AANP Teaching Rounds:

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AMERICAN ASSOCIATION
OF NEUROPATHOLOGISTS

Disclosures

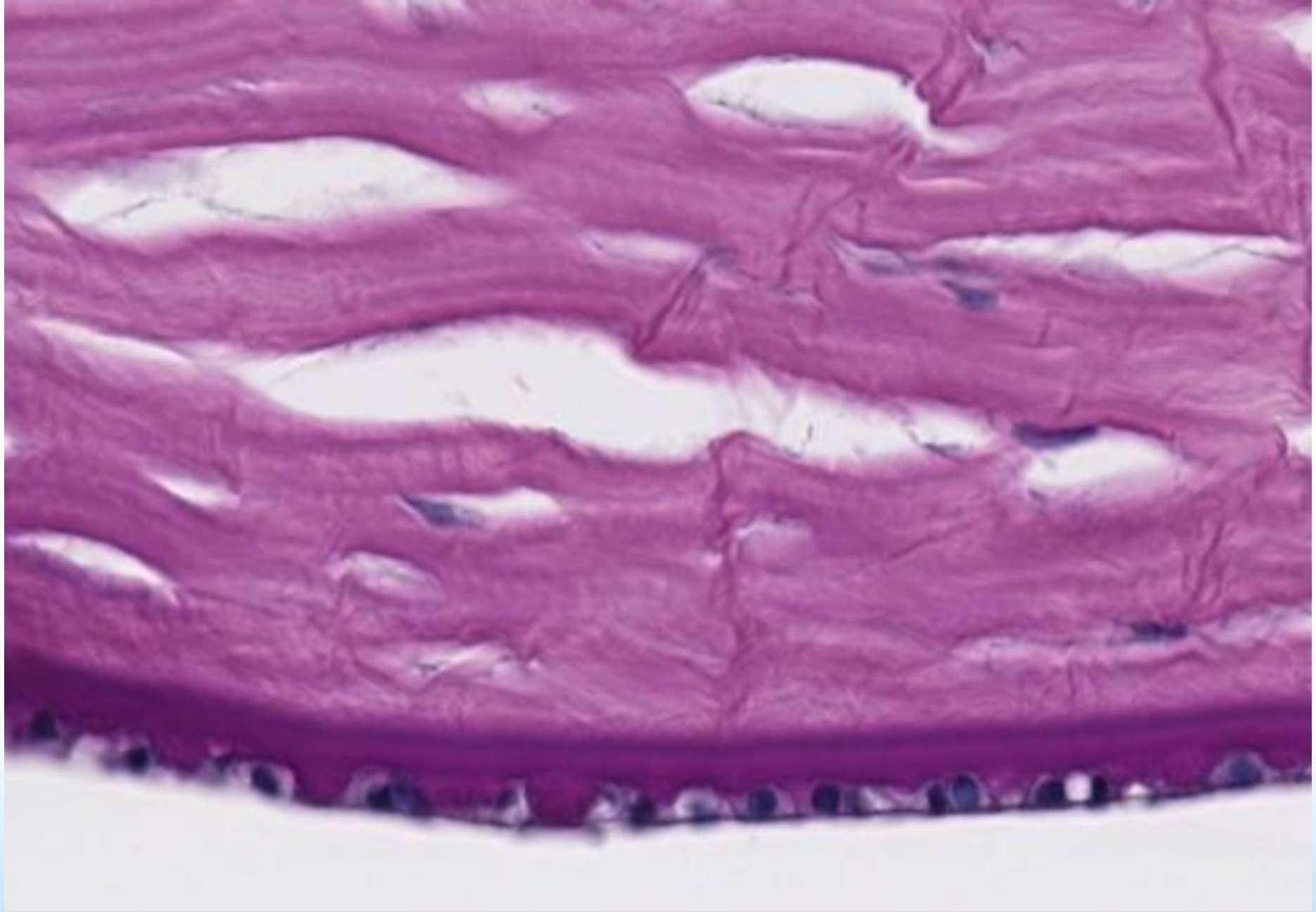
- I have no relevant financial relationships to disclose

