Disclosures
July 7, 2020

Dr. Ankur Sangoi has disclosed a financial relationship with Google (consultant). Dr. Keith Duncan has disclosed a financial relationship with Abbvie (contractor/consultant). South Bay Pathology Society has determined that these relationships are not relevant to the planning of the activity (Dr. Sangoi) or the clinical cases being presented.

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

Presenters:

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Hubert Lau, MD
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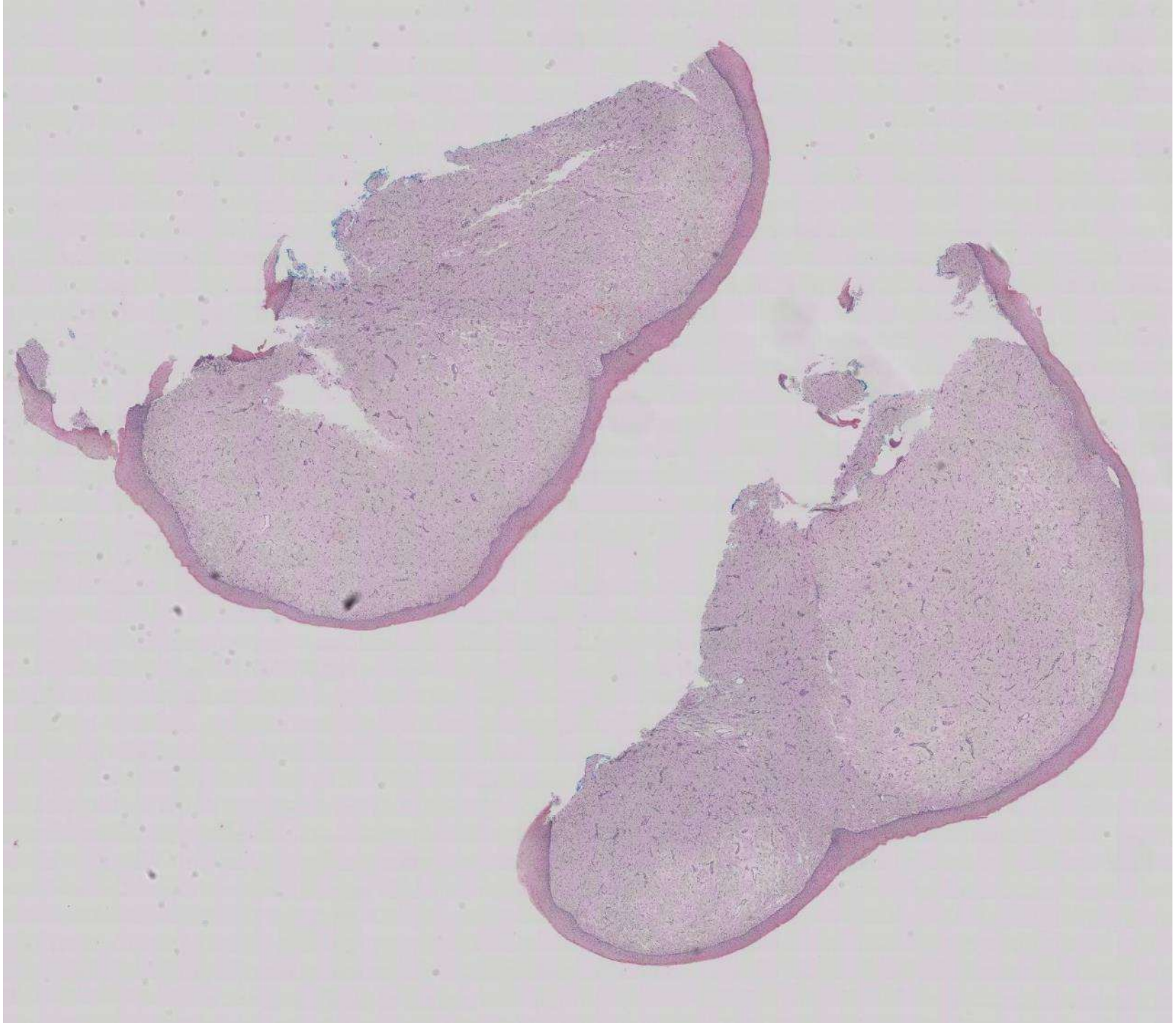
Activity Planners/Moderator:

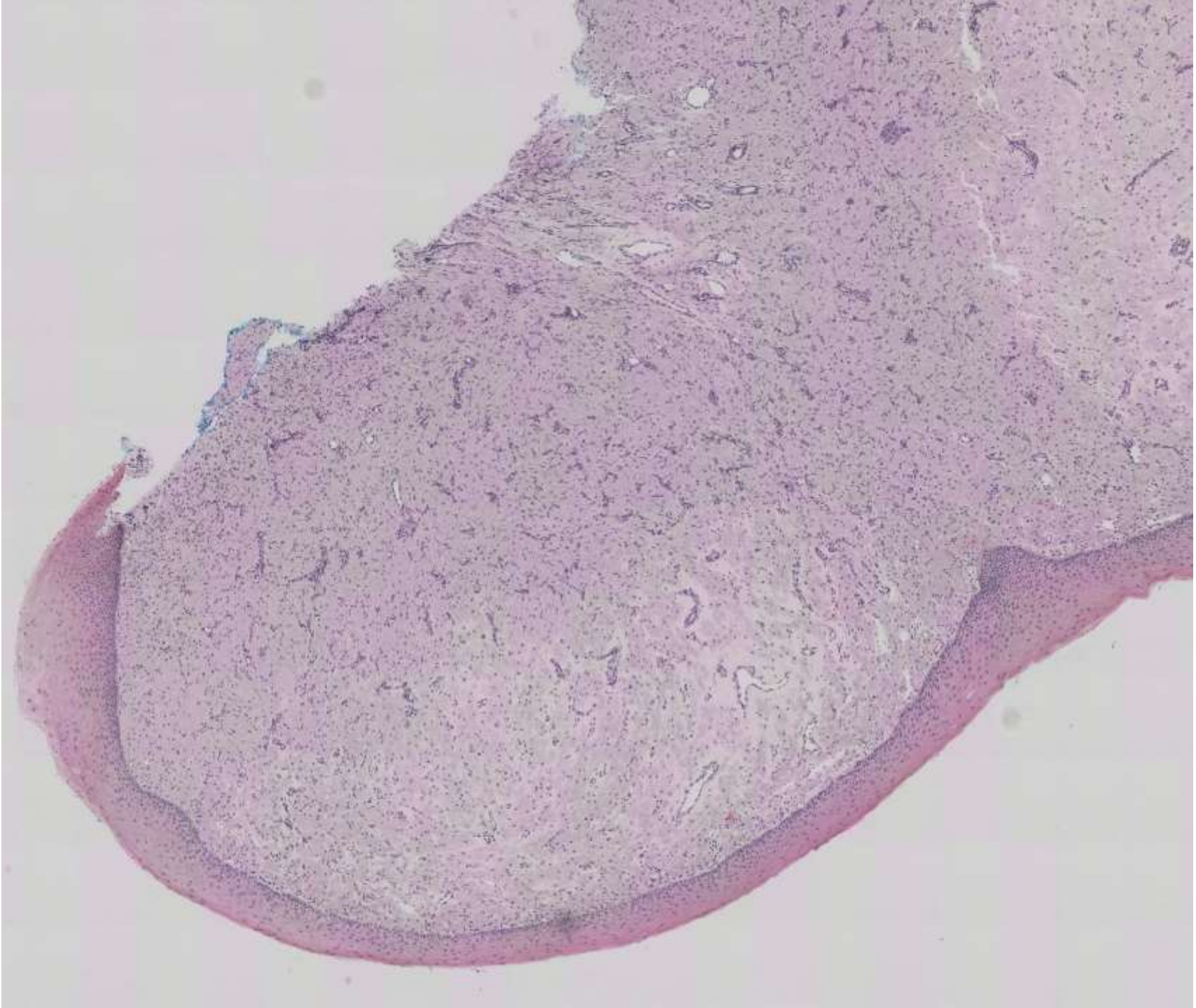
Kristin Jensen, MD
Megan Troxell, MD, PhD

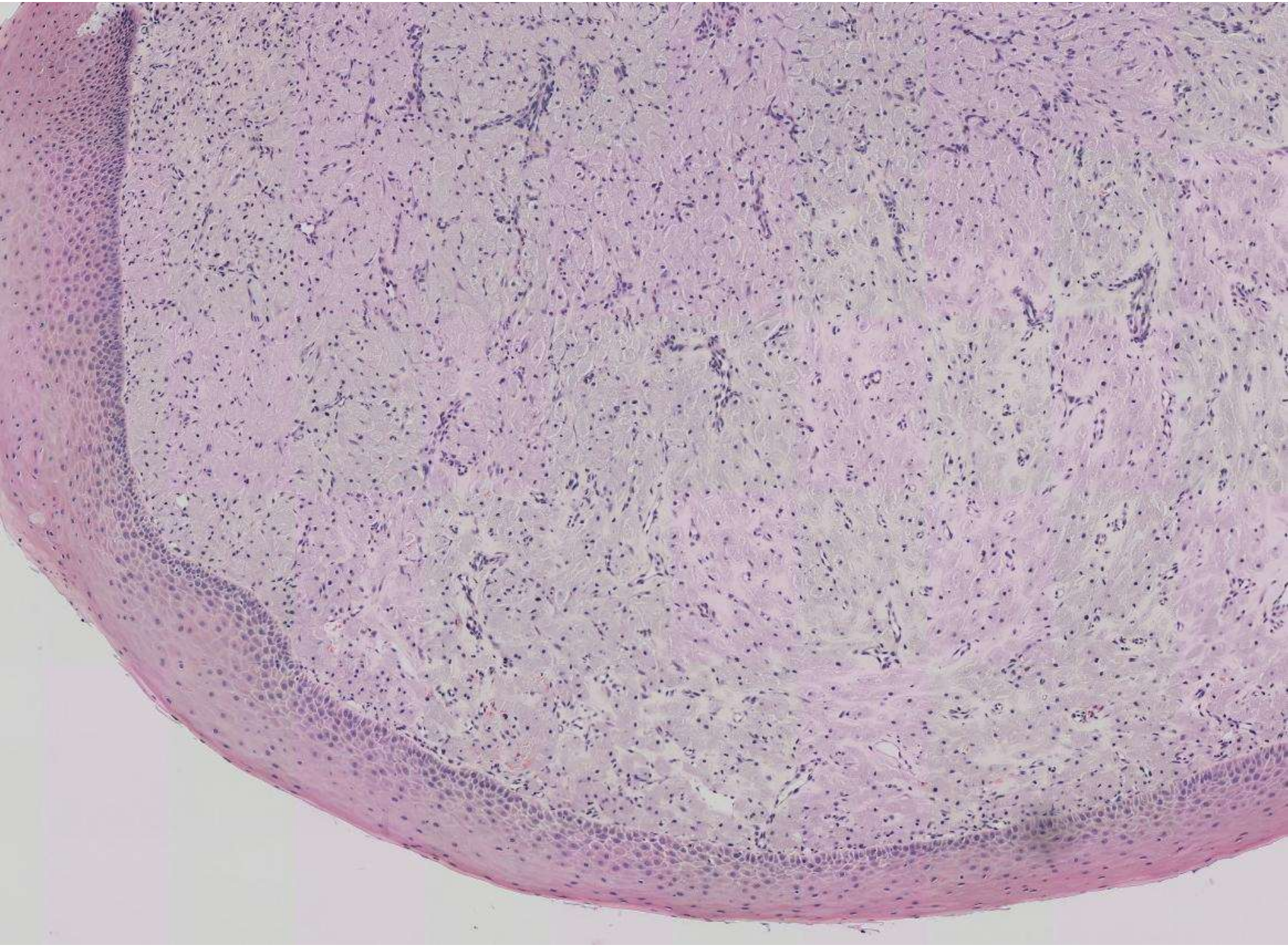
20-0701
scanned slide available!

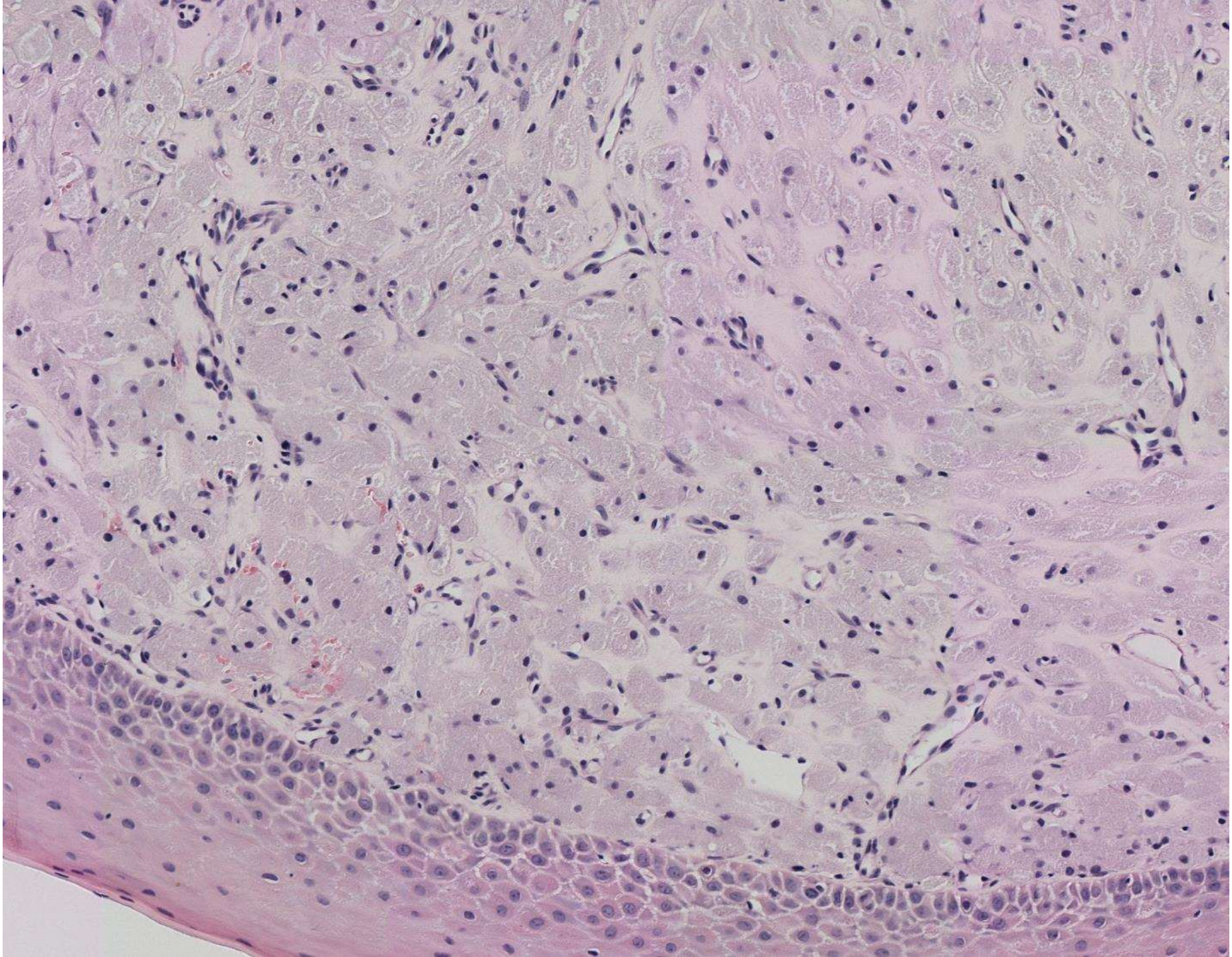
Jordan Taylor/Emily Chan; UCSF

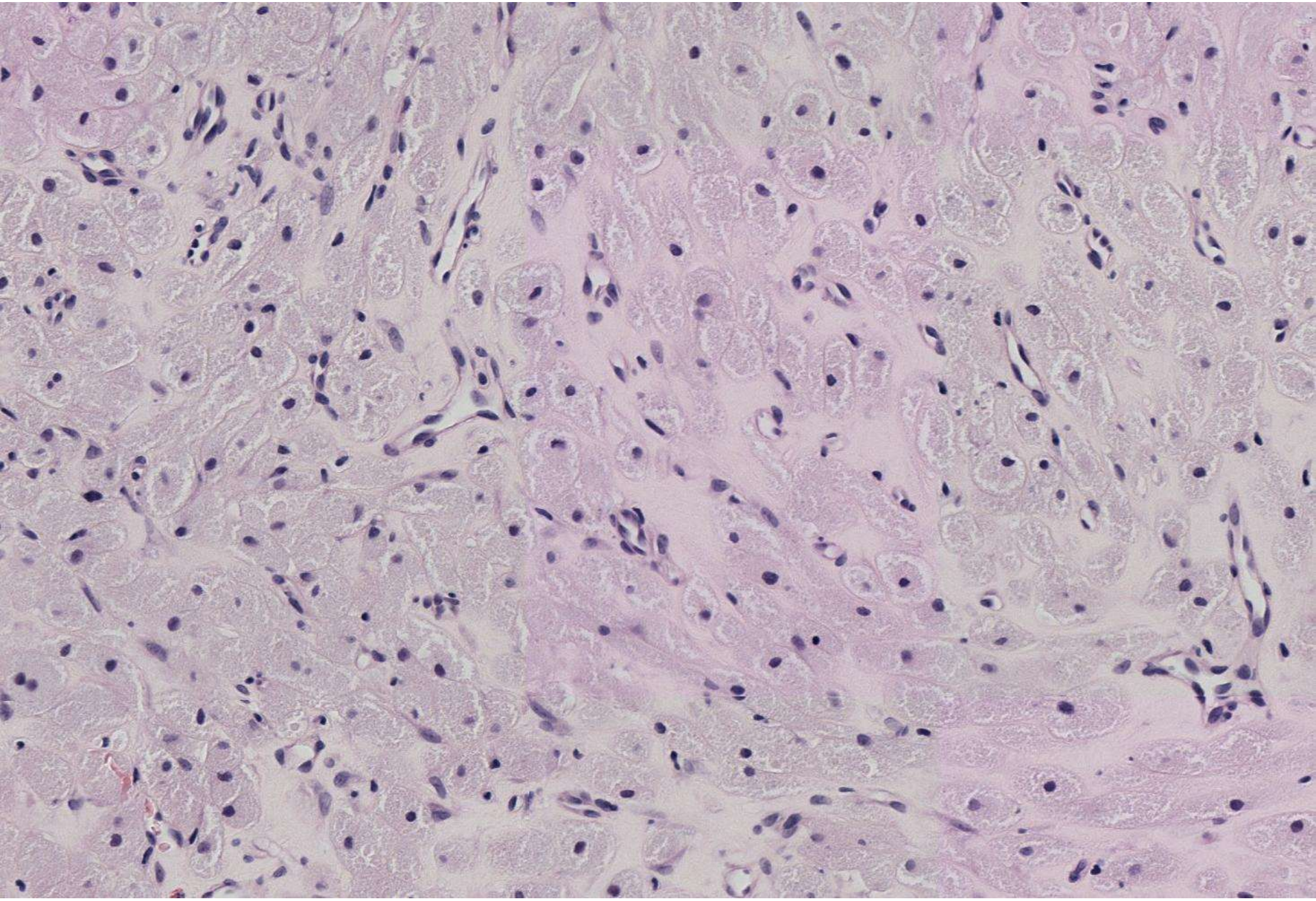
2-day-old with single pedunculated pink firm mass emanating from left mandible alveolar ridge.

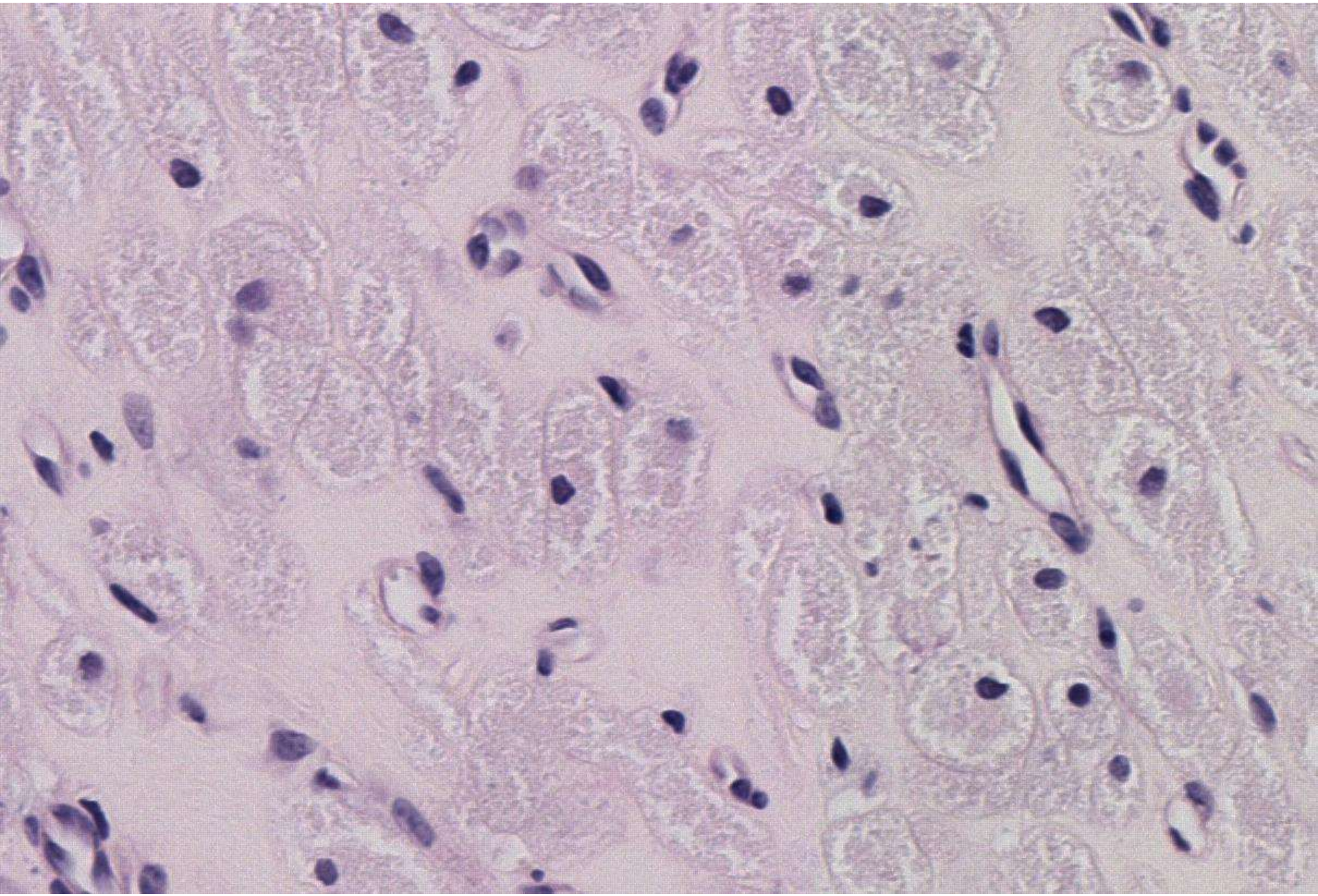




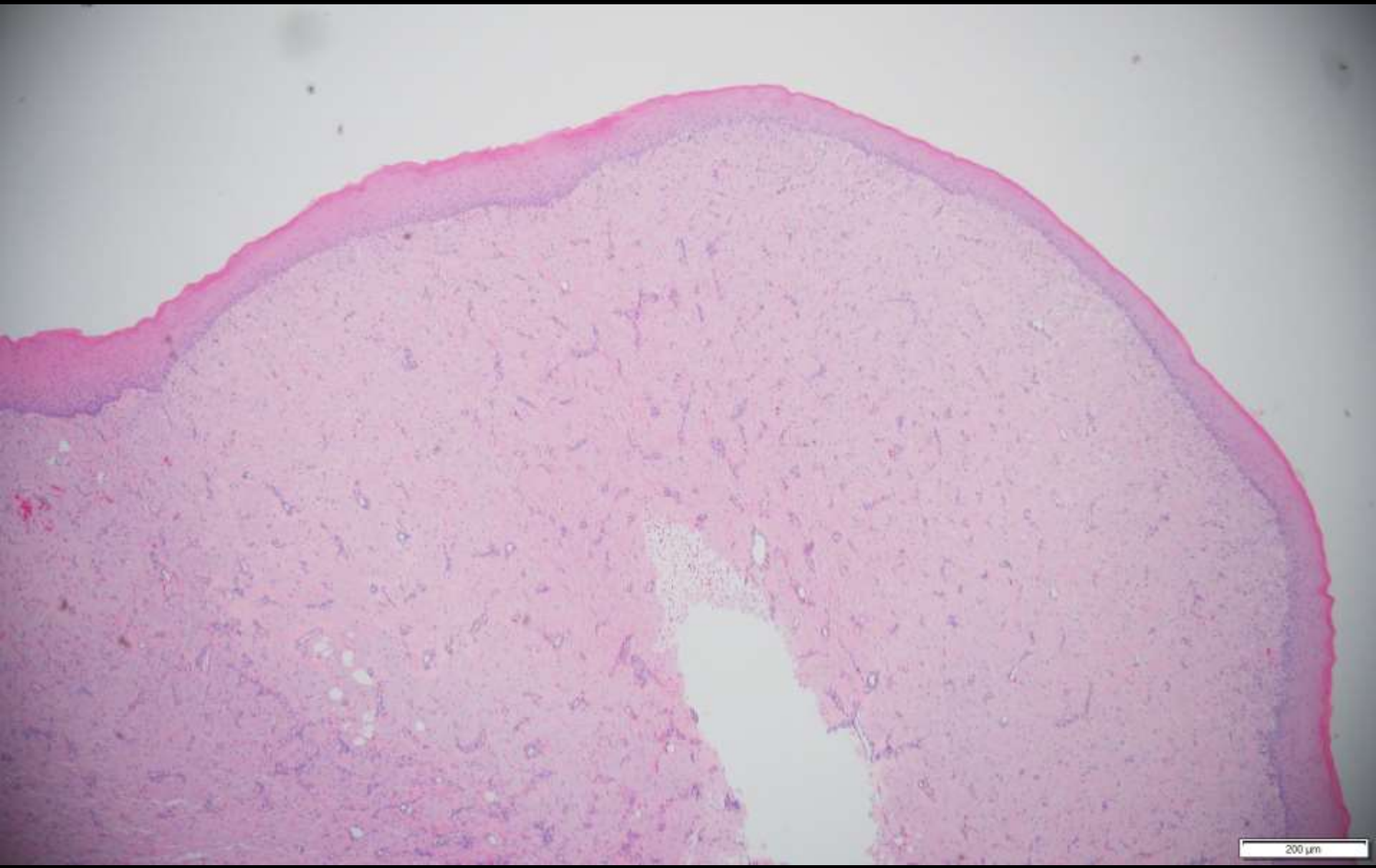


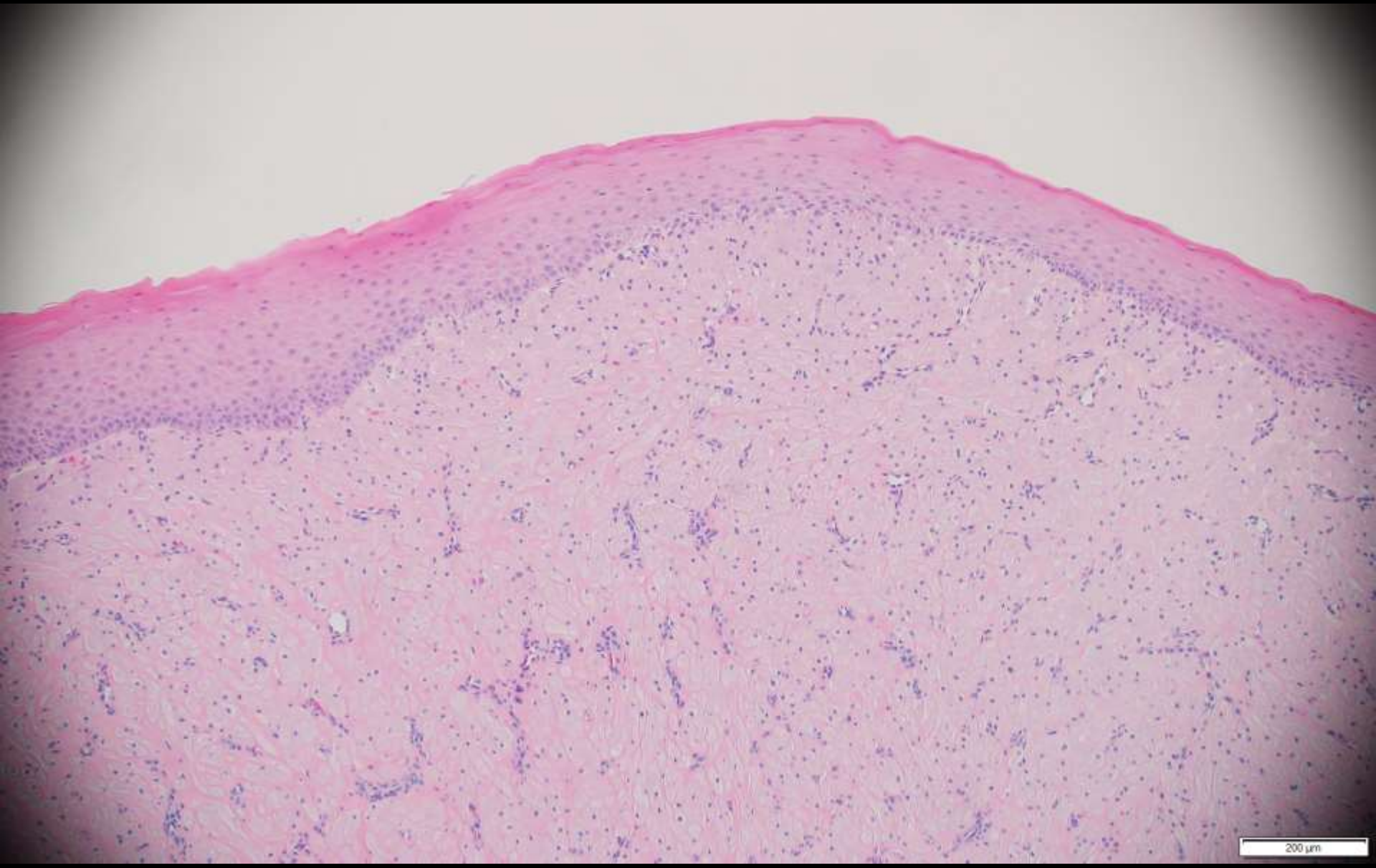






DIAGNOSIS?


200 µm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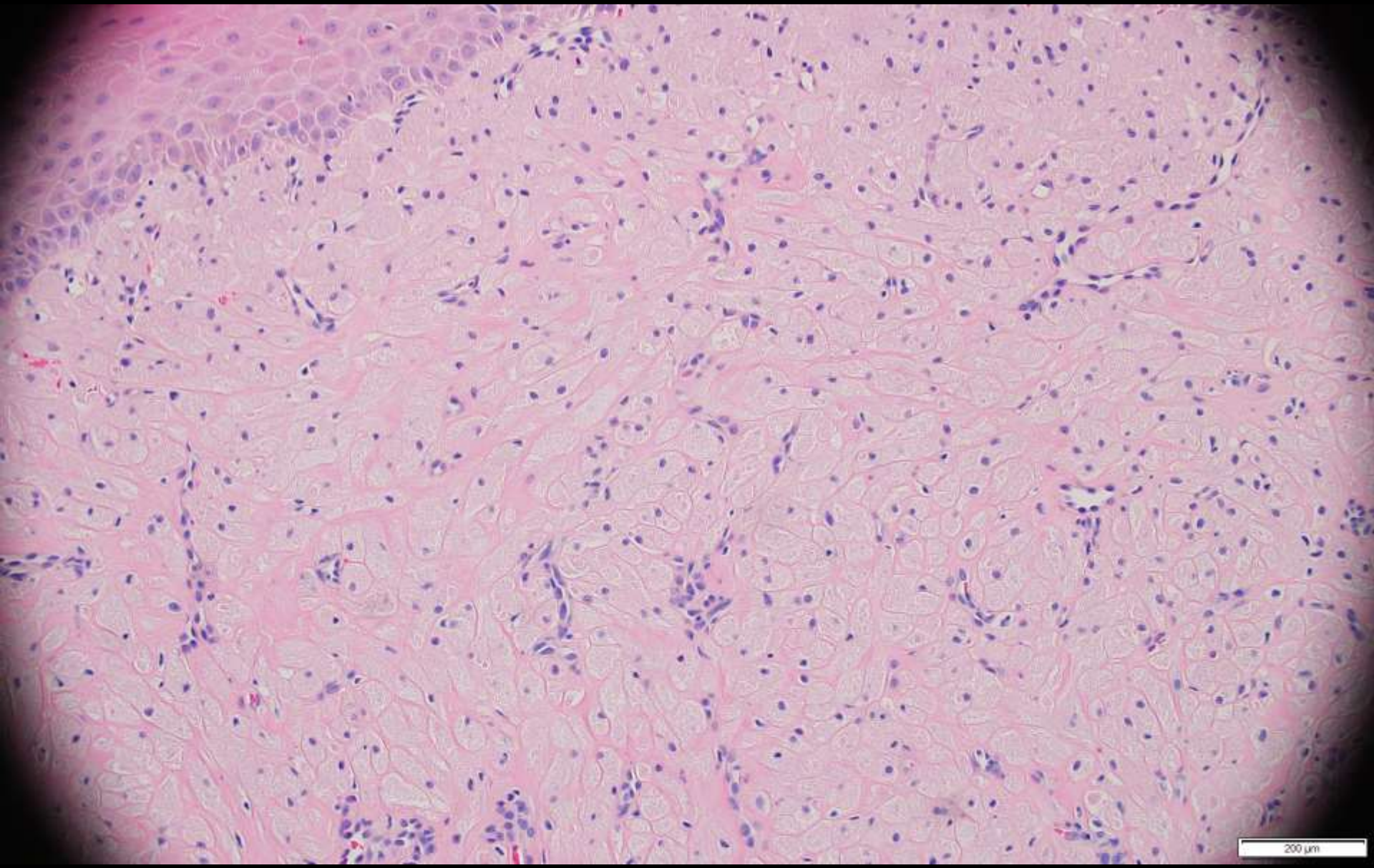
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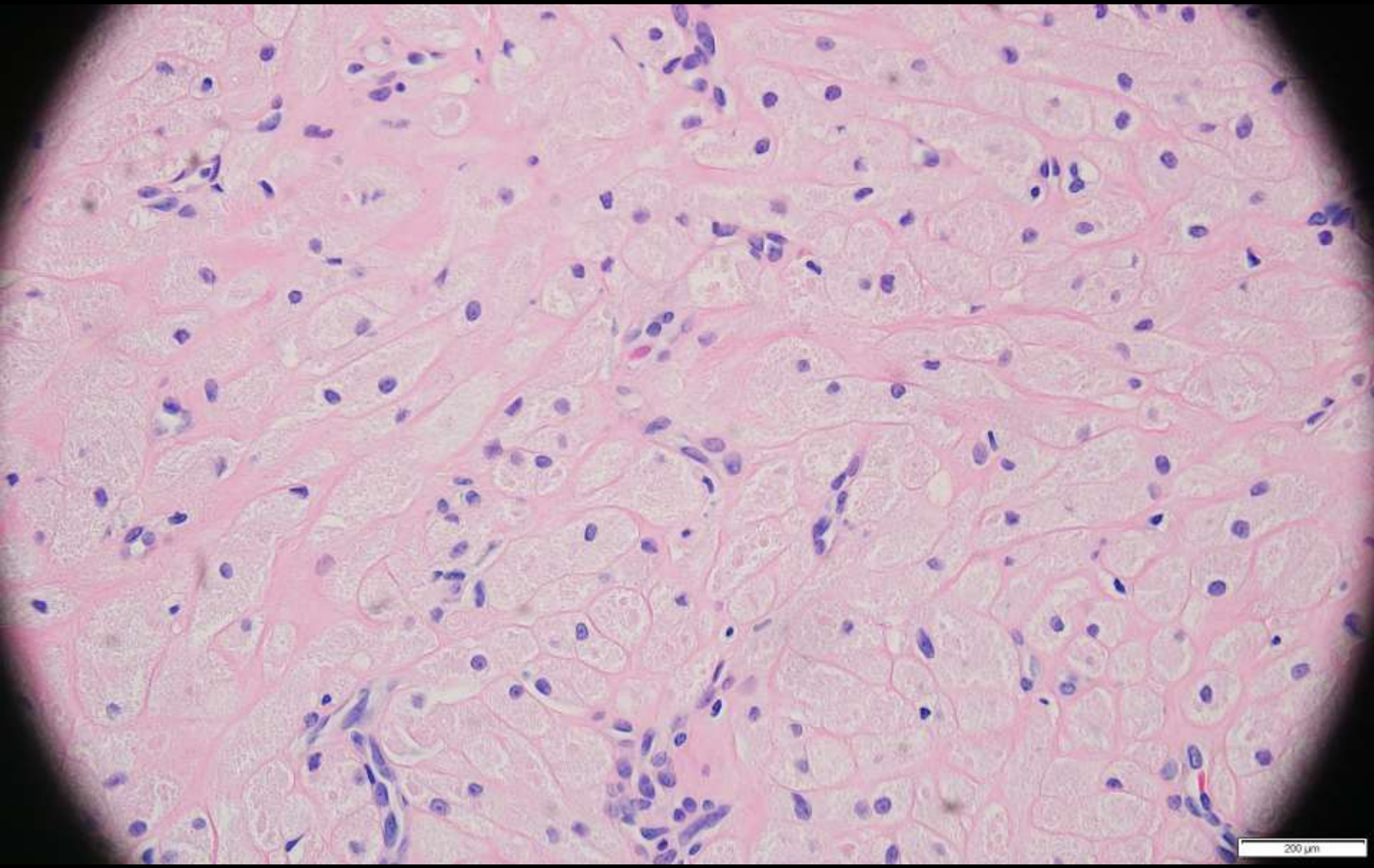
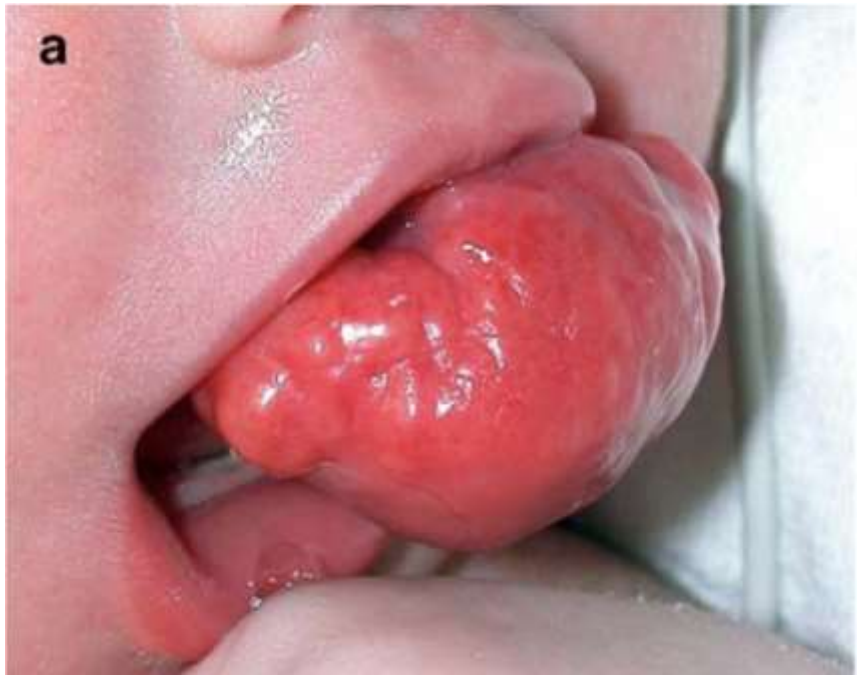

200 µm

Differential diagnosis

- Granular cell tumor
- Gingival granular cell tumor of the newborn (congenital epulis tumor)

Gingival granular cell tumor of the newborn

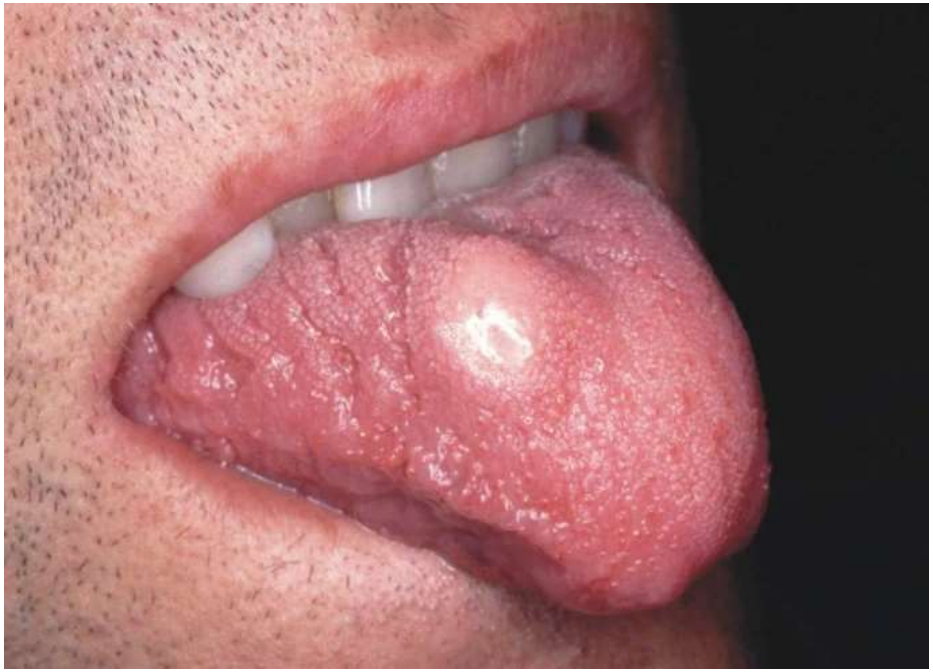
- Exclusively in newborn infants
- Predominately female (9-10:1, F:M)
- Solitary polypoid nodule
- Often attached to the labial aspect of the dental ridge
- 1-2 cm in diameter
  - Some can be > 3 cm
- Rarely recur, even with incomplete excision
- No malignant transformation reported



