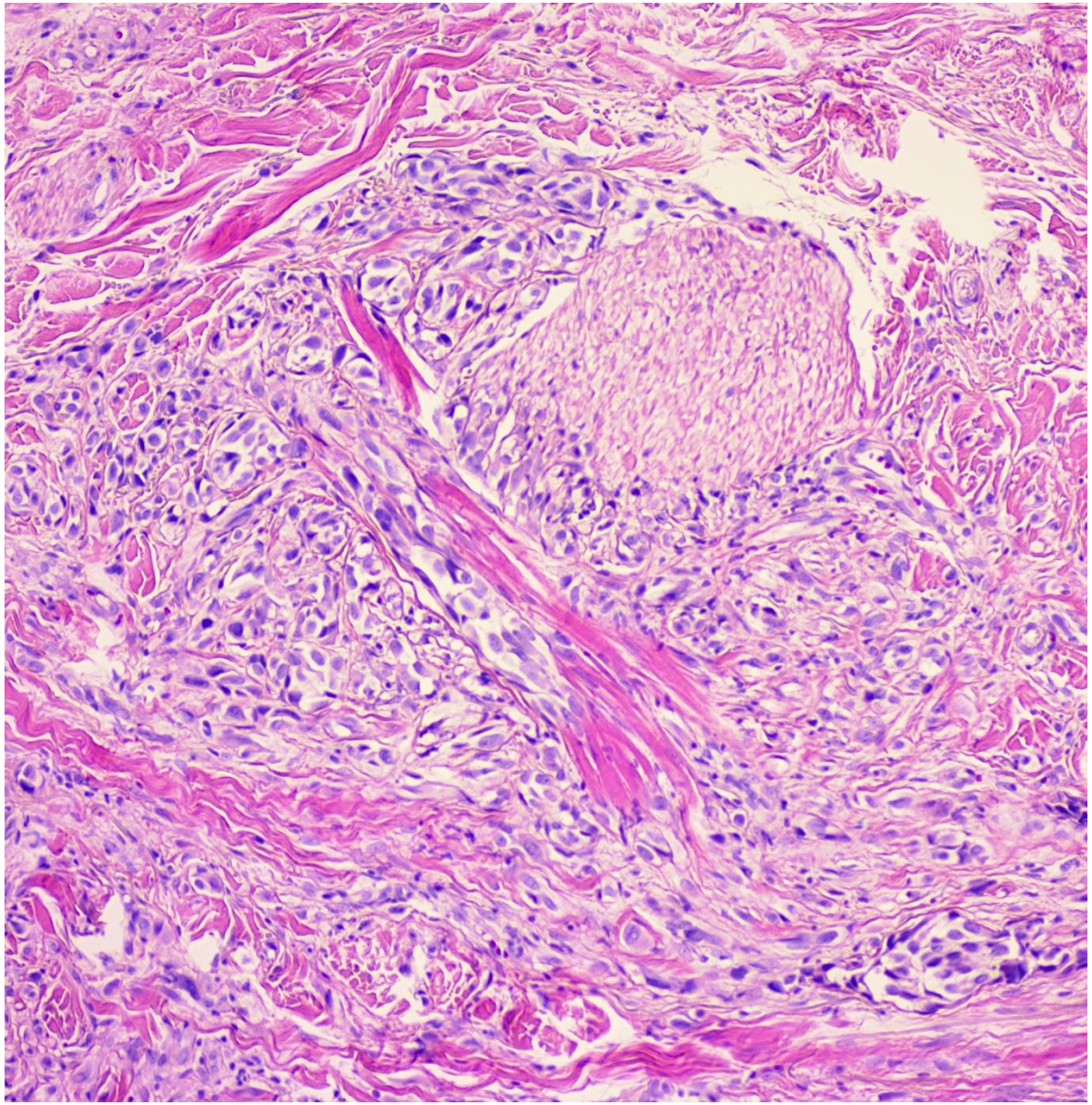
- **Metastatic Breast vs. Primary Cutaneous Adnexal Carcinoma:**
  - **Breast markers (GATA3, ER, mammaglobin) favor breast origin.**
  - **Adnexal tumors may express p63, CK5/6, D2-40 (lymphatic marker in some cases).**
- **Metastatic Lobular Carcinoma vs. Signet-Ring Cell GI Cancer:**
  - **Breast:** E-cadherin–, GATA3+, ER+
  - **GI:** CK20+, CDX2+, E-cadherin+
- **Triple-Negative Breast vs. Melanoma/Sarcoma:**
  - **Breast:** CK7+, GATA3+ (but SOX10– unless basal-like).
  - **Melanoma:** S100+, SOX10+, Melan-A+.
  - **Sarcoma:** Vimentin+, specific sarcoma markers (e.g., CD34, SMA).