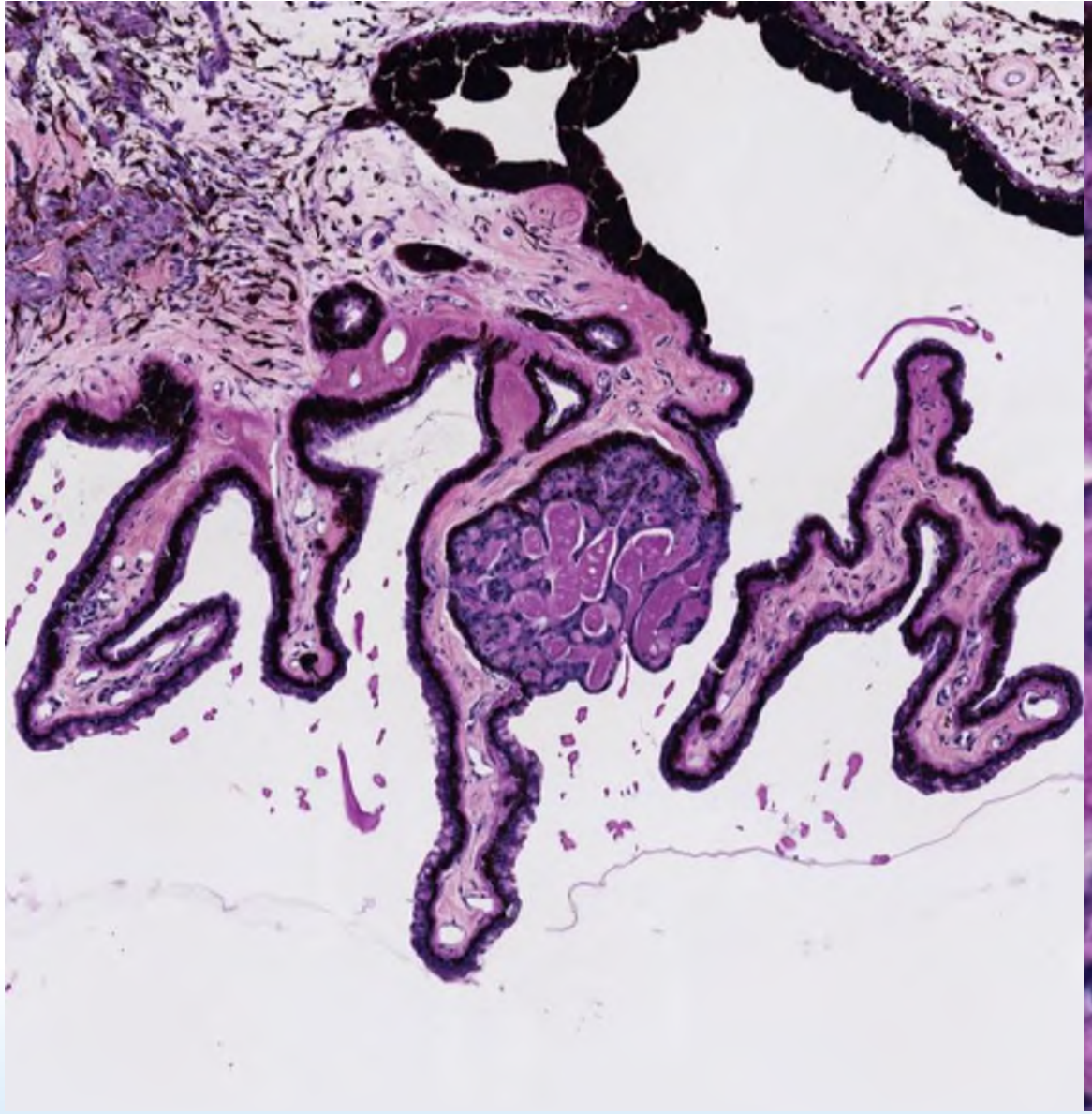
Learning Objectives

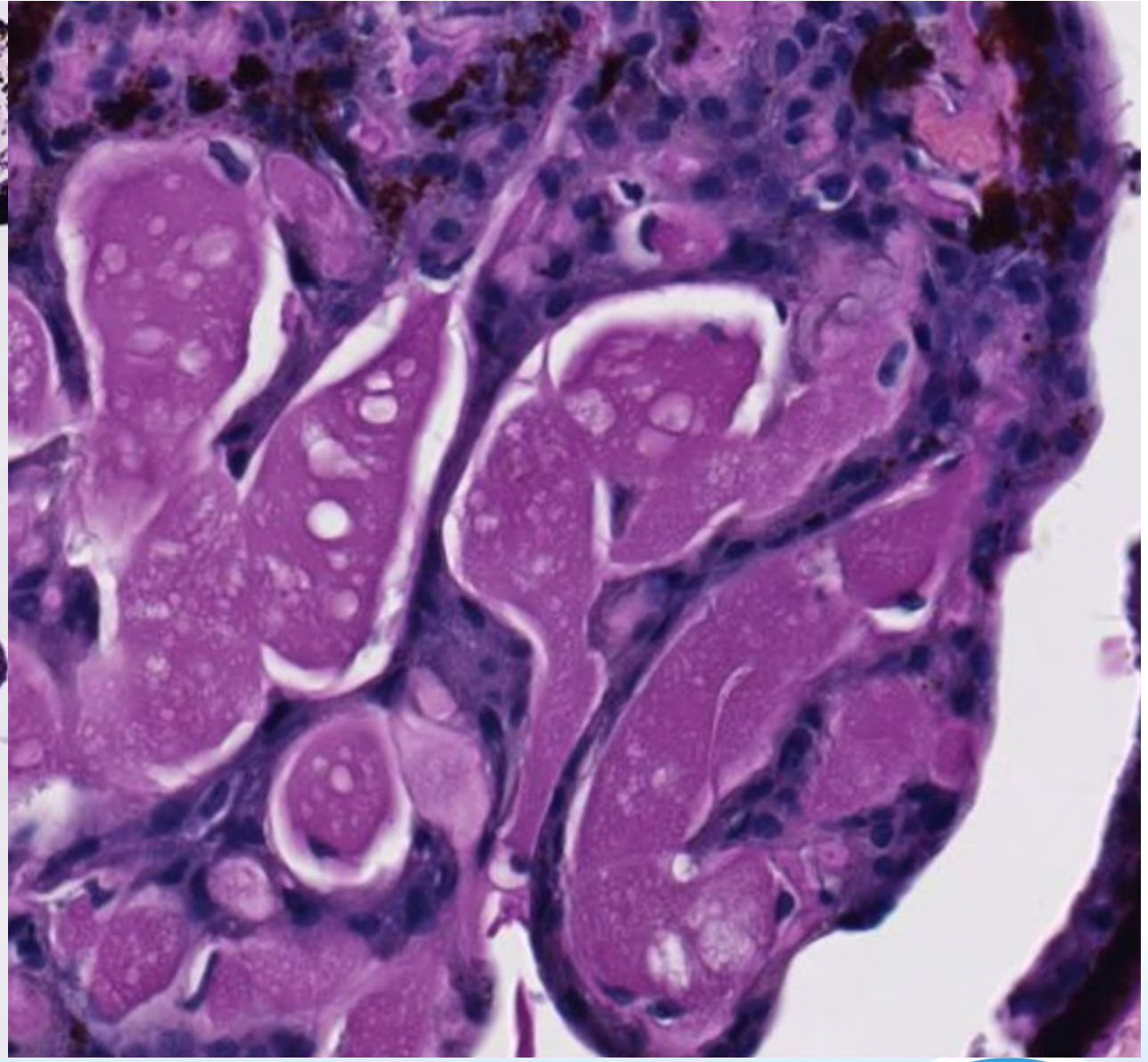
- Learning Objective #1: Outline the differential diagnosis of tumors of the ocular surface
- Learning Objective #2: Recognize the spectrum of ocular infections relevant to ophthalmic pathology
- Learning Objective #3: Recognize the morphologic features of the most common keratopathies and dystrophies

Case 1

- 60-year-old woman with past medical history of hypertension, GERD, Atrial fibrillation and DVT
- Autopsy: acute pulmonary hemorrhage, aortopulmonary fistula, and aortic dissection
- No clinical history of eye disease







Findings

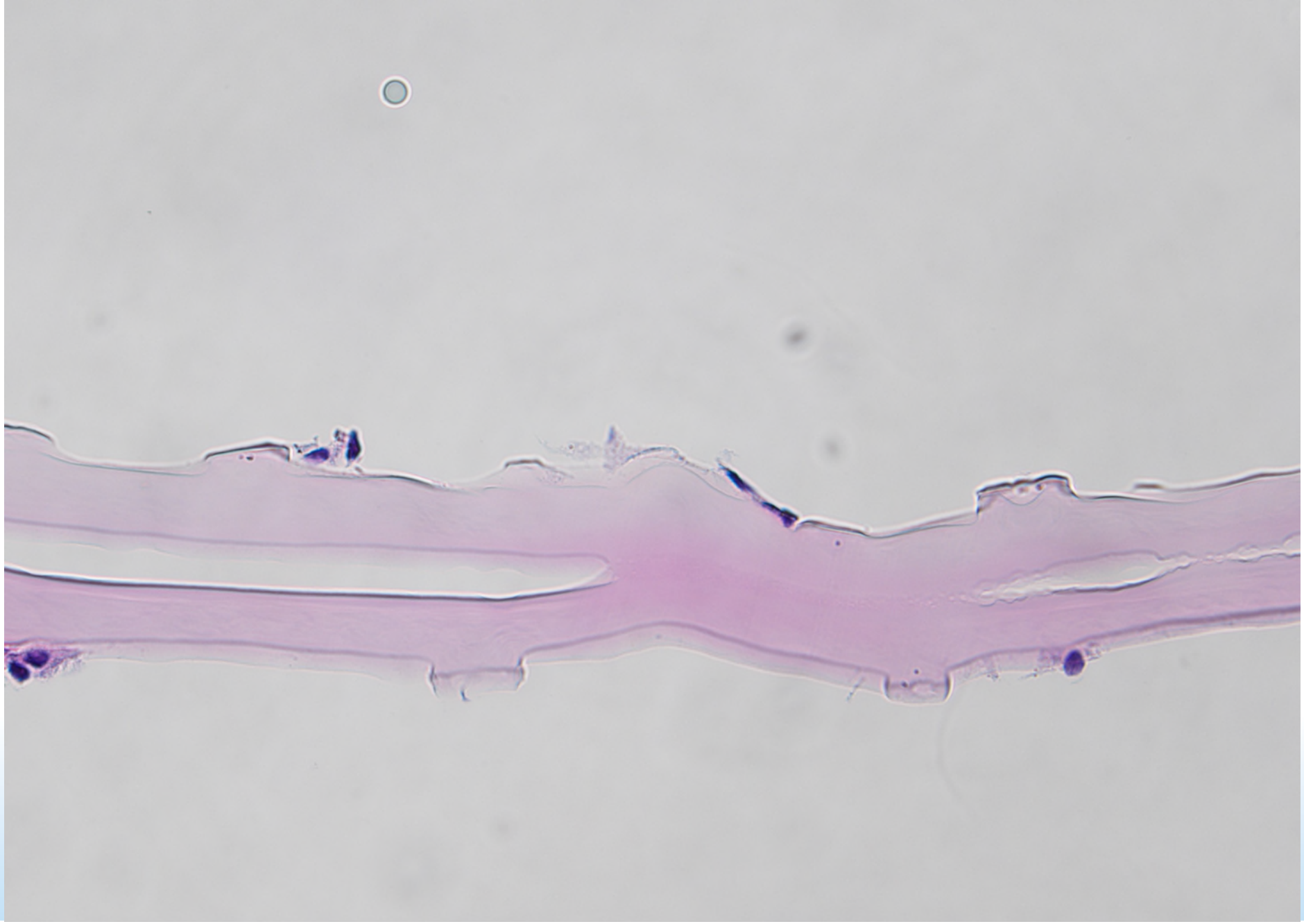
- Fuchs Dystrophy
- Fuchs Adenoma

Case 1
Fuchs Endothelial Corneal Dystrophy

- Most common corneal dystrophy in the US
- Corneal edema in ~5th-6th decade of life
- Primary defect in corneal endothelium
- Relatively easy clinical and pathologic diagnosis
- PAS stain very useful in equivocal cases