Vered, M., et al. Virchows Arch (2009)
Conrad, R., et al. Arch Pathol Lab Med (2014)

Granular cell tumor

- 30 - 60 year-old
- Female predominance (2:1, F:M)
- Painless nodule
- Often on the tongue
- Typically < 3 cm

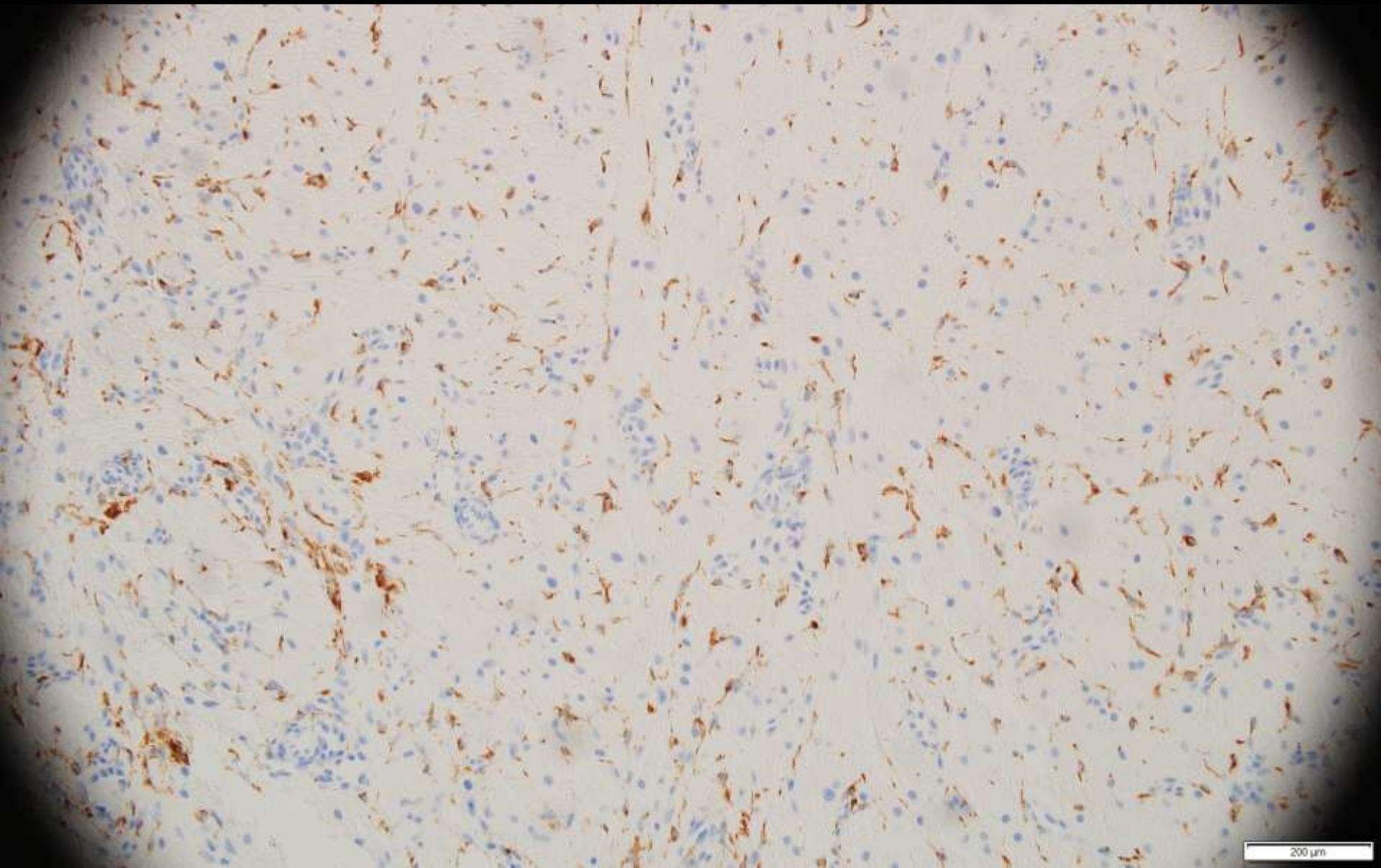


Sena Costa, N., et al. Journal of Medical Case Reports (2012)

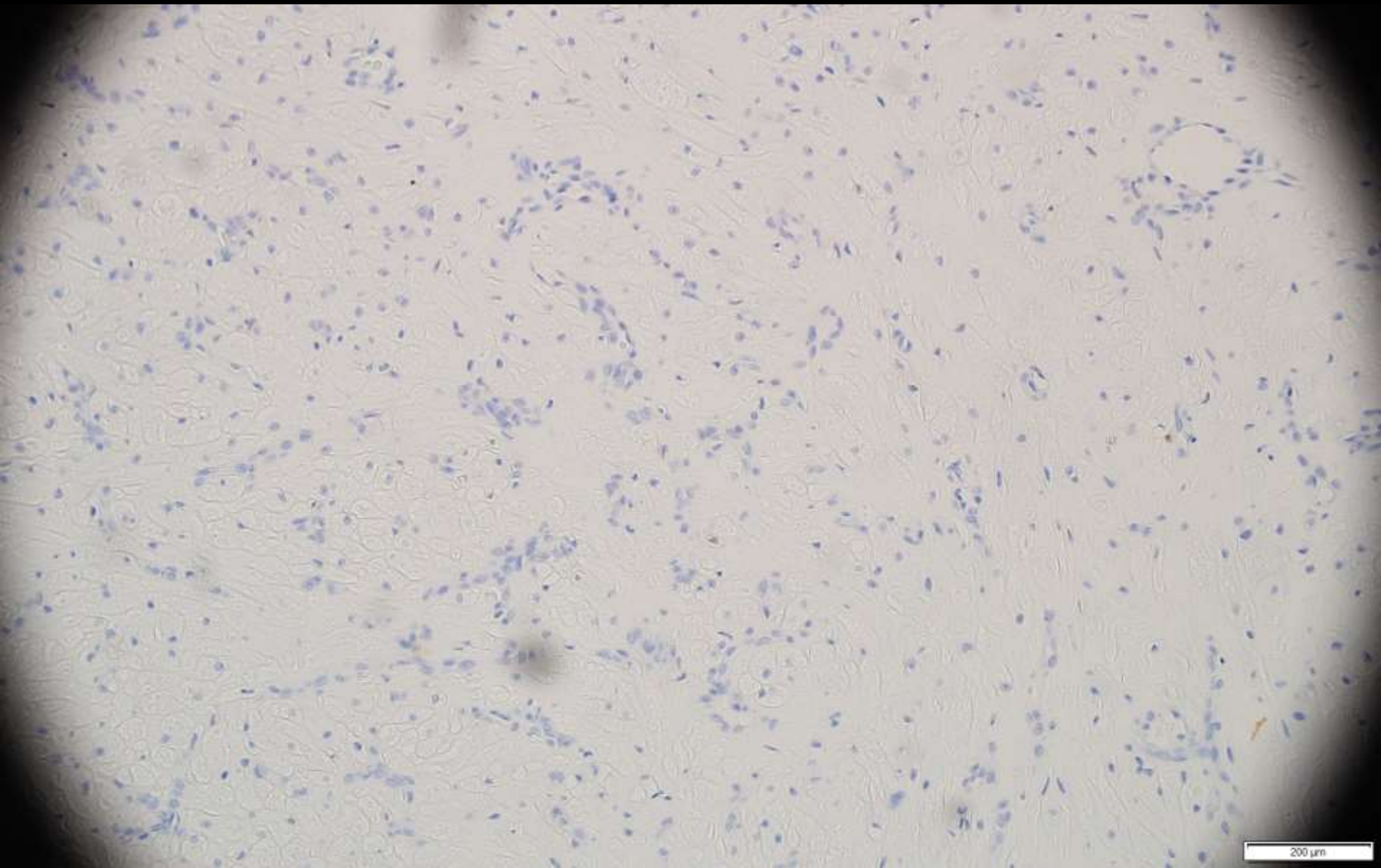
Immunohistochemical stains

- Granular cell tumor (of adults)
  - Positive stains: S100, SOX10, CD68
- Gingival granular cell tumor of the newborn
  - Positive stains: CD68 (variable)
  - Negative stains: S100

S100



CD68



Immunohistochemical stains: congenital epulis

Table 3 Staining pattern (score and intensity) of the granular cells for the various immunohistochemical stains

Specimen #	Vimentin	S-100[a,b]	NSE	CD-68 (KP-1)[a]	CD-68 (PG-1)[a]	Calretinin[a,b]	PGP9.5	NGFR/p75[b]	NKI/C3	Inhibin-α
1	4, +++	–	–	–	–	–	4, ++	–	4, ++	–
2	4, ++	–	3, ++	–	–	–	4, ++	–	4, +++	–
3	4, ++	–	4, ++	–	–	3, ++	4, ++	–	4, ++	–
4	4, ++	–	–	–	–	–	4, ++	–	3, ++	–
5	4, ++	–	–	–	–	–	2, ++	–	4, +++	–

[a] Positive interstitial cells
[b] Positive nerve bundles within the lesion

Vered, M., et al. Virchows Arch (2009)

Immunohistochemical stains

Table 3 Staining pattern (score and intensity) of the granular cells for the various immunohistochemical stains

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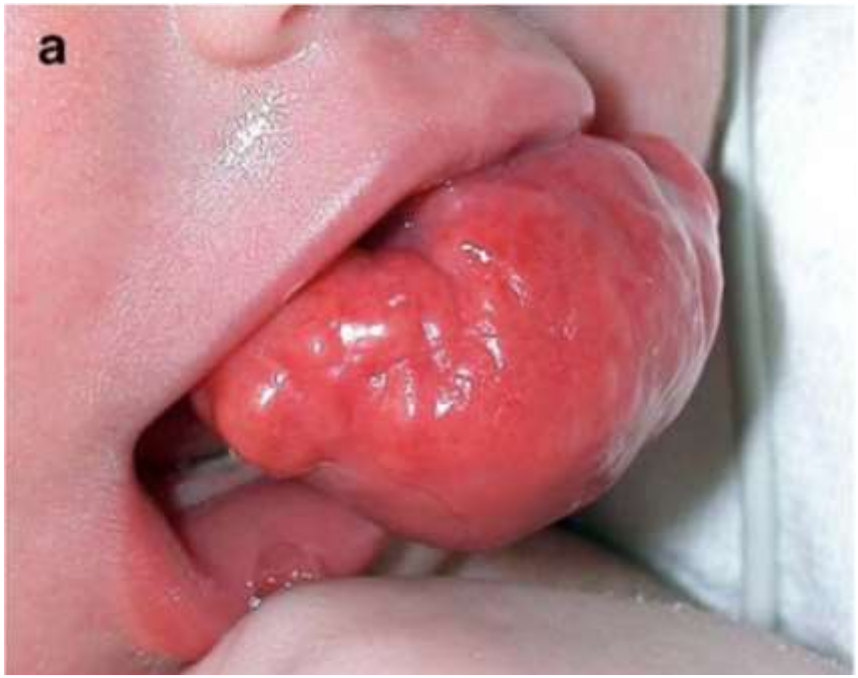
1	4, +++	–	–	–	–	–	4, ++	–	4, ++	–
2	4, ++	–	3, ++	–	–	–	4, ++	–	4, +++	–
3	4, ++	–	4, ++	–	–	3, ++	4, ++	–	4, ++	–
4	4, ++	–	–	–	–	–	4, ++	–	3, ++	–
5	4, ++	–	–	–	–	–	2, ++	–	4, +++	–

[a] Positive interstitial cells
[b] Positive nerve bundles within the lesion

Vered, M., et al. Virchows Arch (2009)

Gingival granular cell tumor of the newborn: take home points

- Newborn female infants
- On alveolar dental ridge
- Large polygonal cells with granular eosinophilic cytoplasm
- S-100 negative
- Resection is generally curative



Vered, M., et al. Virchows Arch (2009)
Conrad, R., et al. Arch Pathol Lab Med (2014)

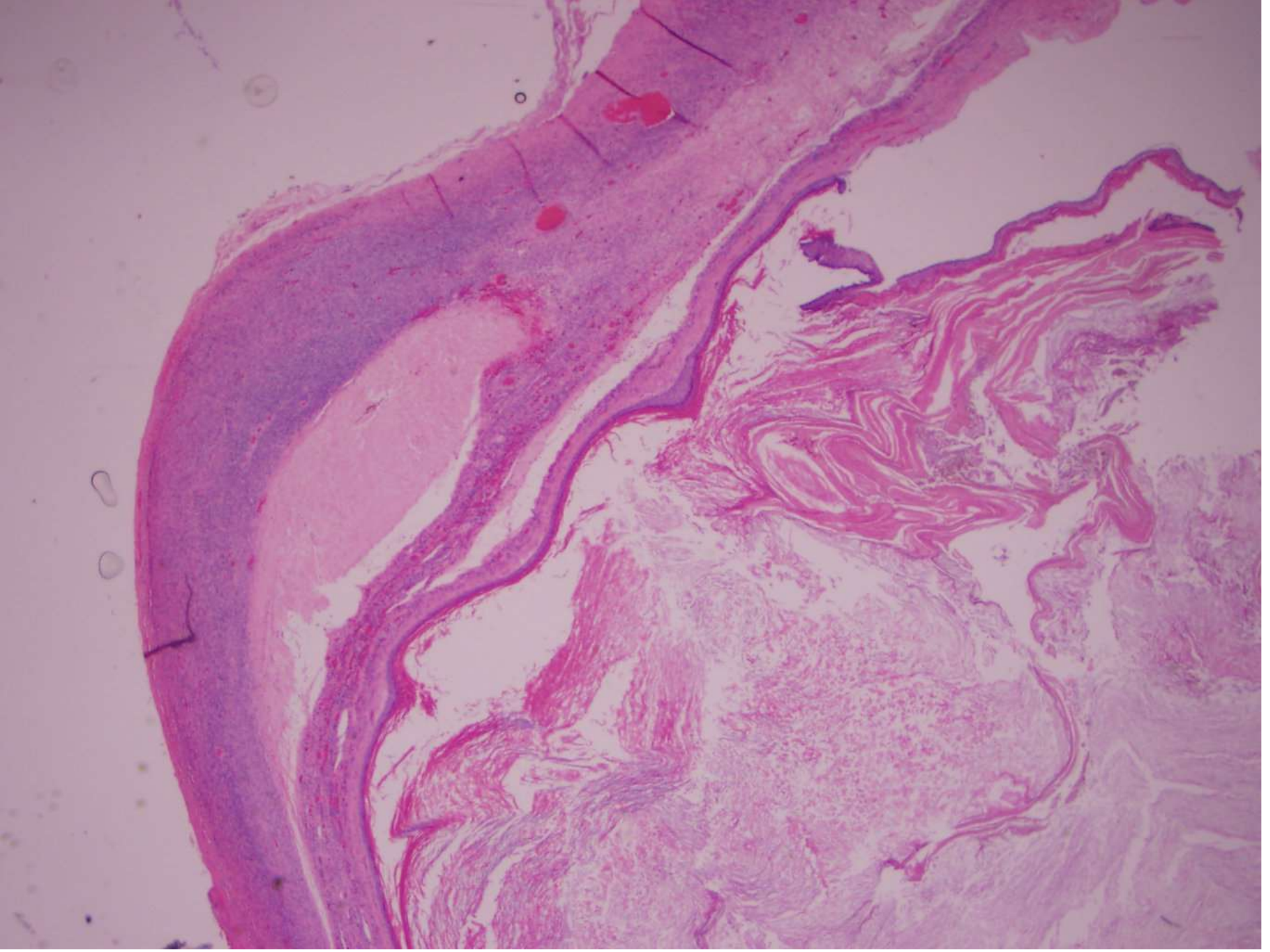
References

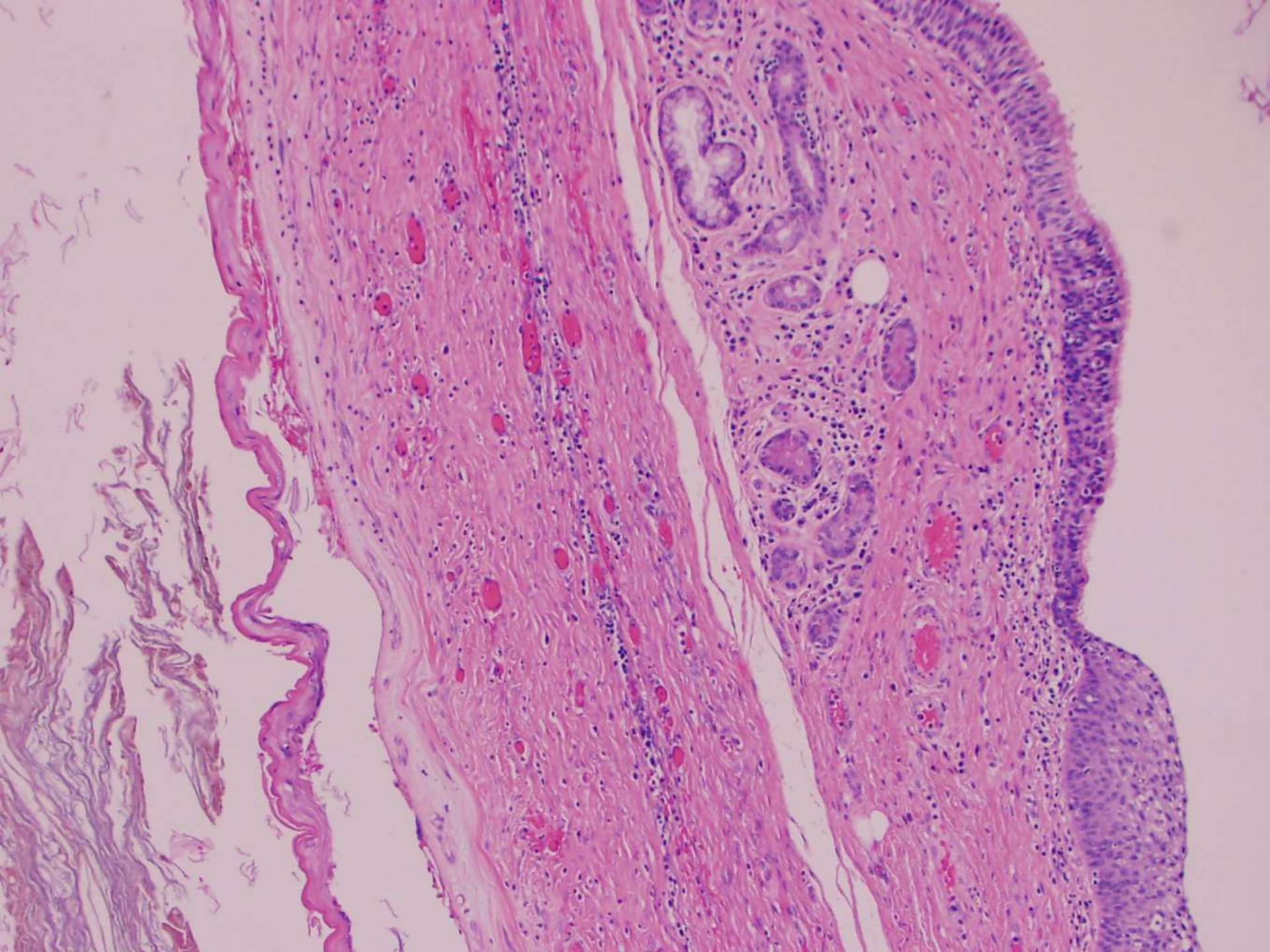
- Conrad, R, et. al. Congenital Granular Cell Epulis, Arch Pathol Lab Med (2014) 138:128-131.
- Vered, M, et. al. Congenital granular cell epulis presents an immunohistochemical profile that distinguishes it from granular cell tumor of the adult. Virchows Arch (2009) 454: 303-310.
- Sena Costa, N.C., Bertini, F., Carvalho, Y.R. *et al.* Granular cell tumor presenting as a tongue nodule: two case reports. *J Med Case Reports* **6,** 56 (2012).

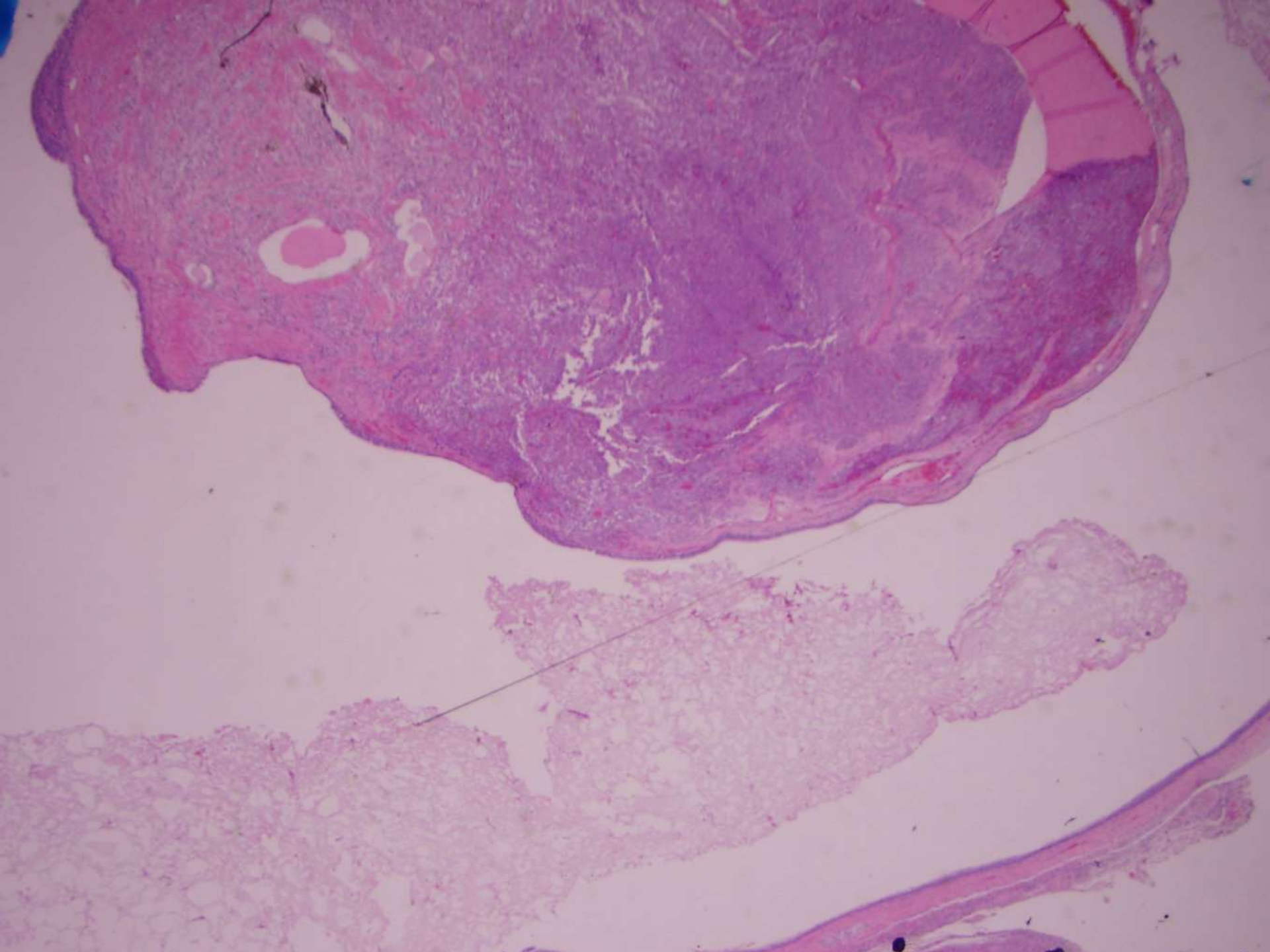
20-0702

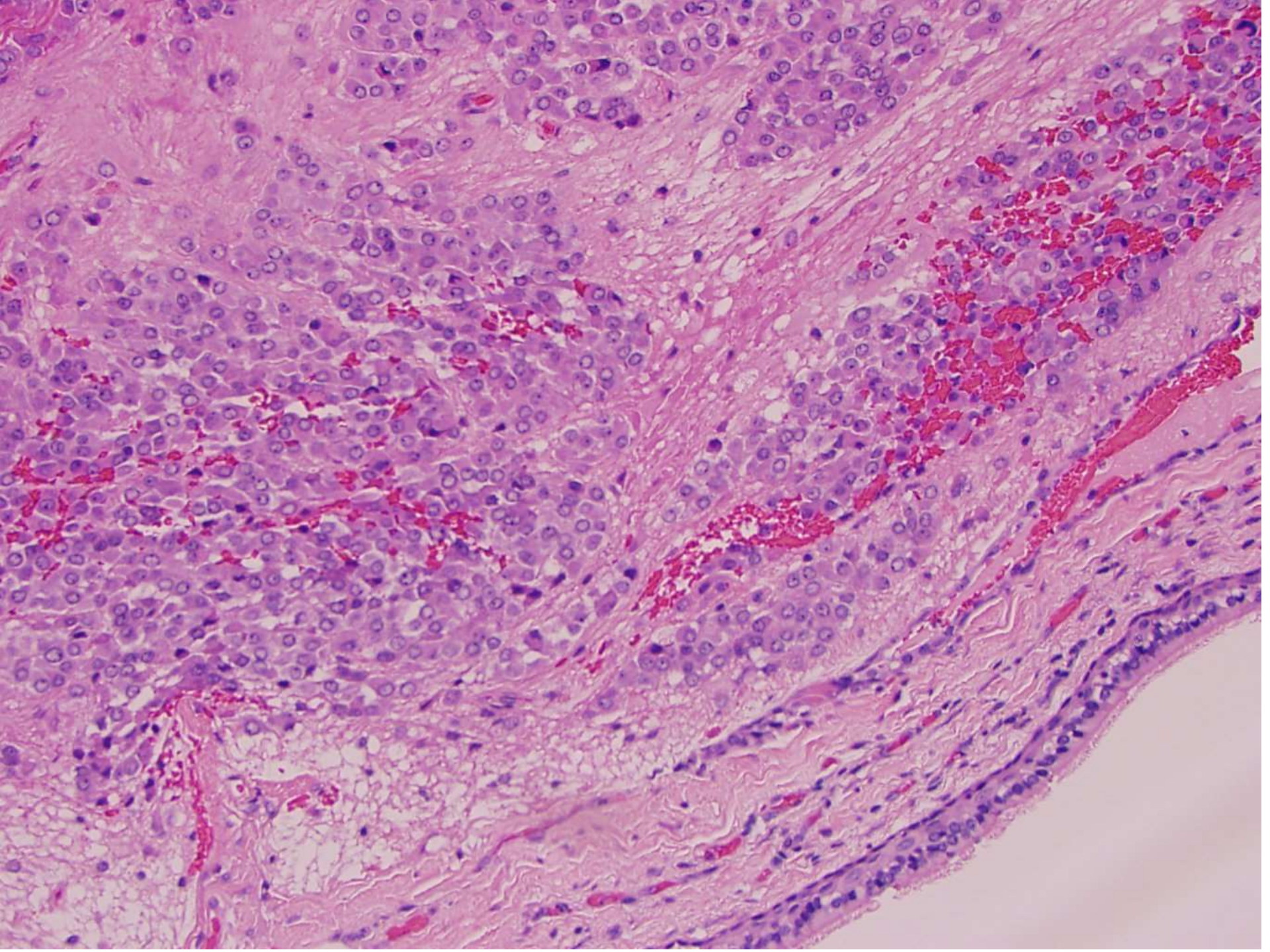
Greg Rumore/Greg Moes; Kaiser Diablo/Kaiser Oakland

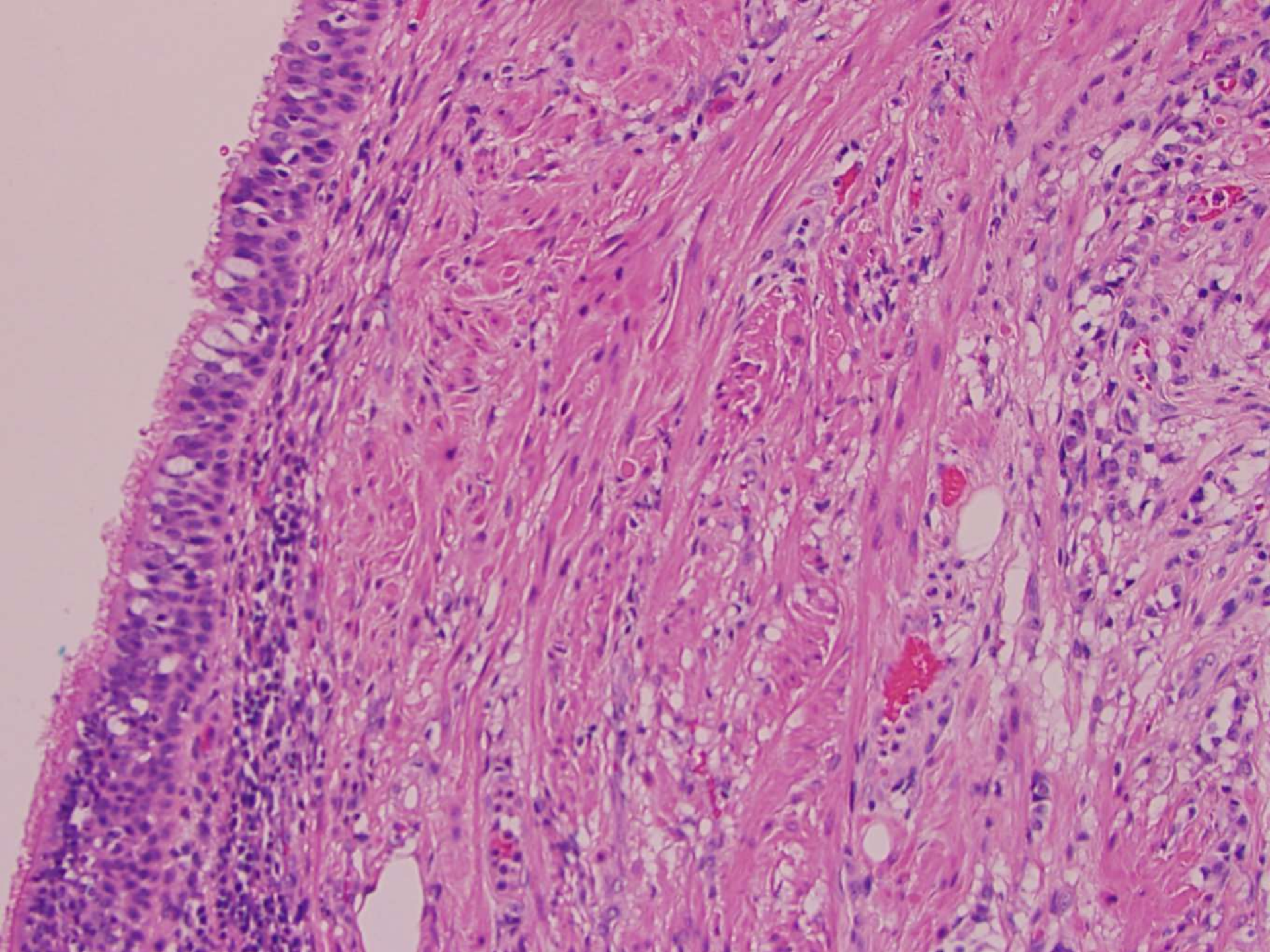
60-year-old F with post-menopausal bleeding and cystic right ovarian mass.