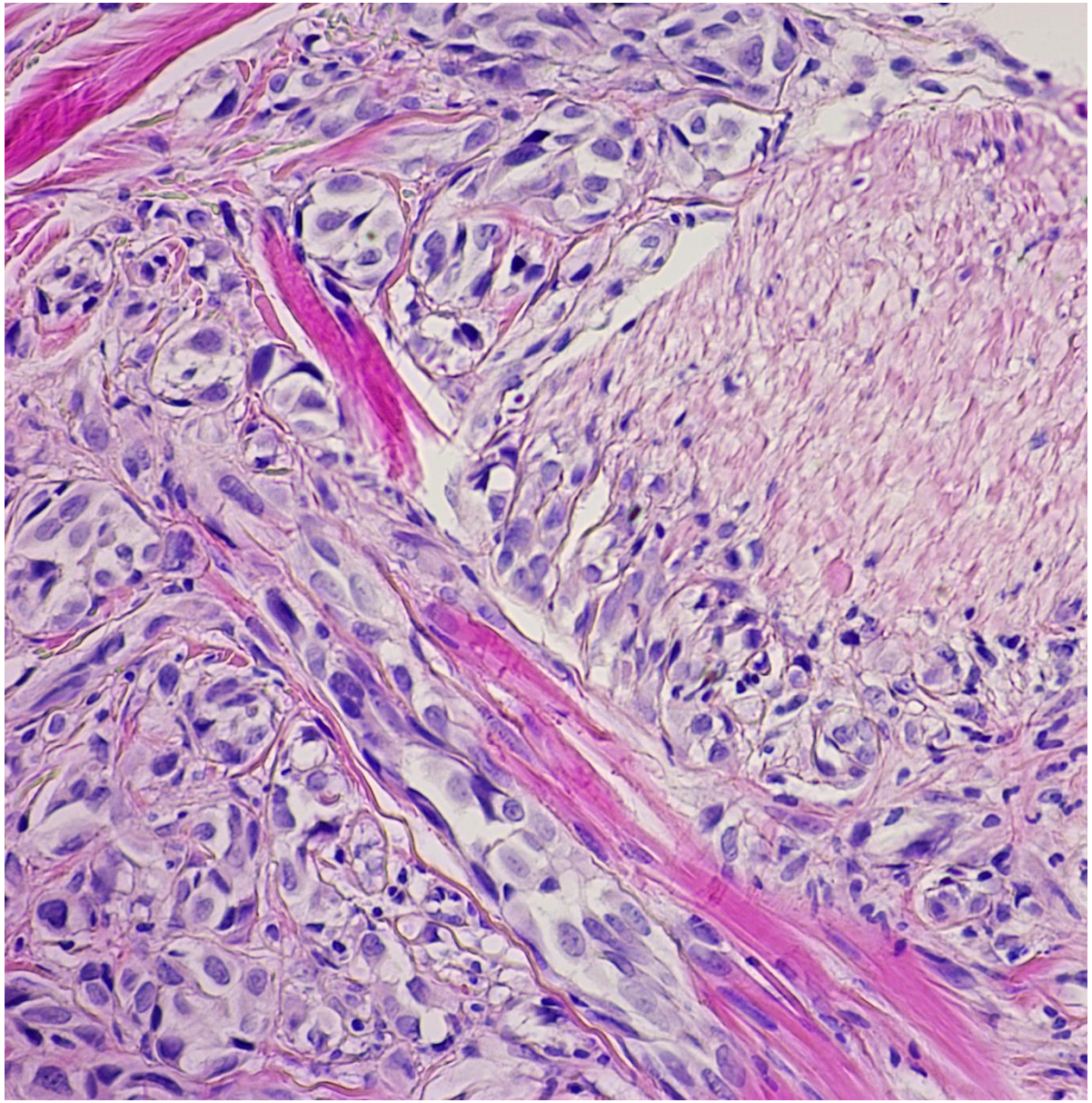
Immunohistochemical markers for breast carcinoma