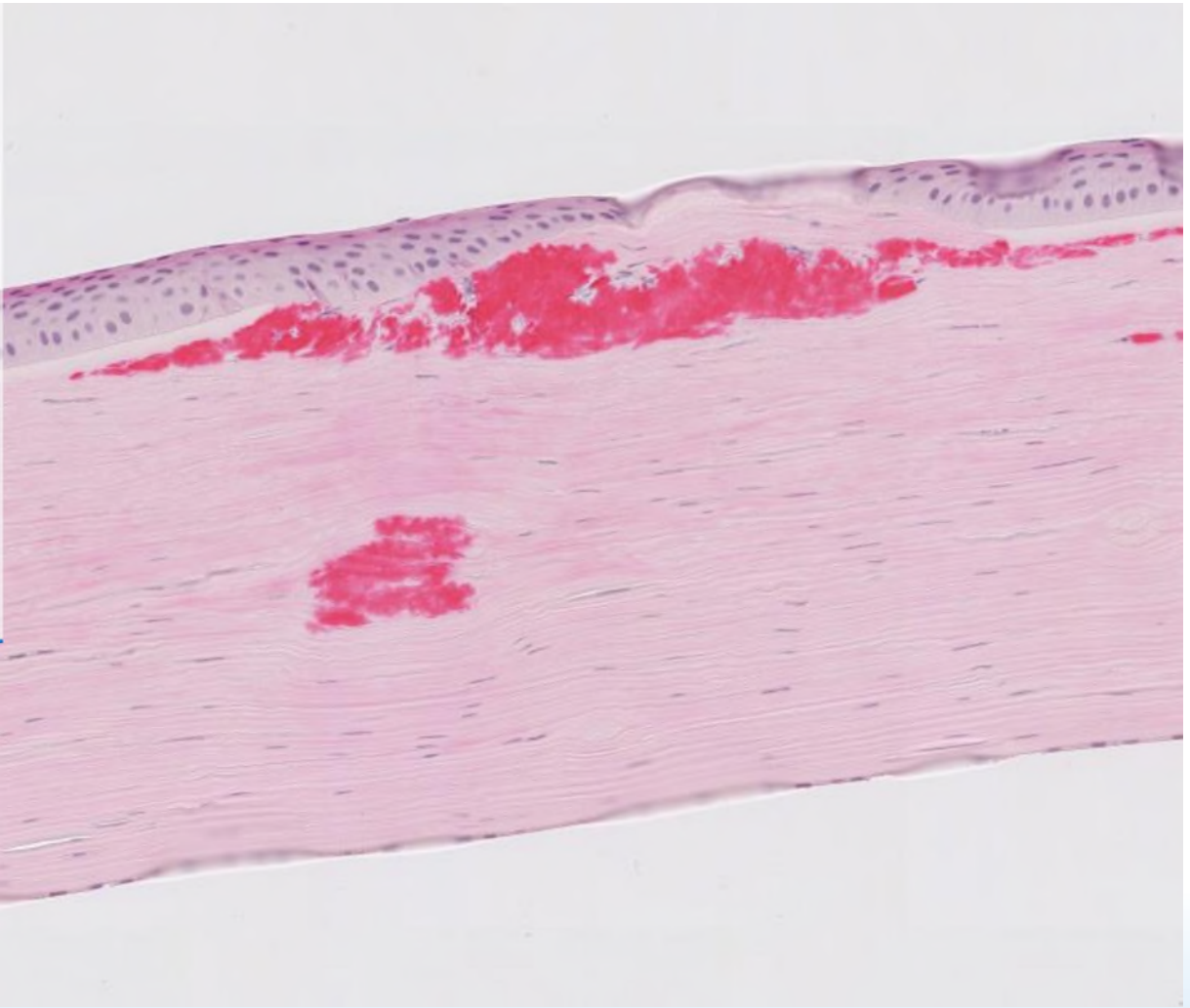
Fuchs adenoma

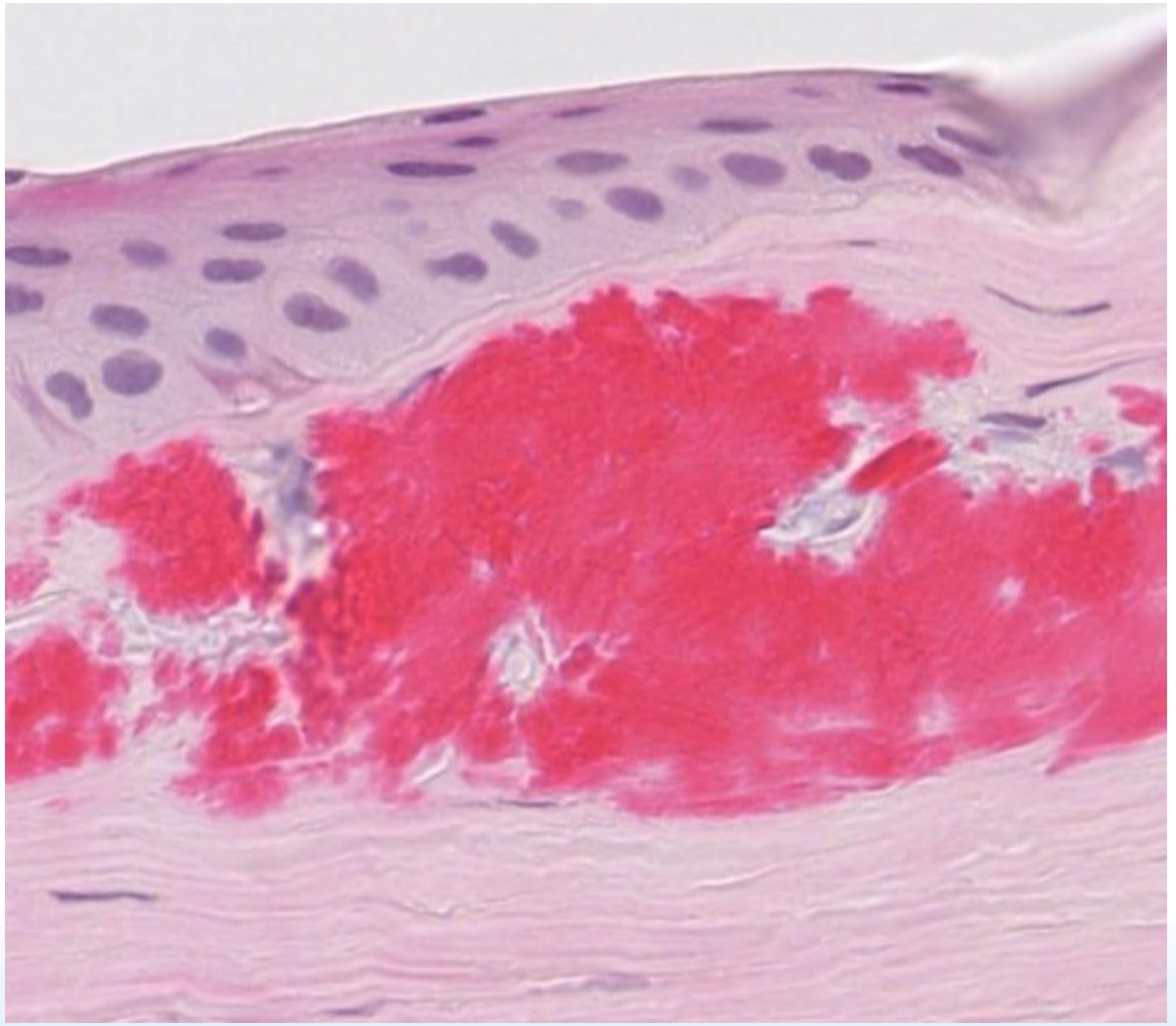
- Benign tumor possibly developing from non-pigmented ciliary epithelium
- Age related
- Typically incidental at autopsy, but may rarely cause iris protrusion, shallowing of anterior chamber or glaucoma