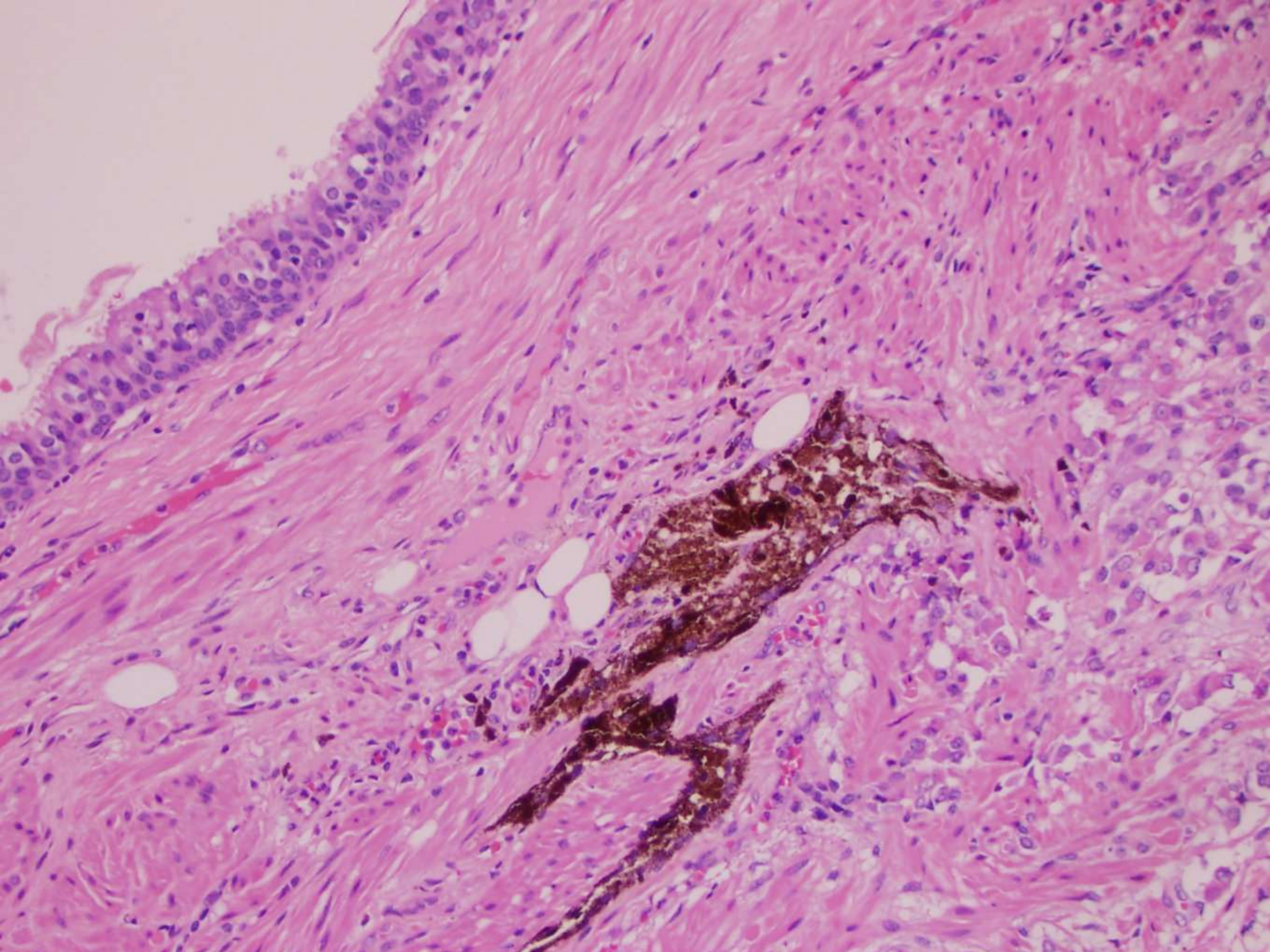


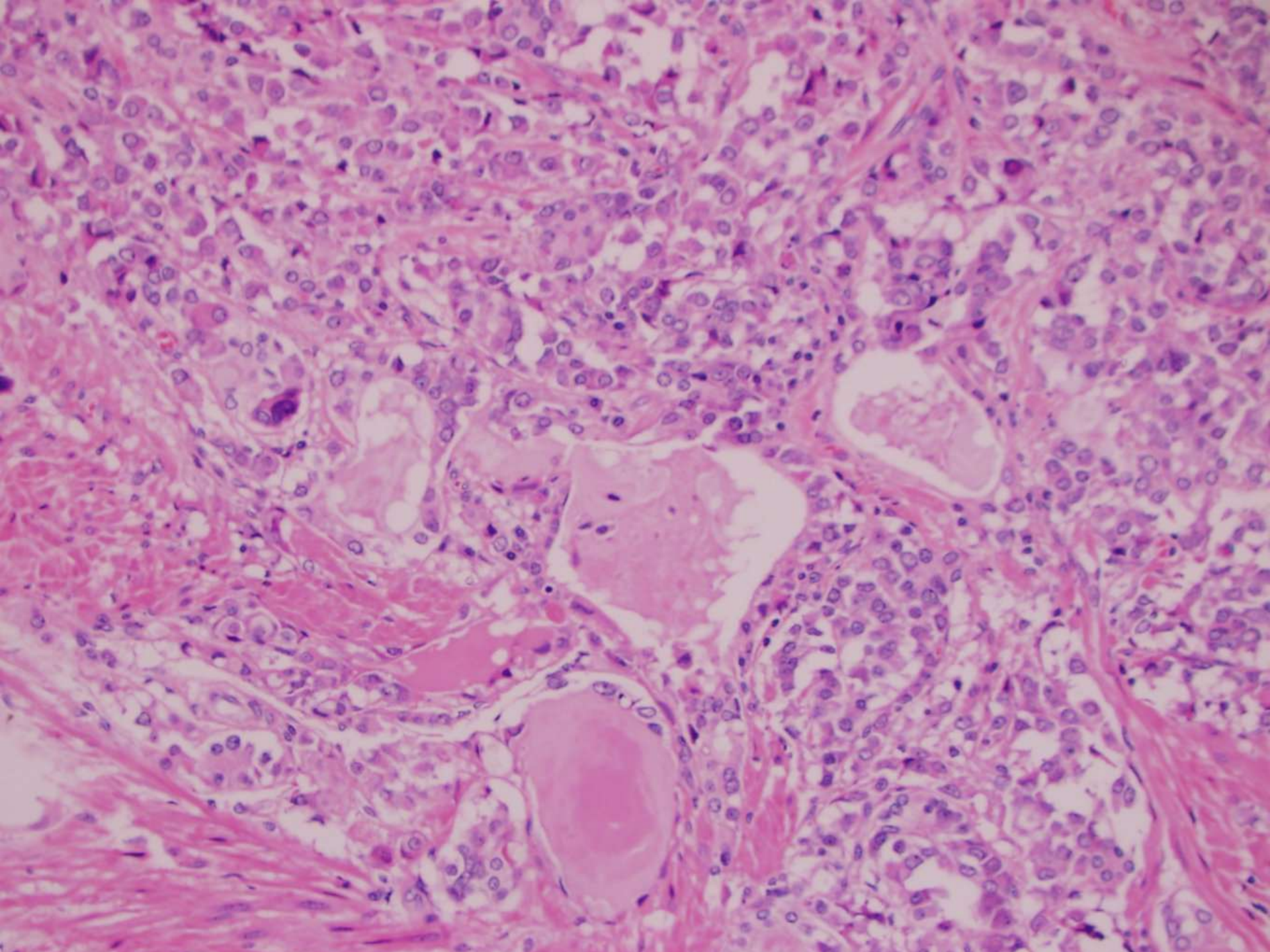


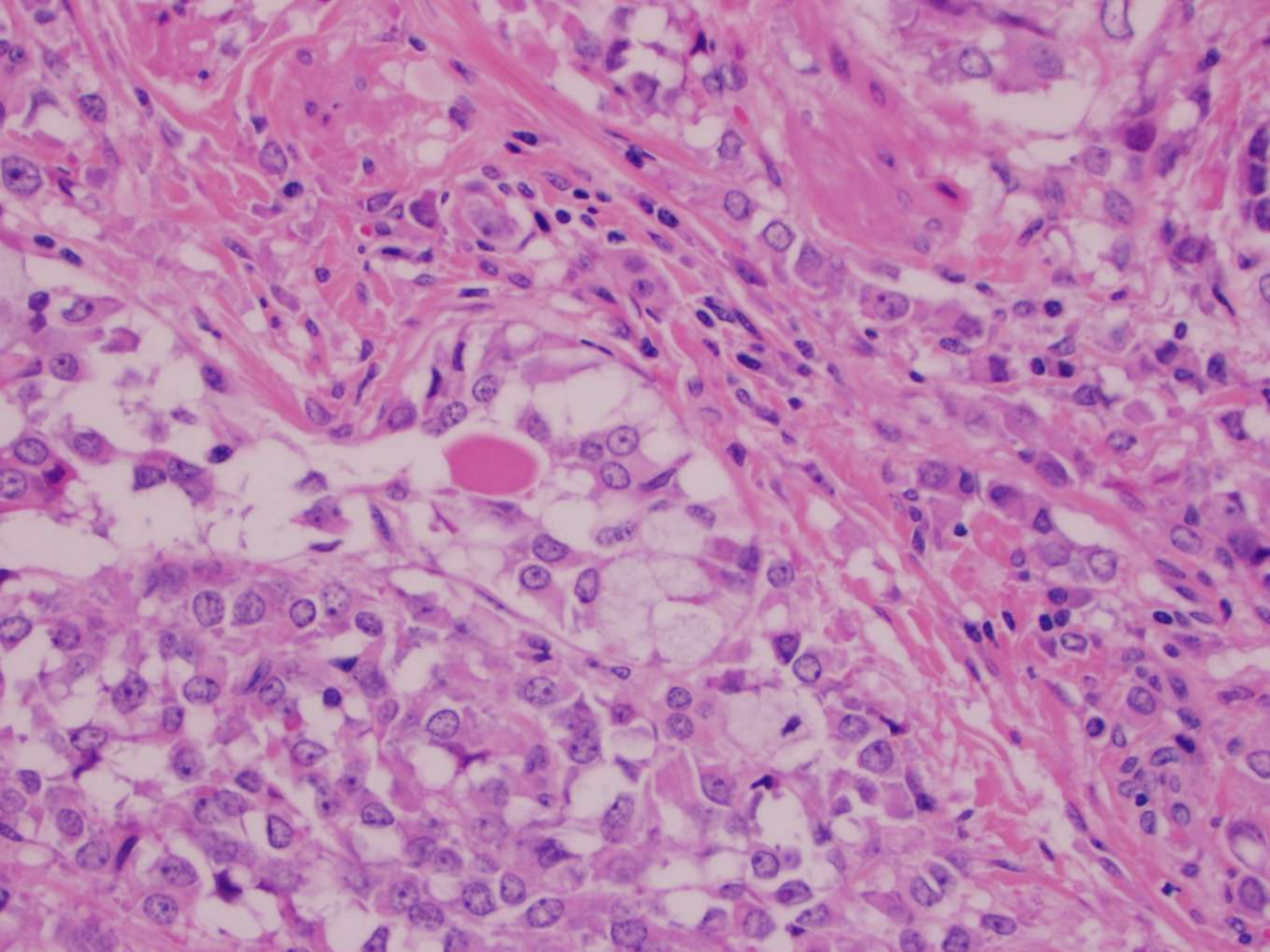


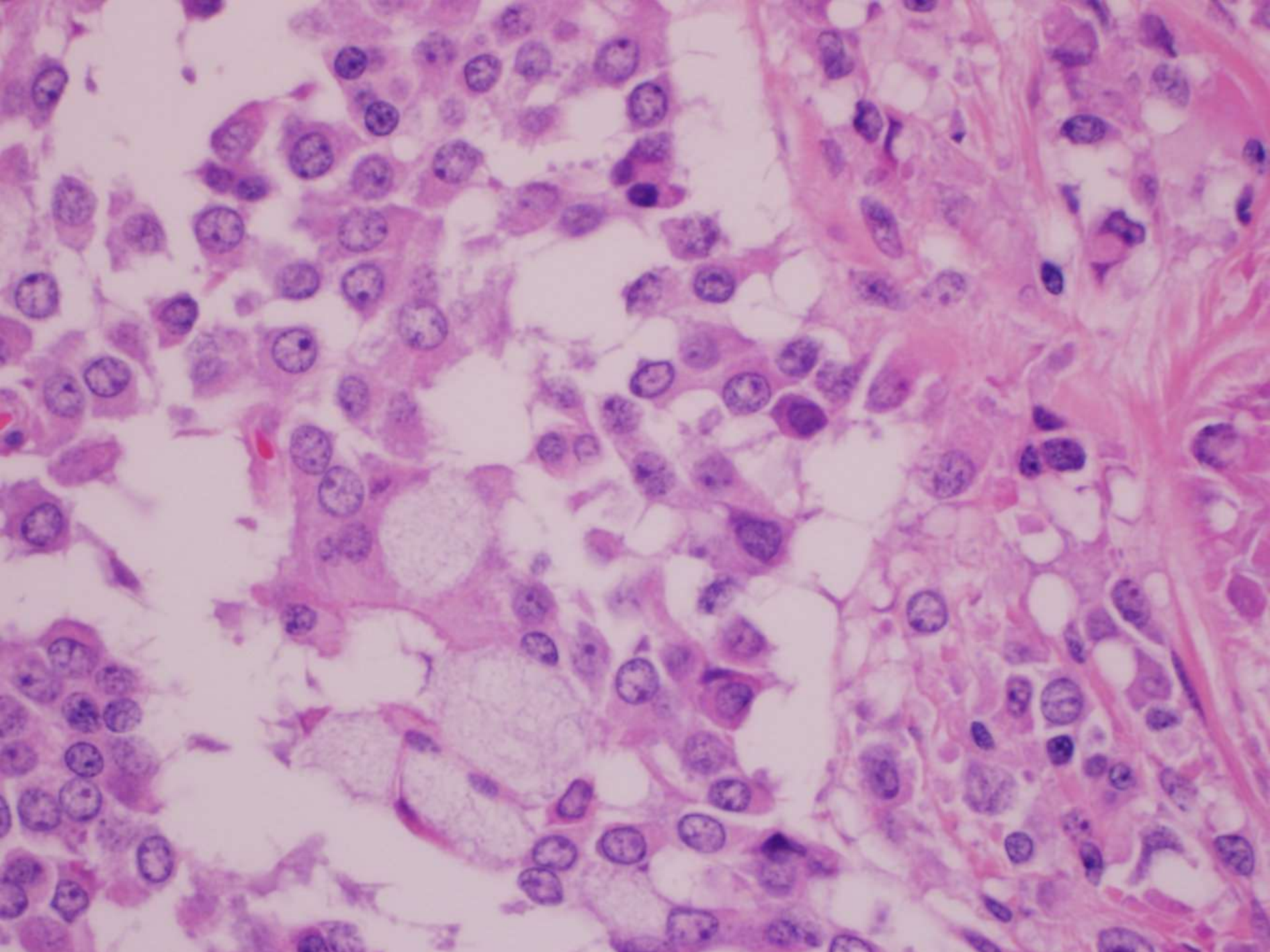


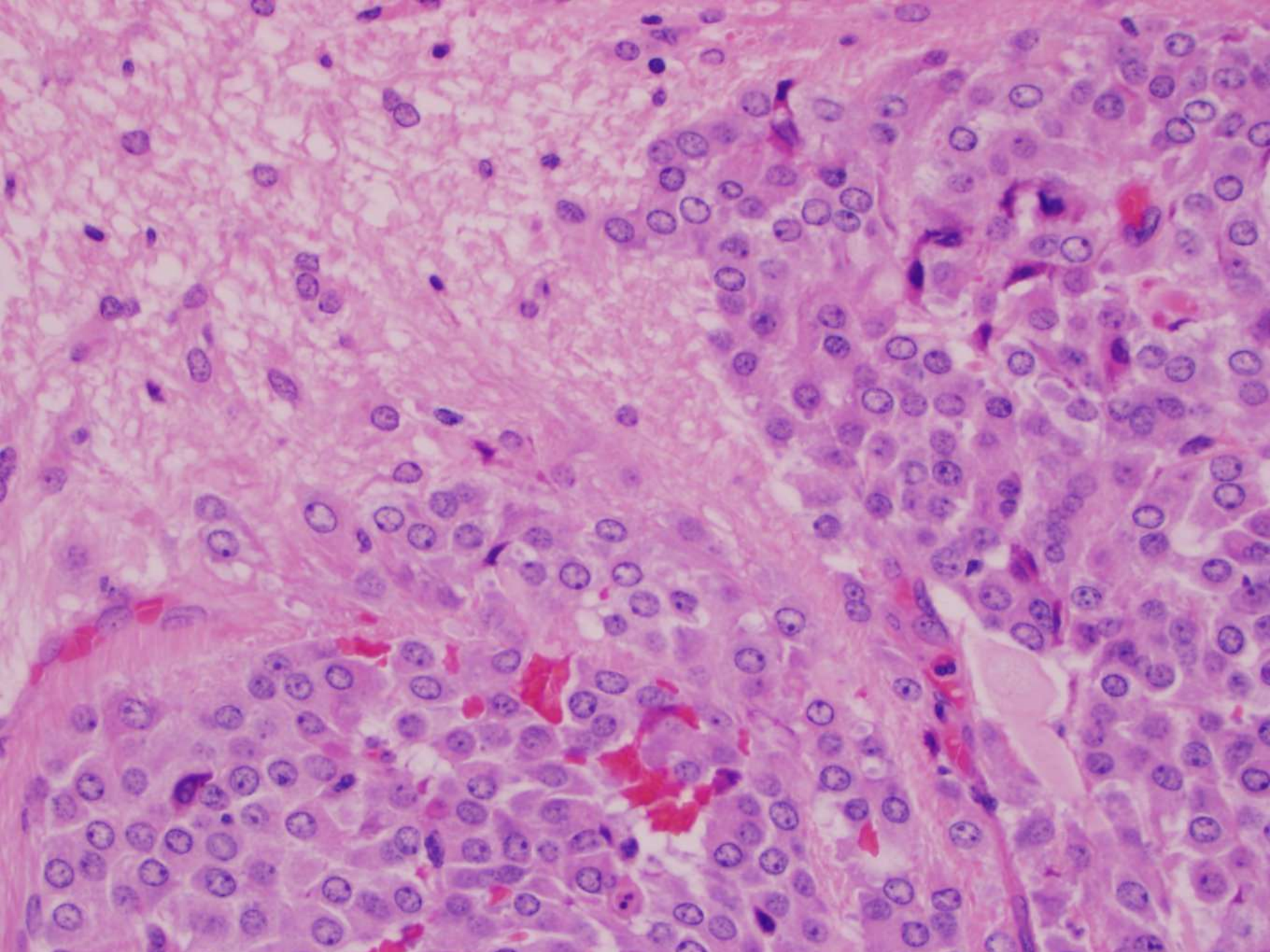


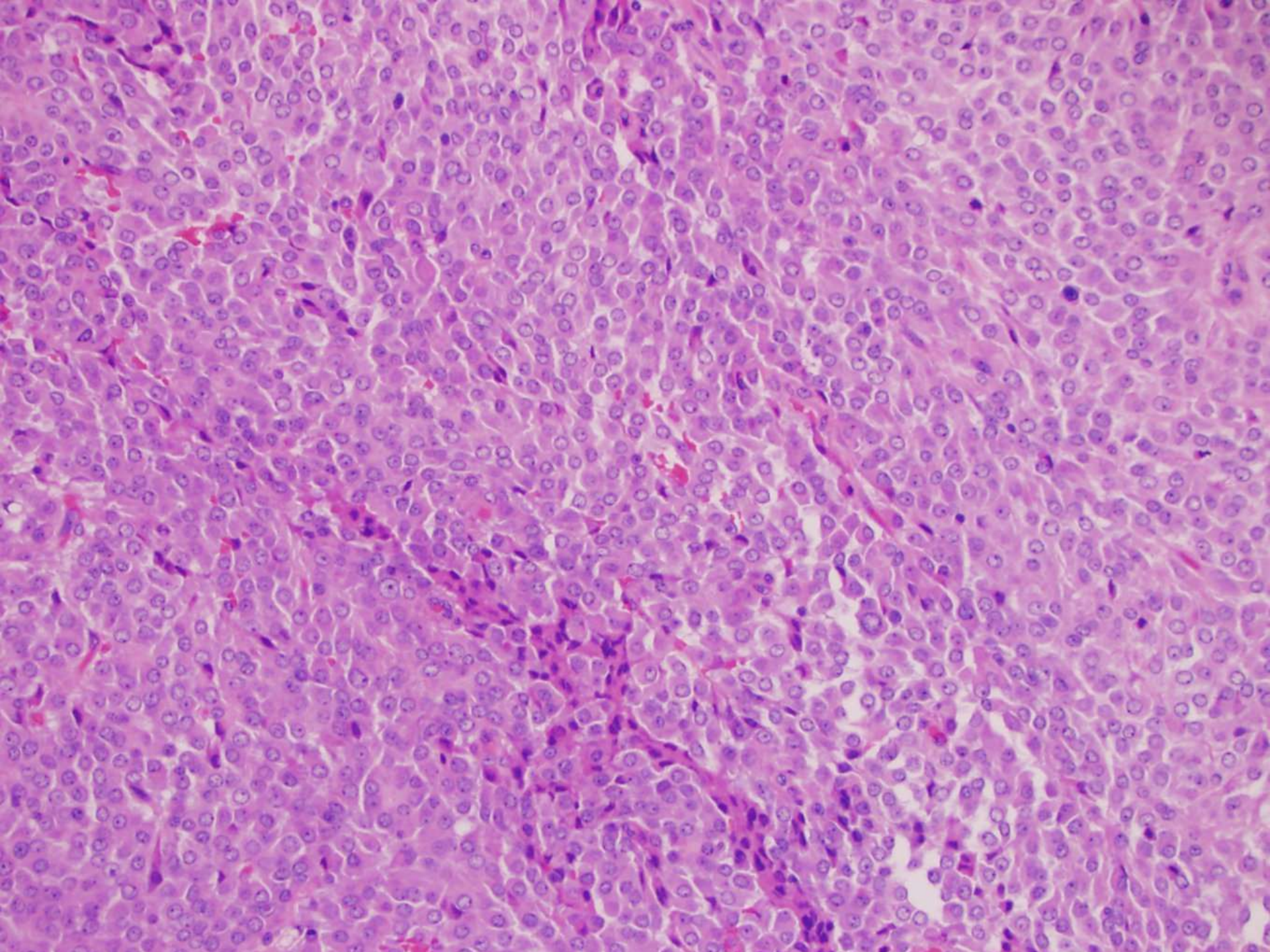


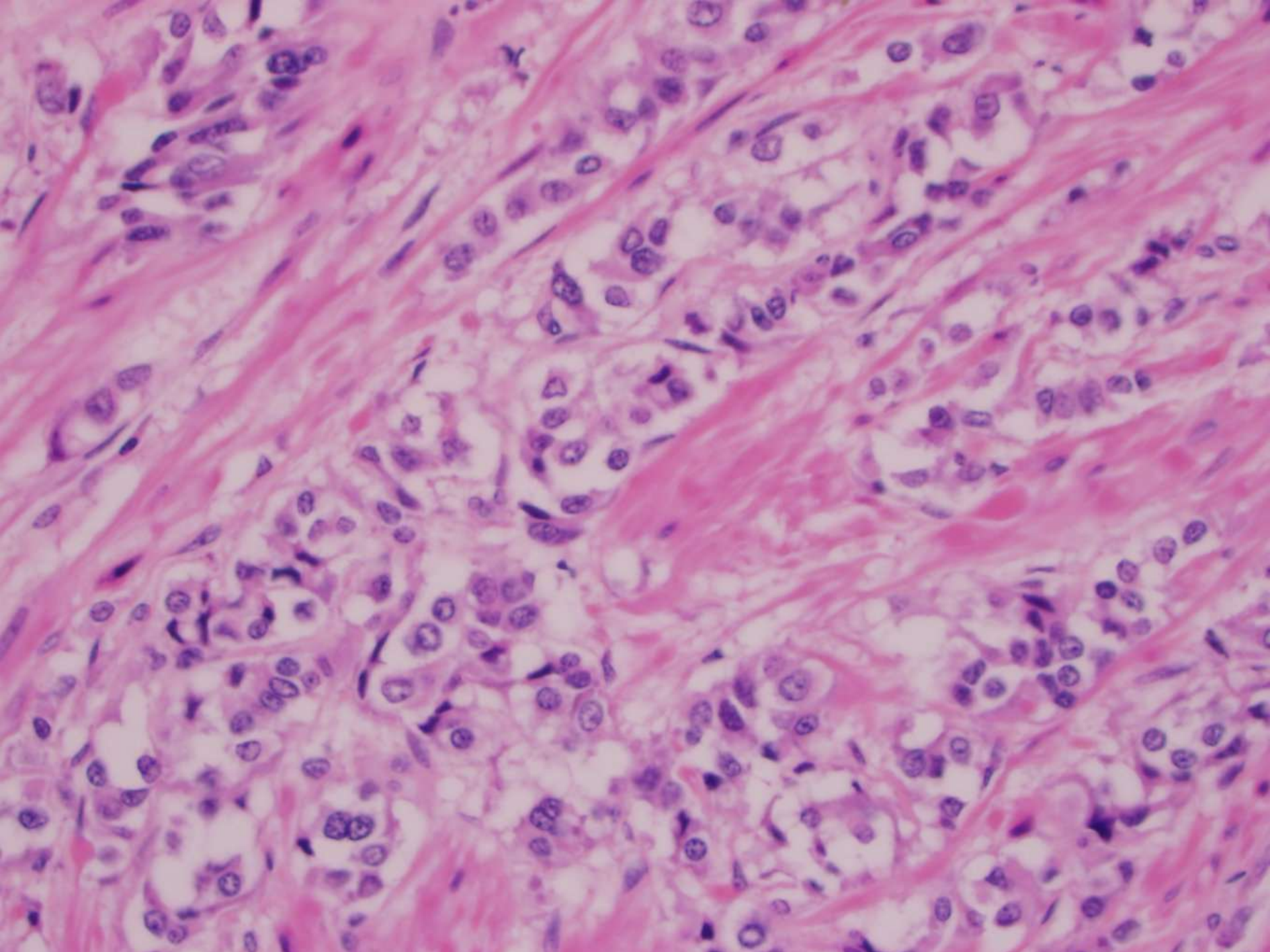


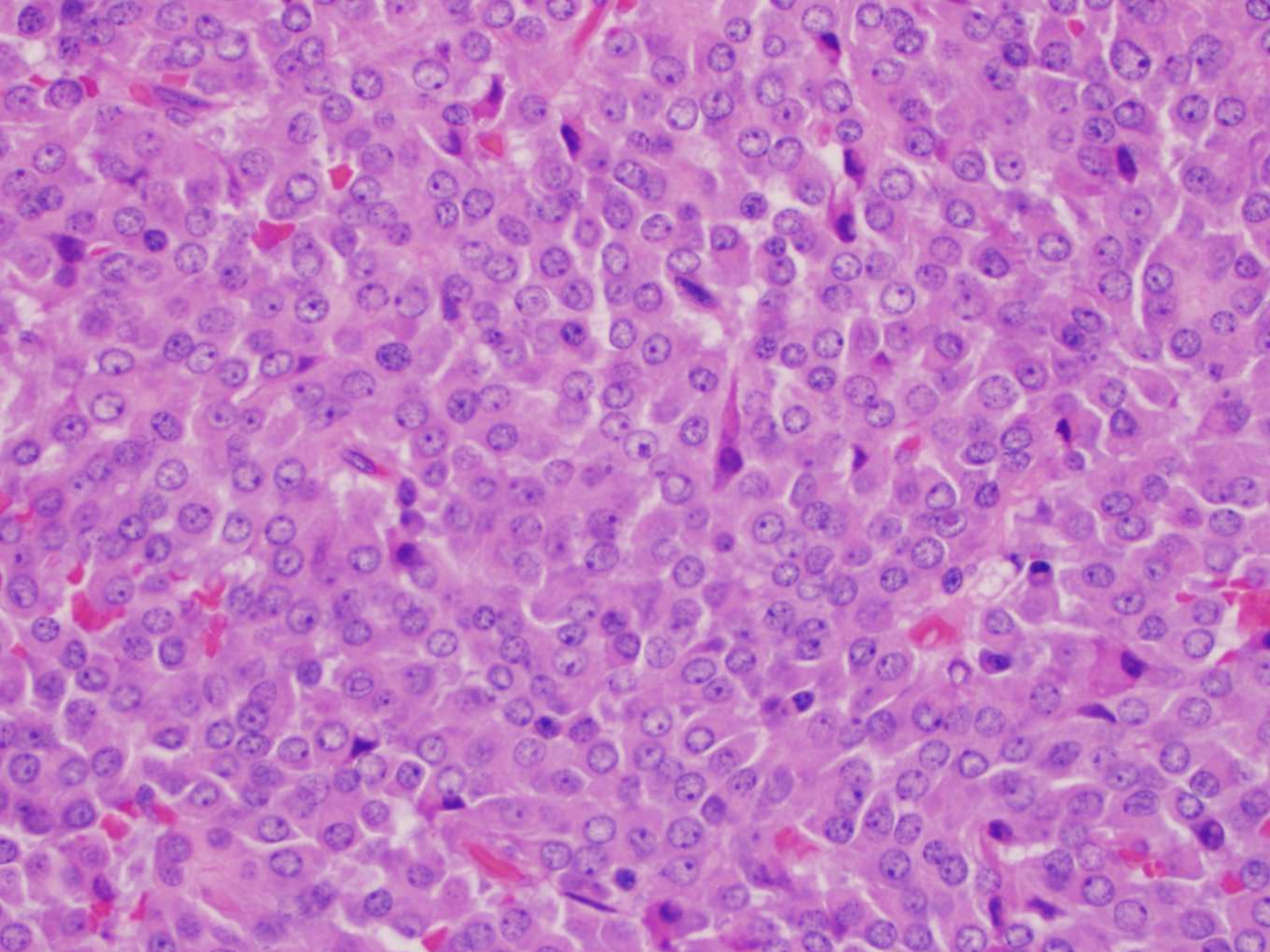


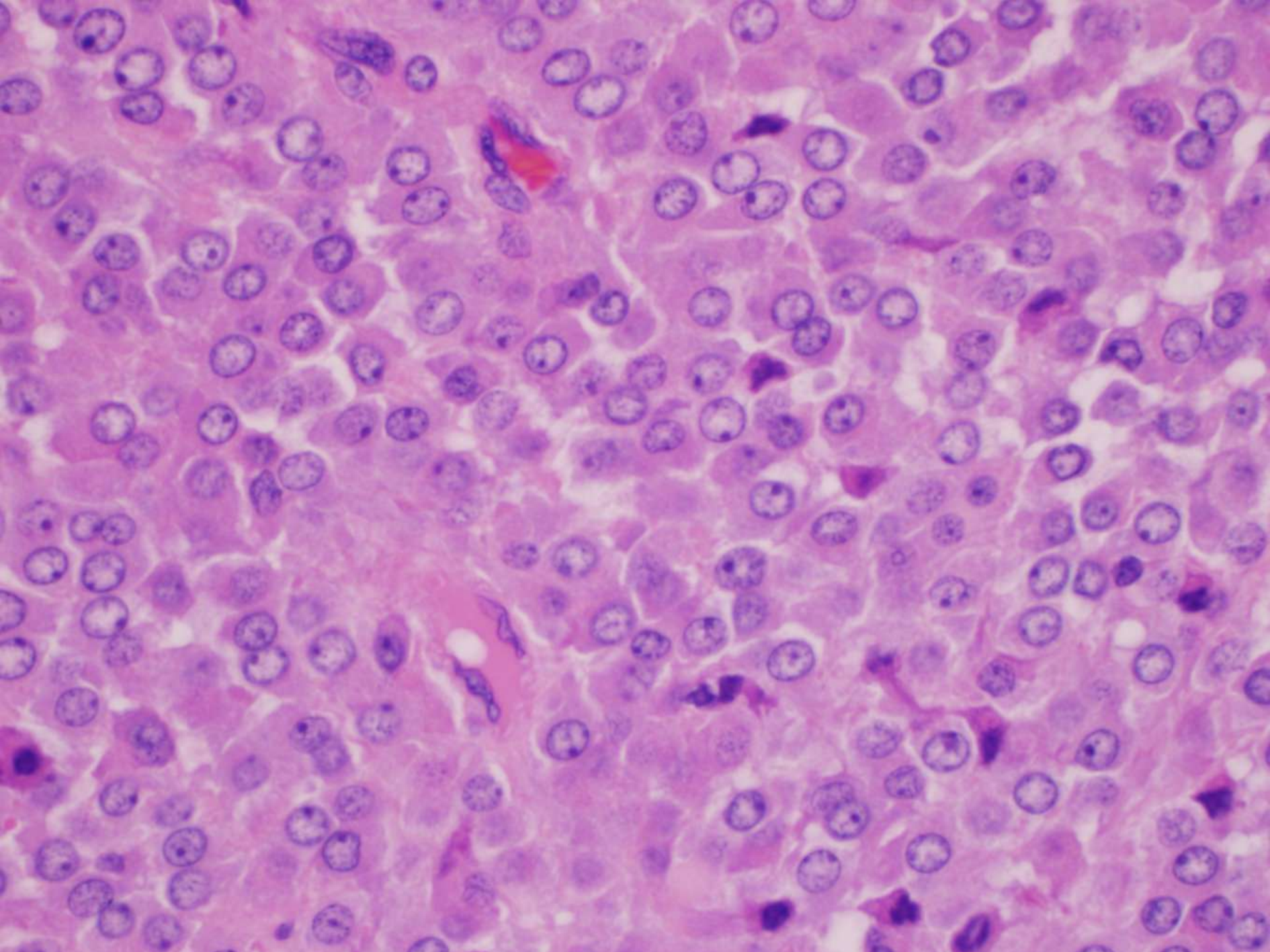








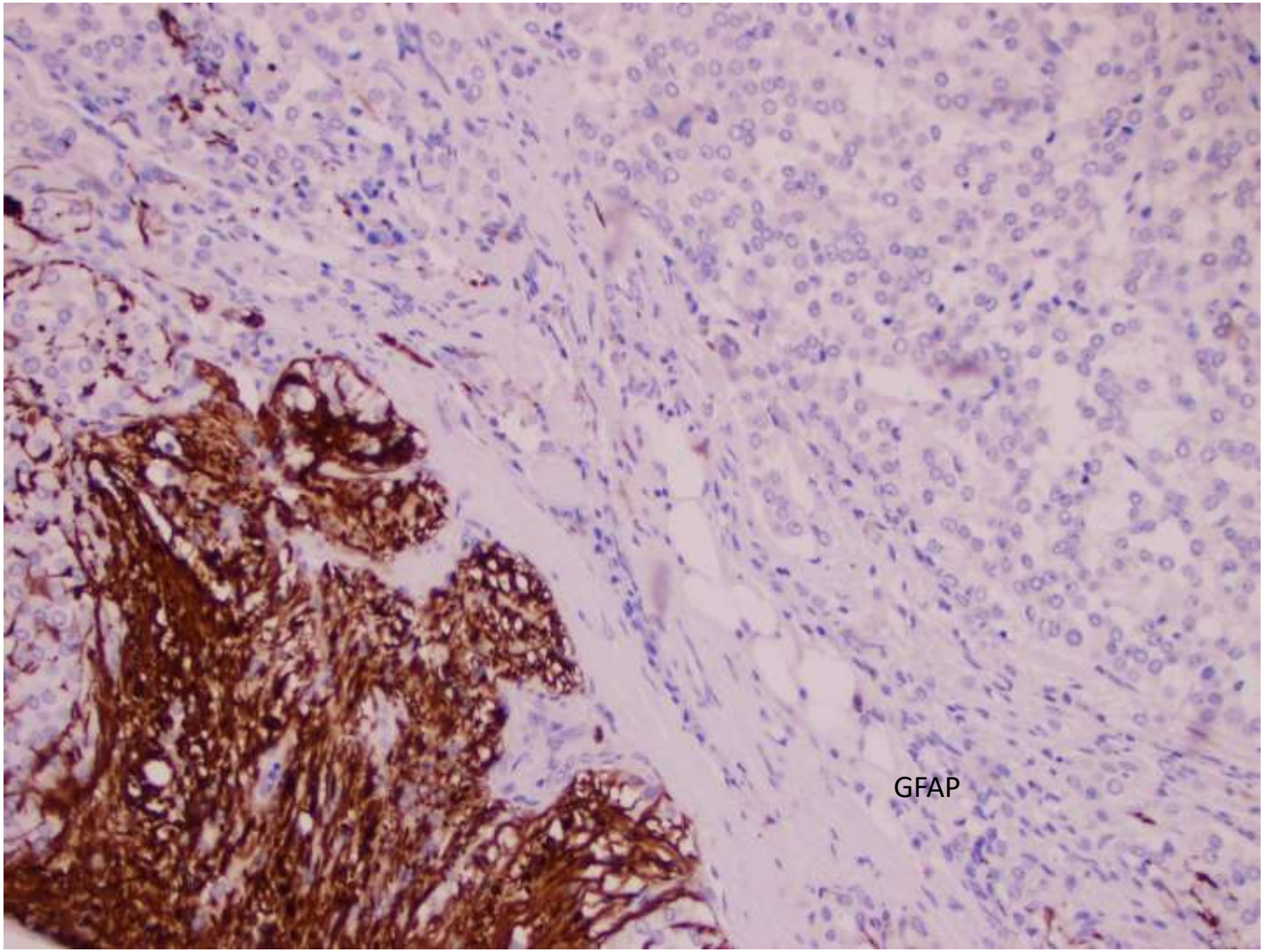




DIAGNOSIS?

Diagnosis:

- Mature Cystic Teratoma with “Double” or Plurihormonal Pituitary Adenoma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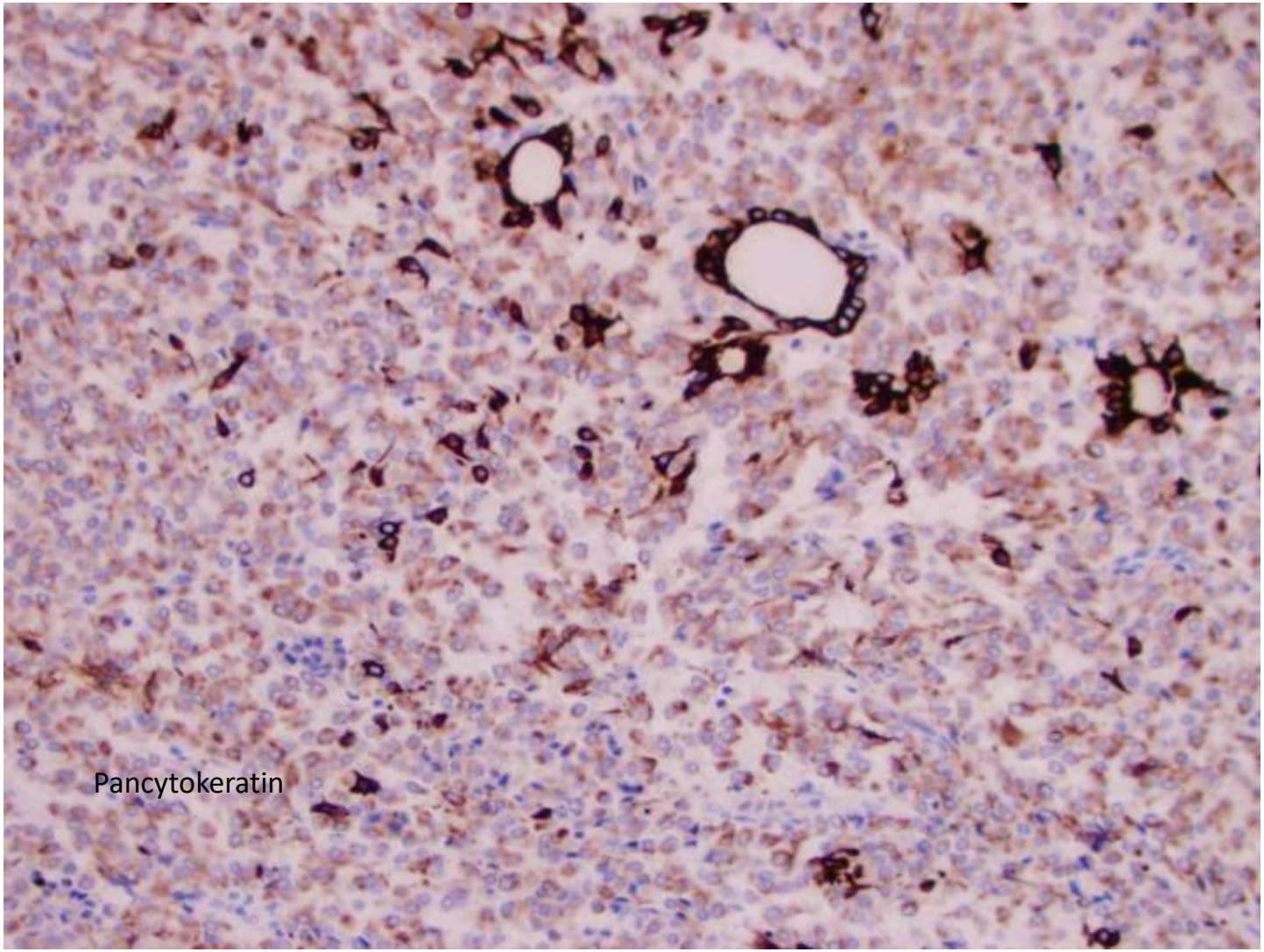
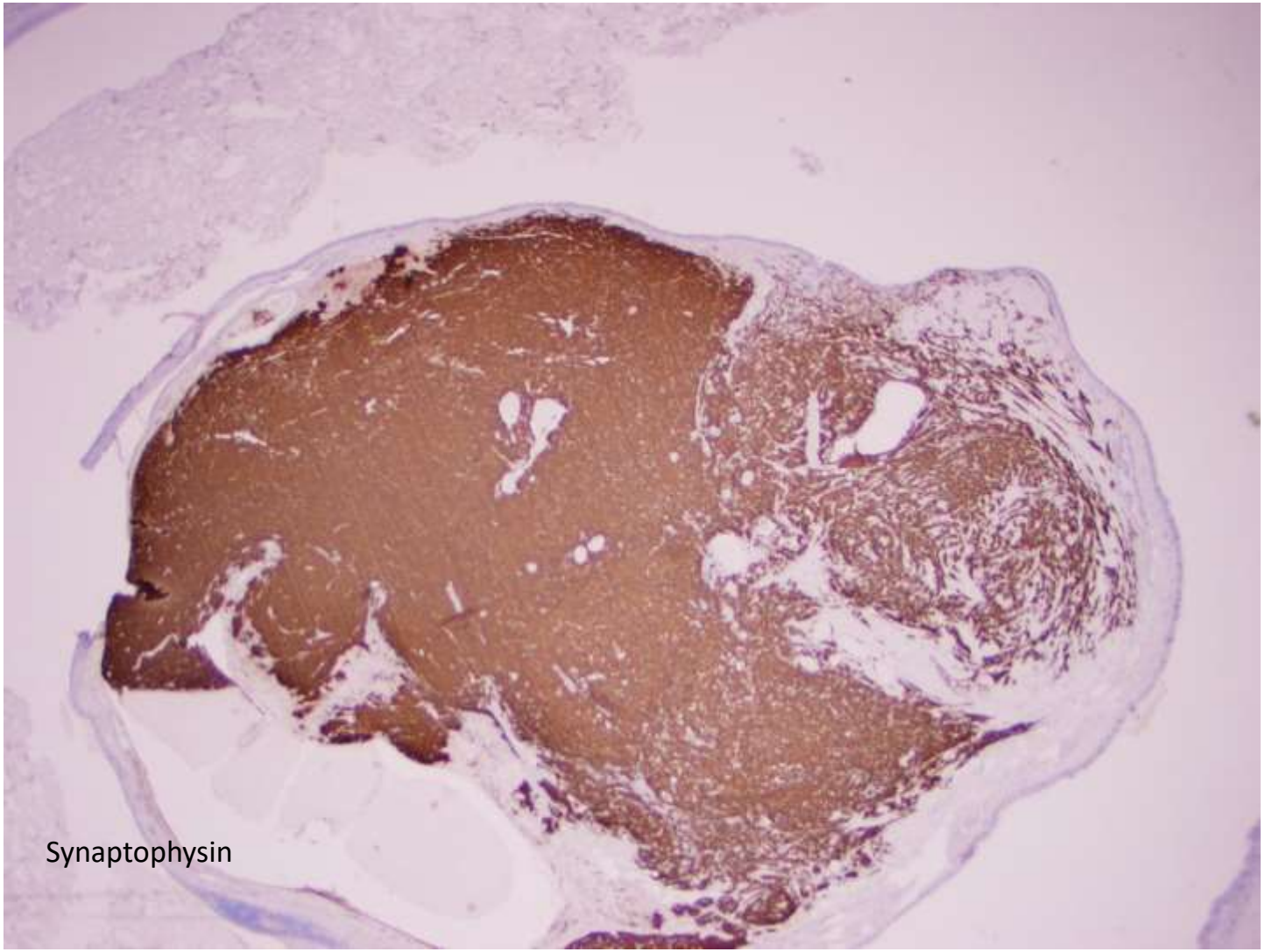
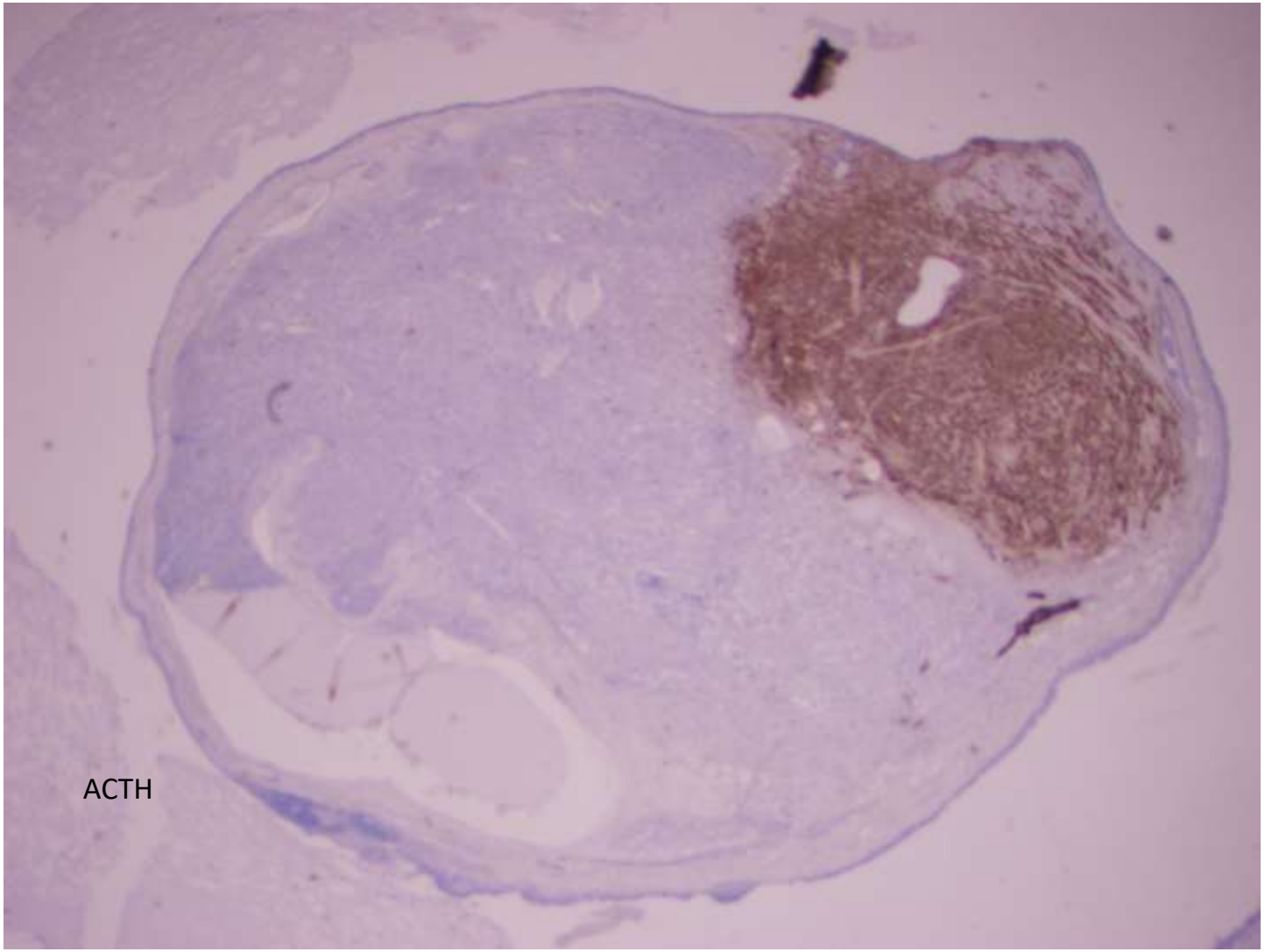