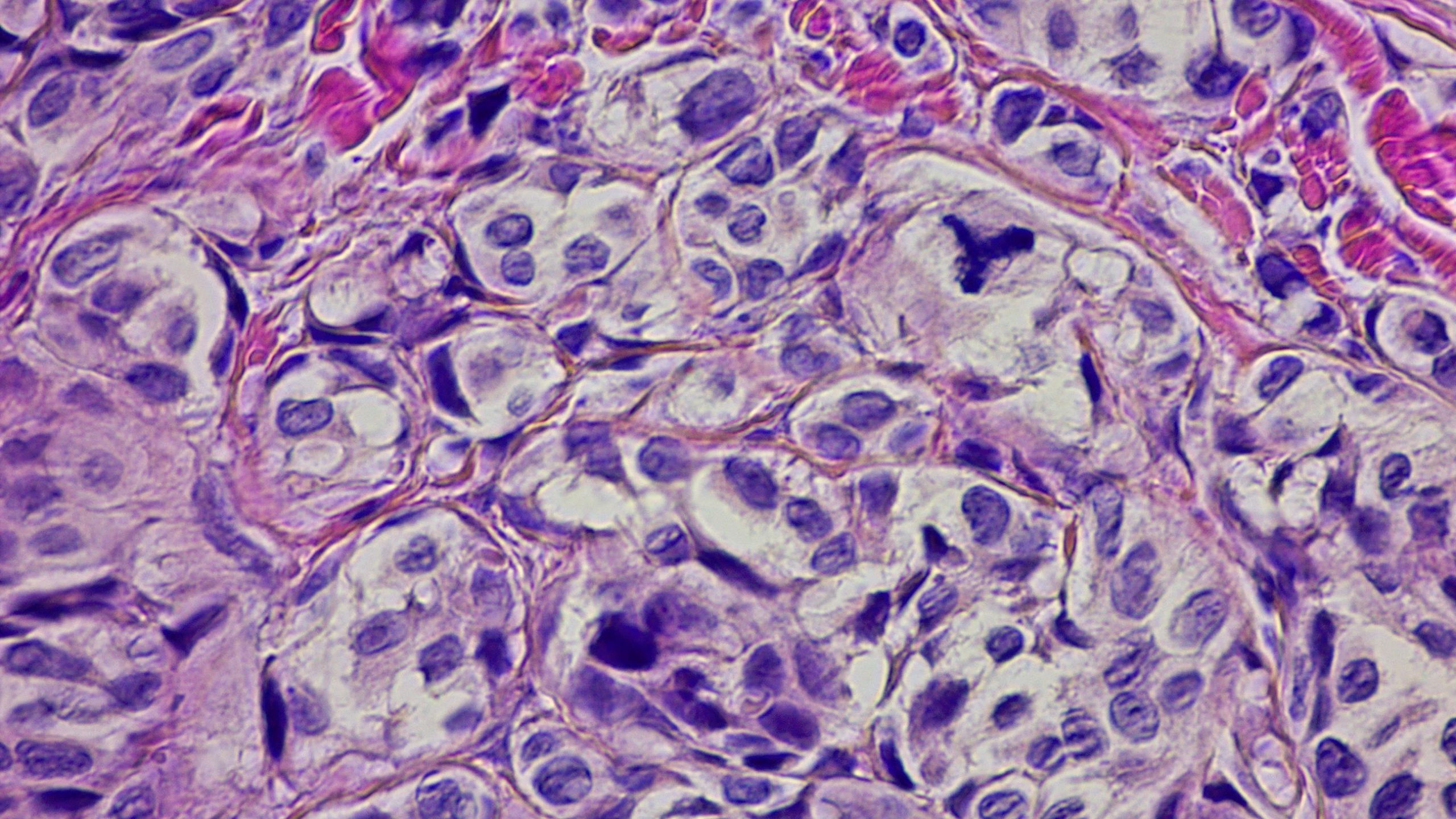
Marker	Ductal Carcinoma (IDC)	Lobular Carcinoma (ILC)	Triple-Negative (TNBC)
CK7	+ (strong/diffuse)	+	+
GATA3	+ (nuclear)	+	+ (most cases)
ER	+ (50-80%)	+ (90%)	–
PR	+ (40-60%)	+ (70%)	–
HER2	+ (15-20%, 3+ IHC or FISH+)	– (rarely +)	–
GCDFP-15	+ (30-50%)	+ (less common)	–
Mammaglobin	+ (50-70%)	+ (variable)	– (rarely +)
E-Cadherin	+ (membranous)	**Loss/lack of staining**	+ (if not lobular)
AR (Androgen Receptor)	+ (some luminal)	+ (some cases)	+ (40-50% of TNBC)
SOX10	–	–	+ (10-30% of TNBC)
CK20	–	–	–
p63	–	–	– (unless metaplastic)