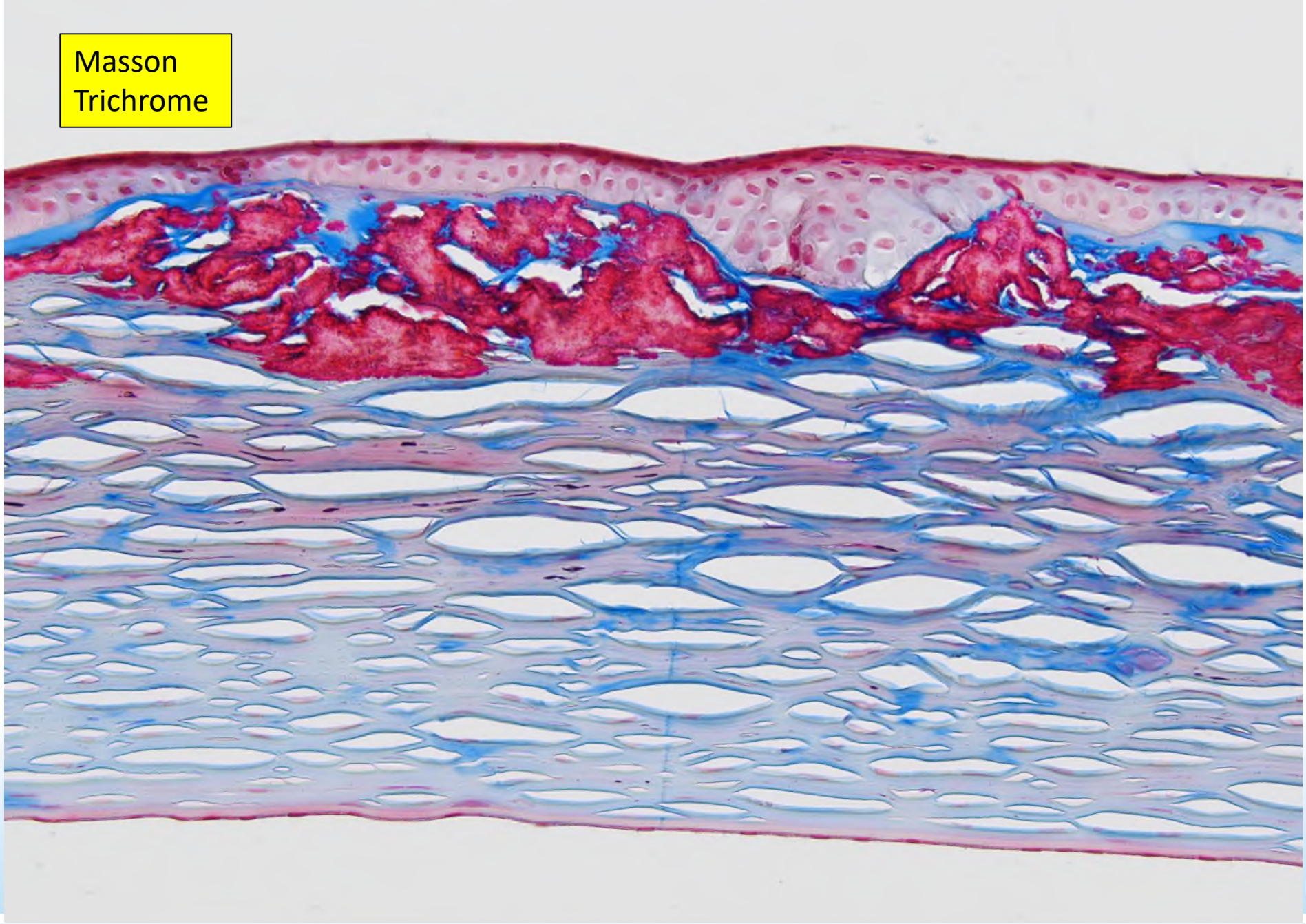
Case 2

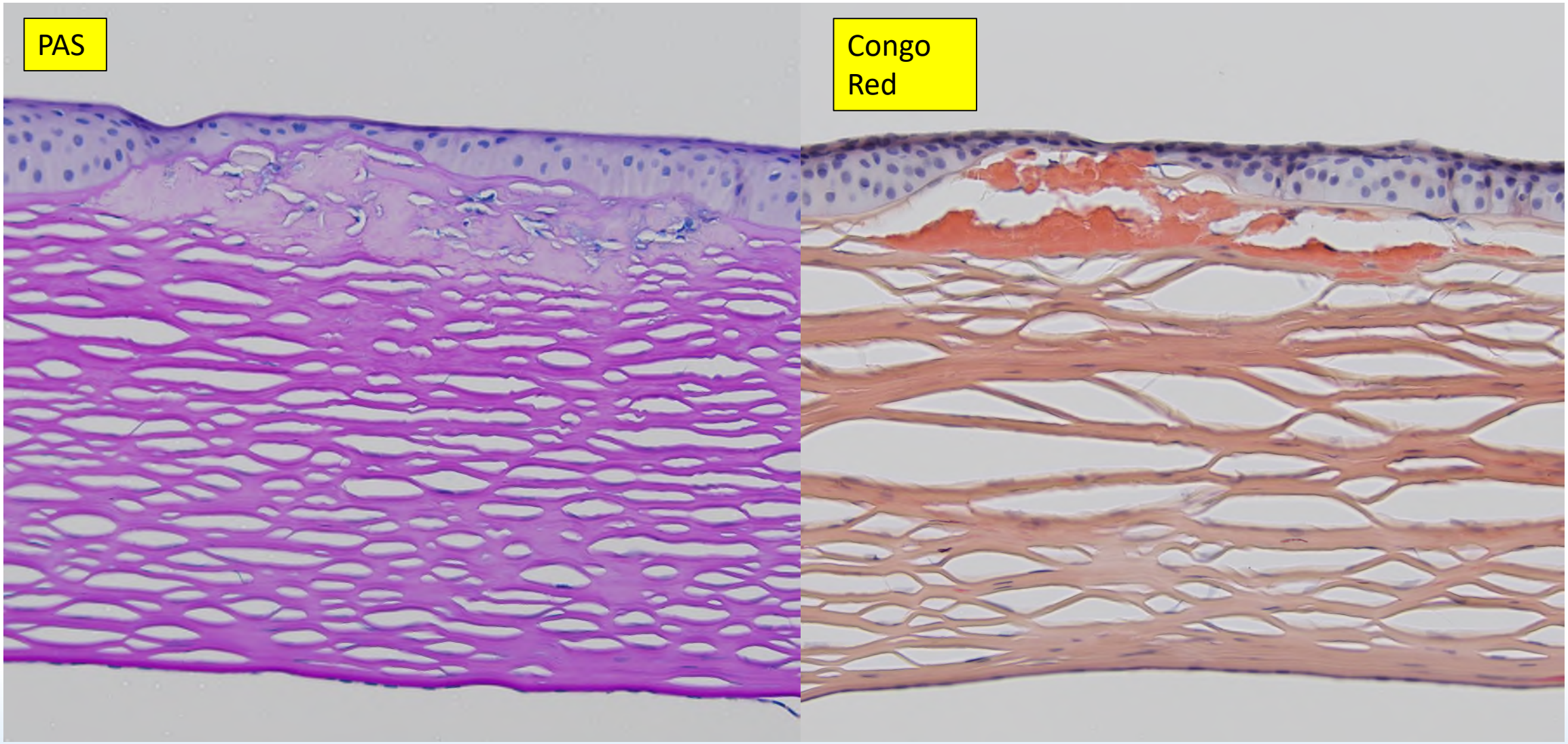
- 54-year-old man with visual loss





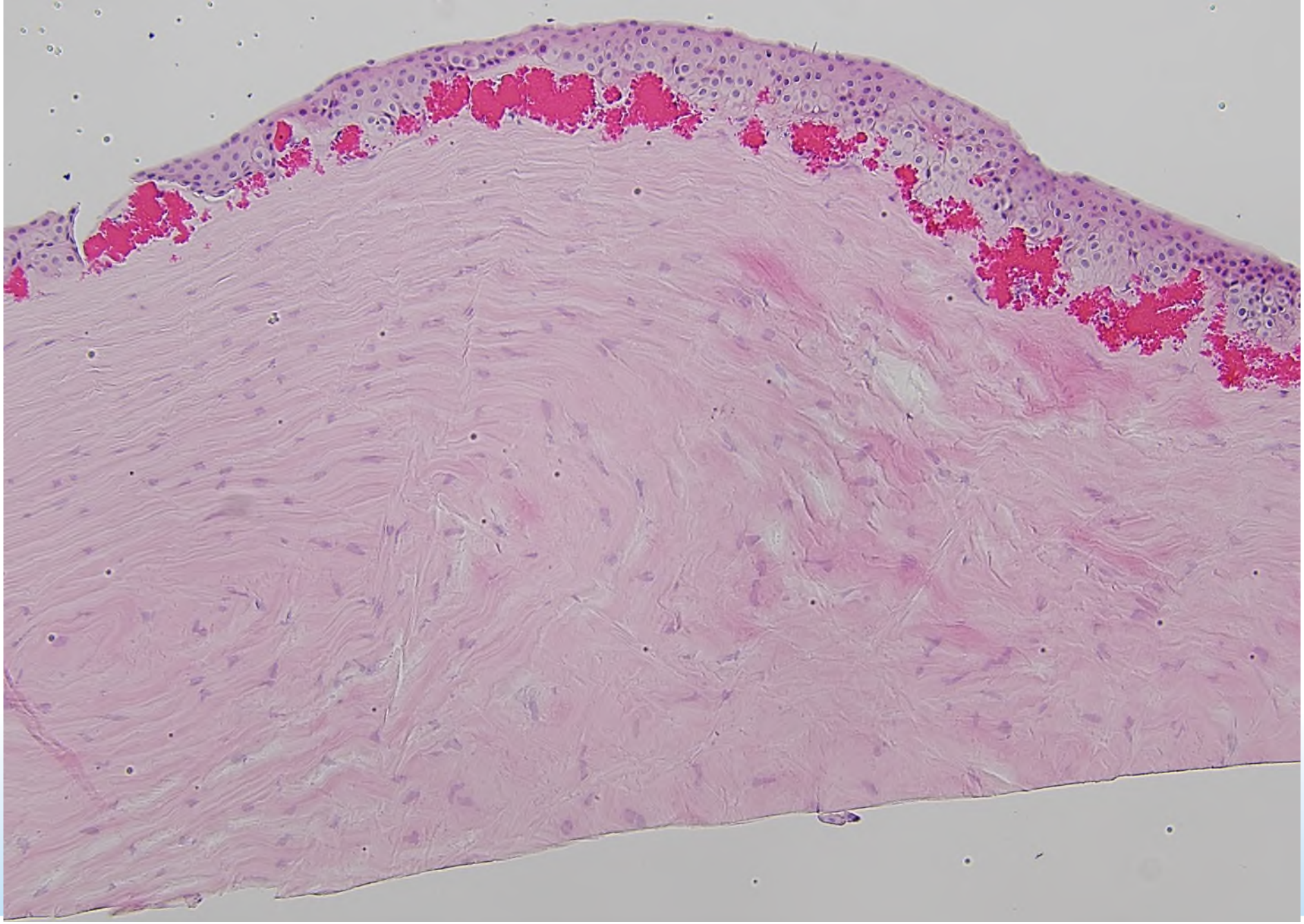
Masson Trichrome




PAS
Congo Red

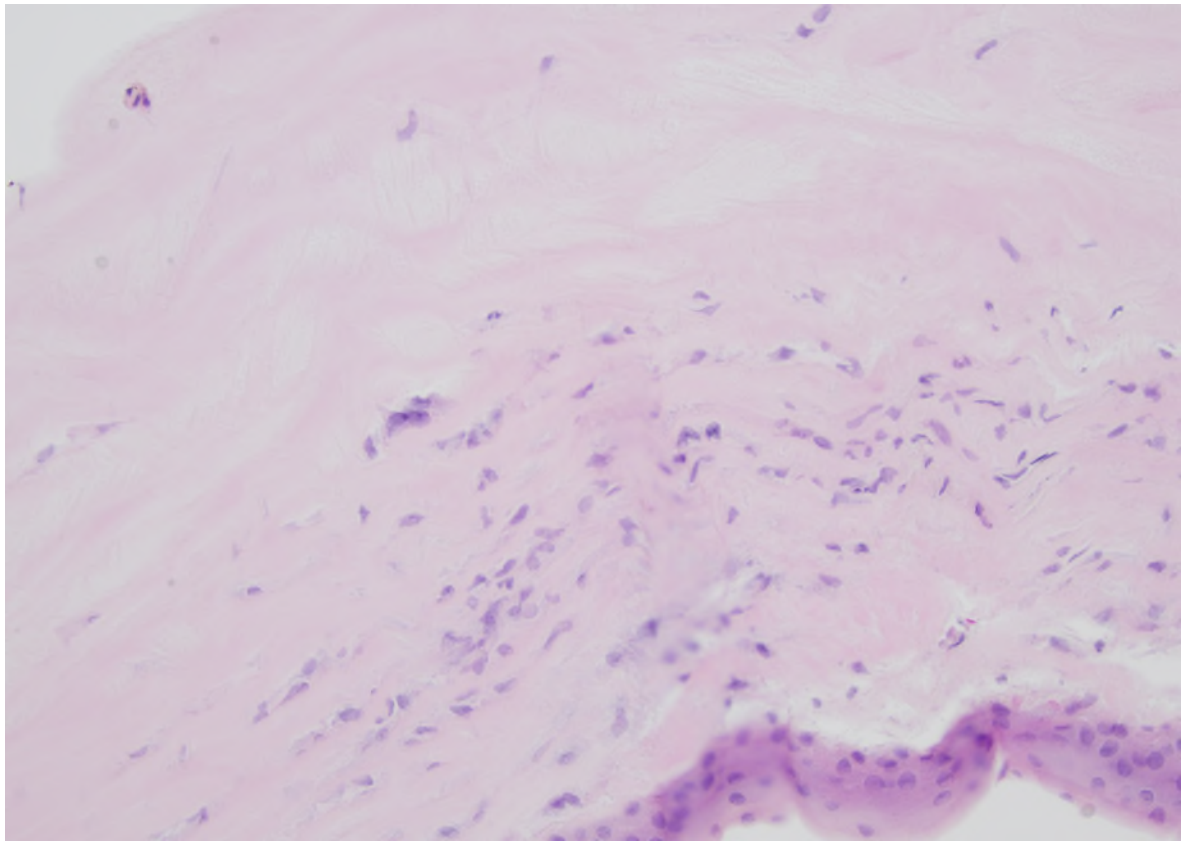
Case 2
Granular Corneal Dystrophy

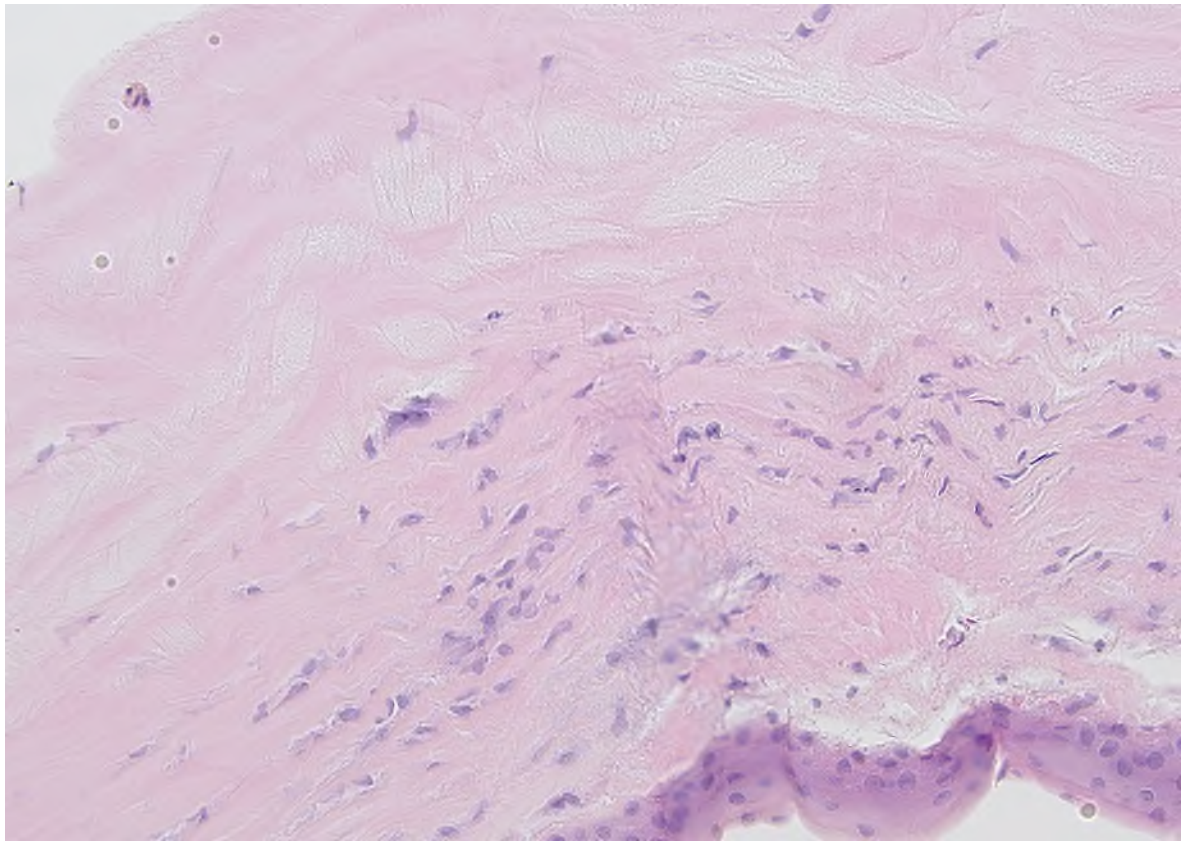
- Visual loss late in life
- May recur in grafts after transplantation
- Autosomal dominant inheritance
    - Transforming growth factor beta (*TGFB1* p.R555W) mutation
- Avellino dystrophy variant: features of Granular (type I)+Lattice
- Other stromal dystrophies more aggressive
  - Lattice corneal dystrophy type I and II (confined and systemic amyloidosis)
  - Macular corneal dystrophy: most aggressive (autosomal recessive, ‘localized mucopolysaccharidosis’)