Pancytokeratin


Synaptophysin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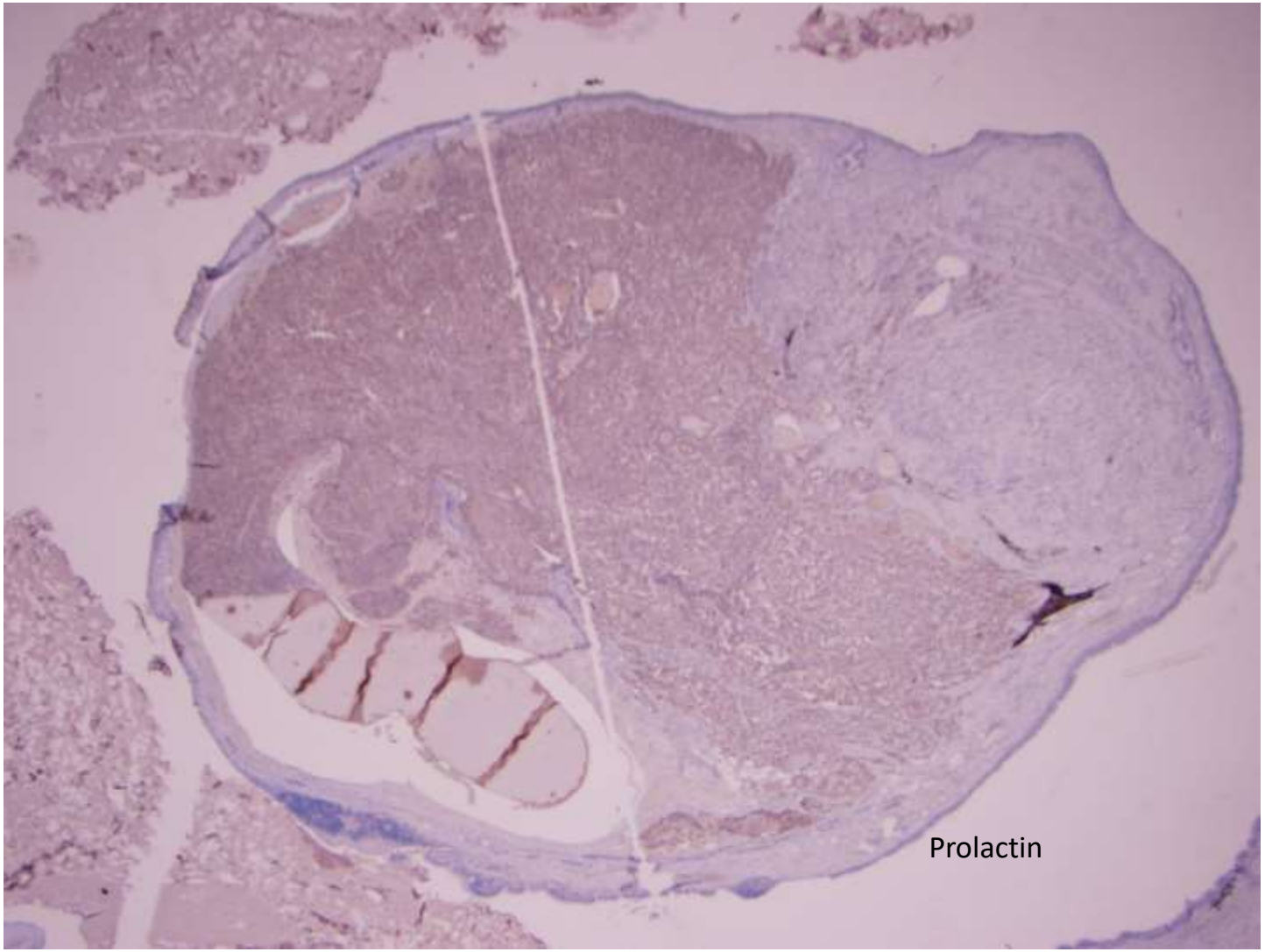
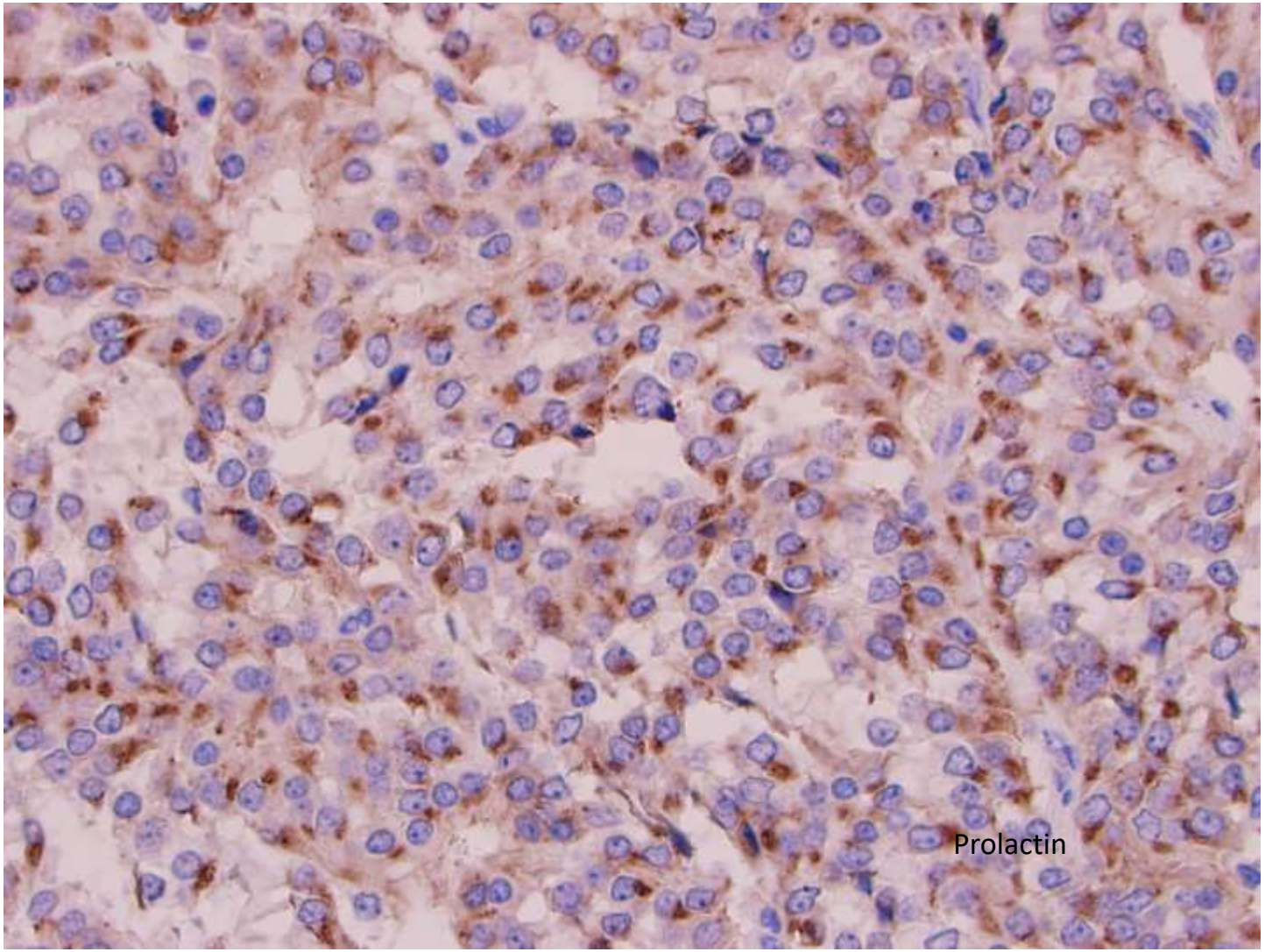

Prolactin


Prolactin

Mature Cystic Teratoma

- Most common ovarian tumor (50%)
- 60% of benign ovarian tumors
- 80% occur during reproductive years
- 15% bilateral

Mature tissues present

- Ectodermal elements predominate-epidermis, skin adnexal structures, neuroectodermal elements (glial, PNS, cerebrum, cerebellum, choroid plexus)
- Mesodermal-smooth muscle, bone, teeth, cartilage, adipose tissue
- Endodermal-respiratory epithelium, GI epithelium, thyroid, salivary gland
- Rare-retina, pancreas, thymus, adrenal, pituitary, lung, kidney, prostate, breast, seminal vesicle

Tumors arising in teratomas

- Strumal tumors
- Carcinoids
- Neuroectodermal tumors
- Somatic-type tumors-SCCA (80%), AdenoCA, Sarcomas, melanomas,lymphomas
- Rare benign tumors-paraganglioma, choroid plexus adenoma, sebaceous adenoma, pituitary adenomas (ACTH, prolactin secreting)

References

- Axiotis, et al, 1987, Corticotroph cell pituitary adenoma within an ovarian teratoma. A new cause of Cushing's syndrome. AJSP 11, 218-224
- Palmer, et al,1990, Prolactinoma in wall of ovarian dermoid cyst with hyperprolactinemia. Obstet Gynecol 75, 540-543
- Other case reports describing ACTH or prolactin producing adenomas in ovarian teratomas

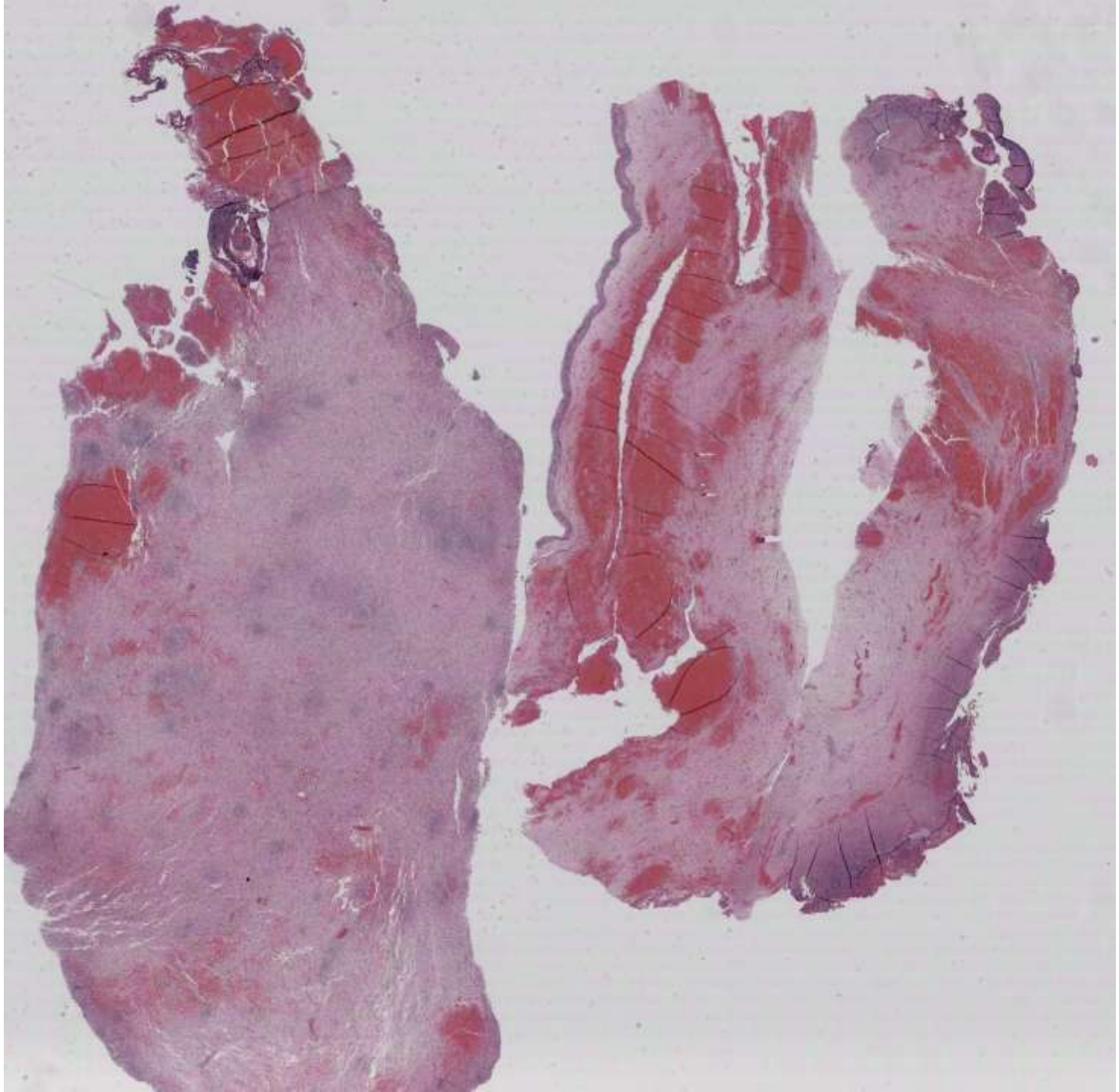
Pituitary Adenoma

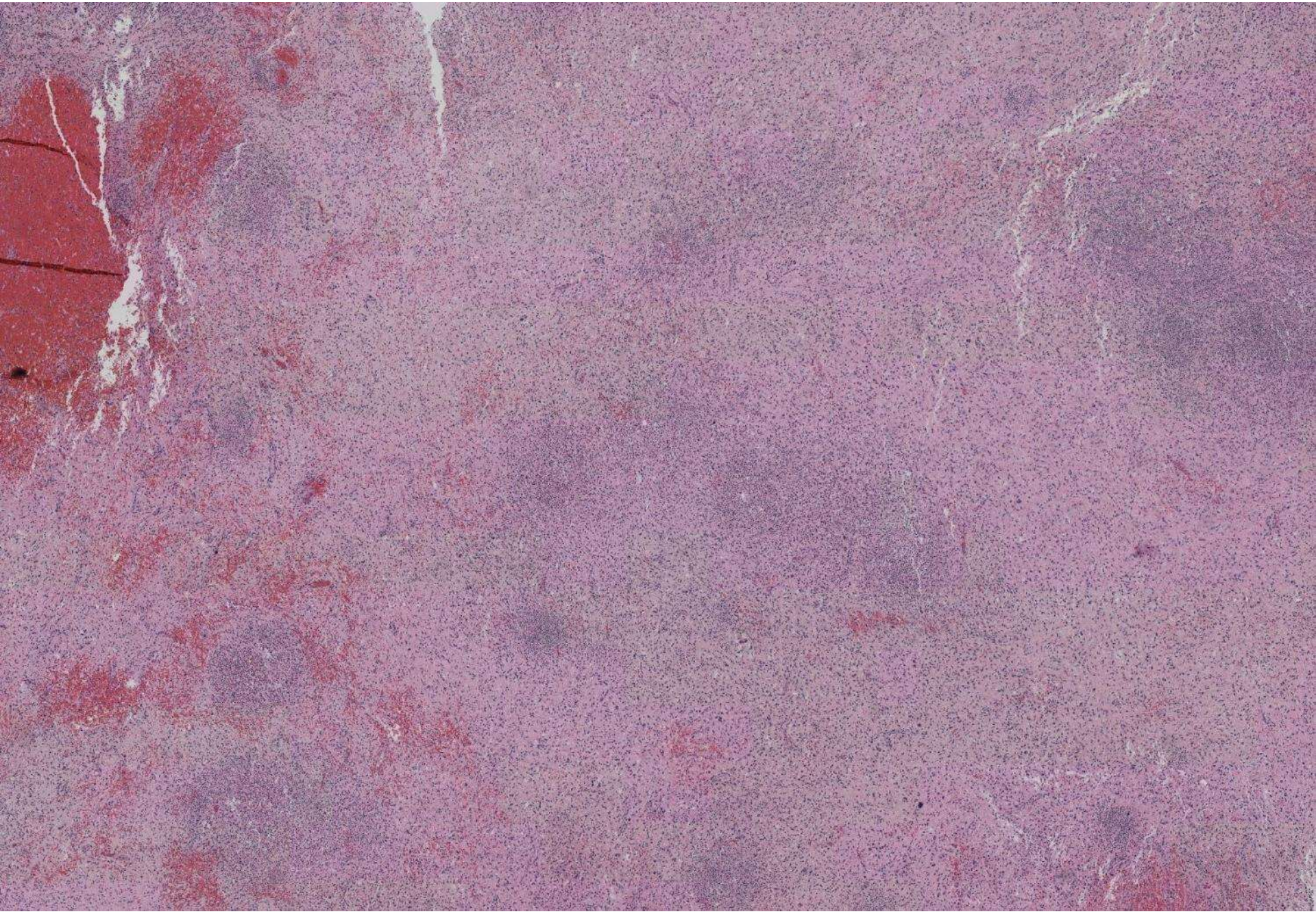
- Workup
  - Endocrine note
  - IHC panel (synaptophysin, CAM 5.2, ACTH, prolactin, HGH, TSH, SF-1, ki-67)
- Types
  - Somatotroph, lactotroph, thyrotroph, corticotroph, gonadotroph, null cell
  - Plurihormonal and double adenomas
- “Atypical”pituitary adenoma
- Vs Pituitary carcinoma

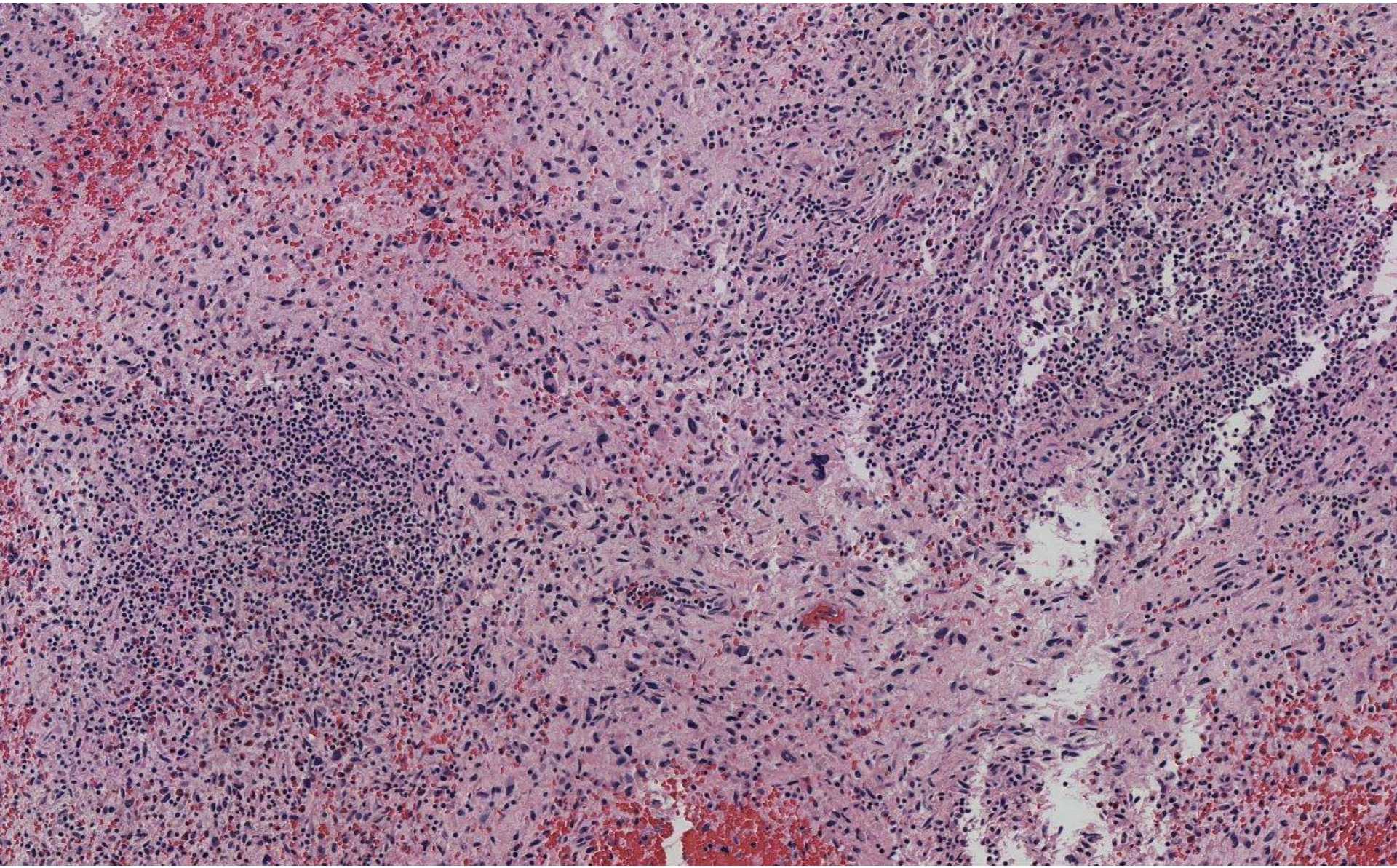
20-0703
scanned slide available!

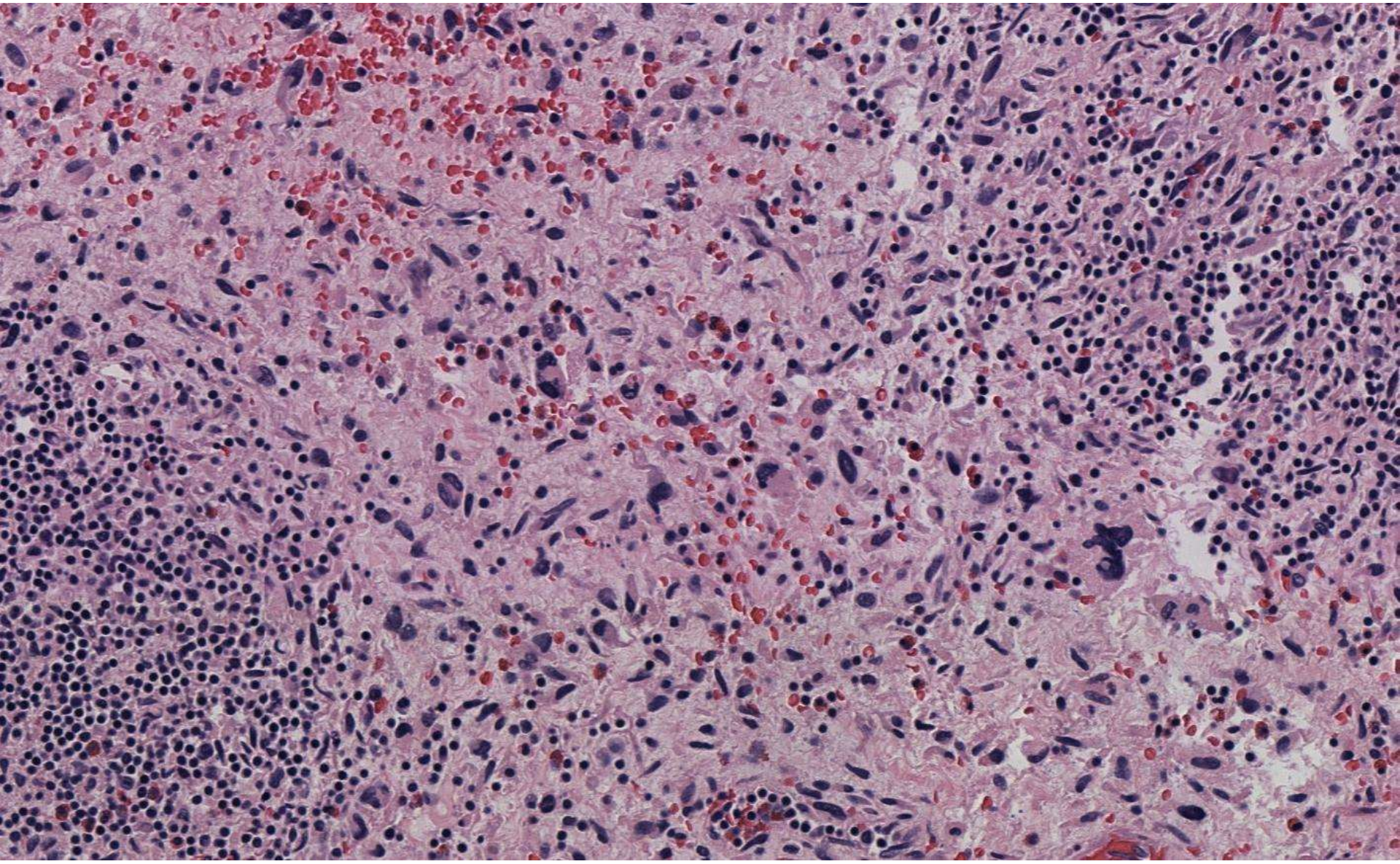
Keith Duncan; Mills-Peninsula

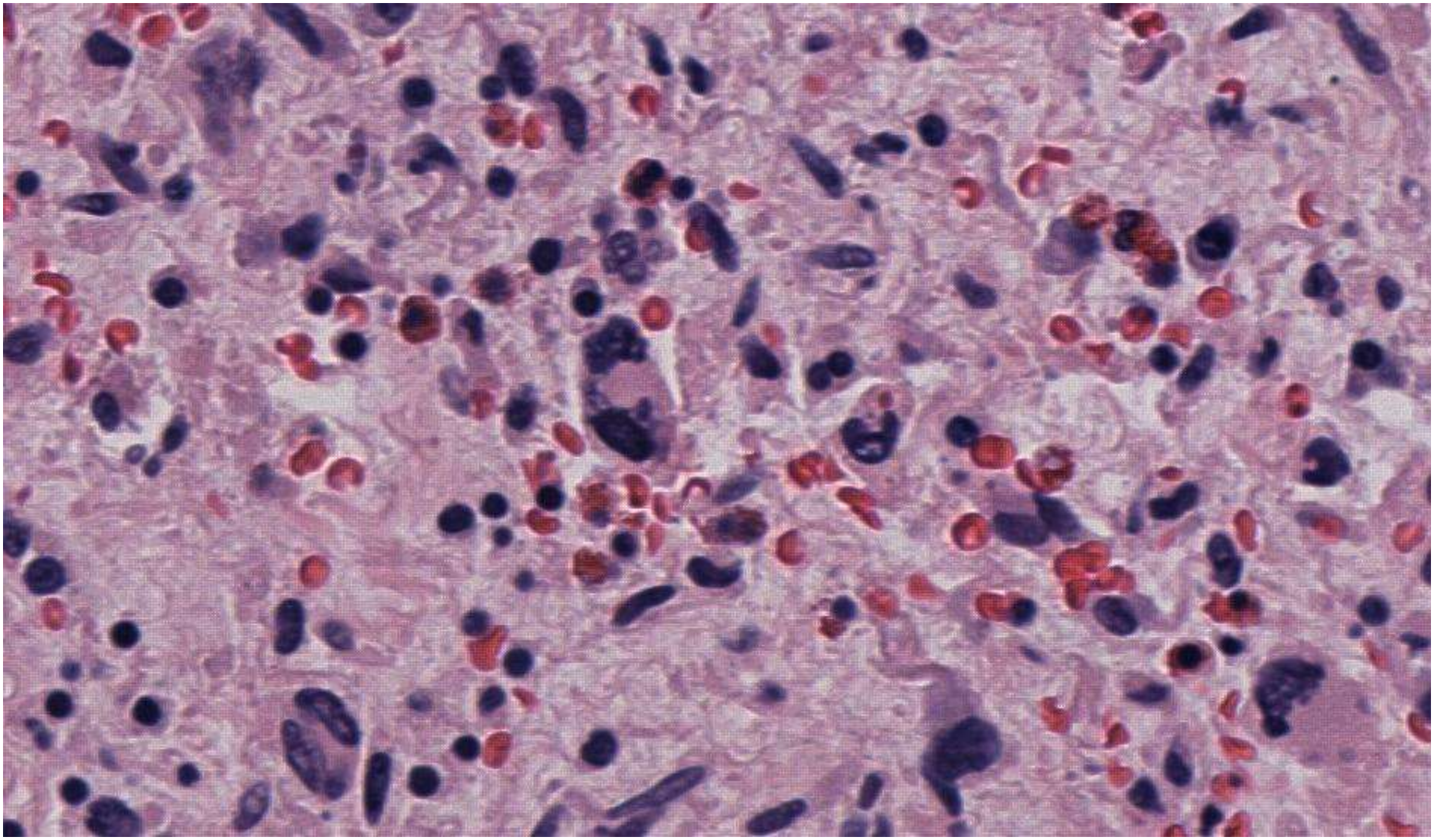
43-year-old M with large liver cysts.

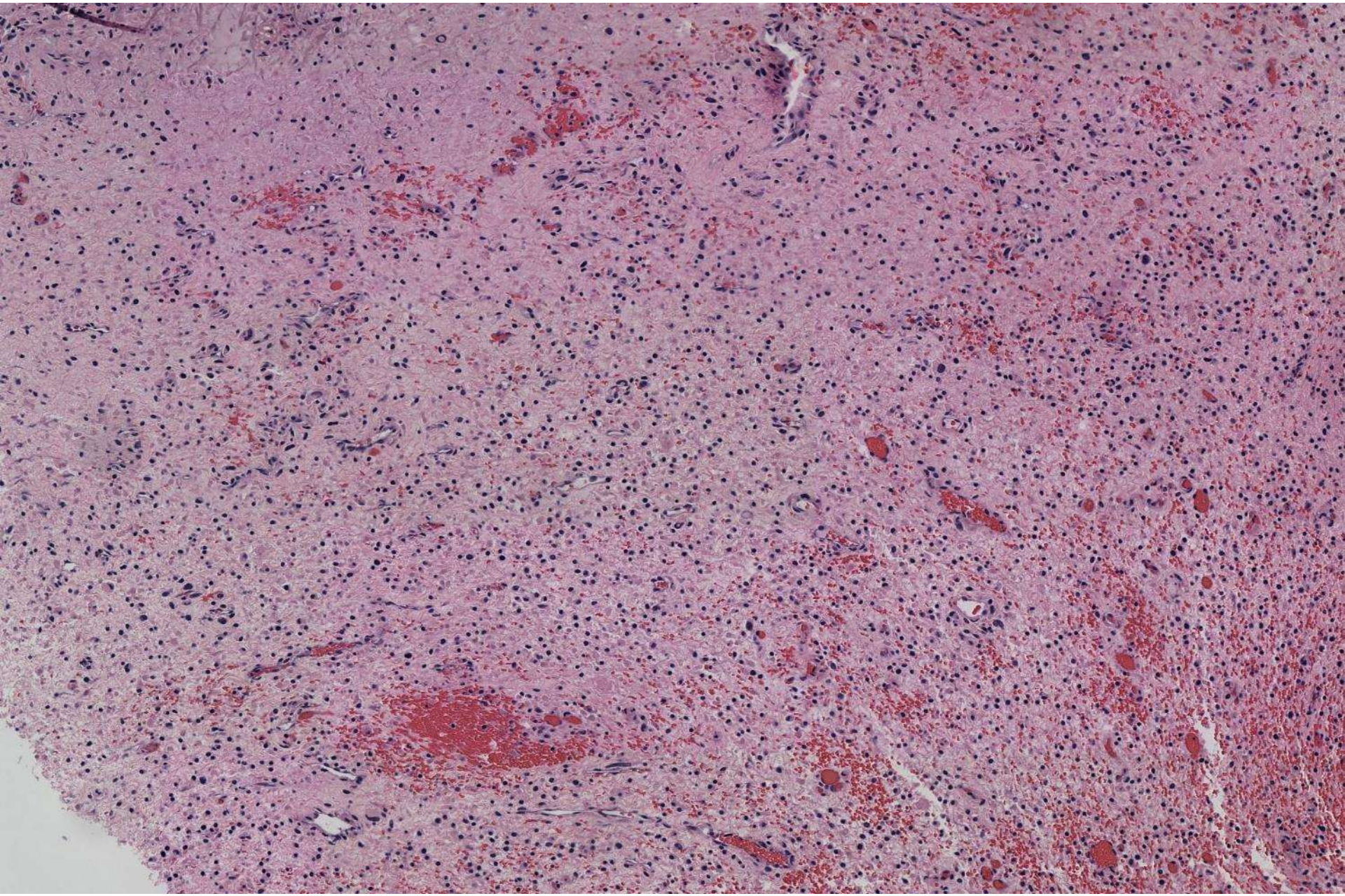


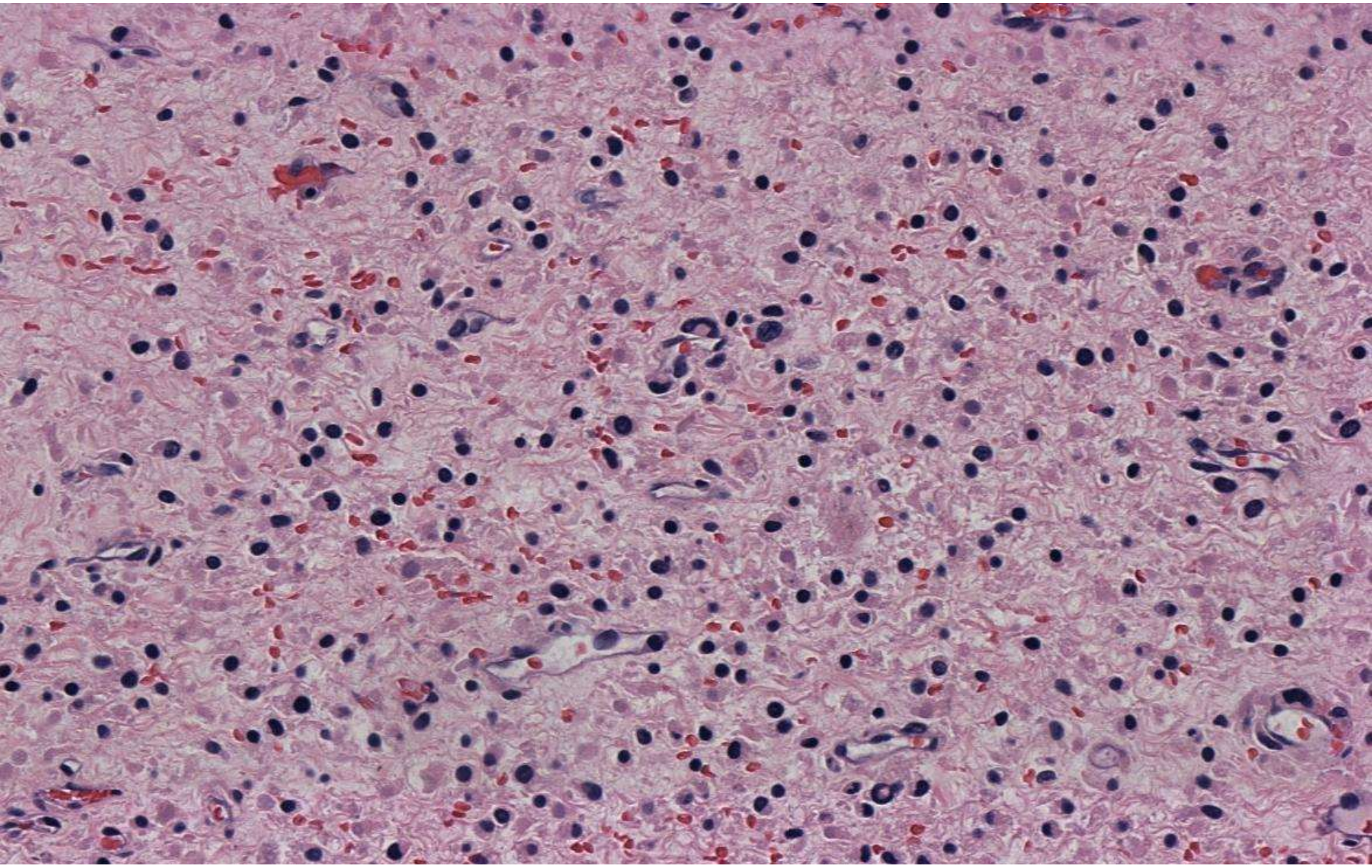


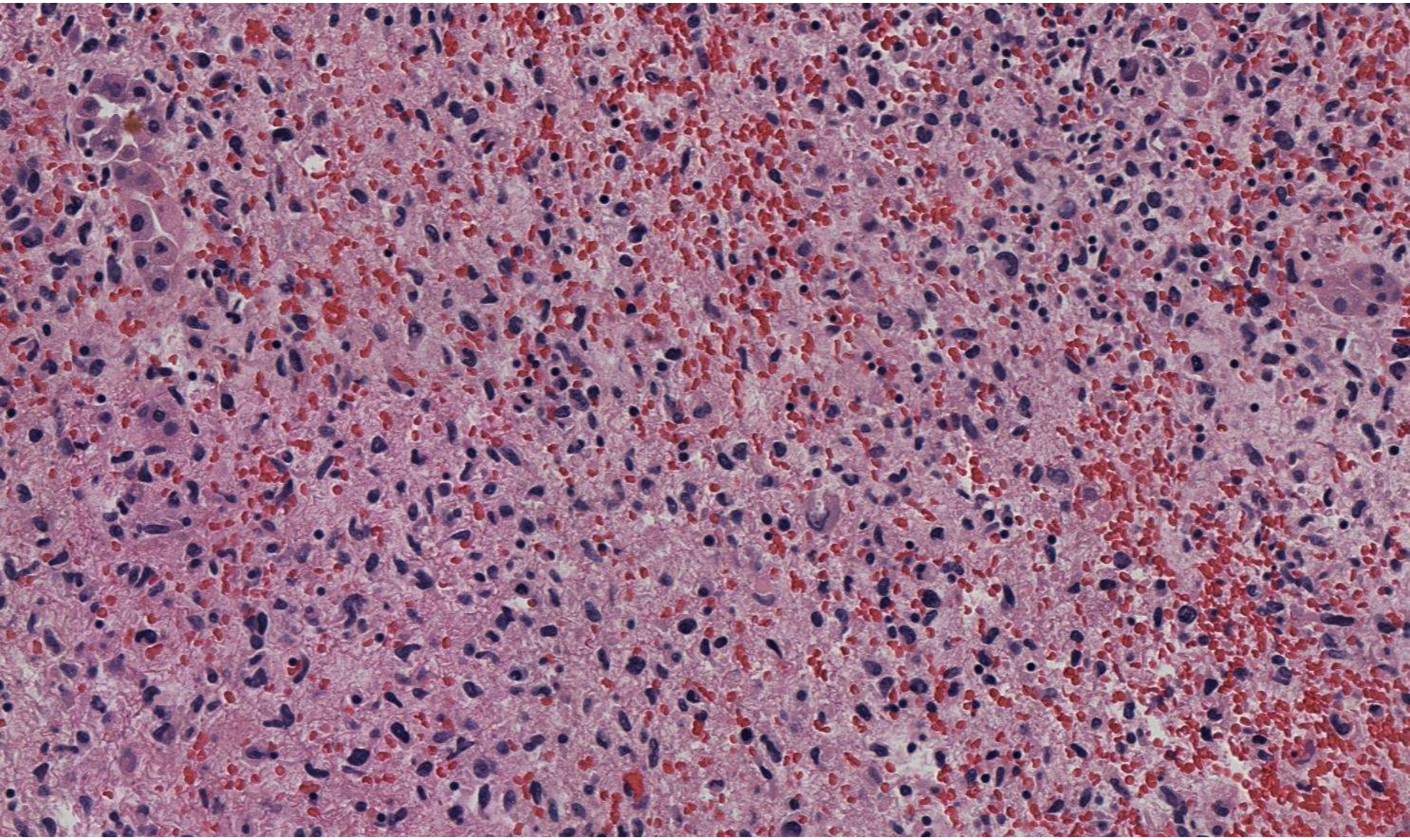


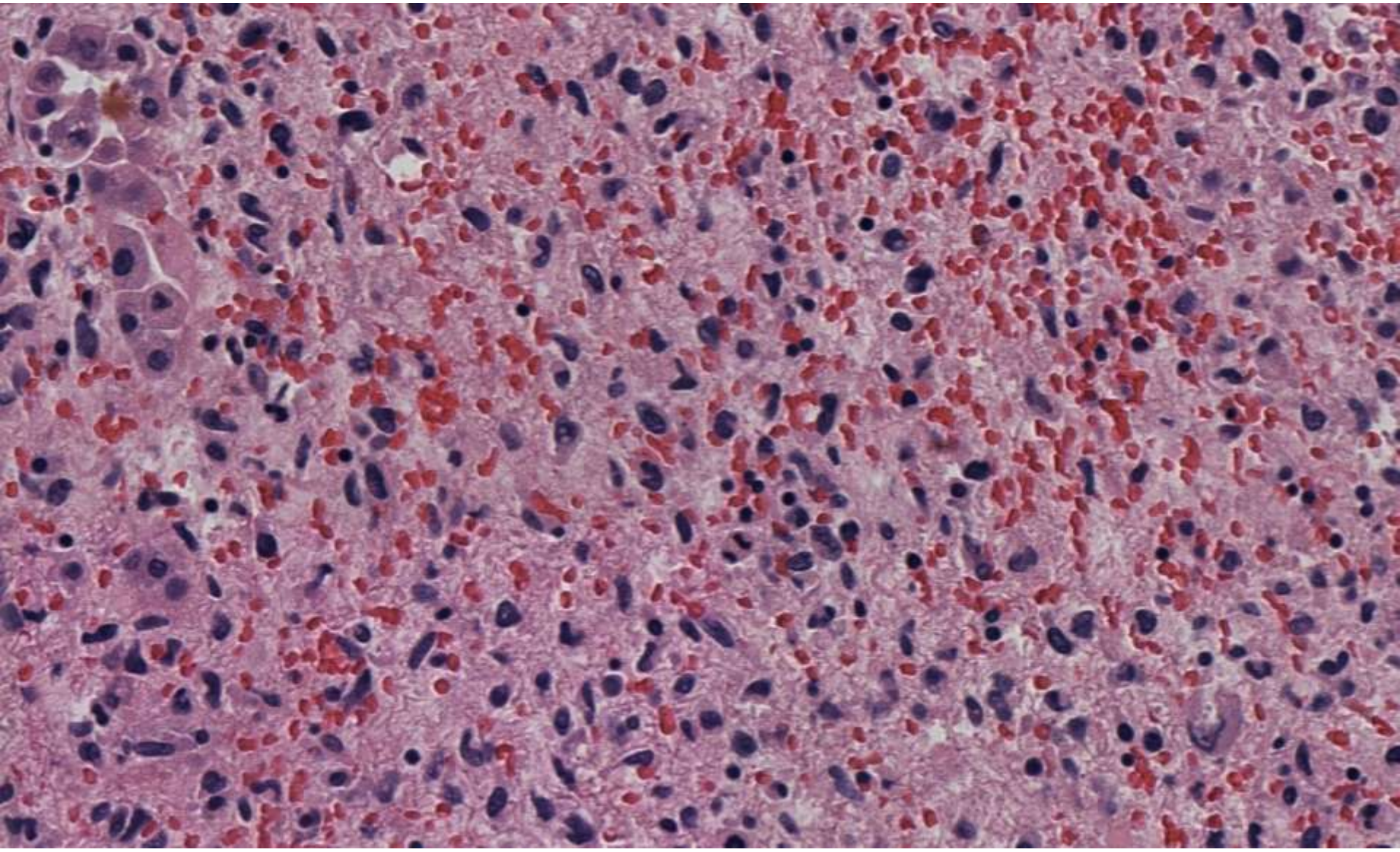


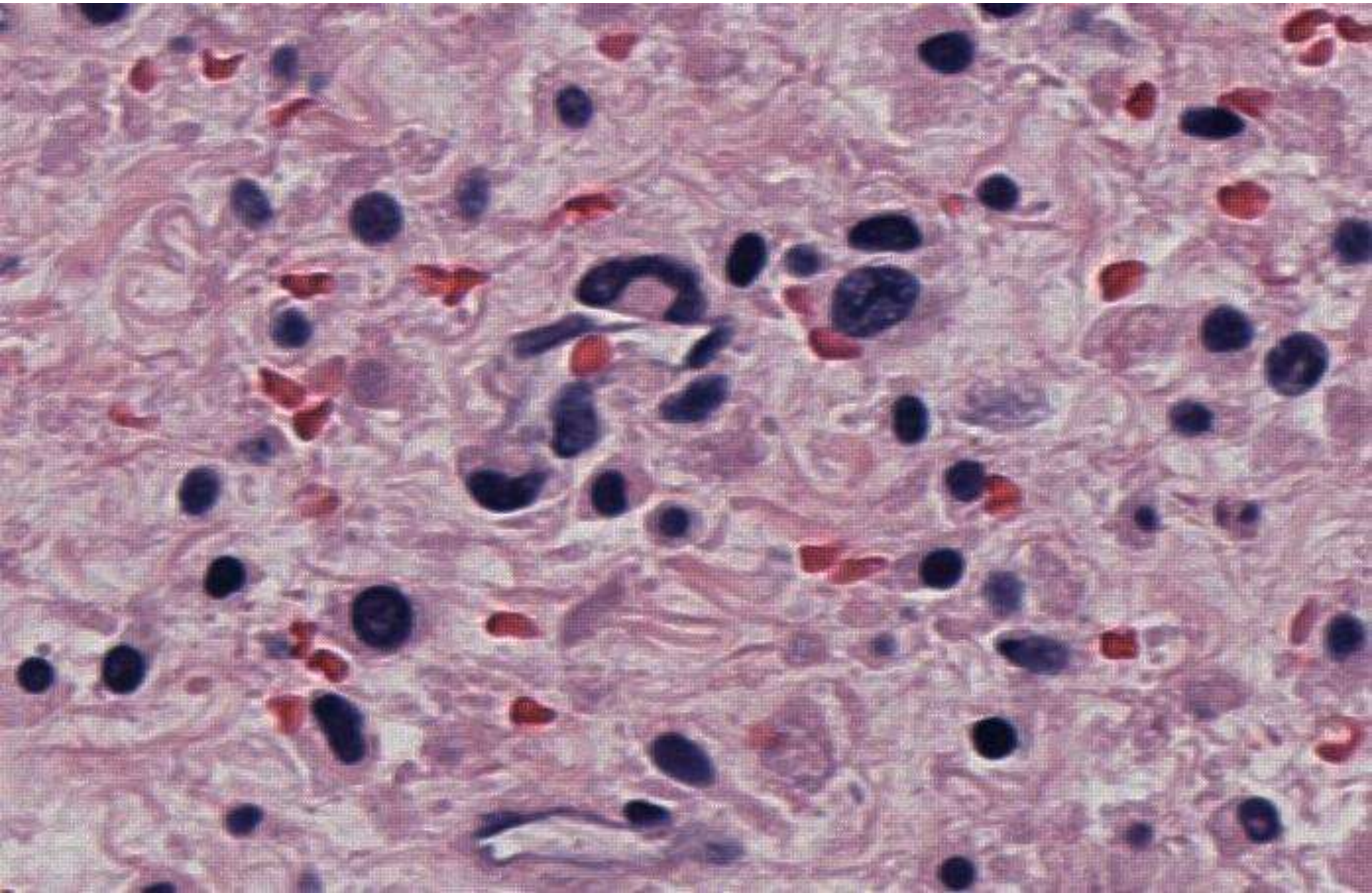












DIAGNOSIS?