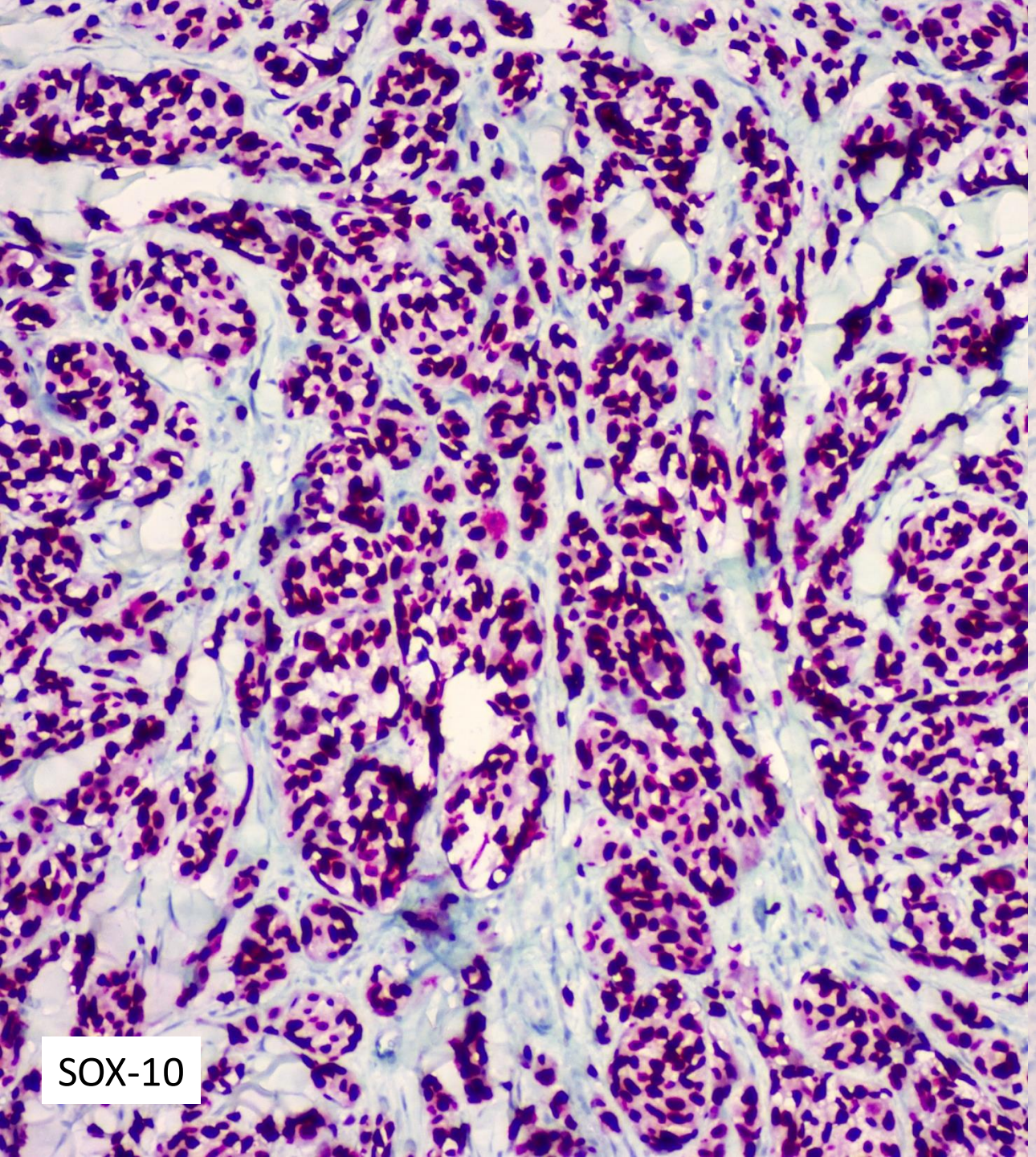


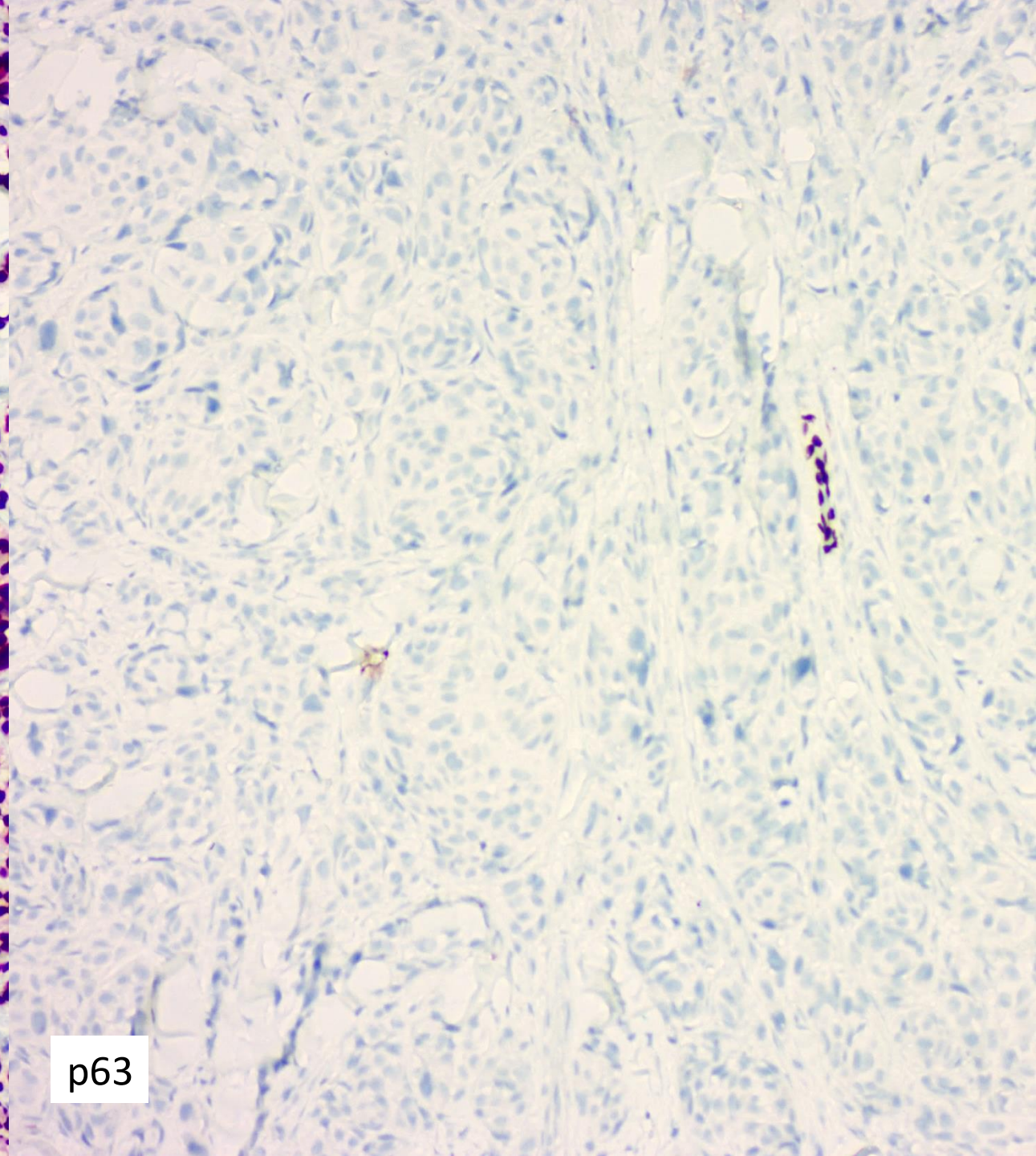









SOX-10


p63

Case 108. 68M, Skin, Left Thigh; New dermal papule, favor evolving dermatofibroma. What is your diagnosis?

A. Dermatofibroma, aneurysmal variant

B. Dermatofibrosarcoma protuberans

C. Angiomatoid fibrous histiocytoma

D. Metastatic melanoma

E. Intradermal melanocytic nevus

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Metastatic melanoma

- History of melanoma with in-transit metastasis on the same thigh
- Patient's IHC: SOX10+, p63-, D2-40-
- **Negative Markers (Used to Rule Out Mimics)**
  - **Epithelial markers (CK7, CK20, EMA)**: Negative (helps exclude carcinoma).
  - **Lymphoid markers (CD45, CD3, CD20)**: Negative (excludes lymphoma).
  - **Sarcoma markers (SMA, desmin, CD34)**: Negative (excludes sarcoma).
  - **GATA3, ER, PR**: Negative (excludes breast carcinoma).
- **Architectural Patterns:**
  - **Nodular/diffuse dermal infiltration** (often spares the epidermis, unlike primary melanoma).
  - **Lack of epidermal involvement** (no "in-situ" component, unlike primary melanoma).
  - **Pushing borders** (well-circumscribed nodules) or **infiltrative growth**.
  - **Lymphovascular invasion** may be present.
- **Cytologic Features:**
  - **Epithelioid cells** (large, round, eosinophilic cytoplasm, prominent nucleoli).
  - **Spindle cells** (fusiform morphology, seen in desmoplastic melanoma).
  - **Pleomorphic/anaplastic cells** (marked nuclear atypia, mitoses).
  - **Pigmentation** (variable; may be absent in amelanotic melanoma).