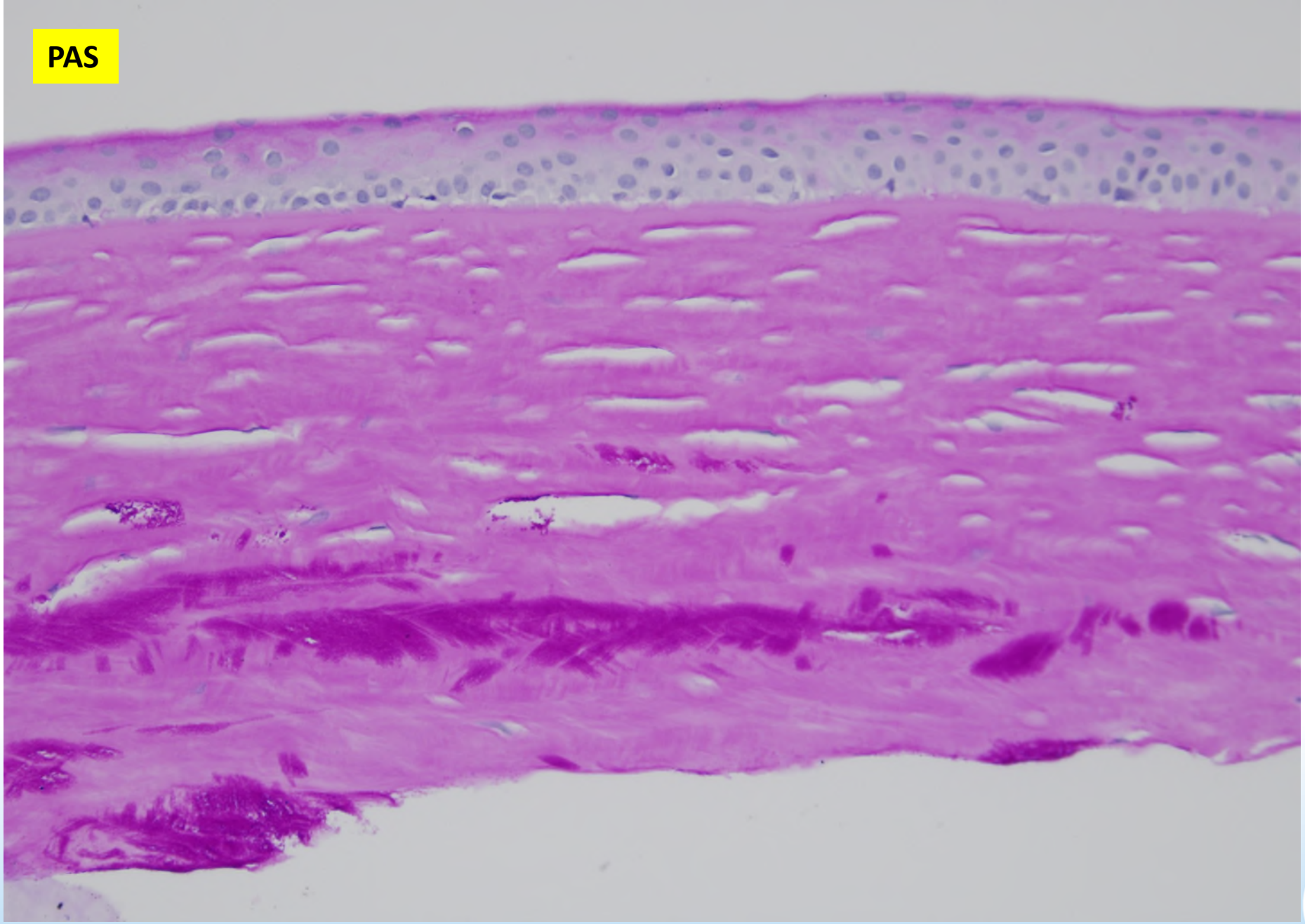


Case 3

- 71-year-old woman with corneal edema



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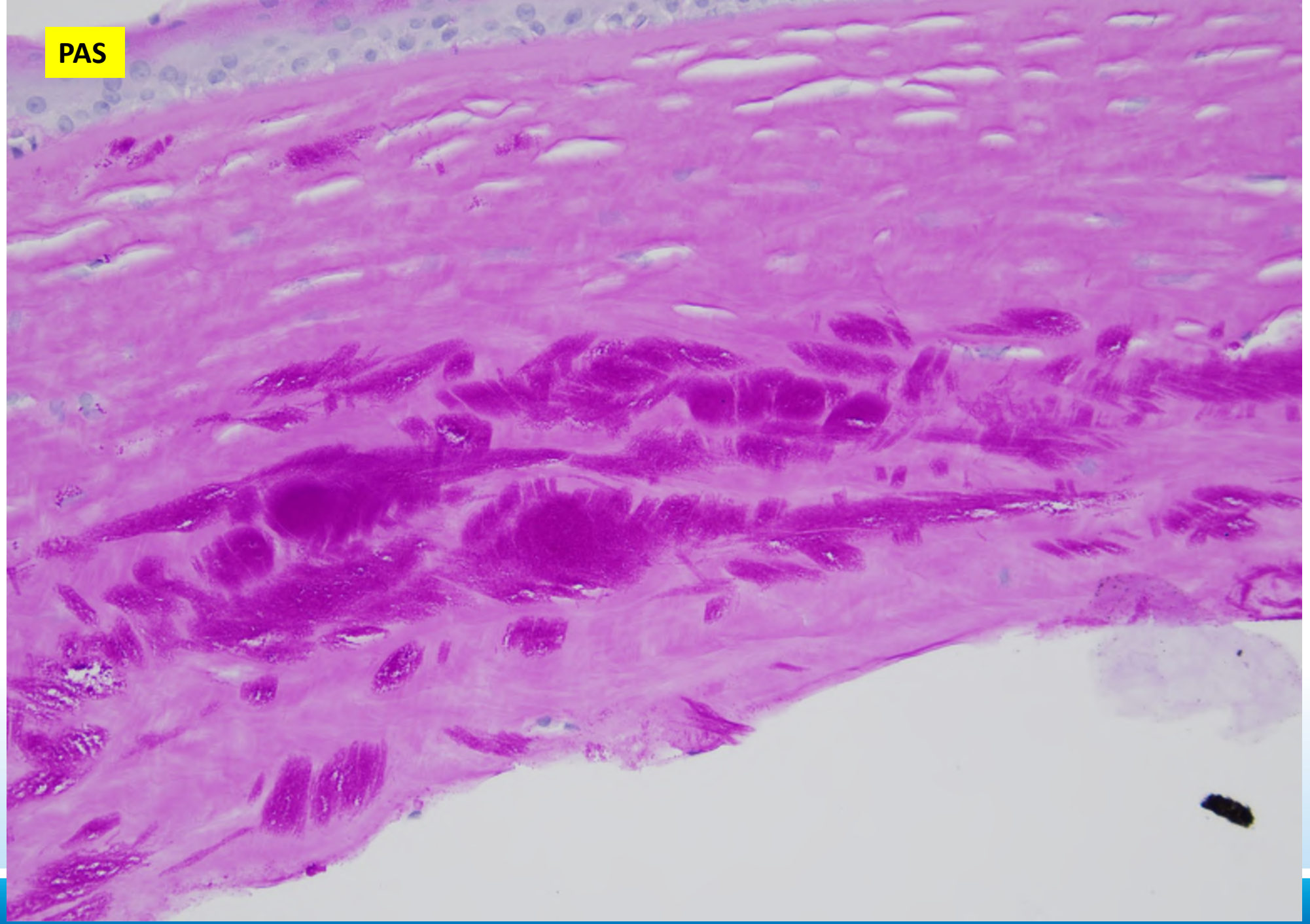
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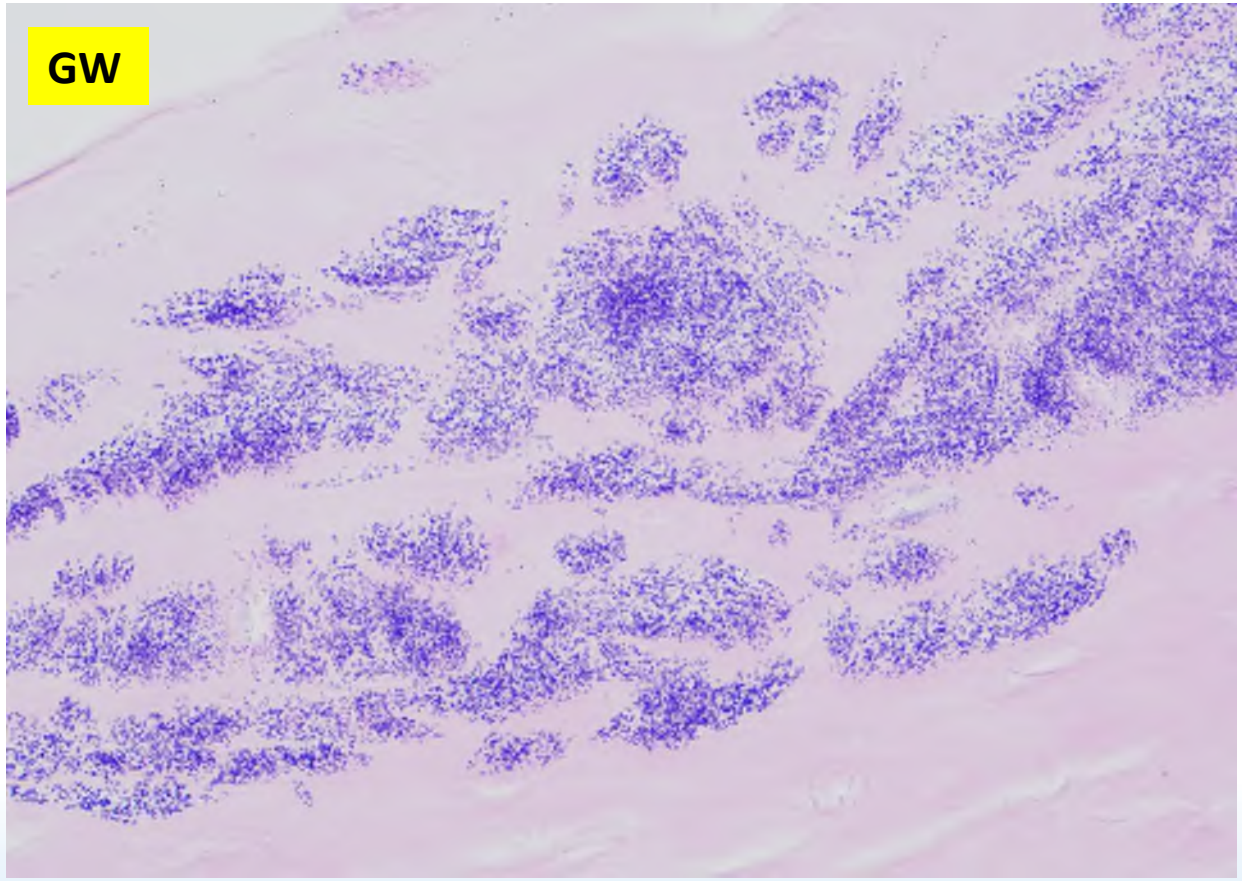
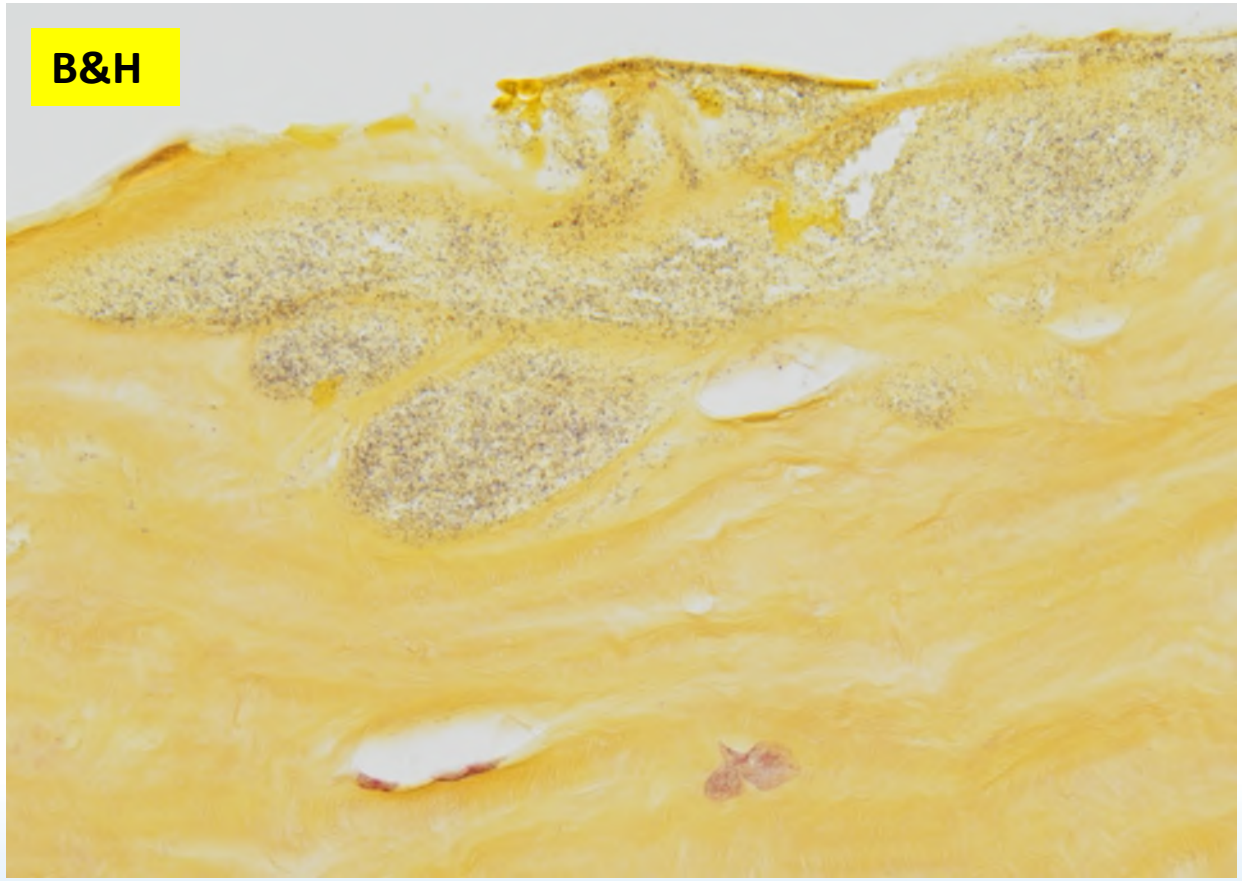
Case 3
Gram Stains