EMBRYONAL SARCOMA

- Malignant mesenchymoma or mesenchymal sarcoma
- 10% of pediatric hepatic tumors (#3 after hepatoblastoma and hepatocellular carcinoma) - usually 6 - 10 years
- In children, often associated with mesenchymal cysts
- Rare in adults
- Primitive mesenchymal neoplasm with possible foci of differentiated sarcoma, such as angiosarcoma
- Typically presents with pain, fever, abdominal mass and normal serum AFP
- Good prognosis - large tumors may rupture & cause death

EMBRYONAL SARCOMA

- **Gross:**
- 10 - 30 cm, solitary, well demarcated, soft tumor with cystic, gelatinous, hemorrhagic & necrotic foci

- **Microscopic:**
- Variably cellular tumor with anaplastic, spindled/oval cells with prominent hyaline globules and ill-defined borders
- Nuclei have stippled chromatin, inconspicuous nucleoli
- Myxoid stroma with thin walled veins
- Bizarre tumor cells with prominent eosinophilic cytoplasm and PAS+ diastase resistant hyaline globules
- Extramedullary hematopoiesis common, frequent mitotic activity

EMBRYONAL SARCOMA

- **Positive stains**
- **PAS**+ diastase resistant hyaline globules, **vimentin**, high **Ki67** index **Glypican 3** (60%), **CD56**, paranuclear dot-like **CK**, **BCL2**, **alpha-1-antitrypsin** and **alpha-1-antichymotrypsin**, variable **muscle markers**

- **Negative stains**
- **Alpha fetoprotein** (hyaline globules), **keratin**, **myogenin**

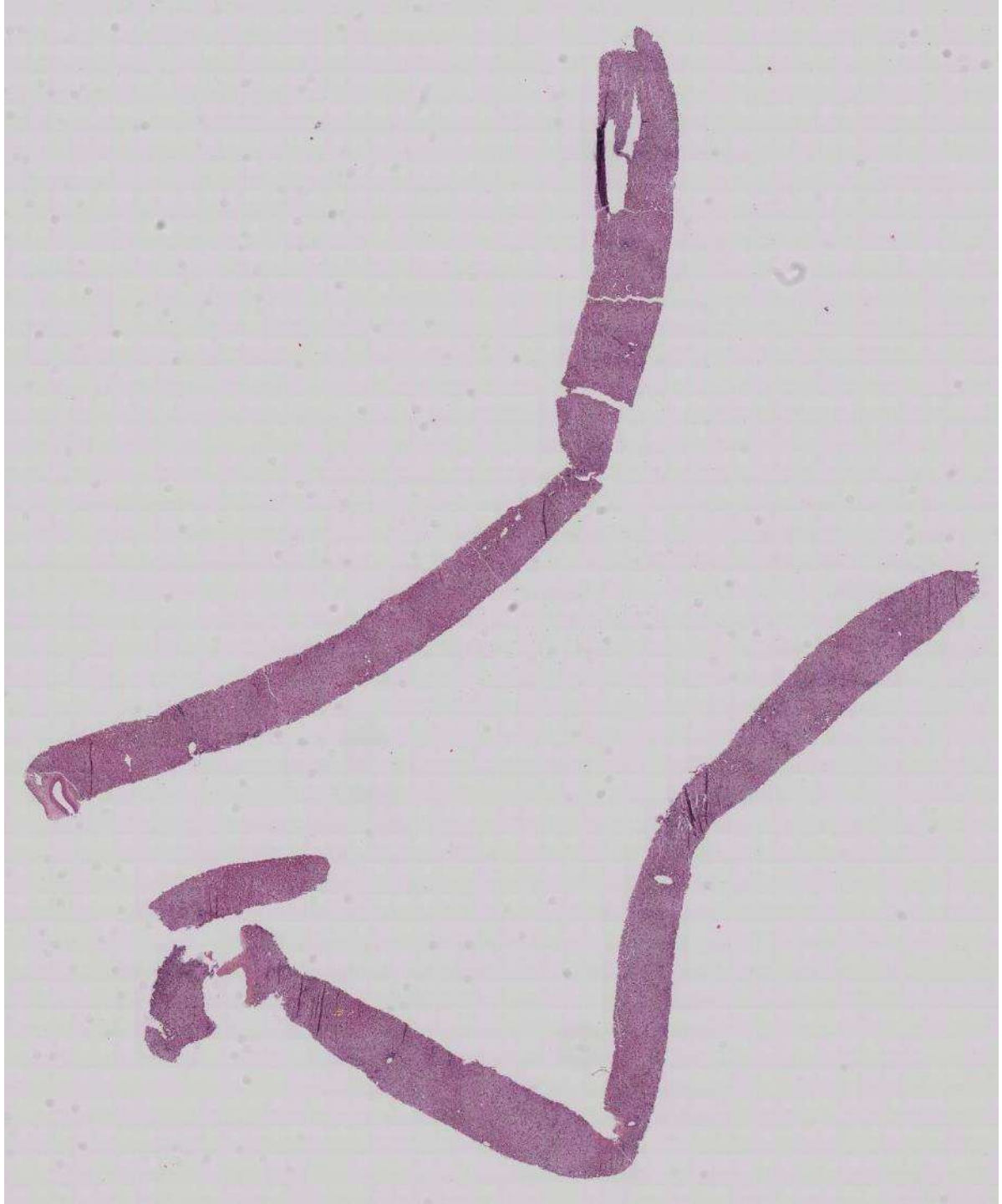
EMBRYONAL SARCOMA

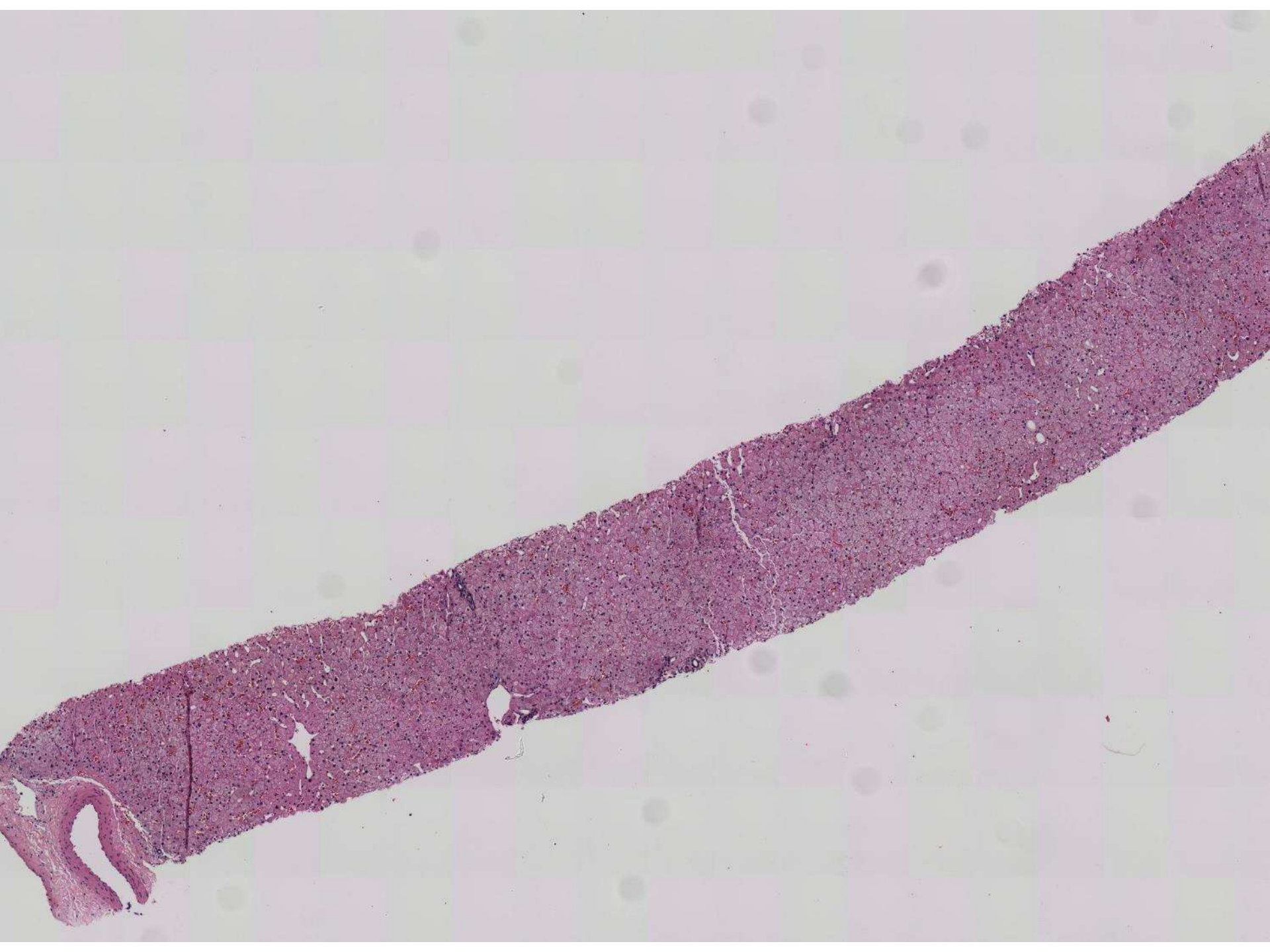
- **Differential diagnosis**
- **Embryonal rhabdomyosarcoma**: children, myxoid mass extending into bile duct, rhabdomyoblastic differentiation with cytoplasmic cross striations, cambium layer present, no diffuse anaplasia or hyaline globules, myogenin+ and MyoD1+
- **Gastrointestinal stromal tumor**: adults, CD117+, DOG1+, CD34+
- **Mesenchymal hamartoma**: usually < 1 yr old, cystic, bland tumor cells -no giant cells
- **Sarcomatoid hepatocellular carcinoma**

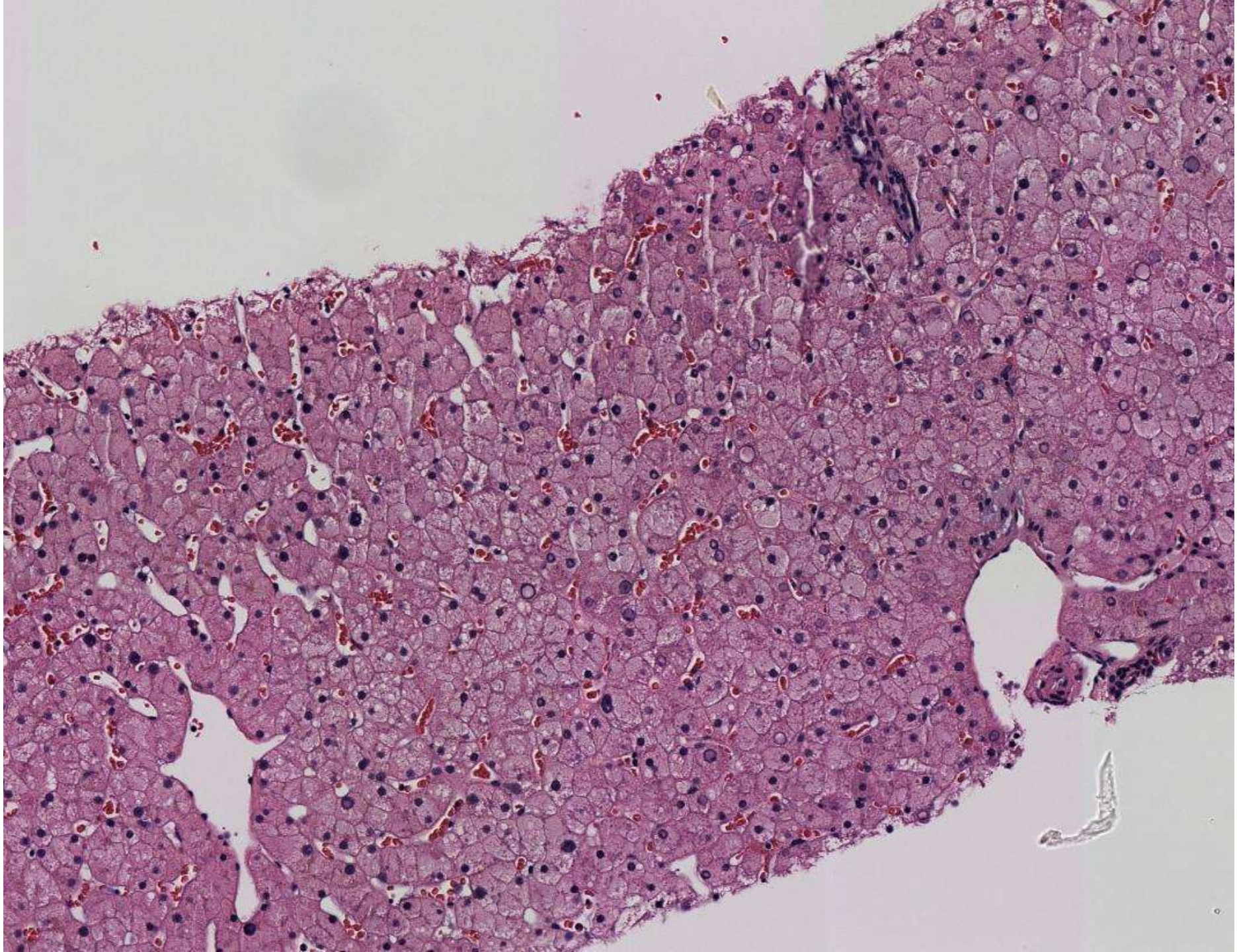
20-0704
scanned slide available!

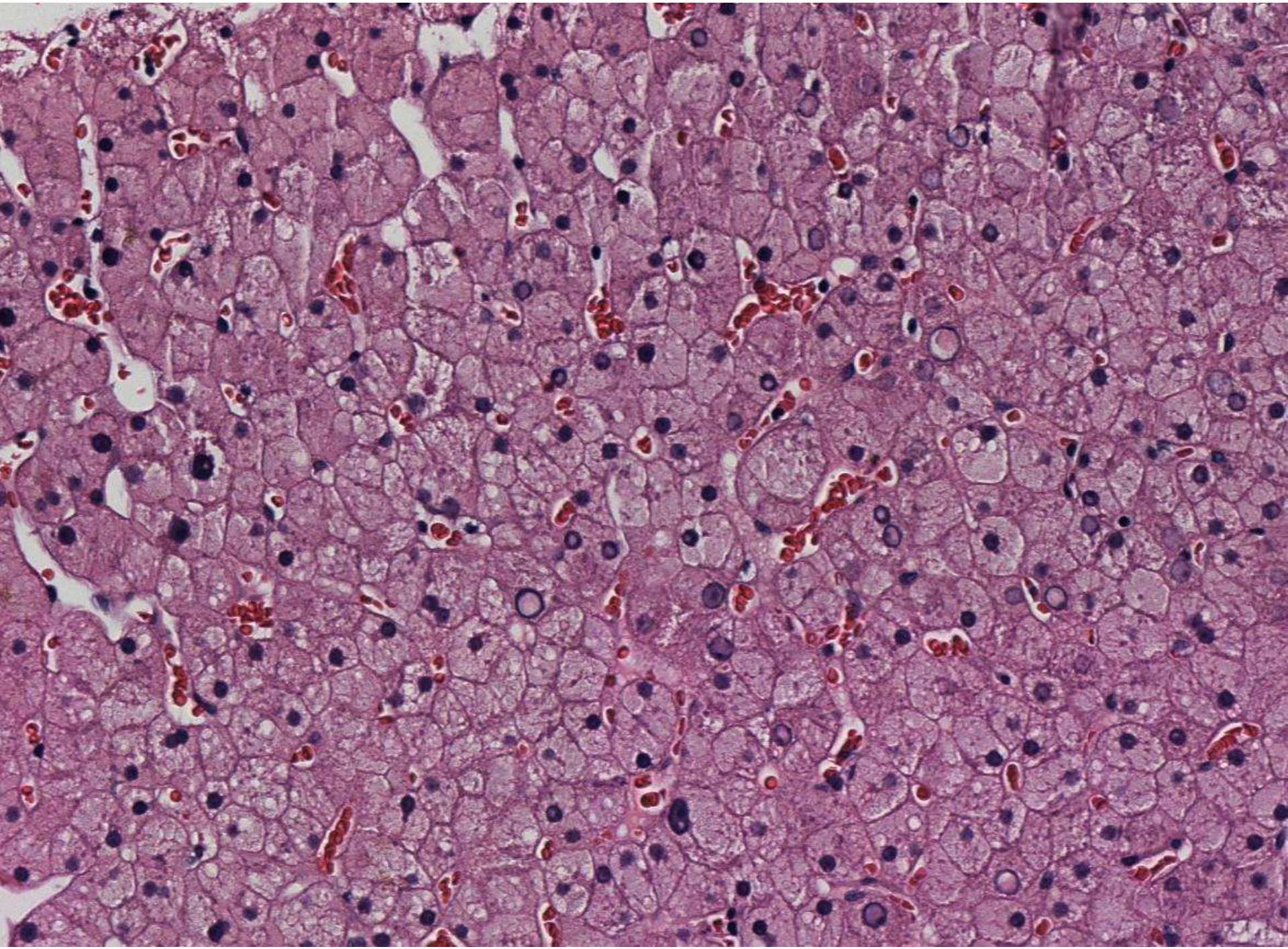
Mahendra Ranchod; Good Samaritan Hospital

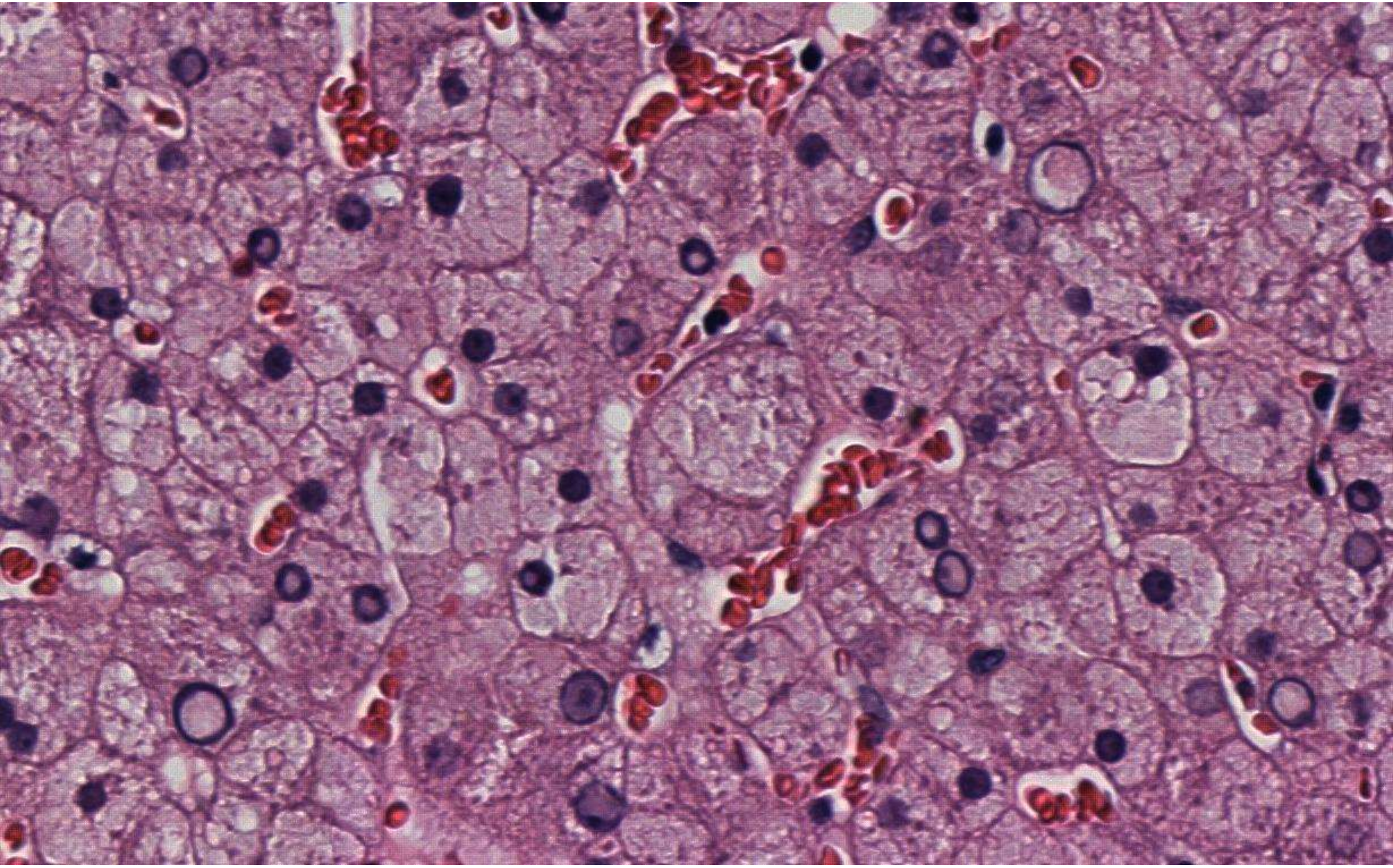
25-year-old M with insulin-dependent type 1 diabetes as well as Hashimoto disease, was found to have abnormal LFTs. Auto-immune hepatitis?

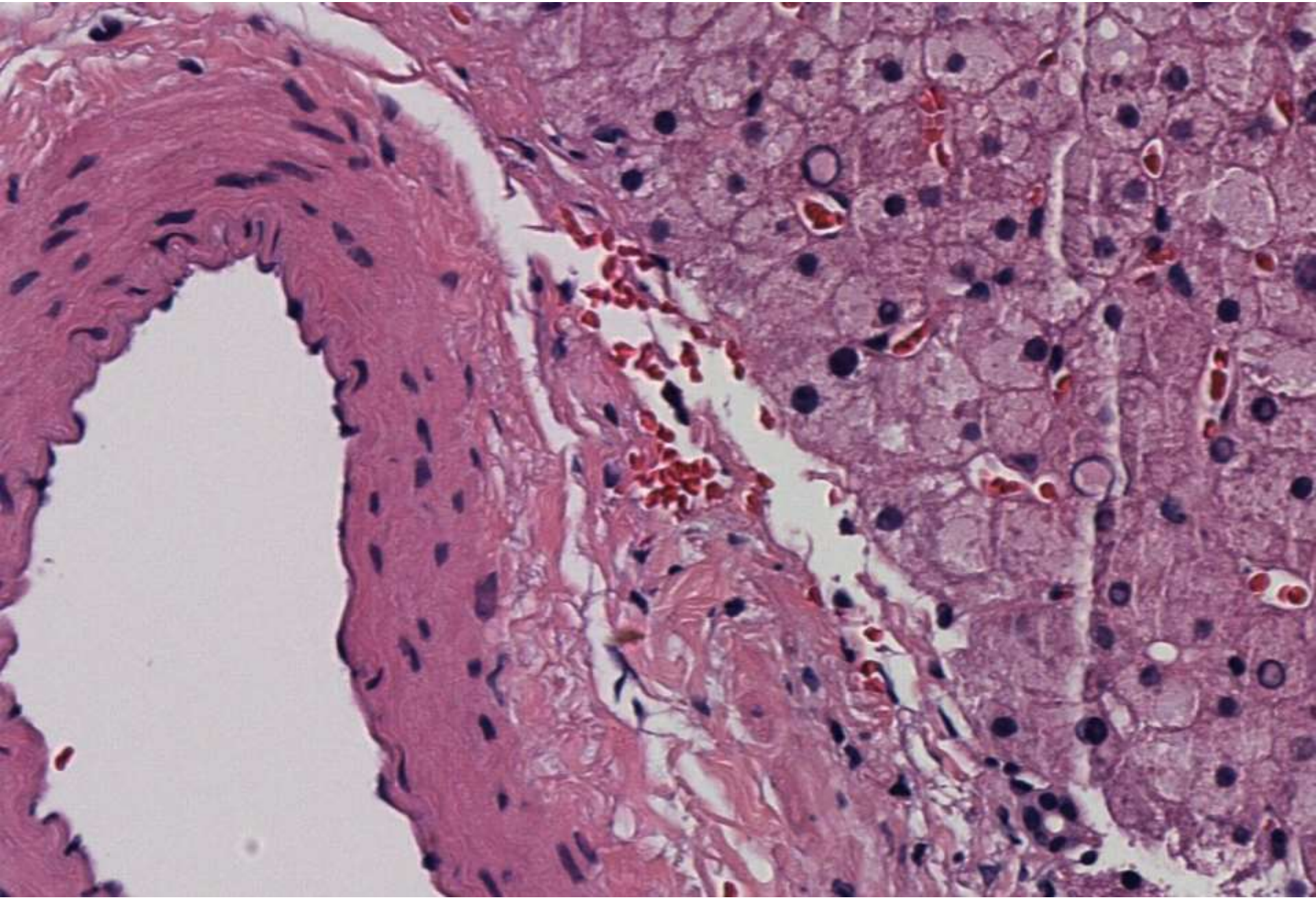


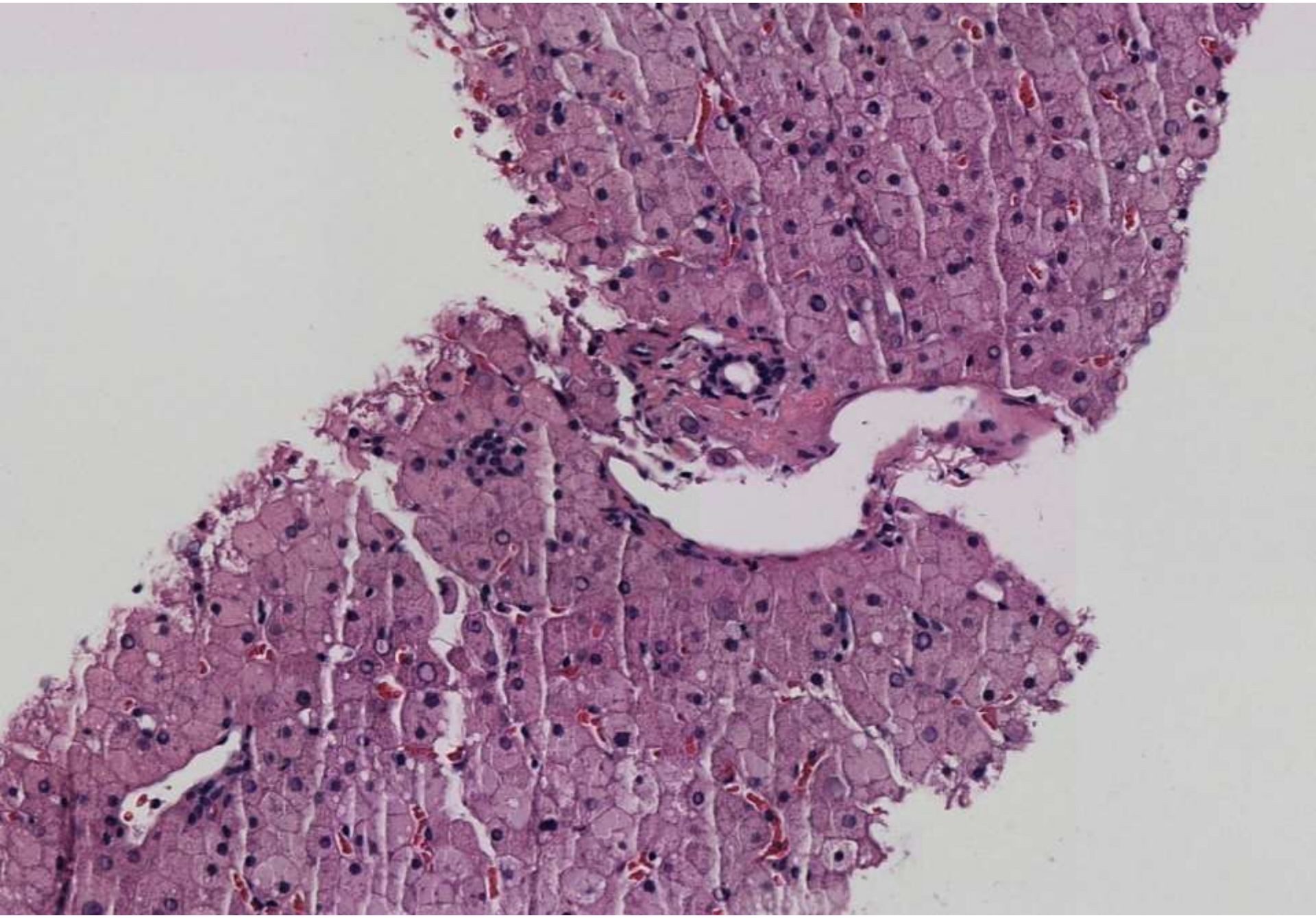


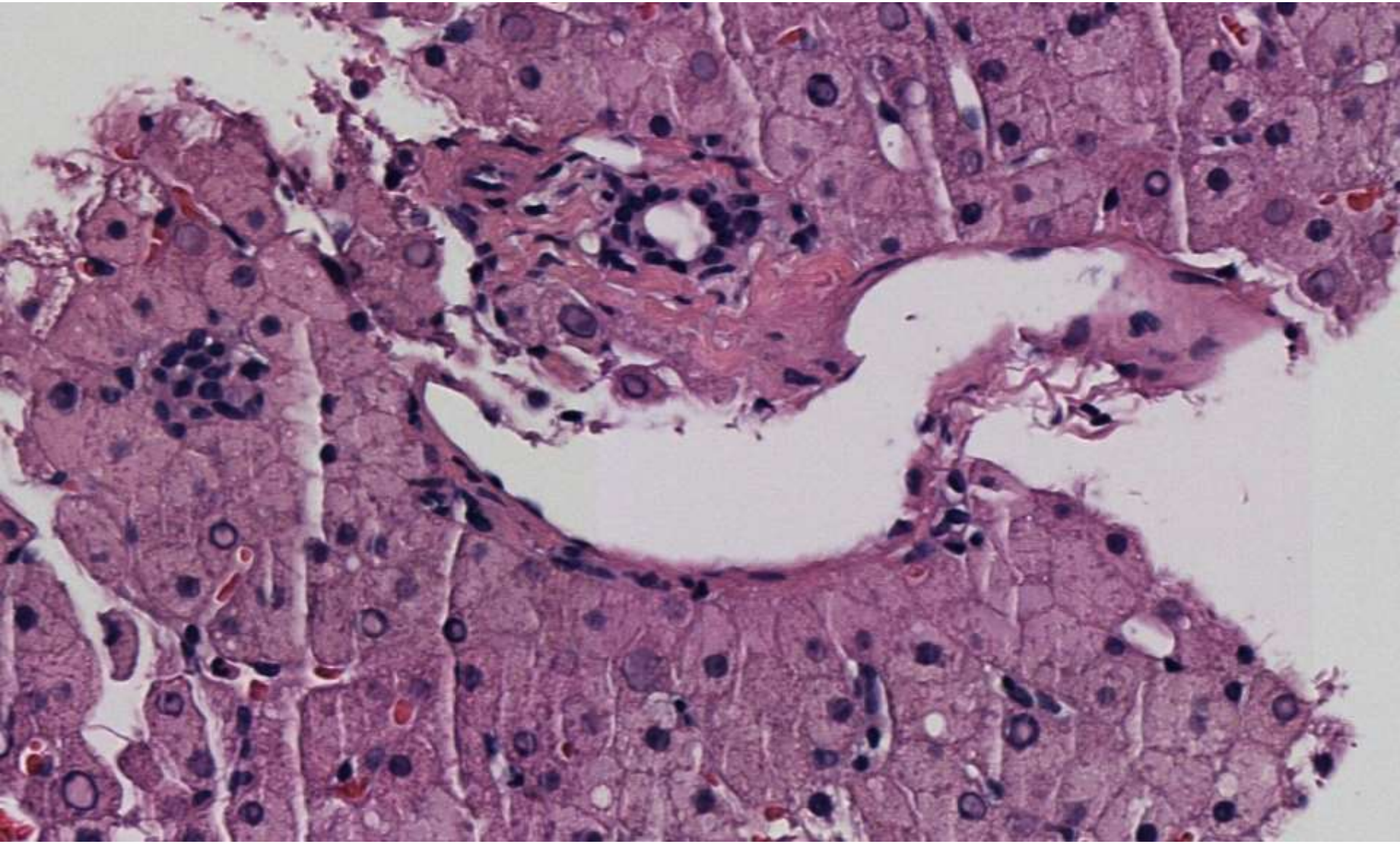


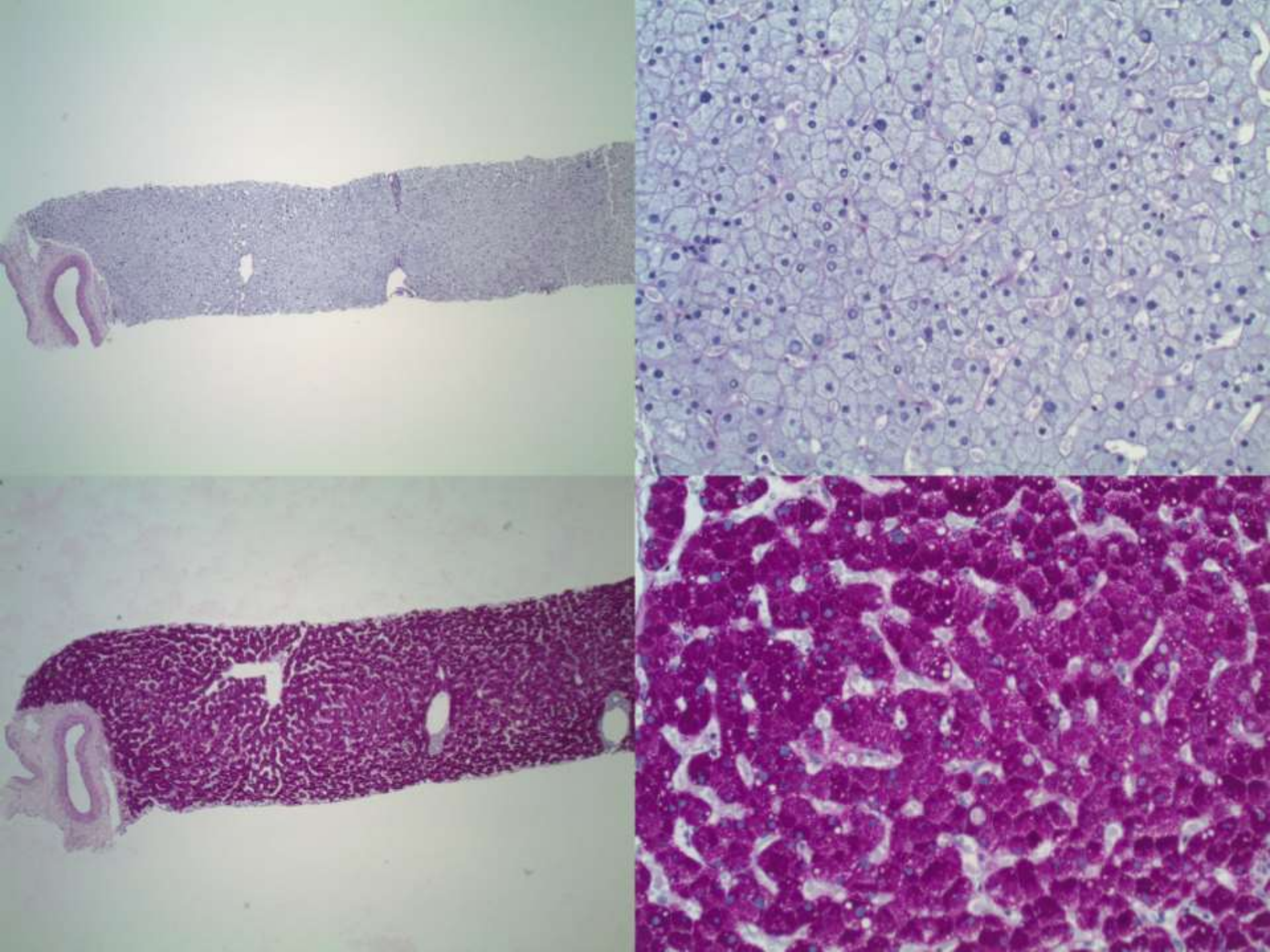












DIAGNOSIS?

Glycogen Hepatopathy

- Young patients with Type 1 DM
- Usually poorly controlled
- Abdominal pain
- Hepatomegaly
- Elevated transaminases (50-1600 IU/L)
- Reversible with control

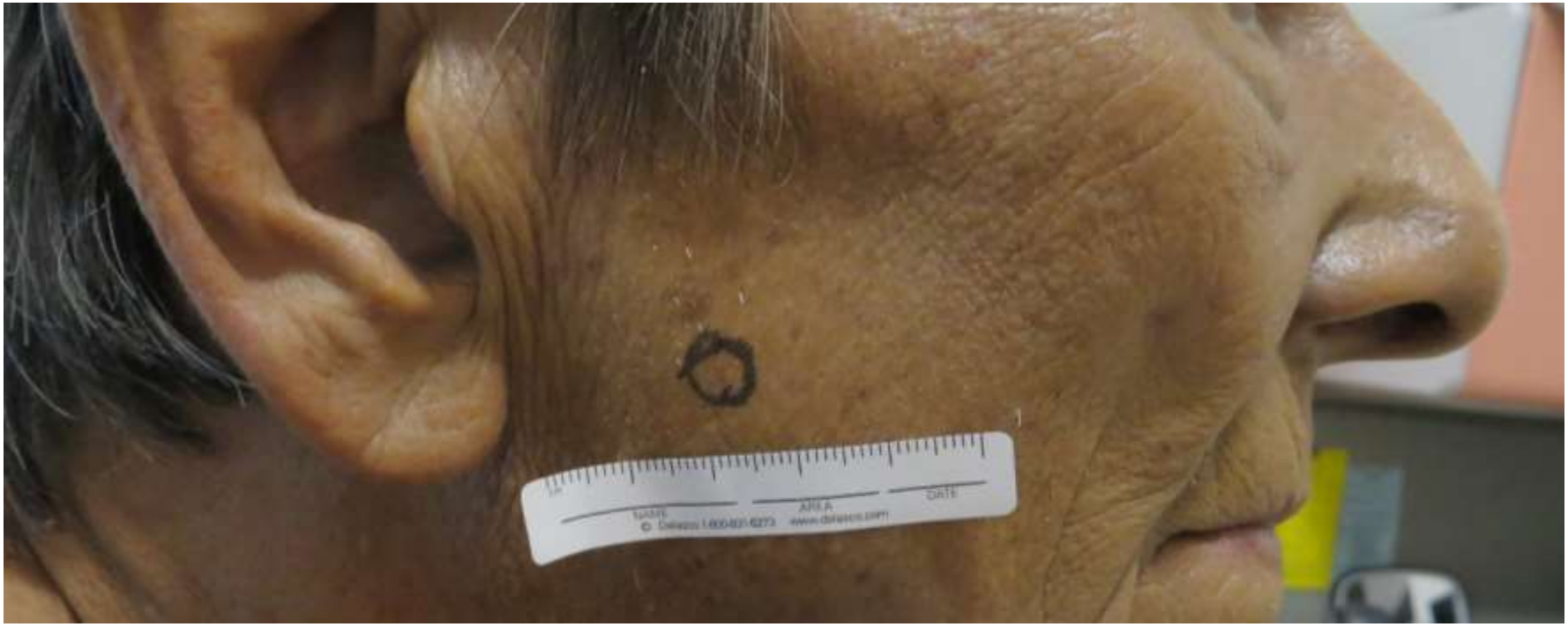
Glycogen Hepatopathy

- Swollen hepatocytes, pale cytoplasm
- Abundant glycogenated nuclei
- PAS and PAS-D confirmatory
- No inflammation
- Incidental fatty change (infrequent)
- Mild portal fibrosis (infrequent, ? unrelated)

20-0705

Jing Zhang/Hubert Lau; VA Palo Alto

77-year-old M with h/o psoriasis. At physical examination, grey discoloration noted on face. Per patient, may have started acutely but has been stable for the past 3 years ("I've been told I look grey for years").