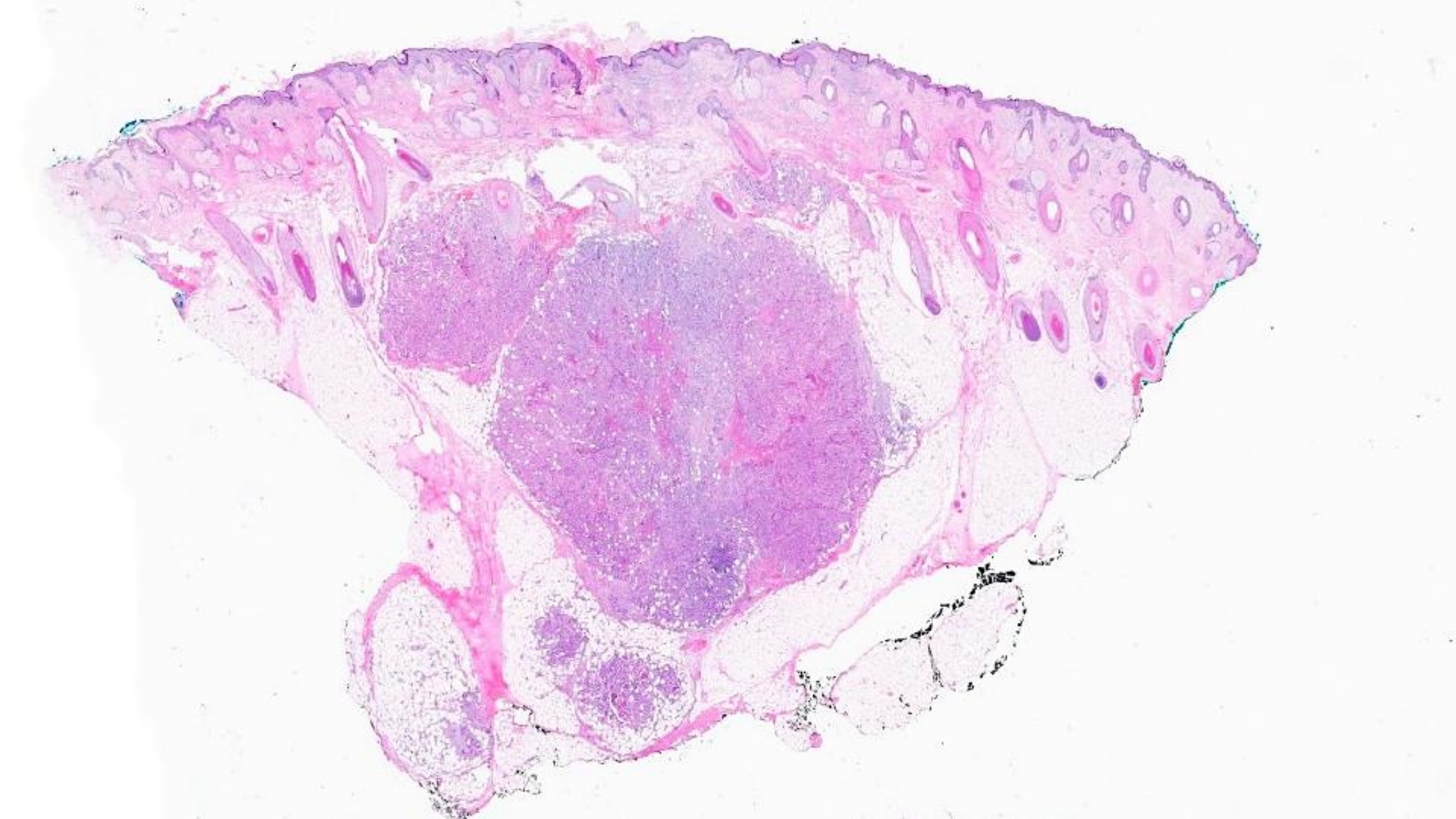
Histologic Differential Diagnosis & Confirmatory Testing