Case 3
Infectious pseudocrystalline keratopathy

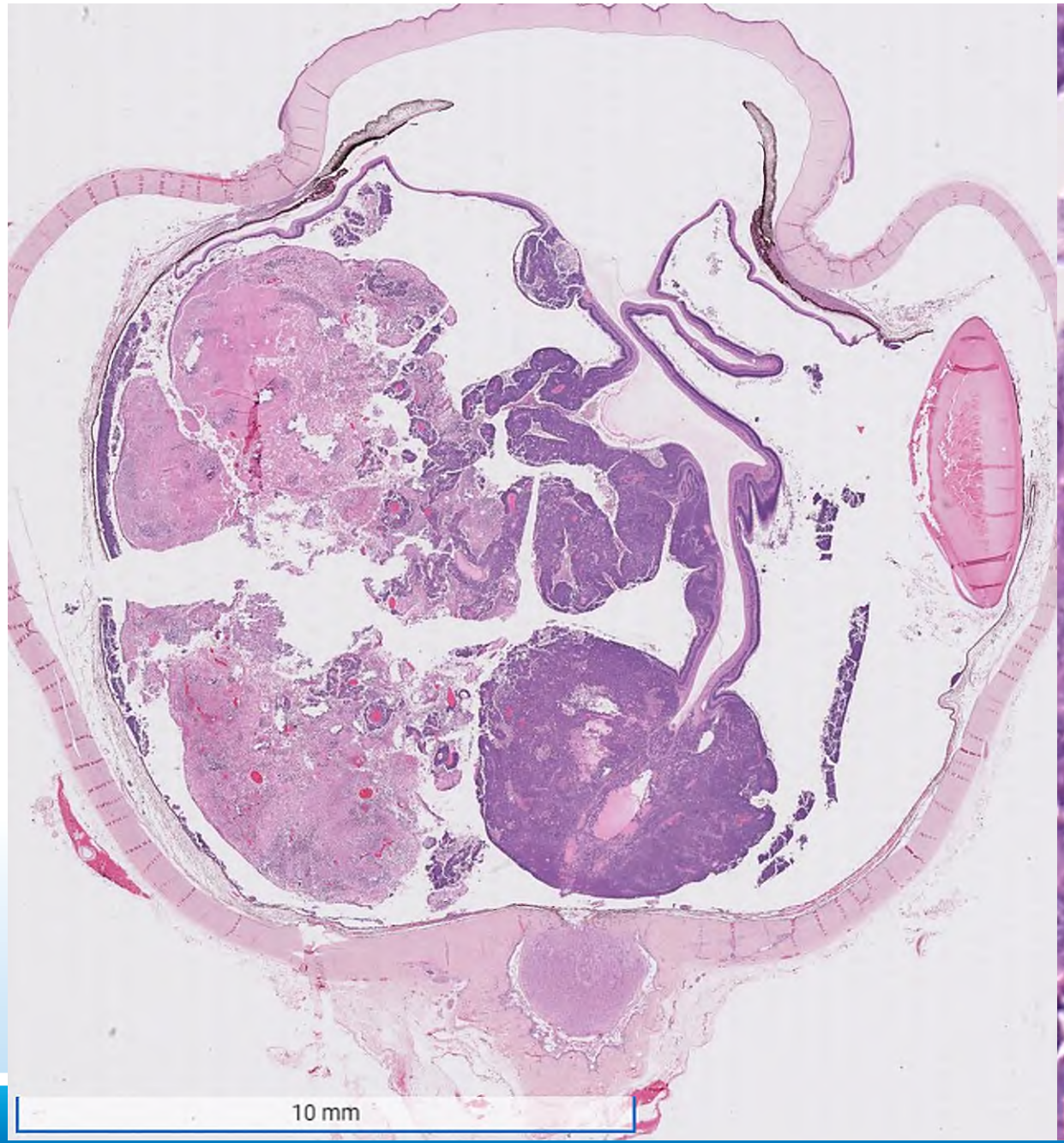
- Indolent corneal infection
- Avirulent streptococcal strains
- Intrastromal opacities in the absence of inflammation
- Complication of corneal surgery, grafts and corticosteroids
- Treatment: aggressive antibiotic therapy or PKA