NAME
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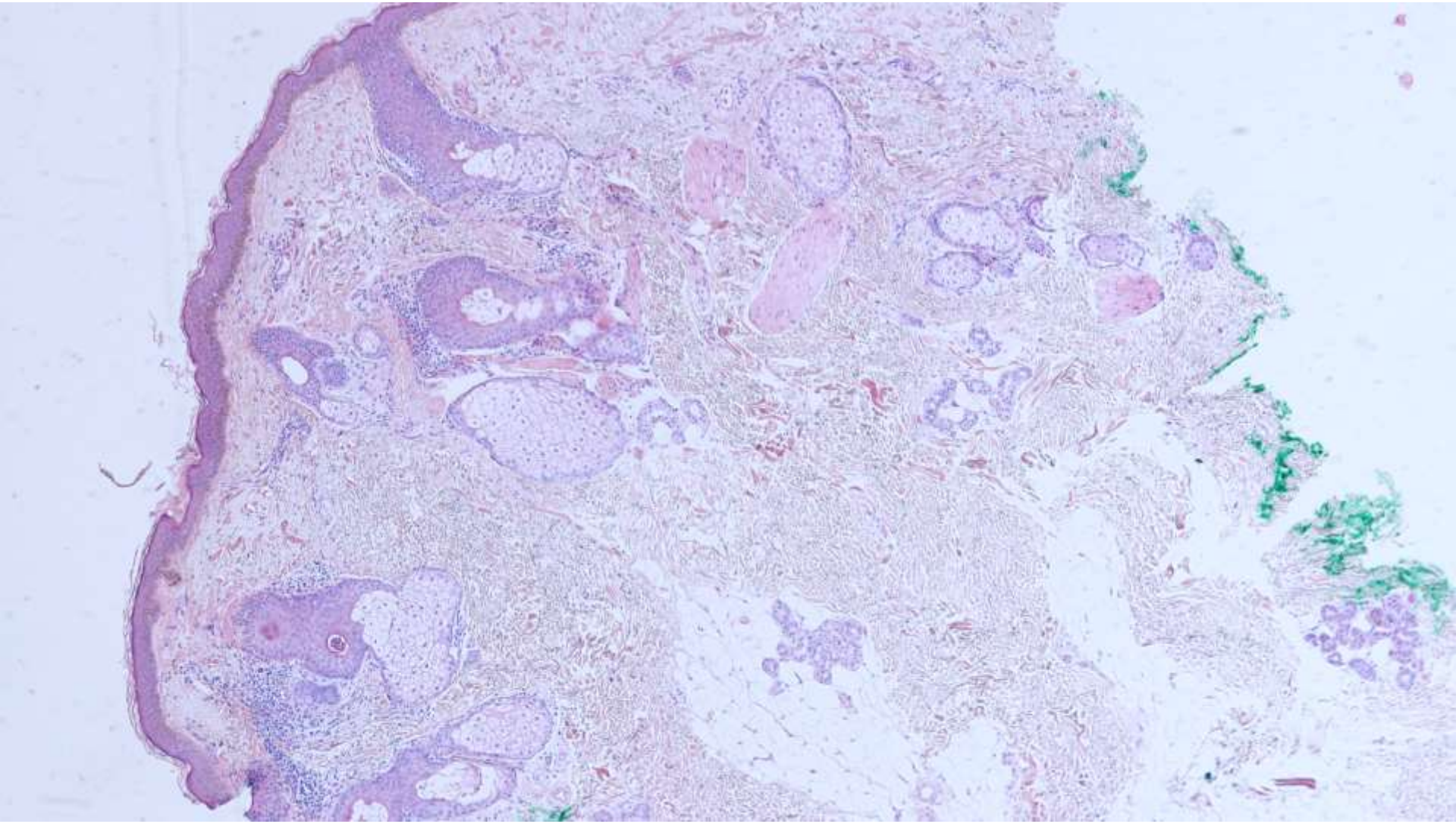
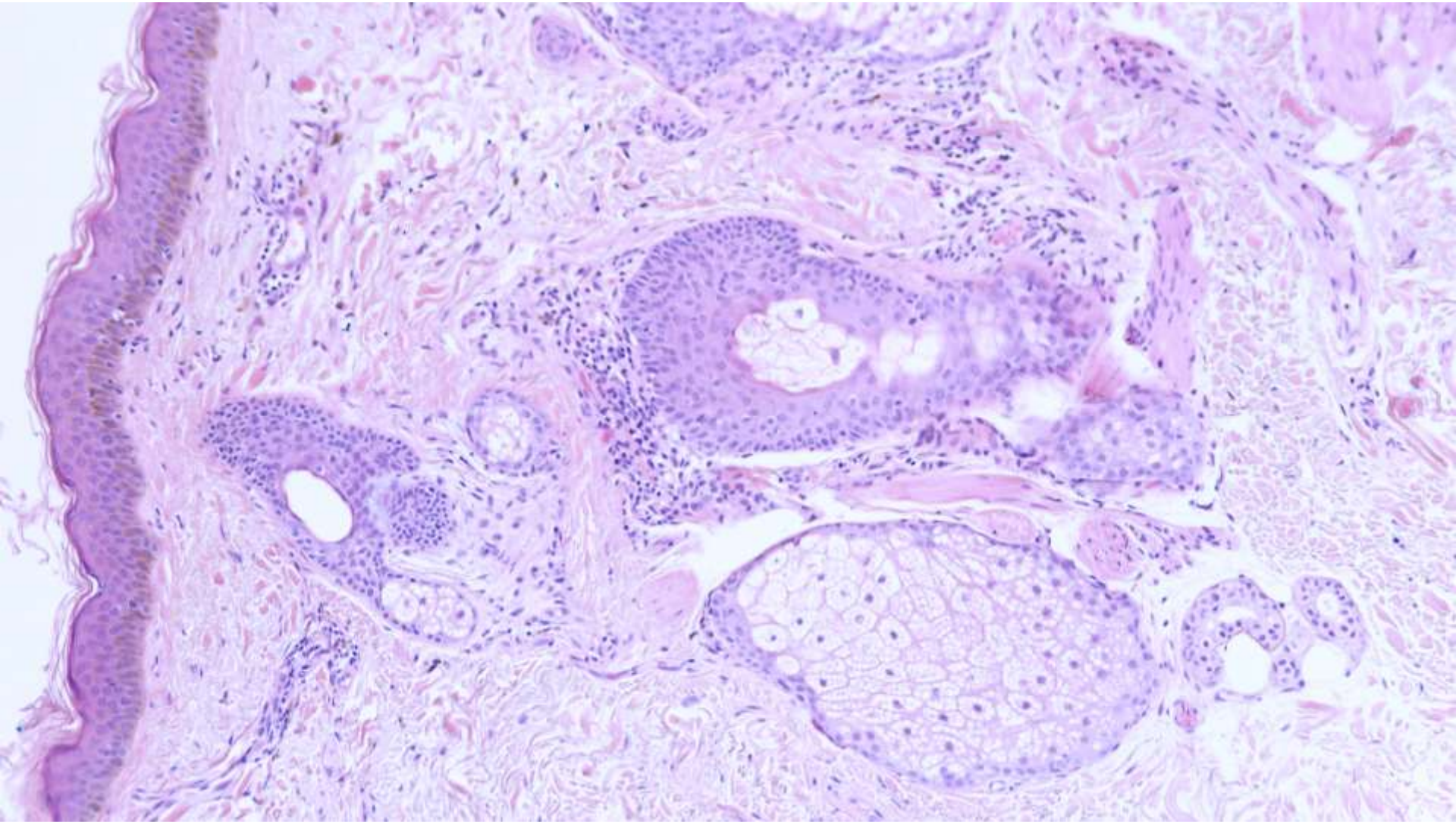
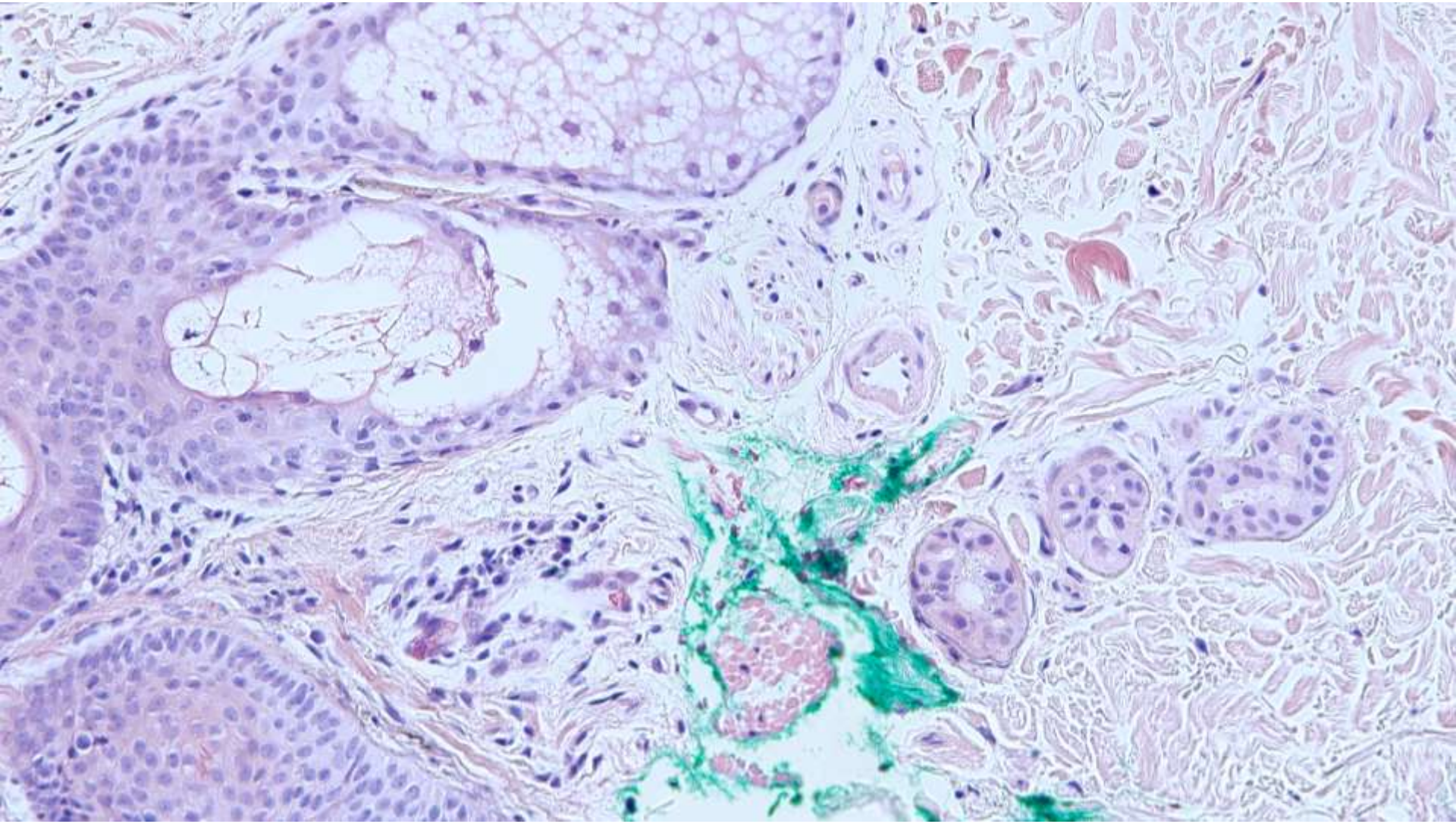
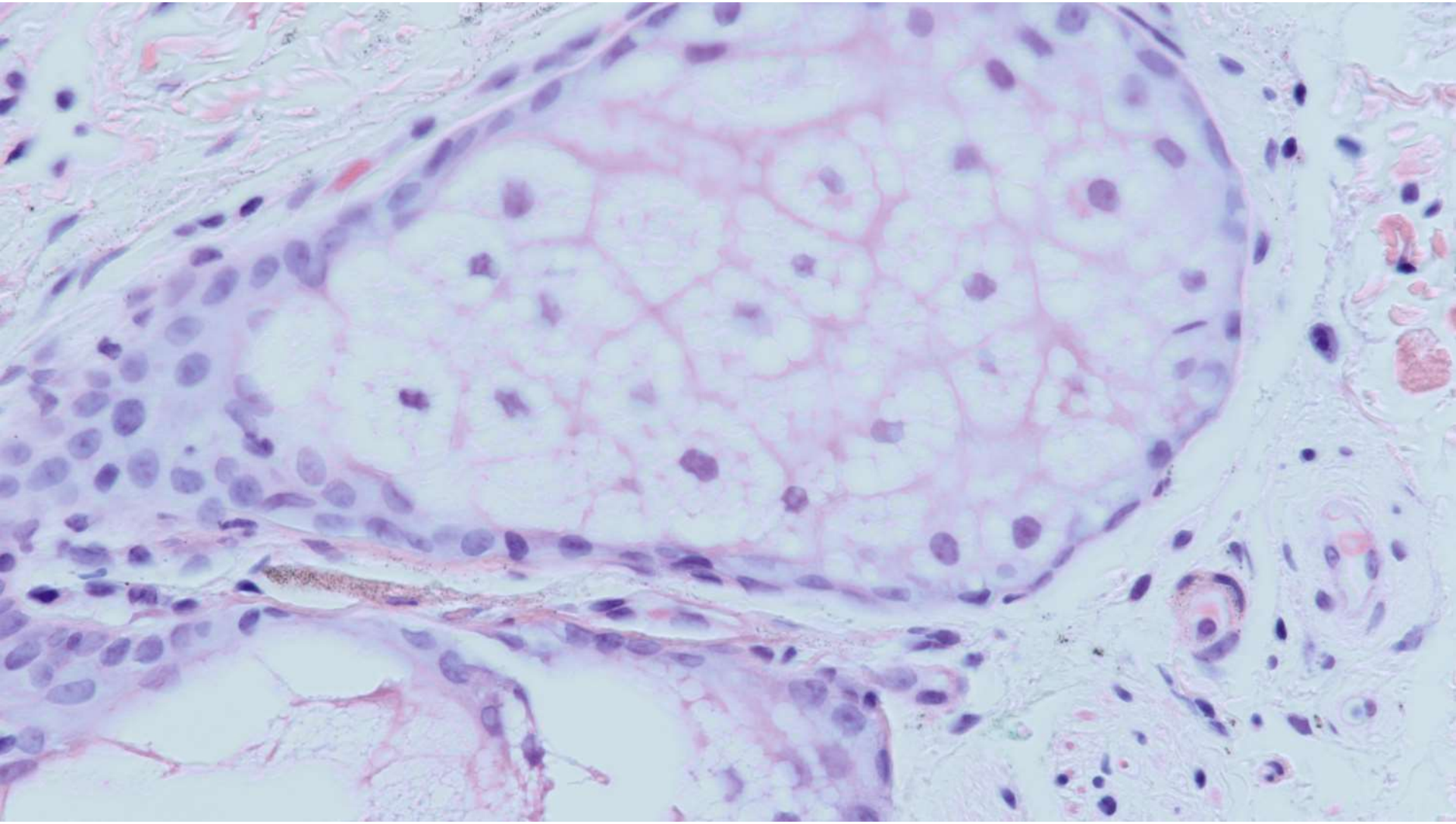
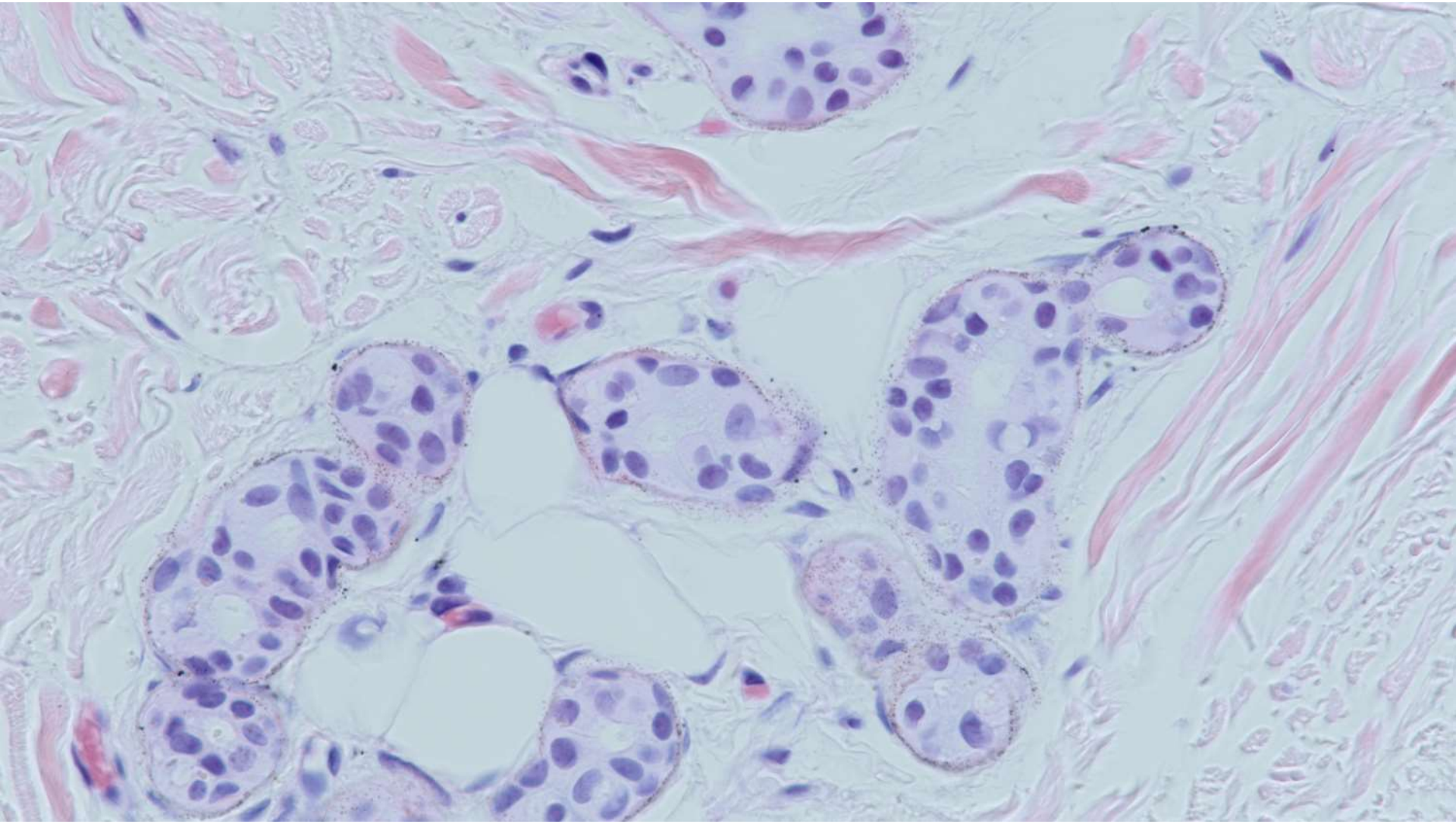










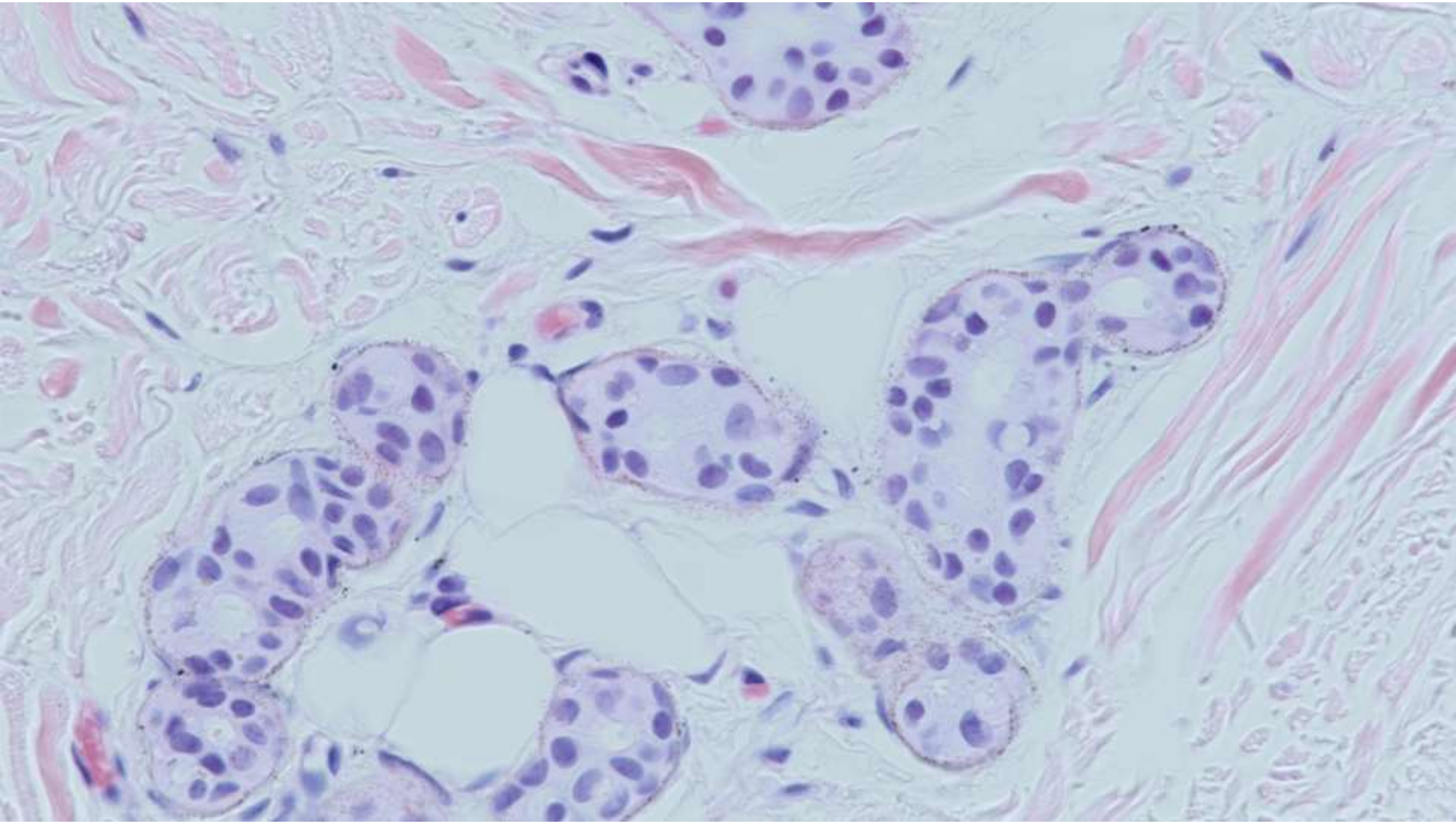
DIAGNOSIS?

Differential diagnosis?

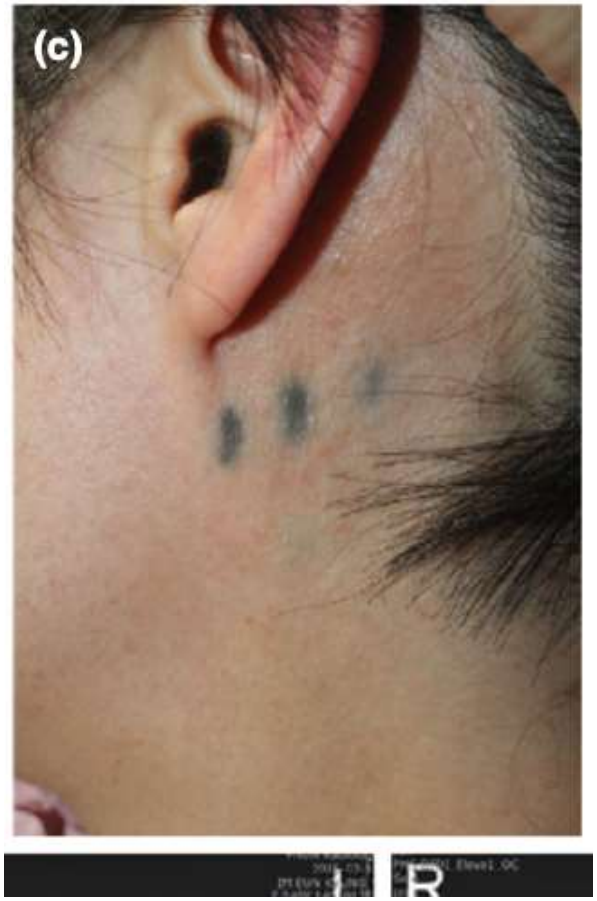
- Tattoo pigment
- Drug hyperpigmentation
  - Minocycline, amiodarone, antimalarials
- Argyria

Diagnosis: Argyria

- Cause: silver exposure (directly through skin or via ingestion)
- Manifestation: Pigmentation of skin that most commonly affects sun-exposed areas, sometimes presents as a macule
- Sources of exposure:
  - Occupational exposure: Silver mining, photographic processing, metal alloy manufacturing
  - Topical medications: creams, eye drops
  - Dental amalgam, acupuncture needles
  - Ingested: colloidal silver dietary supplements
    - highest silver concentrations are found in the skin, liver, spleen and adrenals




DR.OZ
IS IT CANCER?
more quickly?
What is rosacea, and is it the



Park MY, Lee JS, Jin HJ, et al. Localized argyria: troublesome side-effect of acupuncture. J Eur Acad Dermatology Venereol 2018;32:e62–e65.

Letter to the Editor

Cases of Argyria Associated With Colloidal Silver Use

Annals of Pharmacotherapy
2019, Vol. 53(8) 867–870

DOI: 10.1177/1060028019844258
journals.sagepub.com/home/aop
SAGE

- 16 patients
  - 15 patients described chronic use (ongoing >2weeks)
  - Median duration 2 years
  - Common reasons: “boost the immune system, promote well-being, and treat or prevent cold/allergy symptoms”
  - 11 cases: self compounded colloidal silver from a silver wire and generator
  - 2 cases: purchased from a local retailer

  - After discontinuation
    - 8 cases reported permanent argyria
    - 4 mild improvement - complete resolution (3 required treatment)

Takeaways

- The ingestion and application of silver is a practice that can lead to specific pathologic abnormalities
- Generally thought to be a benign condition but there are reports of neurologic deficits, renal problems, hepatic complications
- Histological findings include brown-black granules, singly or in clusters, in the basement membrane zone surrounding the sweat glands and connective tissue sheaths around the pilosebaceous structures
  - Other sites: renal biopsies, GI biopsies
  - Can be subtle! Clinical history is important!

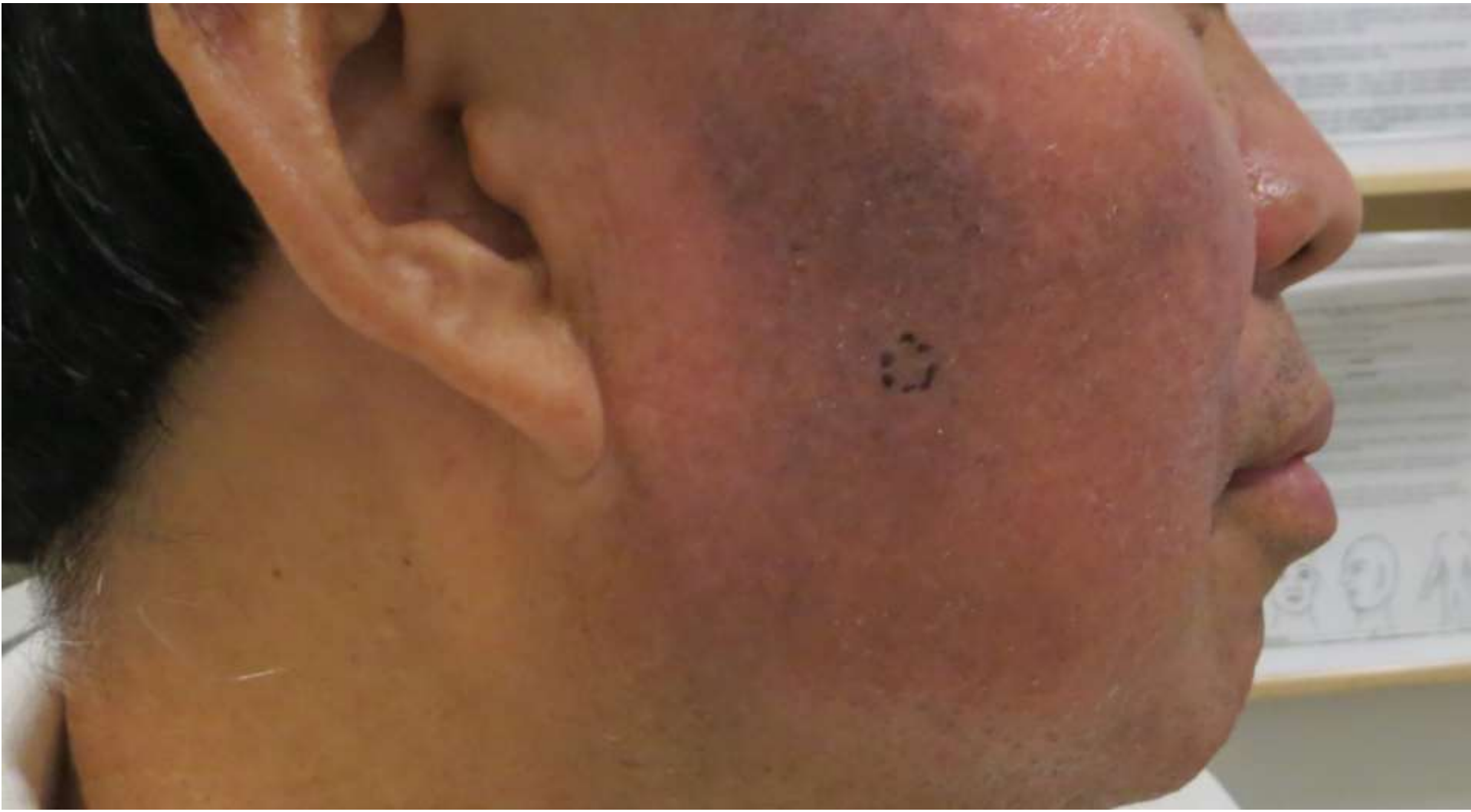
Sources cited:

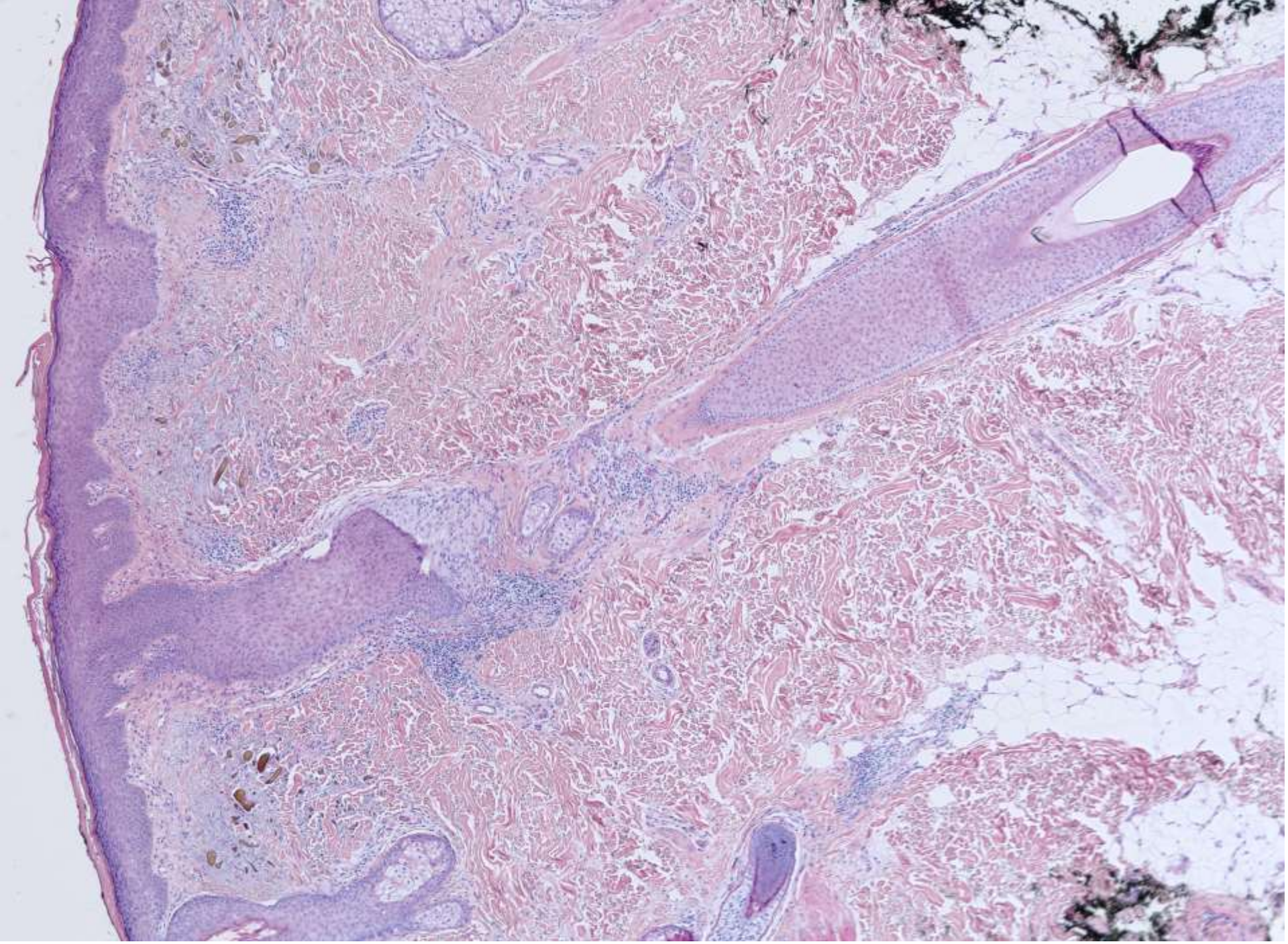
- Kim JJ, Konkel K, McCulley L, et al. Cases of Argyria Associated With Colloidal Silver Use. Ann Pharmacother 2019;53:867–870.
- Rumayor Piña A, Martínez Martínez M, Toral Rizo VH, et al. Cutaneous amalgam tattoo in a dental professional: An unreported occupational argyria. Br J Dermatol 2012;167:1184–1185.
- Park MY, Lee JS, Jin HJ, et al. Localized argyria: troublesome side-effect of acupuncture. J Eur Acad Dermatology Venereol 2018;32:e62–e65.

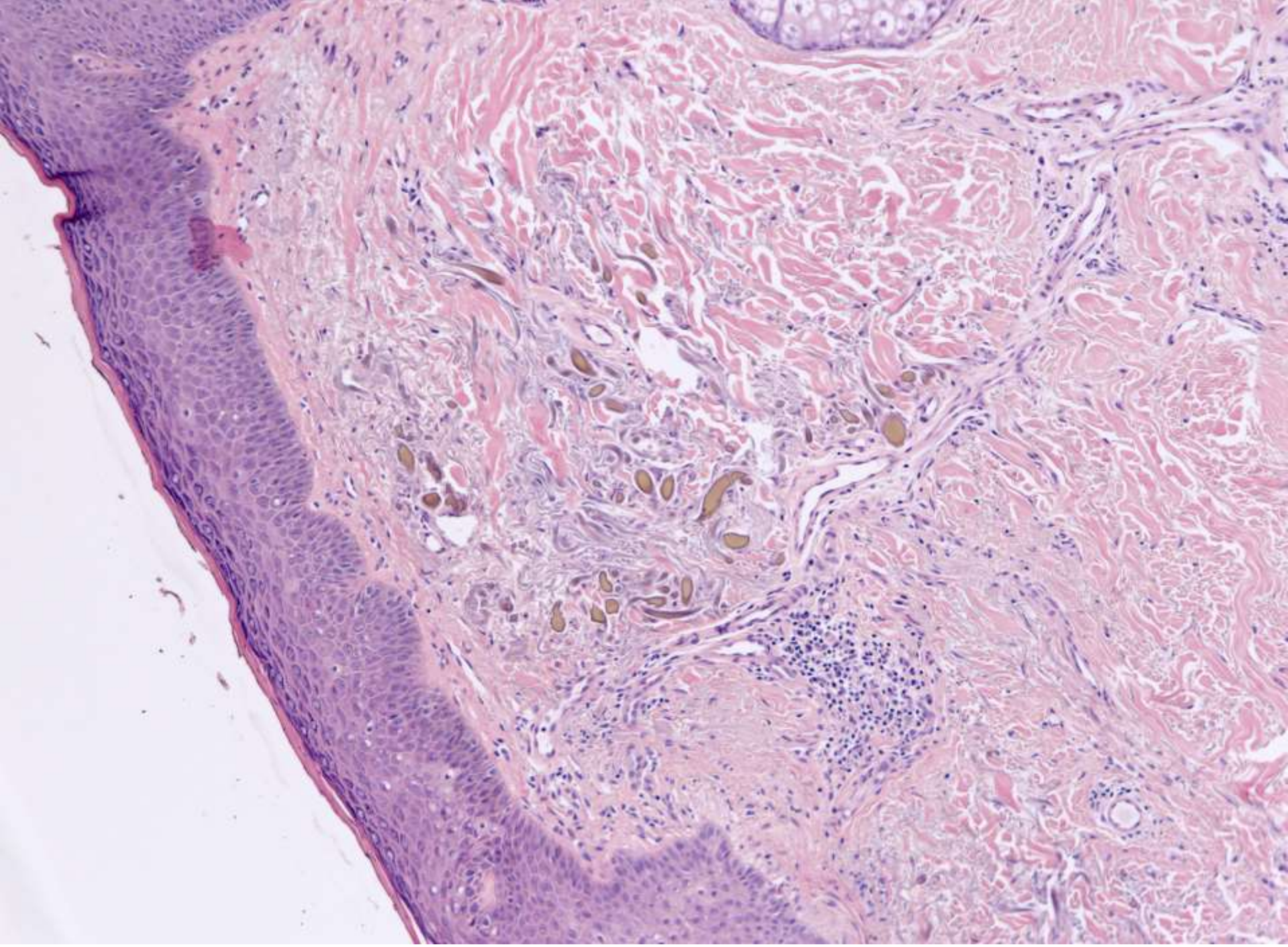
20-0706

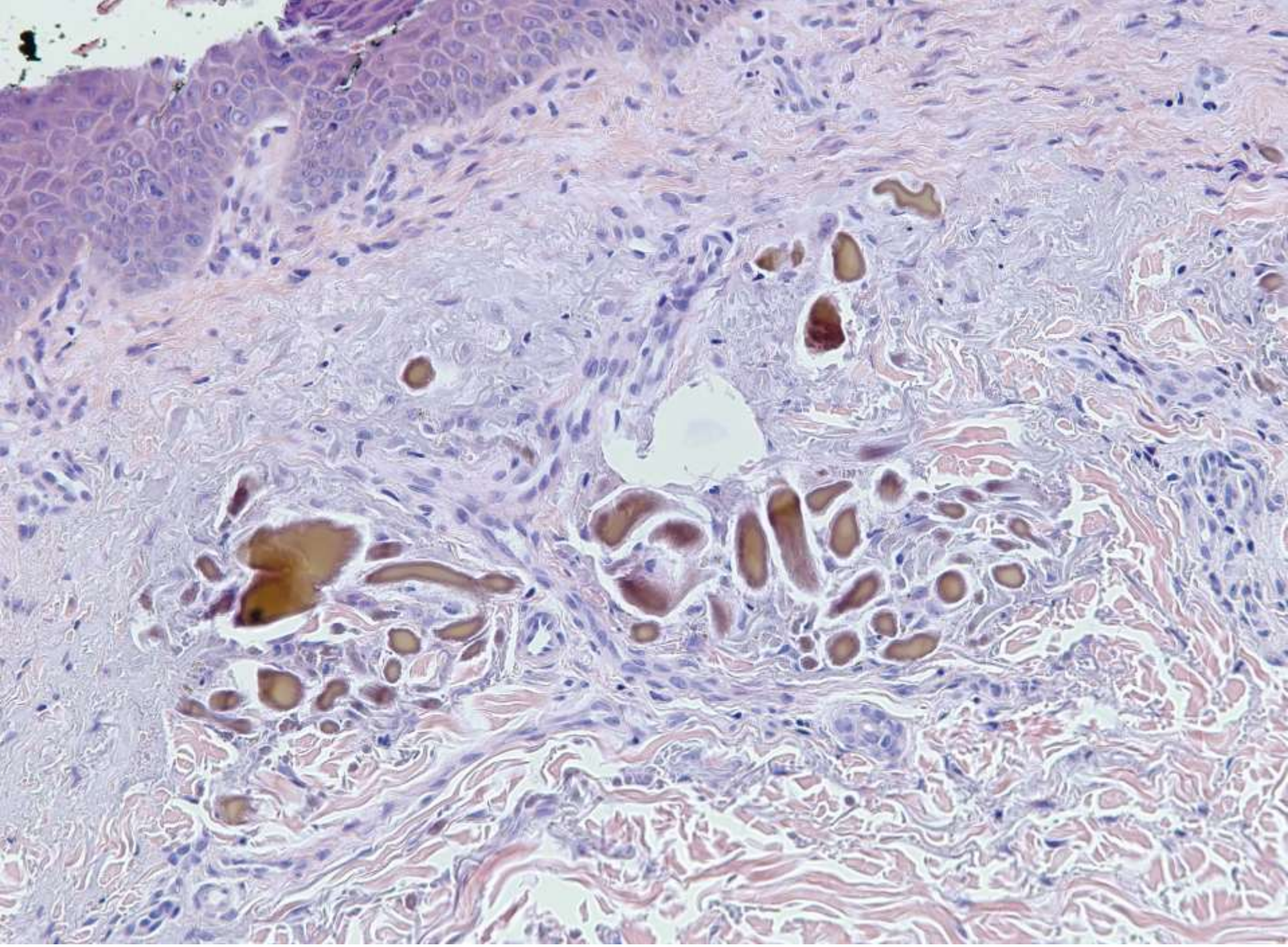
Sara Zadeh/Hubert Lau; VA Palo Alto

63-year-old M with h/o gout, being treated with allopurinol, presented with darkening of cheeks, ongoing for multiple years. Per patient, may have started after starting allopurinol.