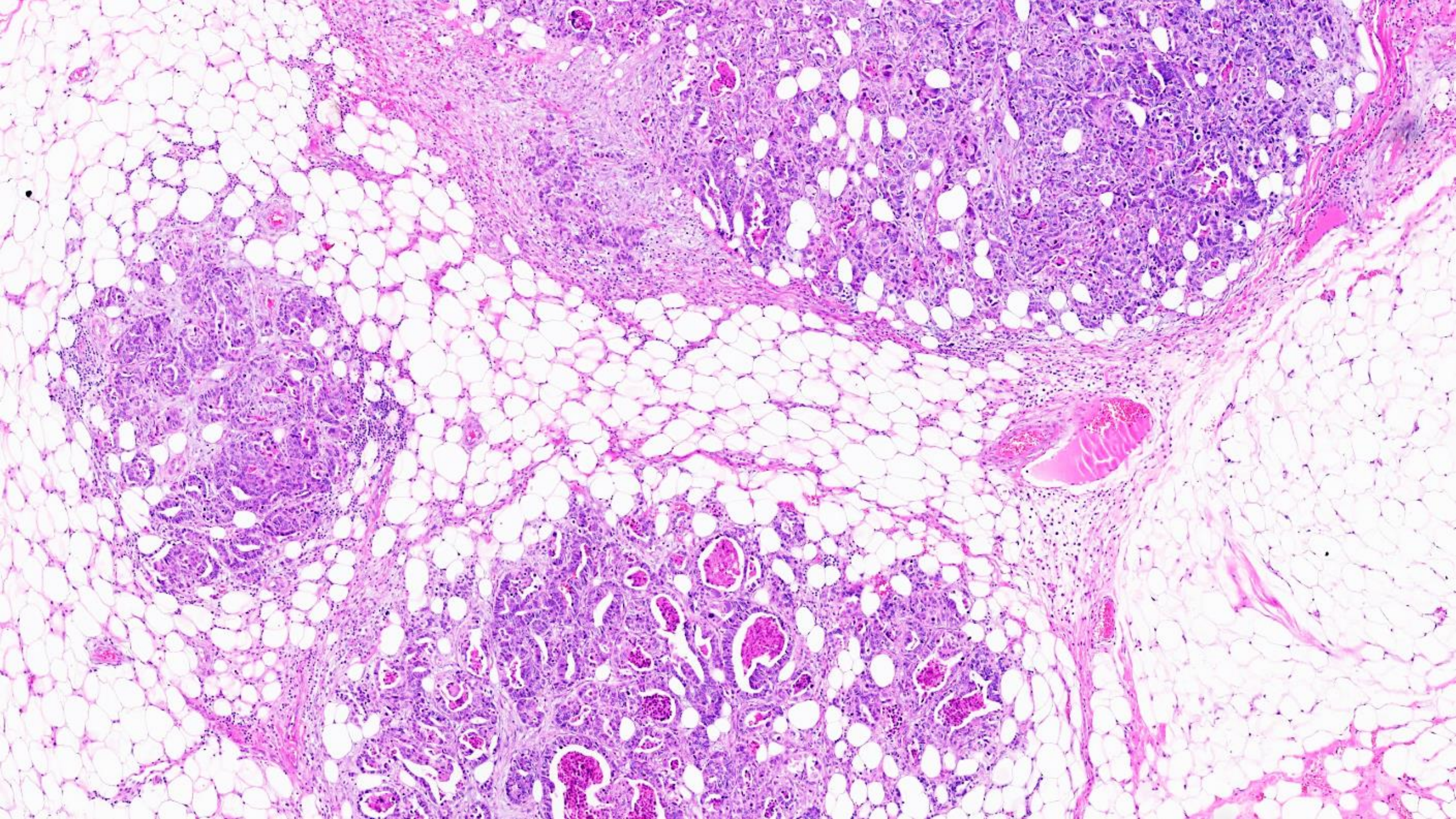
A. Metastatic Melanoma vs. Primary Cutaneous Melanoma

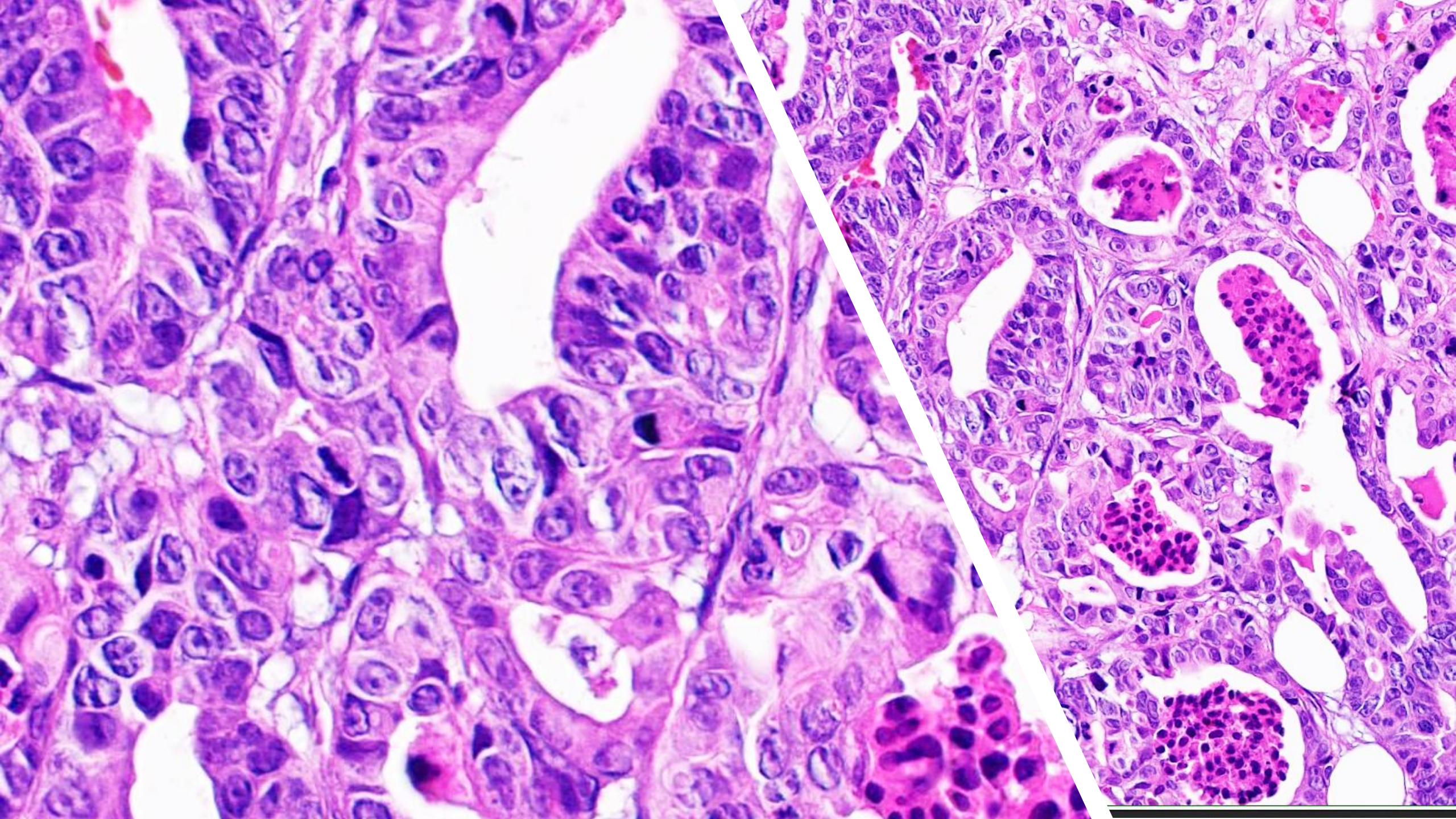
Feature	Metastatic Melanoma	Primary Melanoma
Epidermal involvement	Usually absent	Present (junctional component)
Nevus remnants	Absent	May be present (if arising from a nevus)
Ulceration	Less common	More common
Clinical history	Known primary melanoma	New lesion

B. Metastatic Melanoma vs. Other Cutaneous Metastases

Mimic	Key Differentiating Features	IHC Markers
Poorly differentiated carcinoma	Glandular/squamoid features	**CK+, S100-, SOX10-**
Sarcoma	Spindle cells, myxoid stroma	**SMA+, CD34+, S100-**
Lymphoma	Discohesive cells, lymphoid markers	**CD45+, S100-**
Clear cell sarcoma	Deep soft tissue origin, EWSR1 rearrangement	**S100+, Melan-A+, HMB-45+, EWSR1+**







Case 109. 58M, rapidly growing mass, left cheek. What is your diagnosis?

A. Invasive eccrine carcinoma with ductal differentiation

B. Metastatic esophageal squamous carcinoma

C. Metastatic ductal carcinoma, breast primary

D. Metastatic lung adenocarcinoma

E. Metastatic gastrointestinal adenocarcinoma

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Metastatic esophageal adenocarcinoma

- Patient has h/o esophageal carcinoma
- Patient's IHC:
  - positive for CK7, HER2, CDX2 (focal), P504S (focal) and c-erb B-2/HER-2
  - negative for SATB2, CK20, CK5/6, and p40
  - Low probability of MSI-H

- Summary:
  - **Best IHC panel for metastatic esophageal SCC:**
    - **p40 + CK5/6 + CK7-** (exclude adenocarcinoma).
  - **Best IHC panel for metastatic esophageal adenocarcinoma:**
    - **CK7 + CDX2 + HER2 + MUC5AC** (rule out gastric/colorectal).
  - **Clinical history is critical** (endoscopy/biopsy correlation).