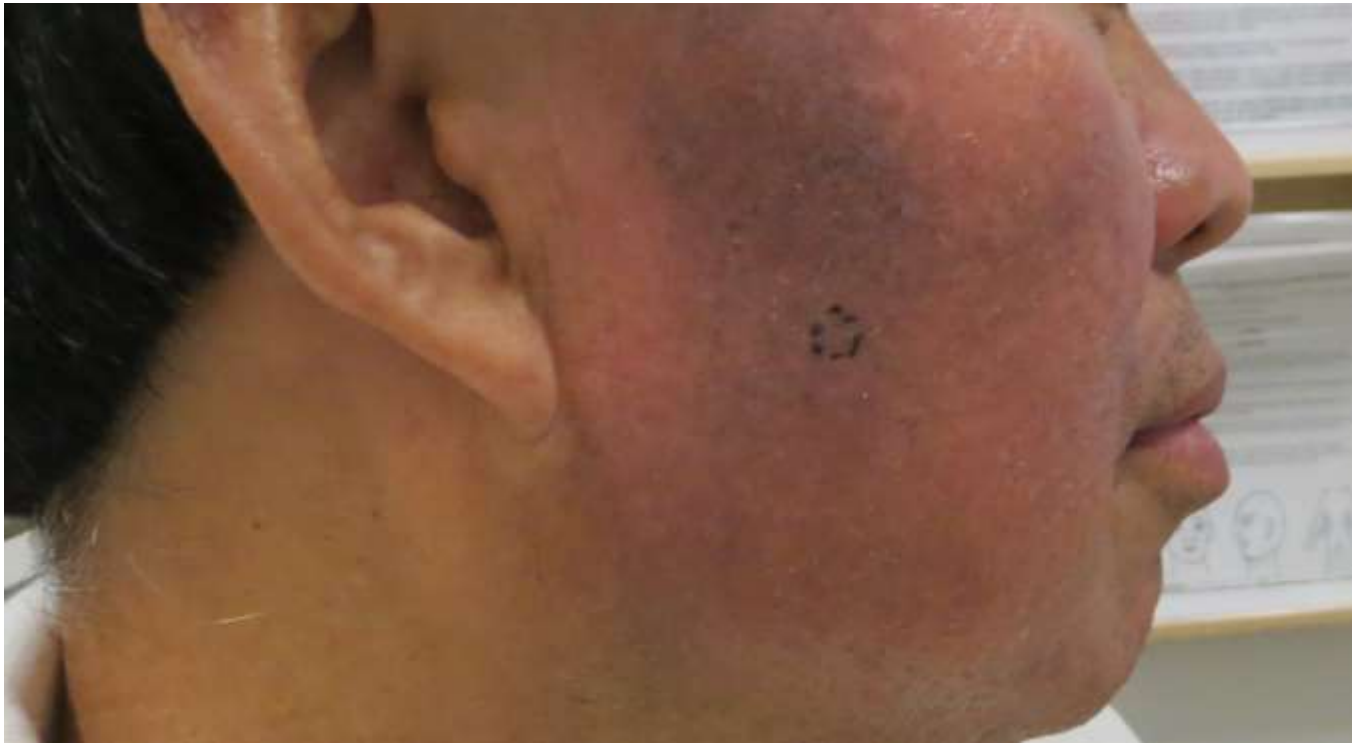


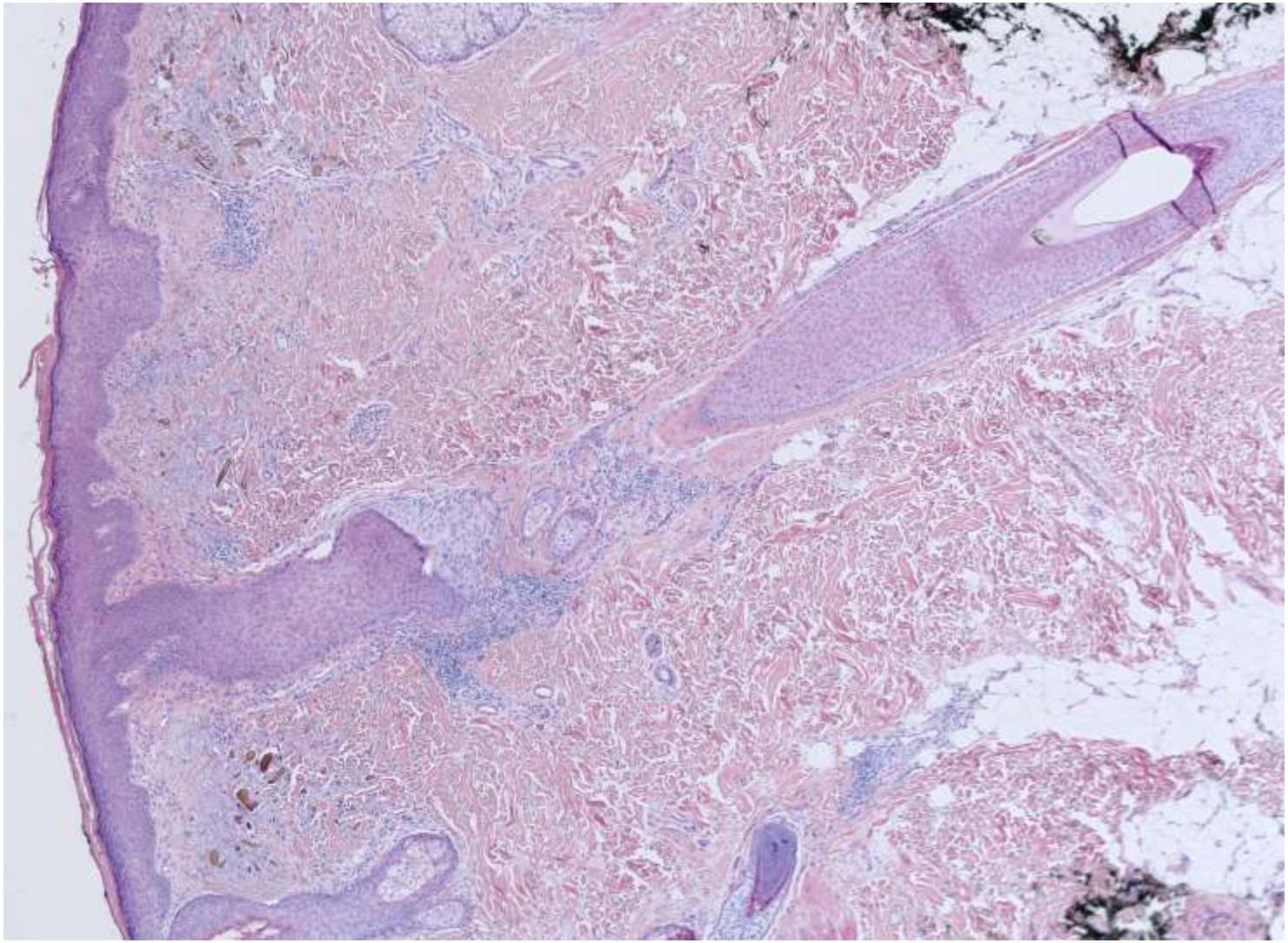


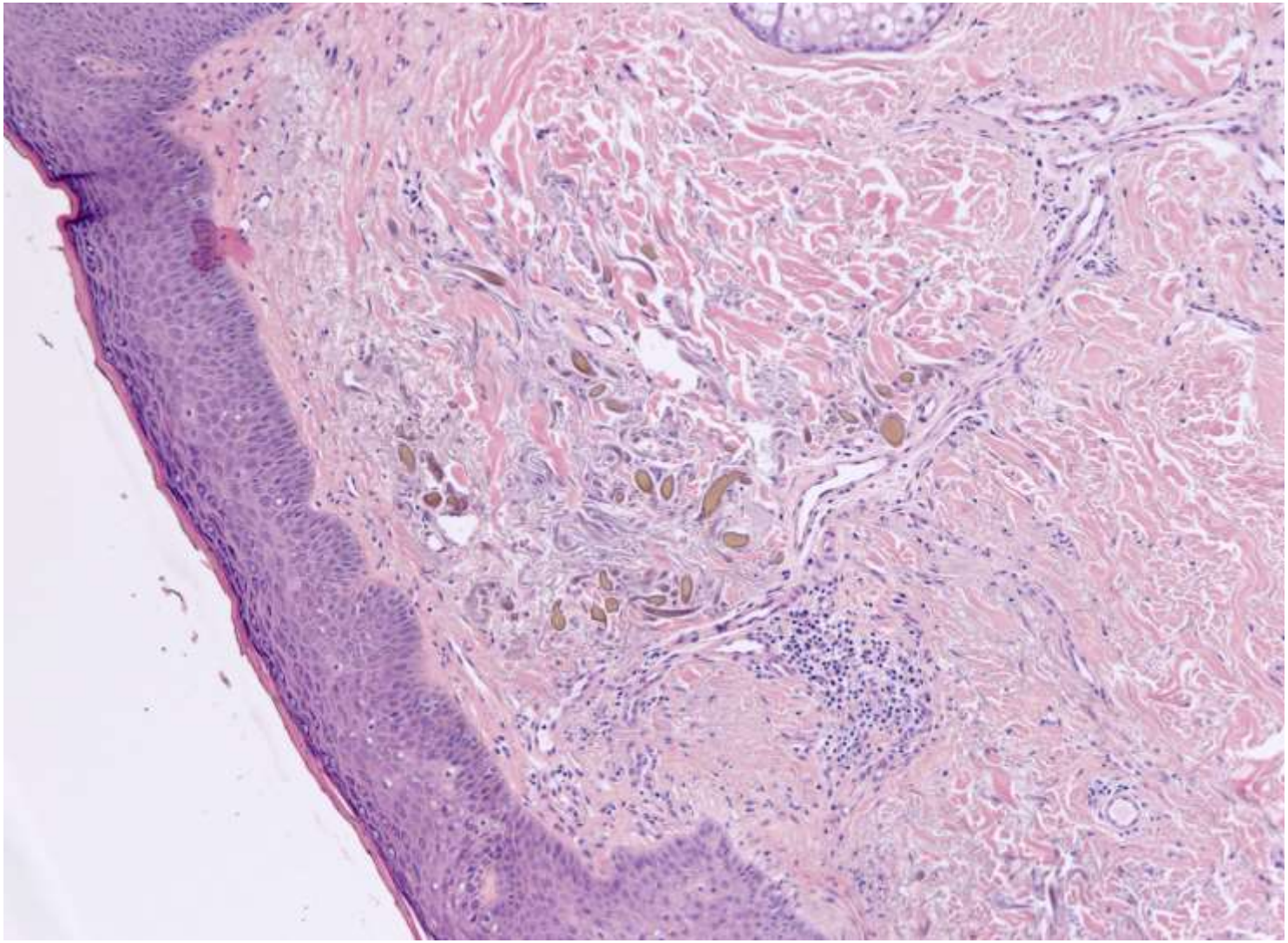
DIAGNOSIS?

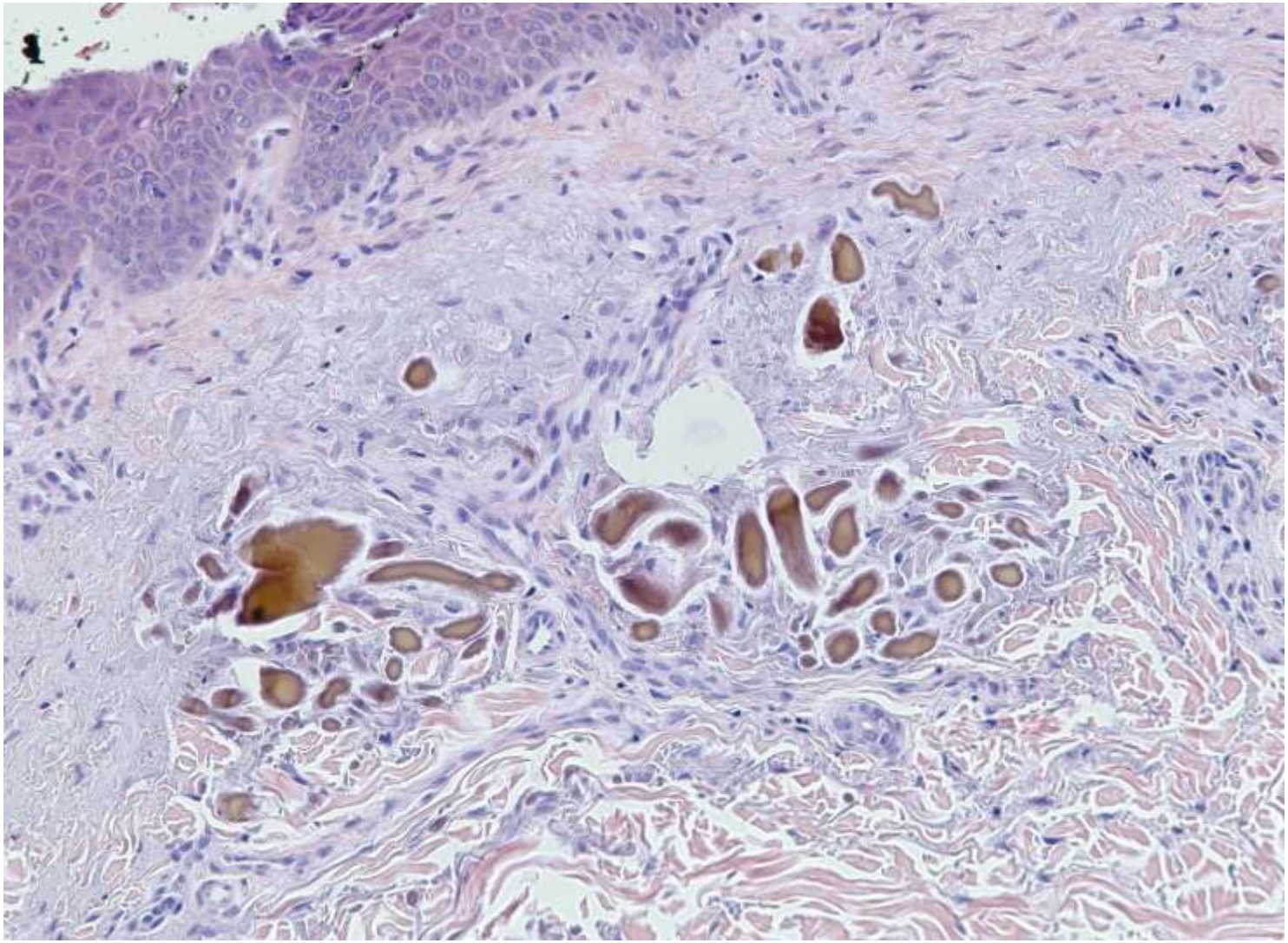
Clinical history

- 63-year-old man, history of gout, being treated with allopurinol
- Presented for darkening of cheeks, ongoing for multiple years
  - Per patient, may have started after starting allopurinol









DIAGNOSIS:
SKIN, RIGHT LATERAL CHEEK, PUNCH BIOPSY
-- CONSISTENT WITH OCHRONOSIS (SEE COMMENT)

Endogenous ochronosis

- Occurs in alkaptonuria (rare autosomal recessive disorder caused by a mutation in the *HGD* gene, which codes for homogentisate 1,2-dioxygenase)
- Accumulated homogentisic acid is excreted in the urine (urine homogentisic acid test used for diagnosis of alkaptonuria) and deposited in connective tissues, including cartilage, skin, sclerae, and heart valves

Exogenous ochronosis

- Deposition of homogentisic acid in the dermis, most commonly cheeks, temples, and neck, following excessive or prolonged exposure to a variety of topical products used in skin-lightening agents
  - **Hydroquinone**, resorcinol, phenol, mercury, picric acid
- Asymptomatic, localized blue-gray discoloration of the skin with hyperchromic, pinpoint papules
- Diagnosis often requires skin biopsy, as it can clinically resemble post-inflammatory hyperpigmentation, melasma, and pigmented contact dermatitis

Exogenous ochronosis

- The offending medication should be stopped, and although the ochronosis may improve slowly, it is generally considered permanent
- There is no known effective treatment, but topical agents including retinoic acid, dermabrasion, cryotherapy, and various laser treatments have been used with inconsistent results

Clinical follow-up

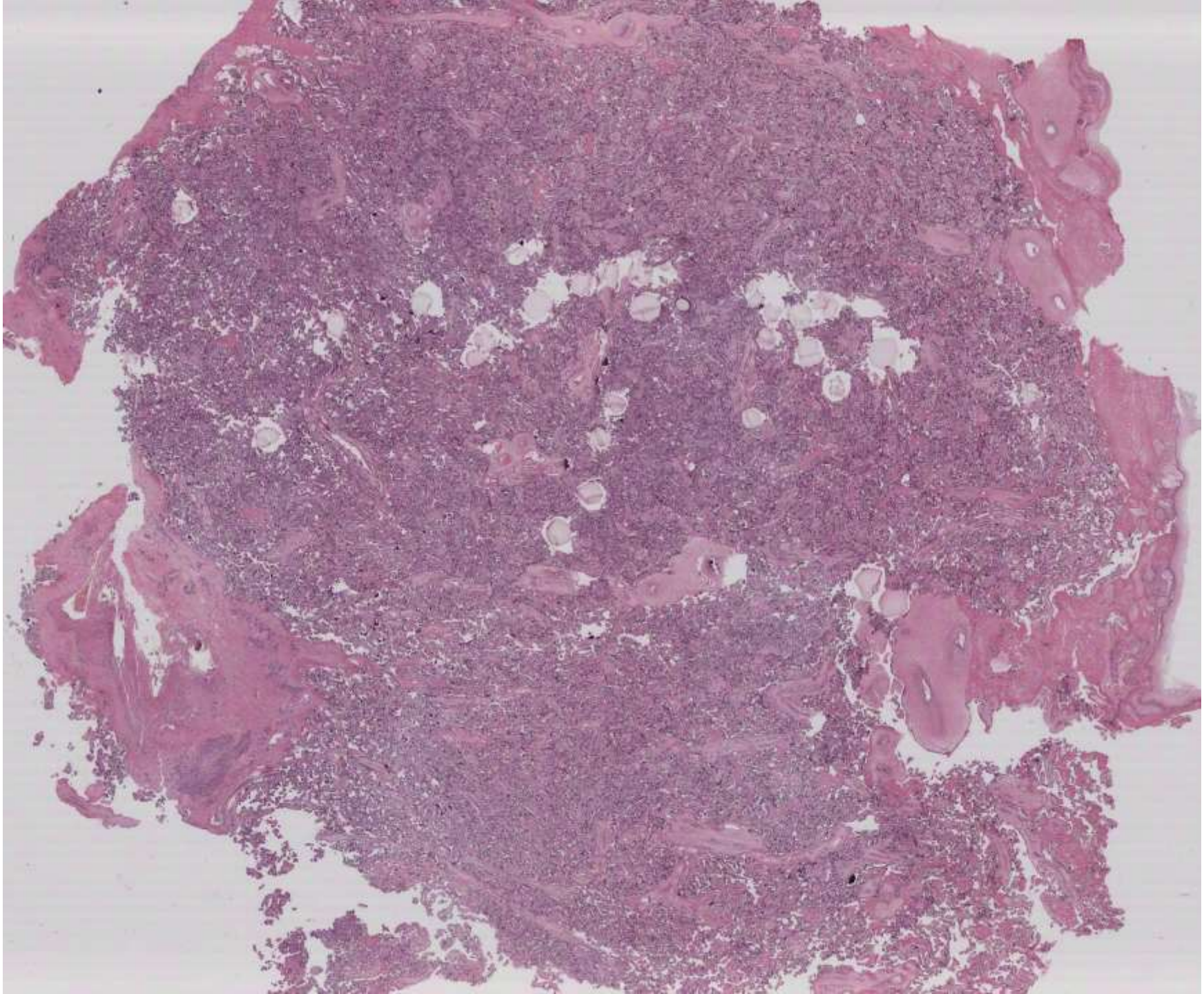
- Patient revealed that he did use a skin lightening cream given to him by a friend
- No clinical or laboratory evidence of alkaptonuria
- Patient has been using 0.1% tretinoin cream with mild improvement

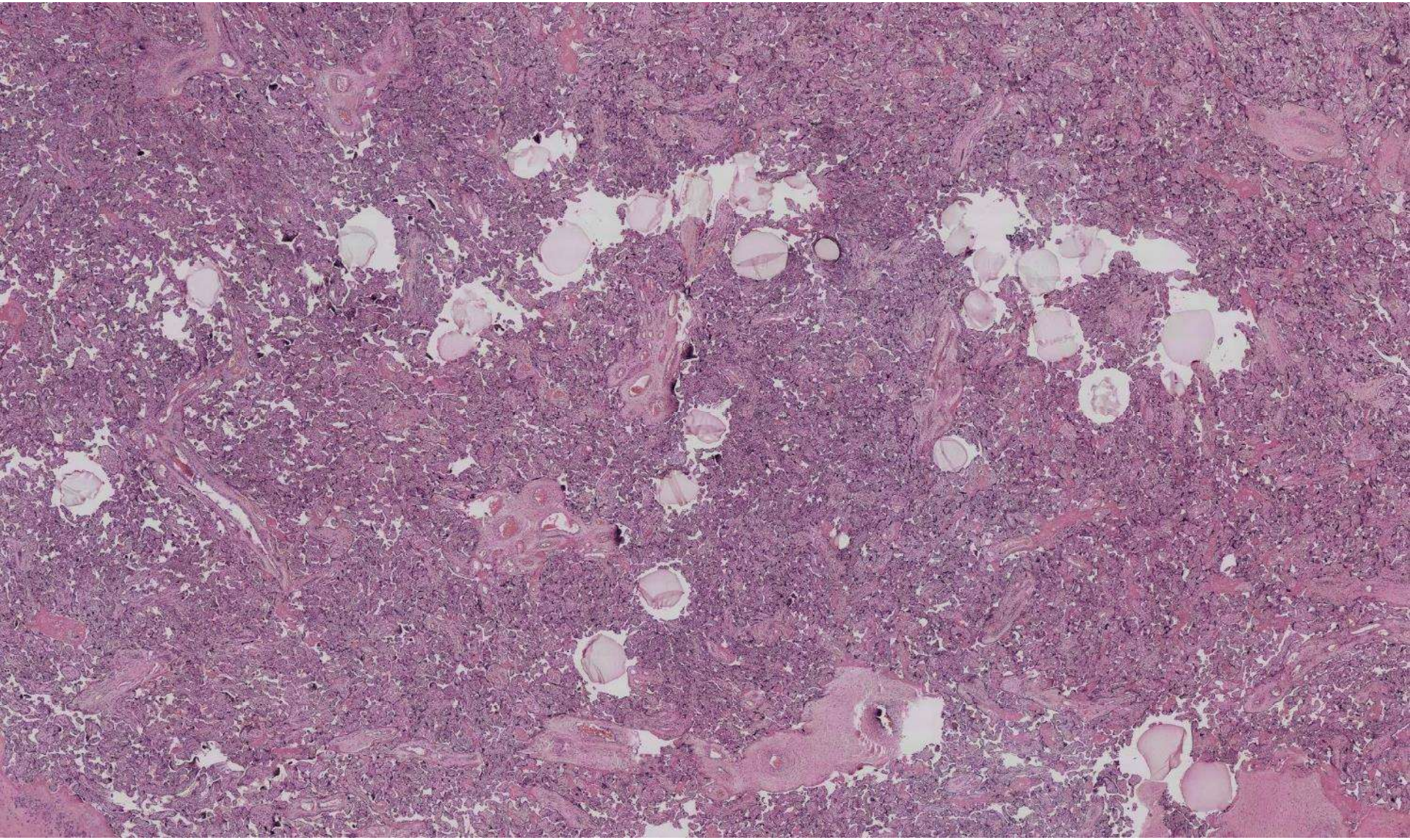
20-0707
scanned slide available!

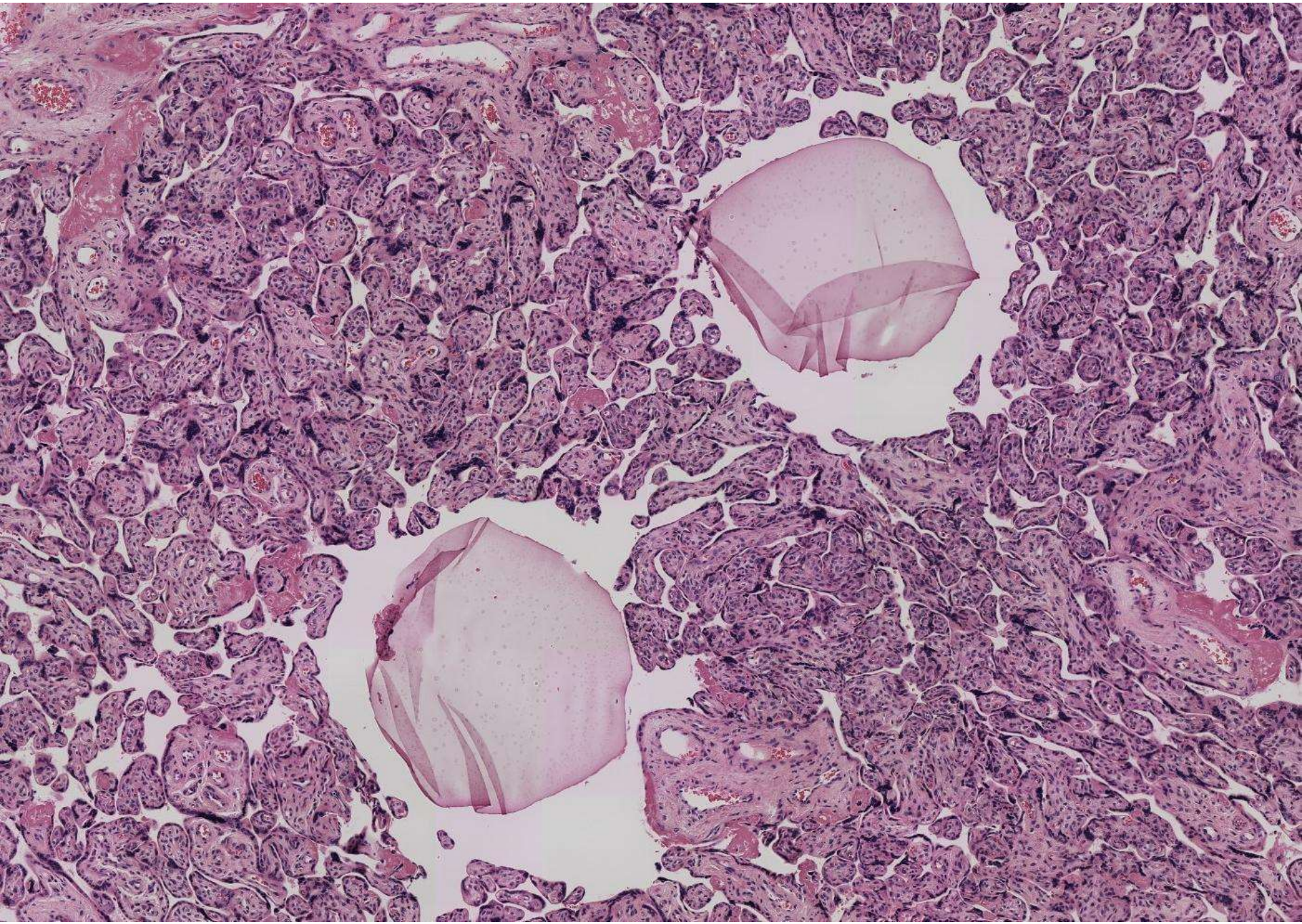
Ankur Sangoi; El Camino Hospital

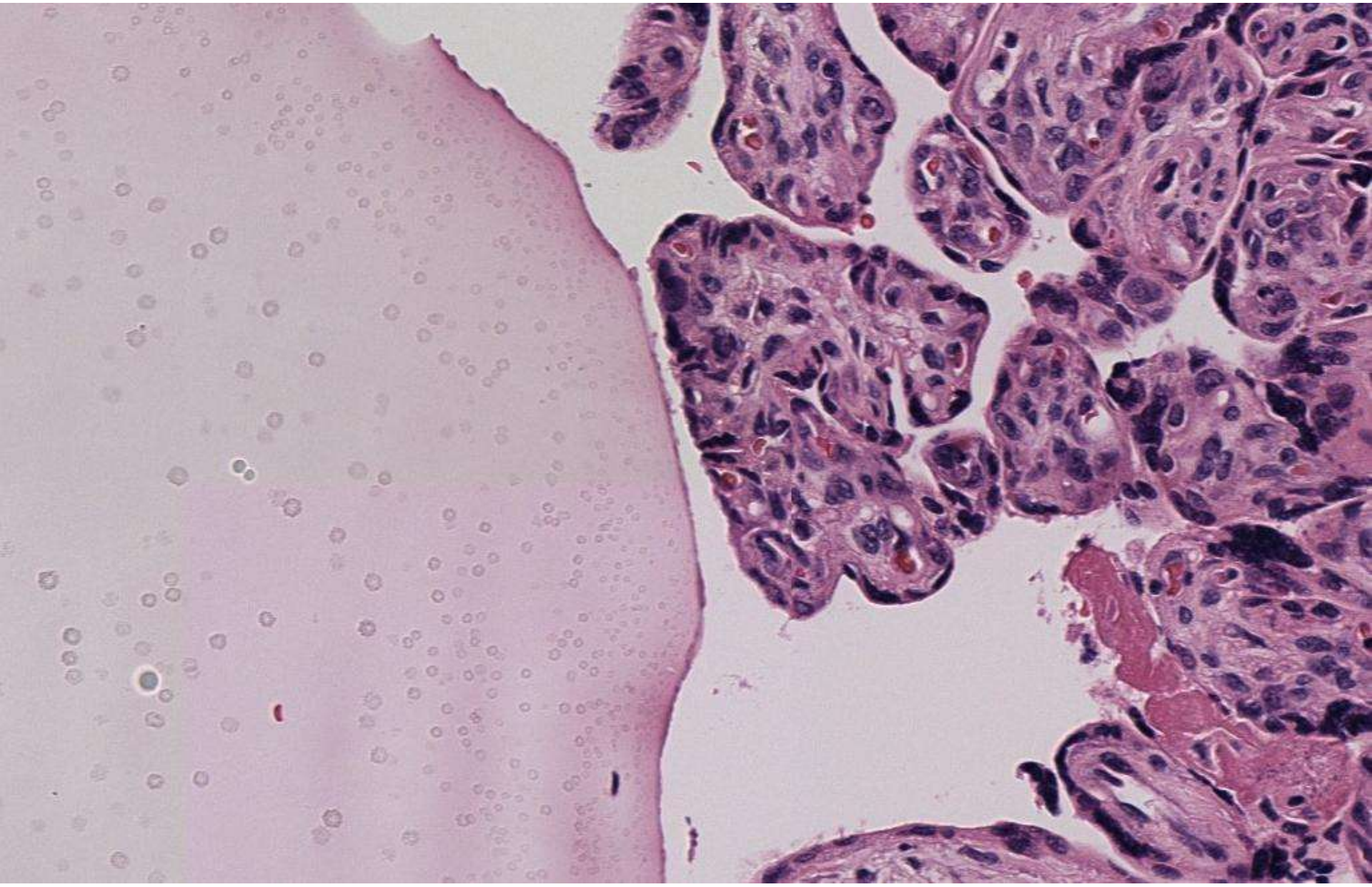
44-year-old F with postpartum hemorrhage and retained complete placenta. Cut section of placental disc showed multiple 1mm grey/green embedded nodules.

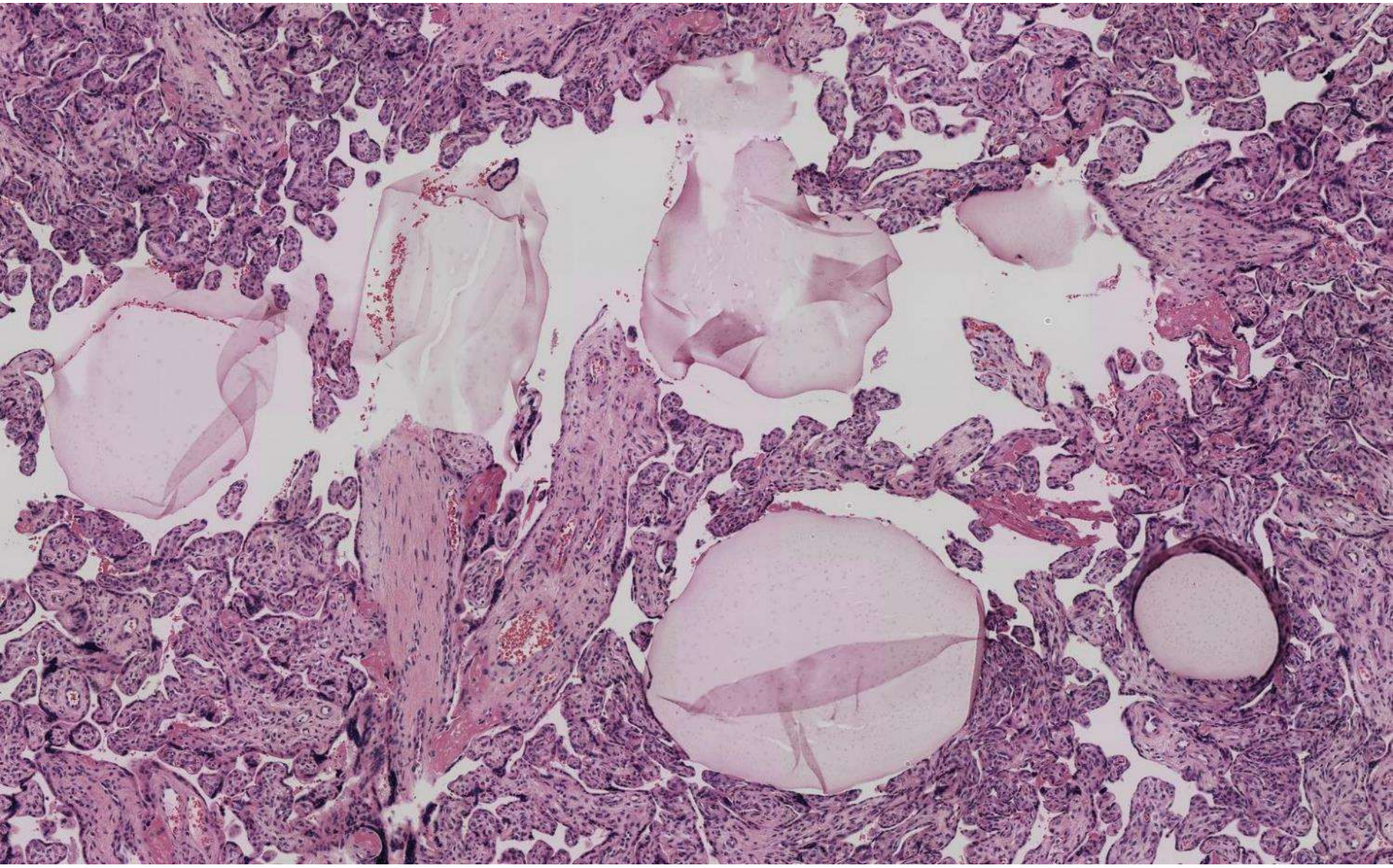

cm
1
2

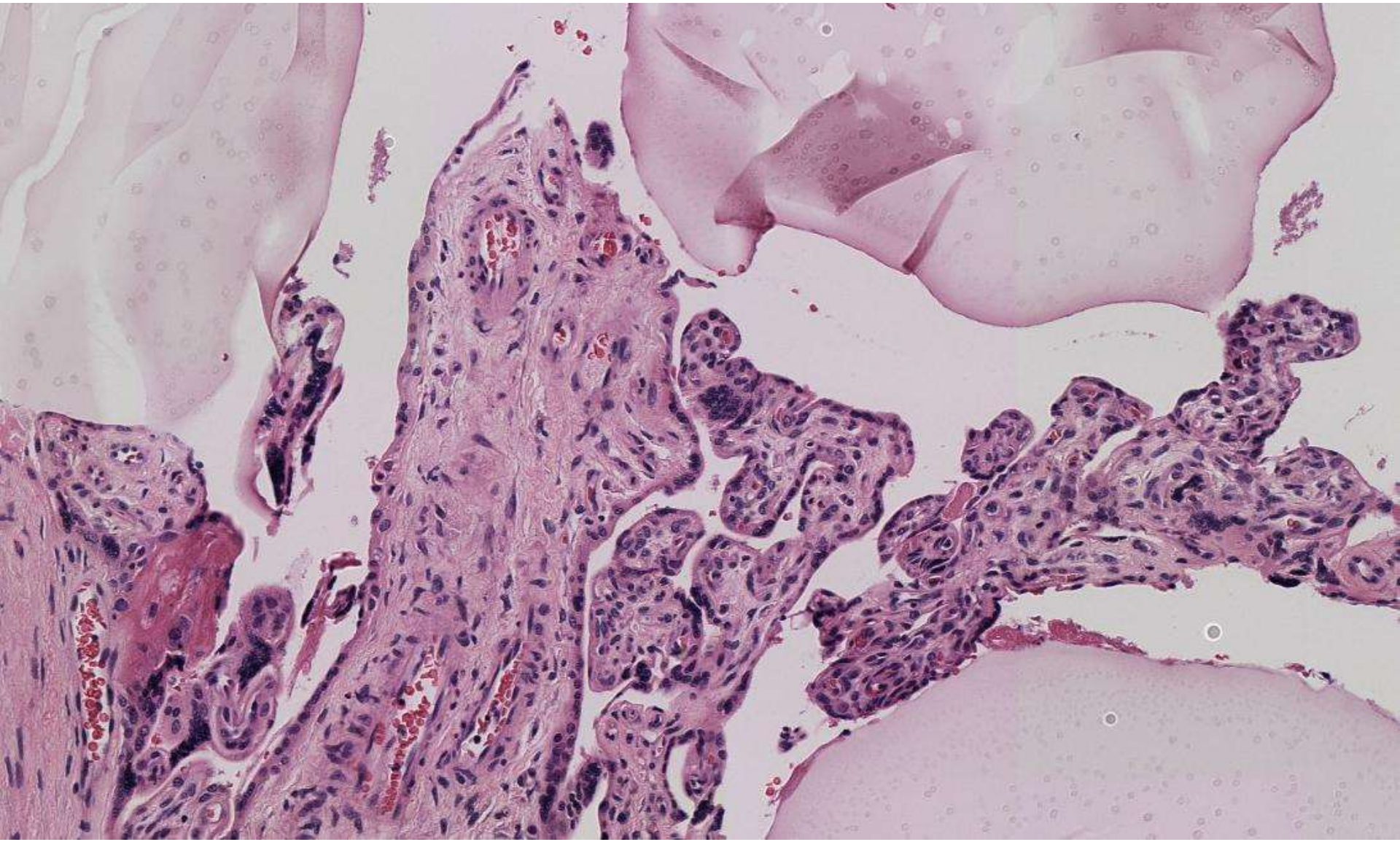


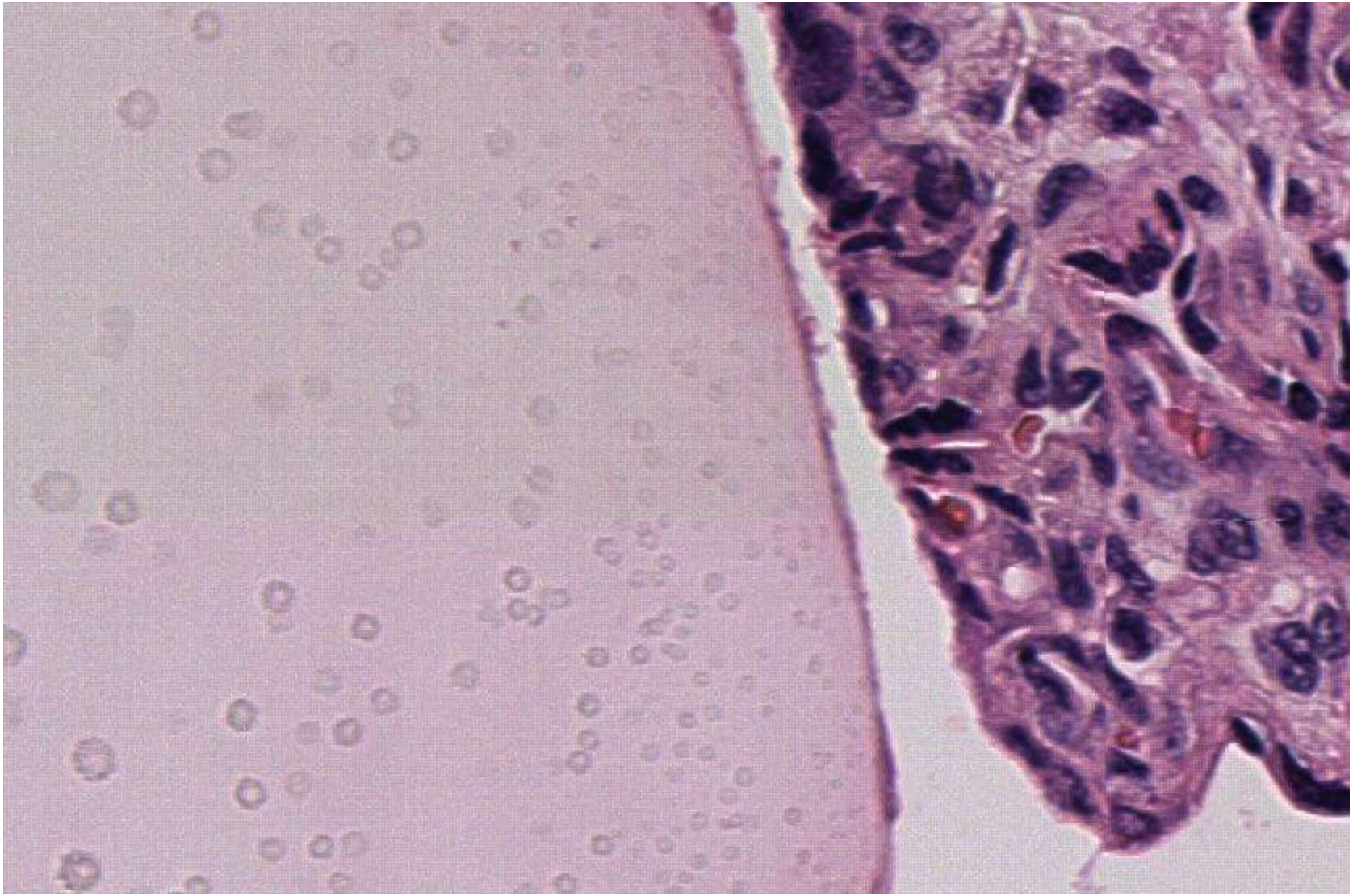


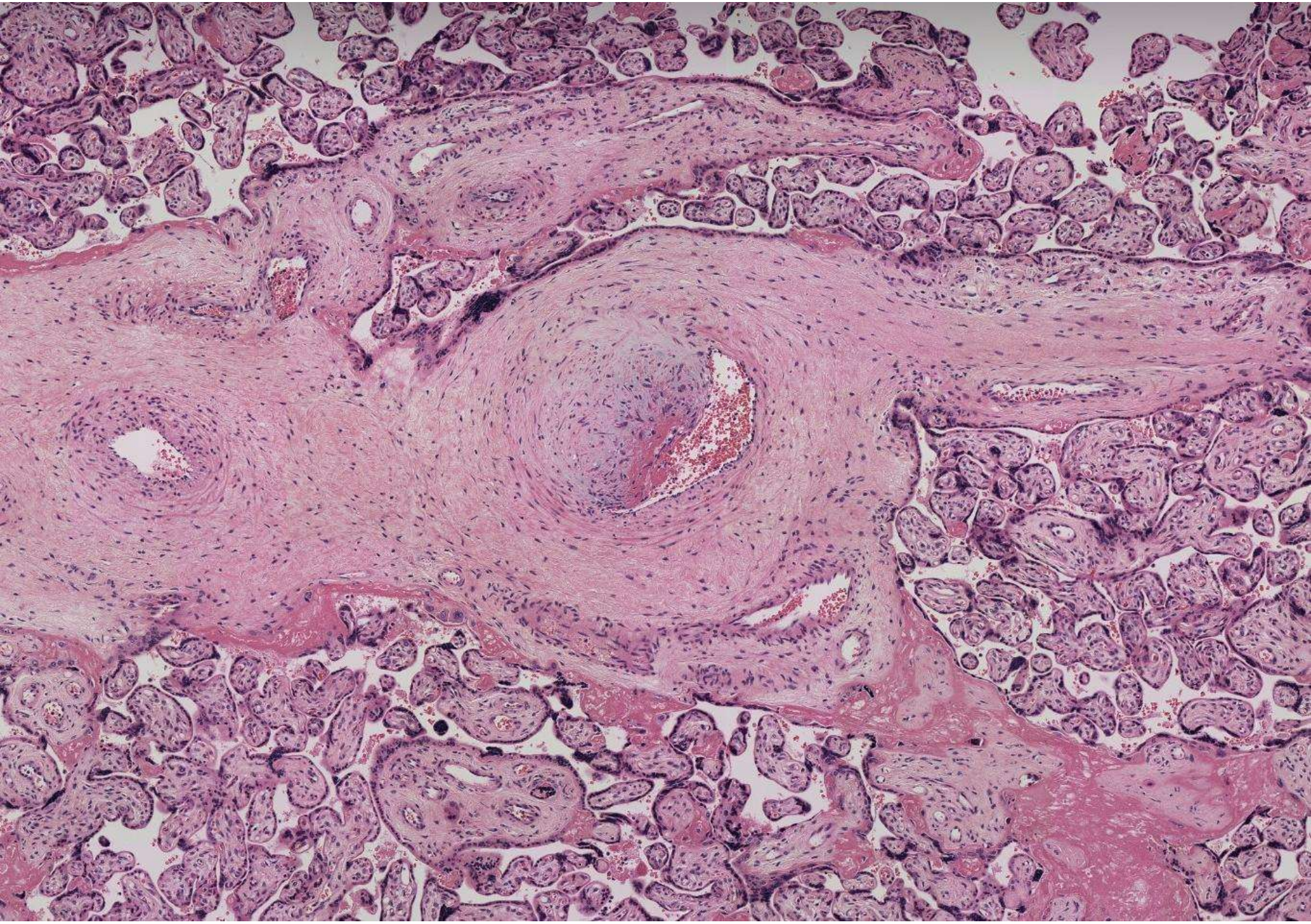


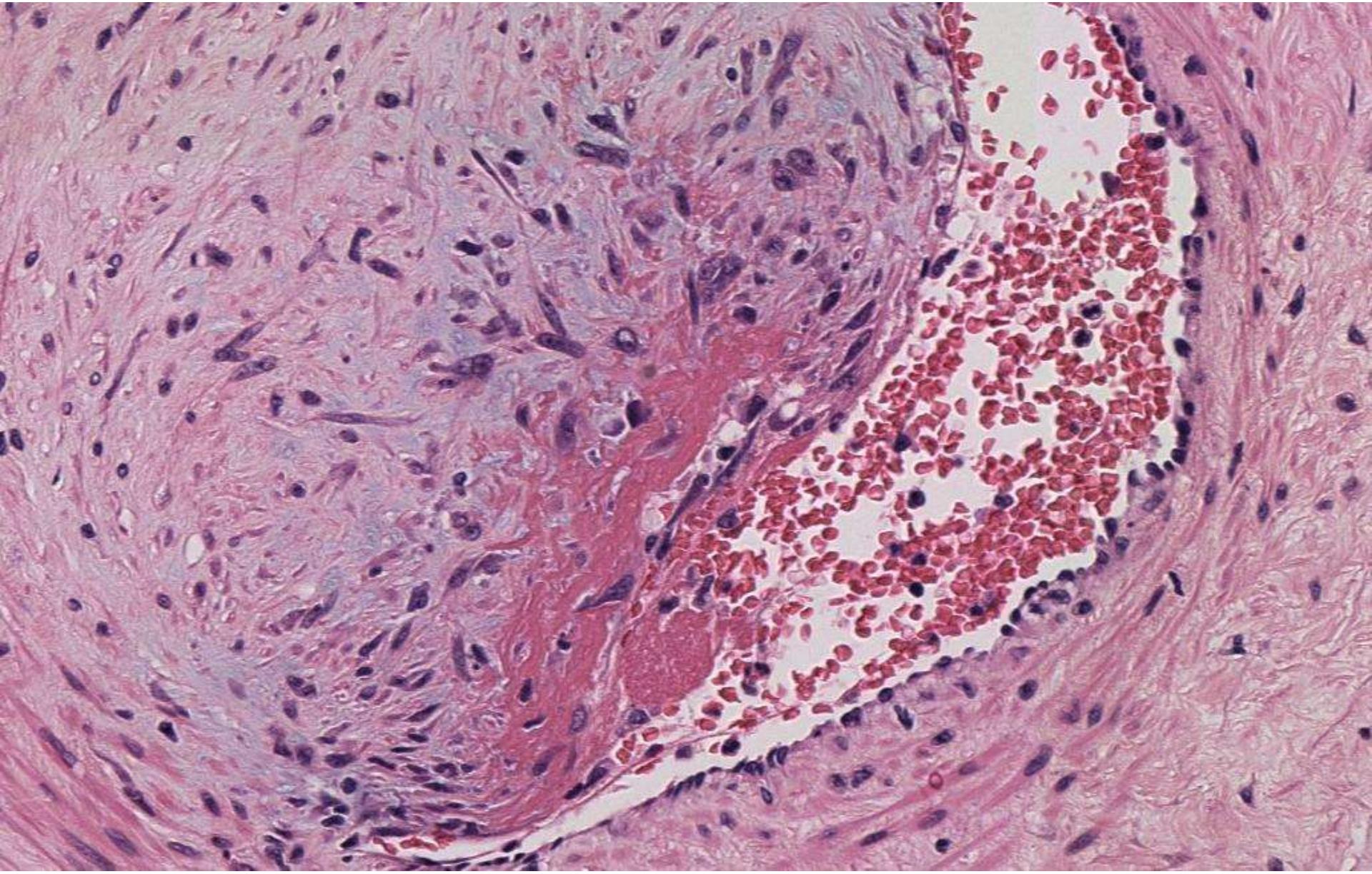












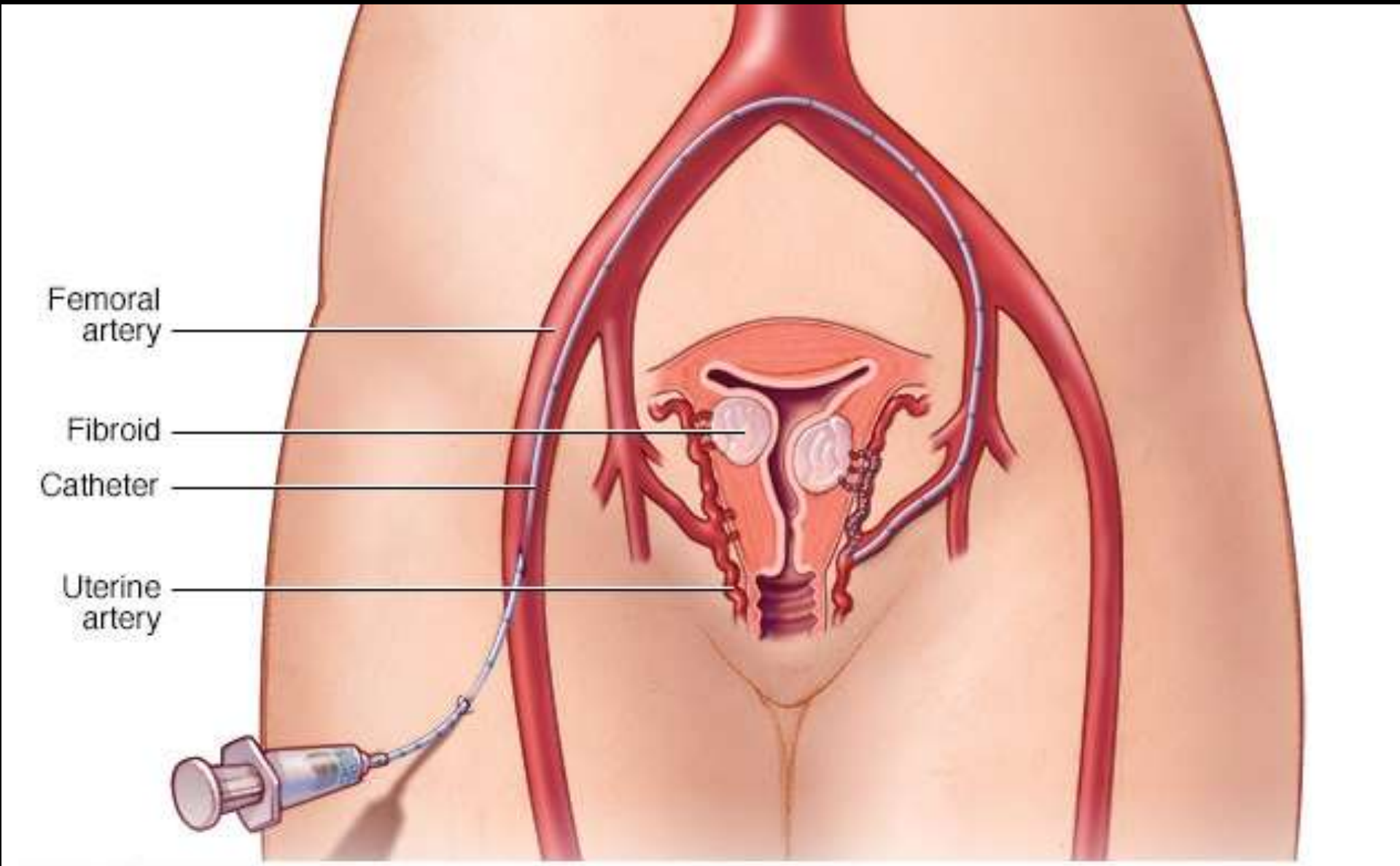
DIAGNOSIS?

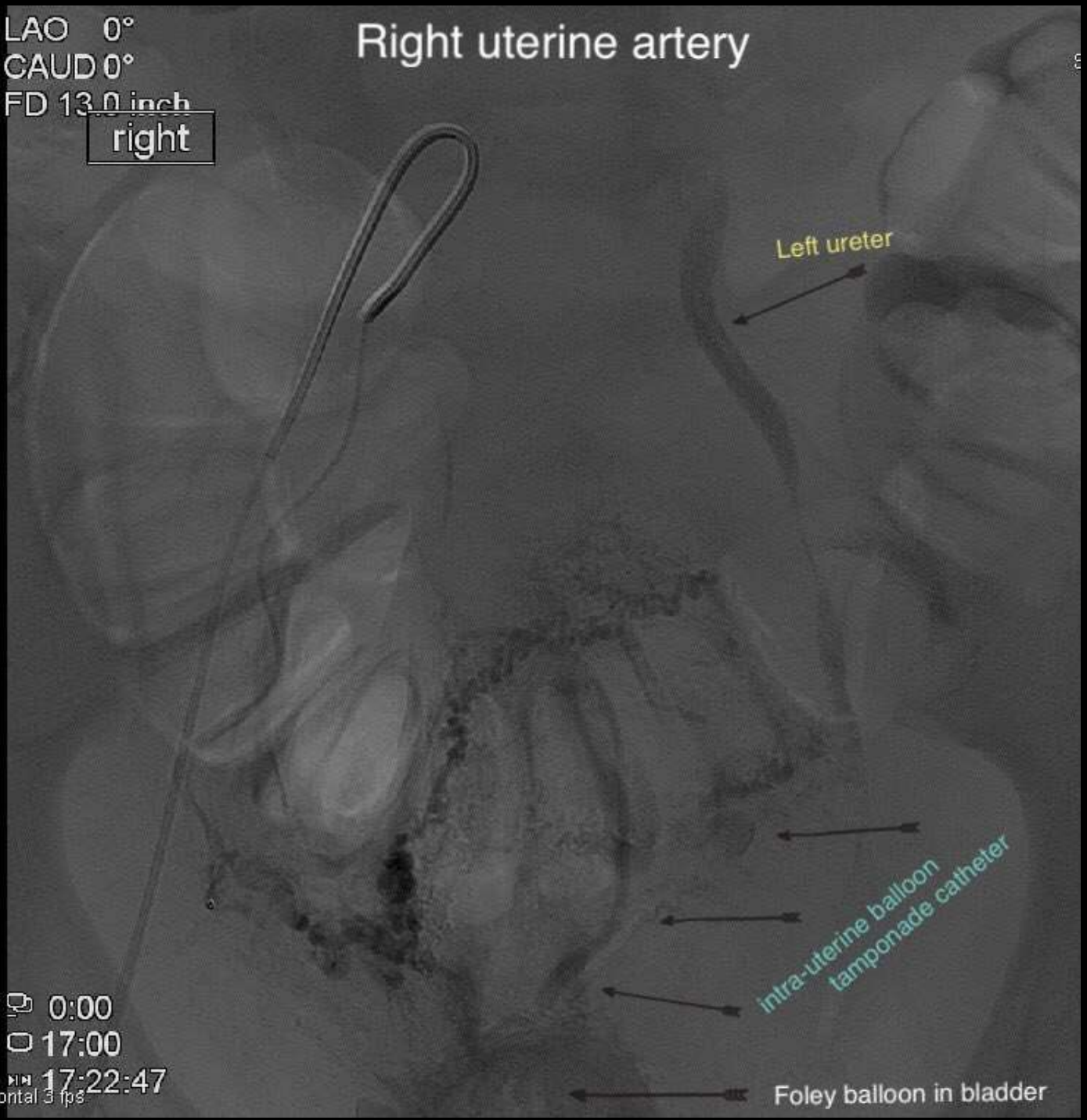
DDx

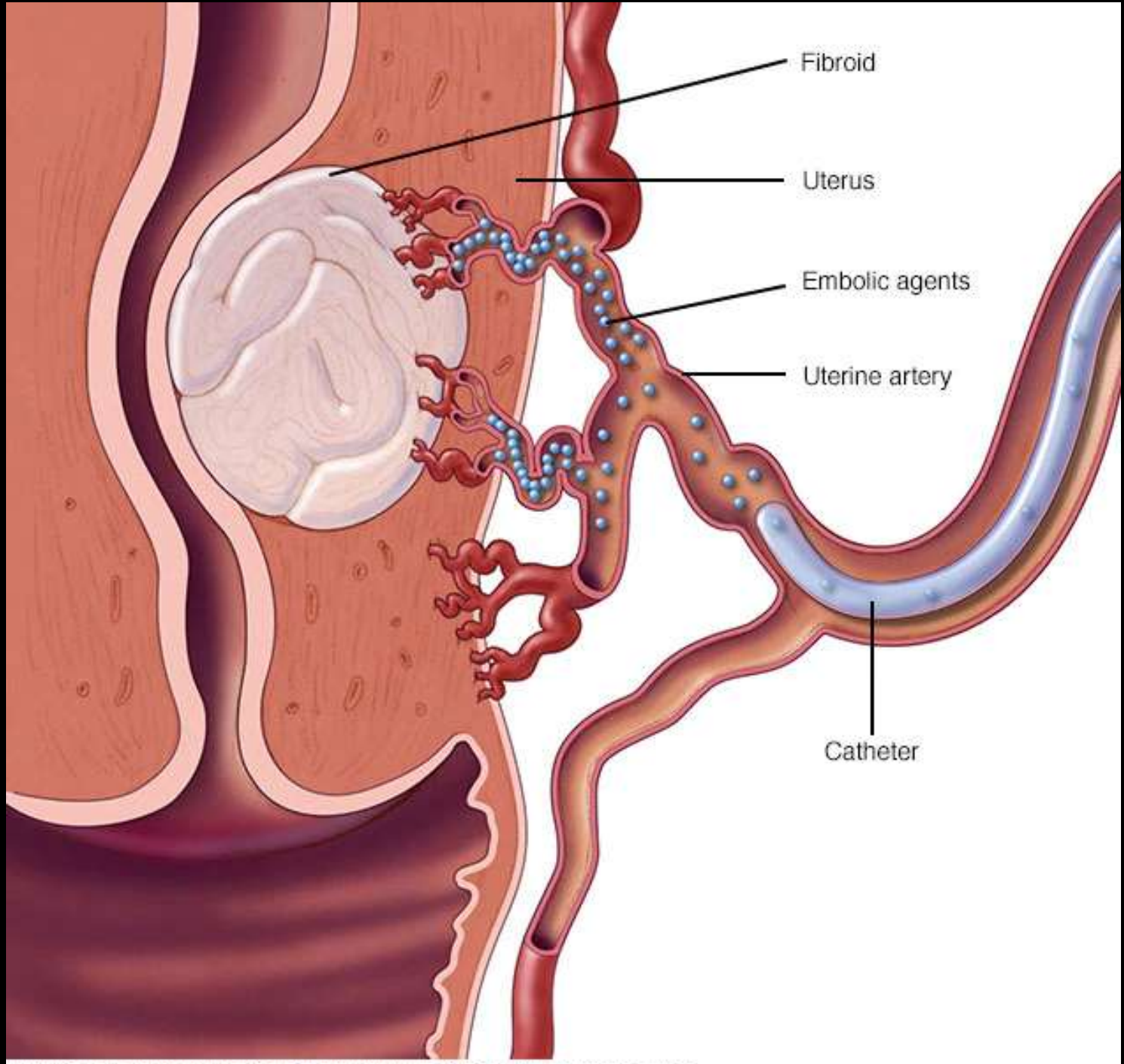
- Embolization material
- Parasitic organism

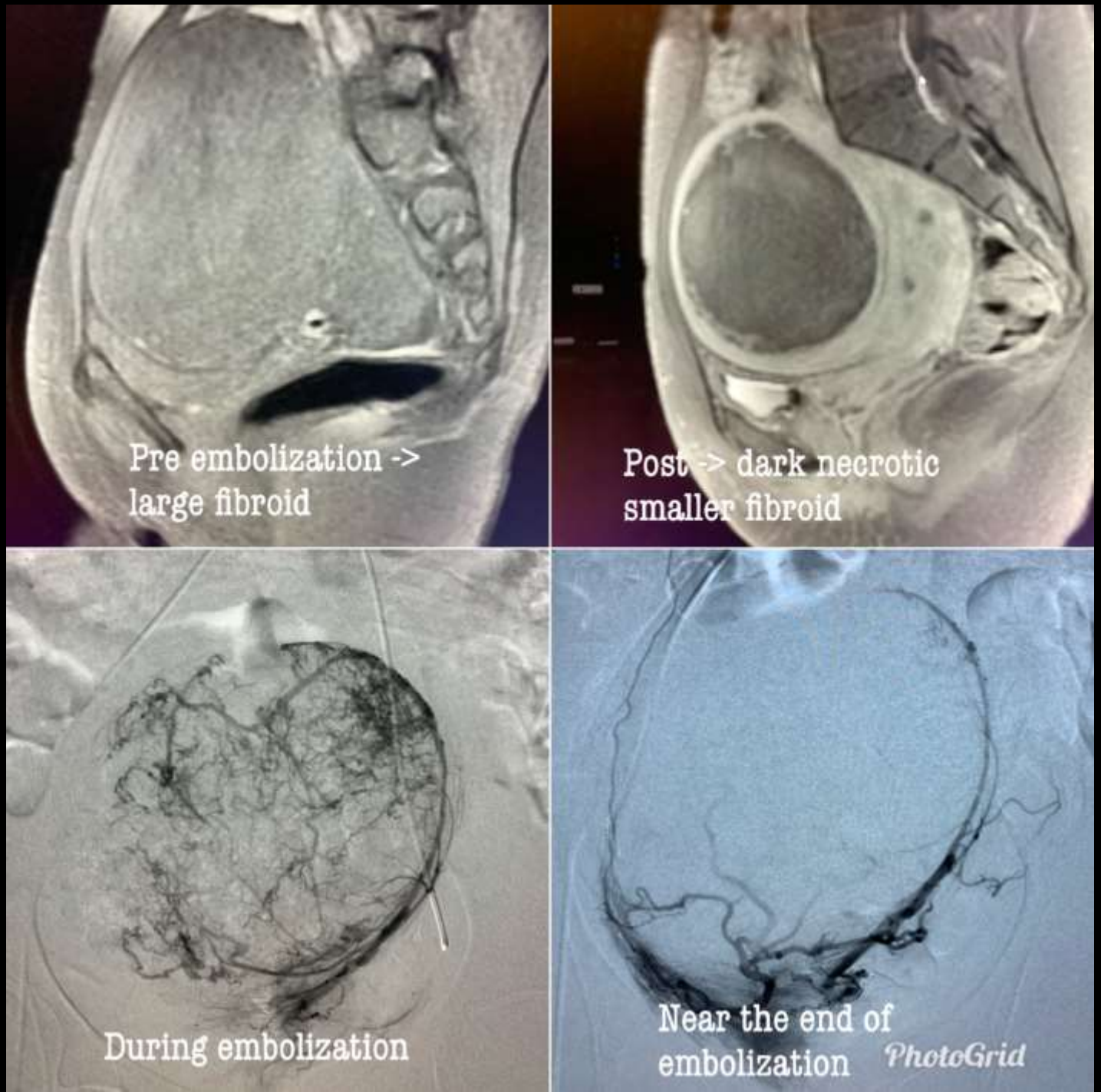
Final Dx

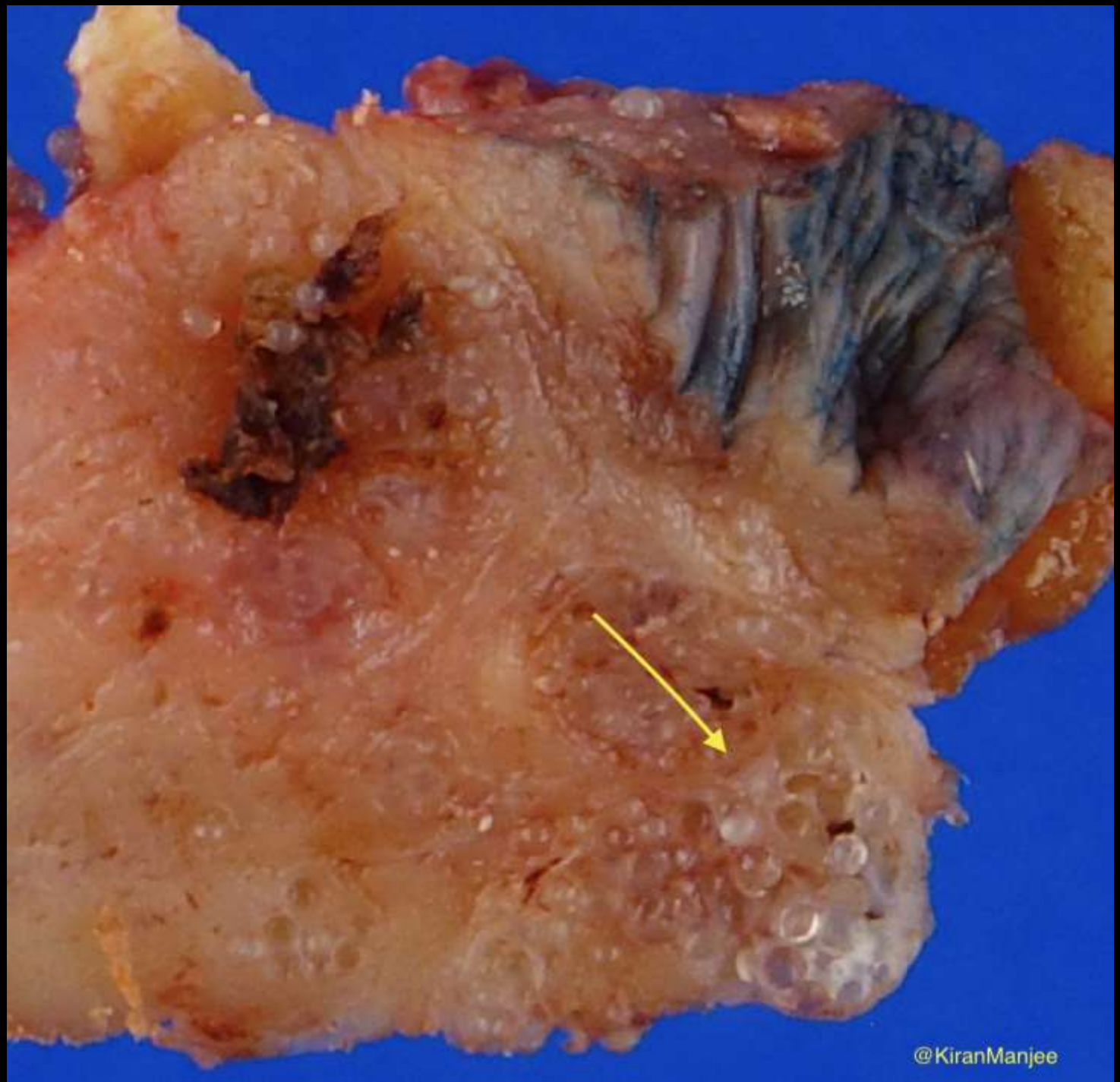
- **Embolization material**
  - Used to Tx post-partum hemorrhage

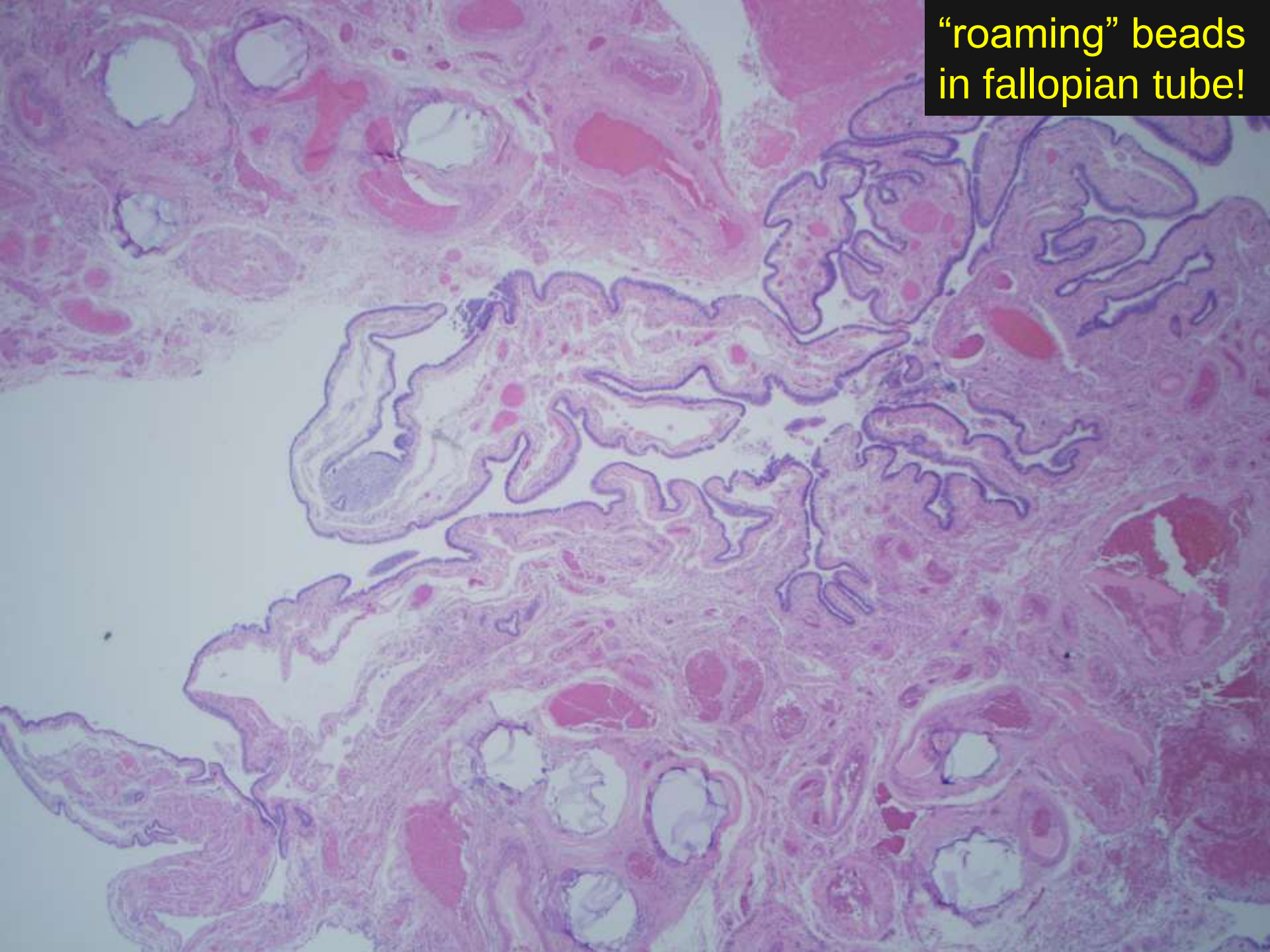


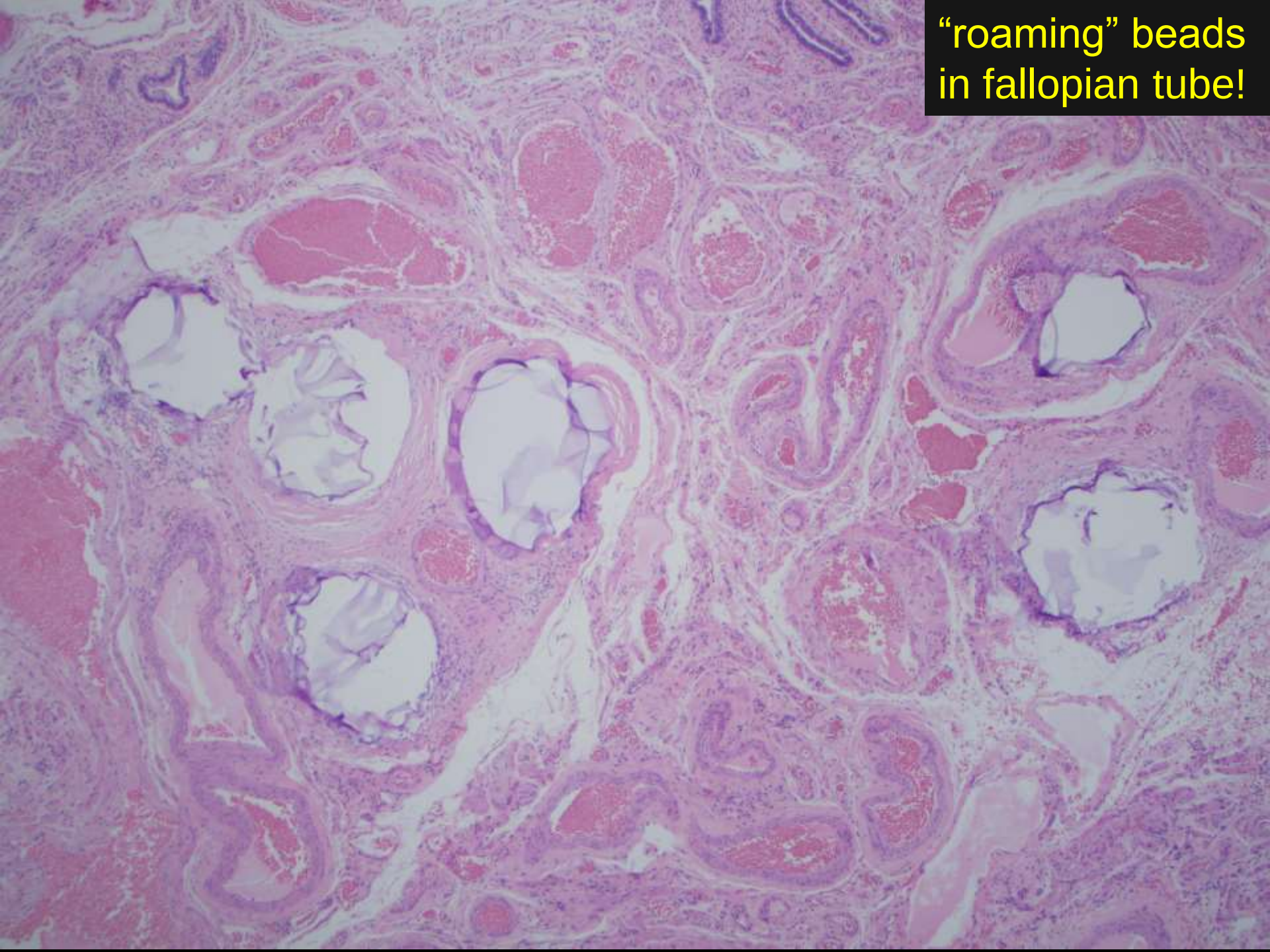

LAO 0°
CAUD 0°
FD 13.0 inch
right
Right uterine artery
Left ureter
intra-uterine balloon tamponade catheter
Foley balloon in bladder
0:00
17:00
17:22:47
ontal 3 fps

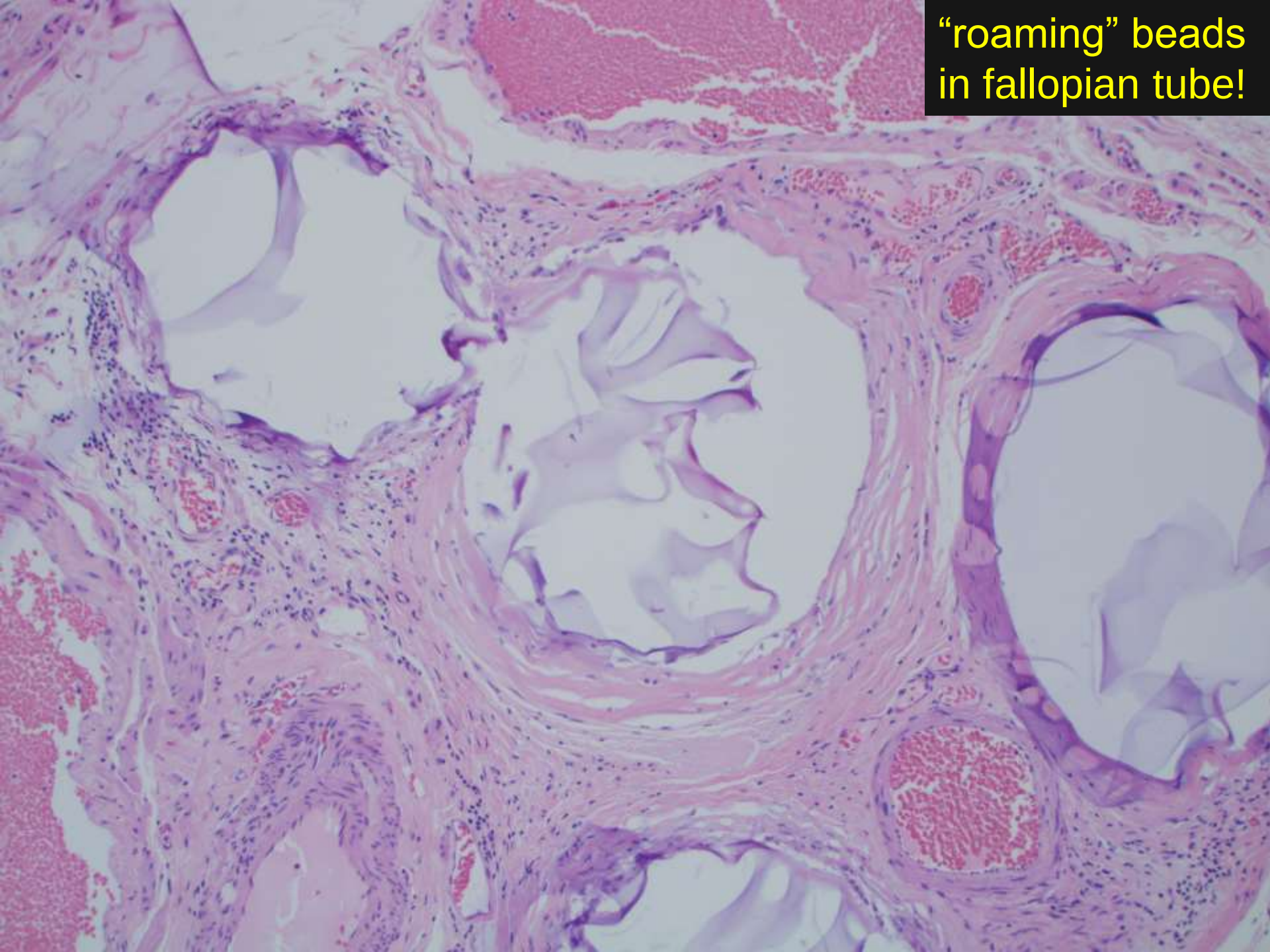



Pre embolization ->
large fibroid
Post -> dark necrotic
smaller fibroid
During embolization
Near the end of
embolization
PhotoGrid


@KiranManjee


“roaming” beads
in fallopian tube!


“roaming” beads
in fallopian tube!


“roaming” beads
in fallopian tube!

Uterine artery embolization

- **Typically used to Tx fibroids or adenomyosis, sometimes pre-operatively**
  - Occasionally used in post-partum hemorrhage
    - Most patients still able to have successful pregnancy after procedure
- **Be aware of “roaming” bead histology!**