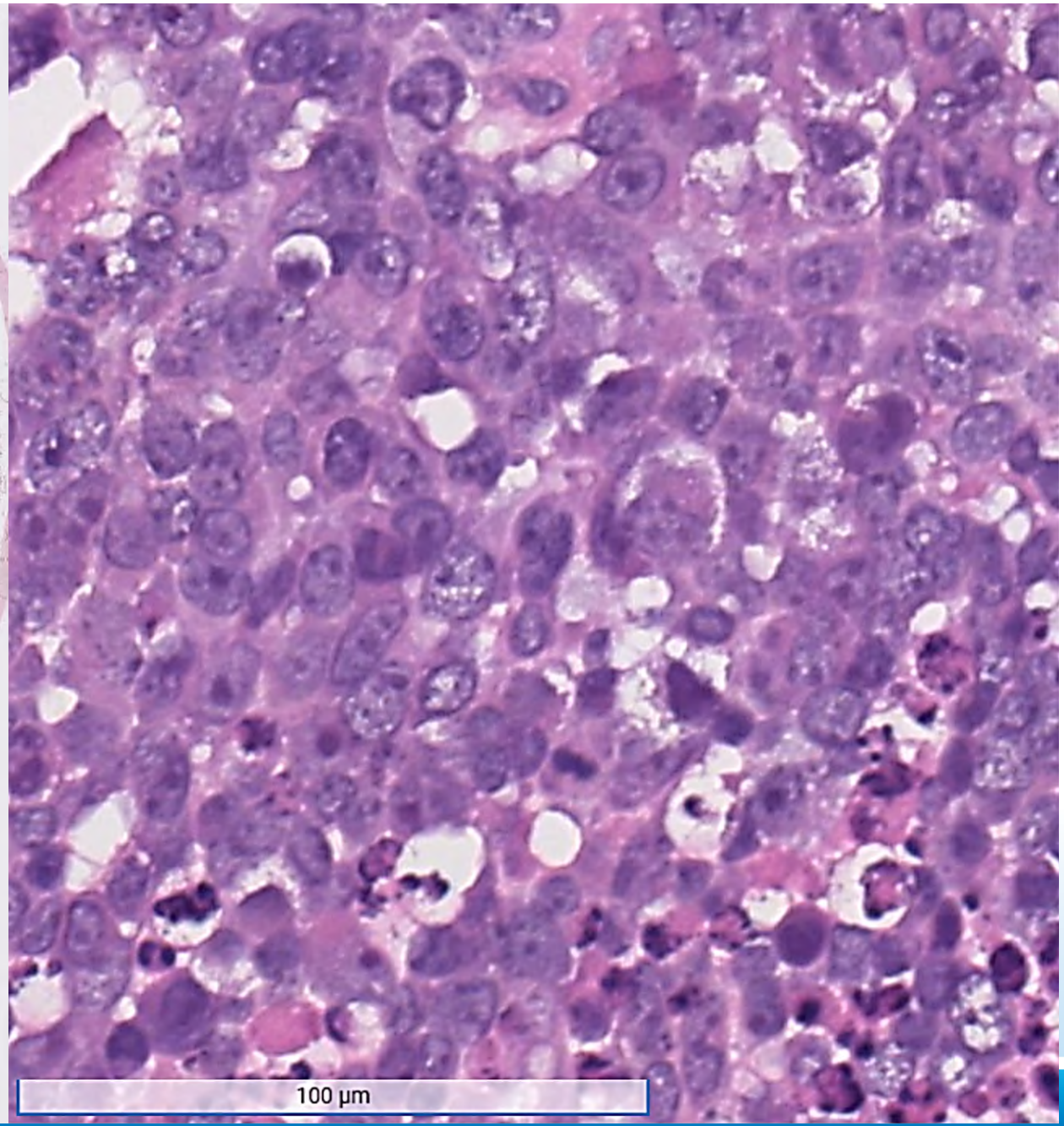
Case 3
Infectious keratitis

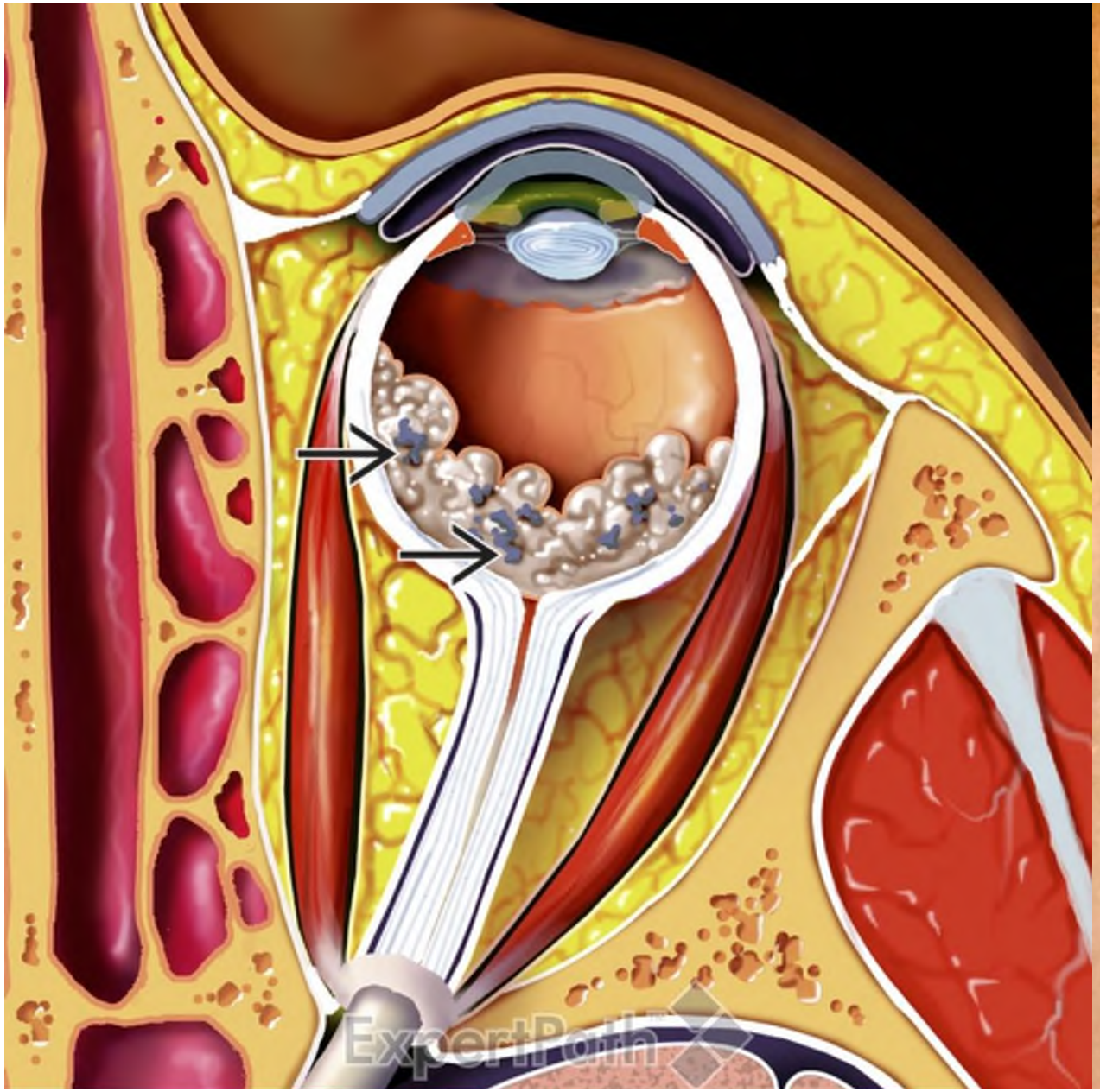
- Bacterial
- Mycobacteria
- Viral (Herpes simplex, Varicella zoster)
- Fungal (Candida, Asperigillus, Fusarium)
- Acanthamoeba

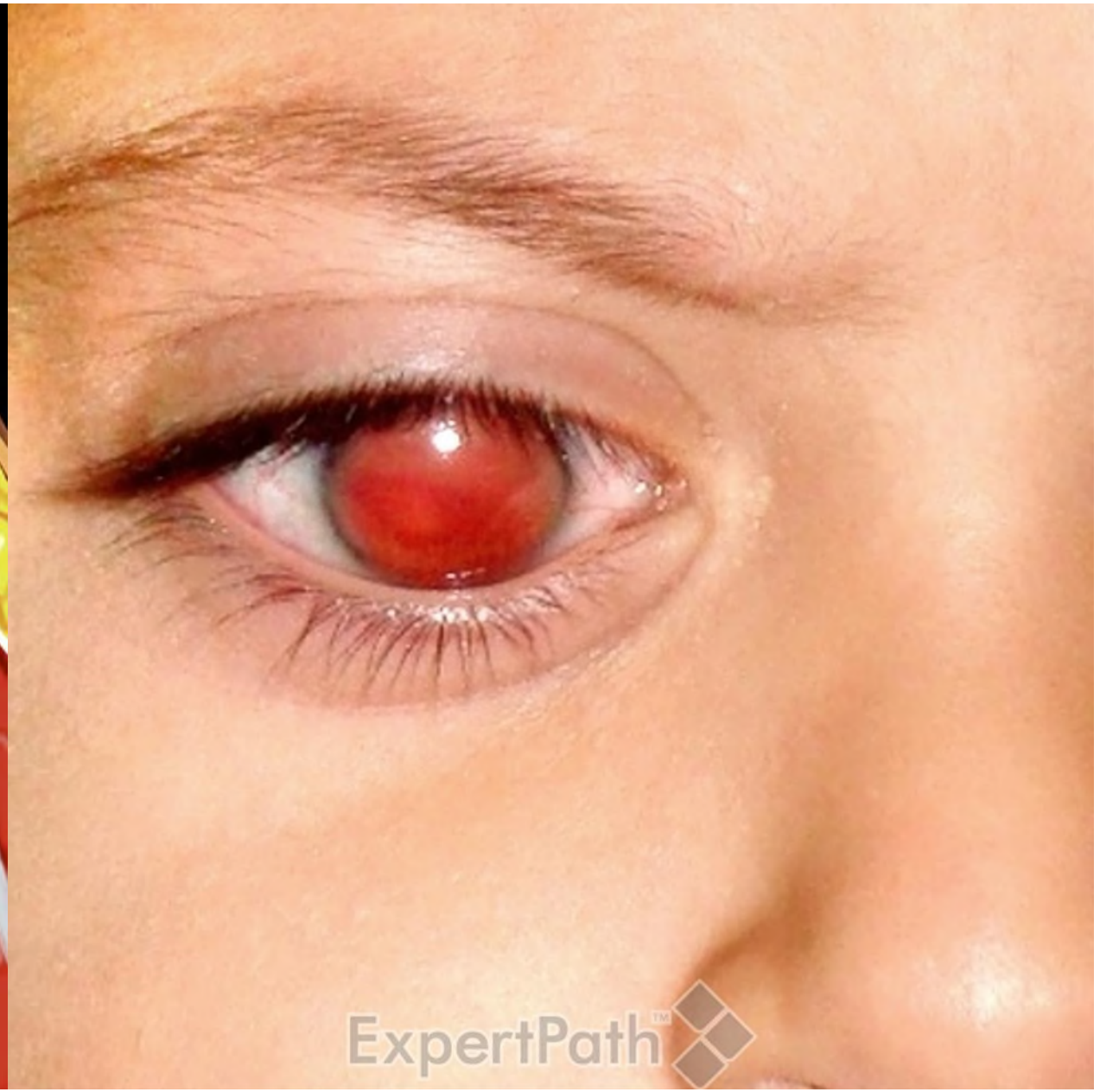
Case 4

- 6-month-old boy with intraocular mass


10 mm


100 µm


ExpertPath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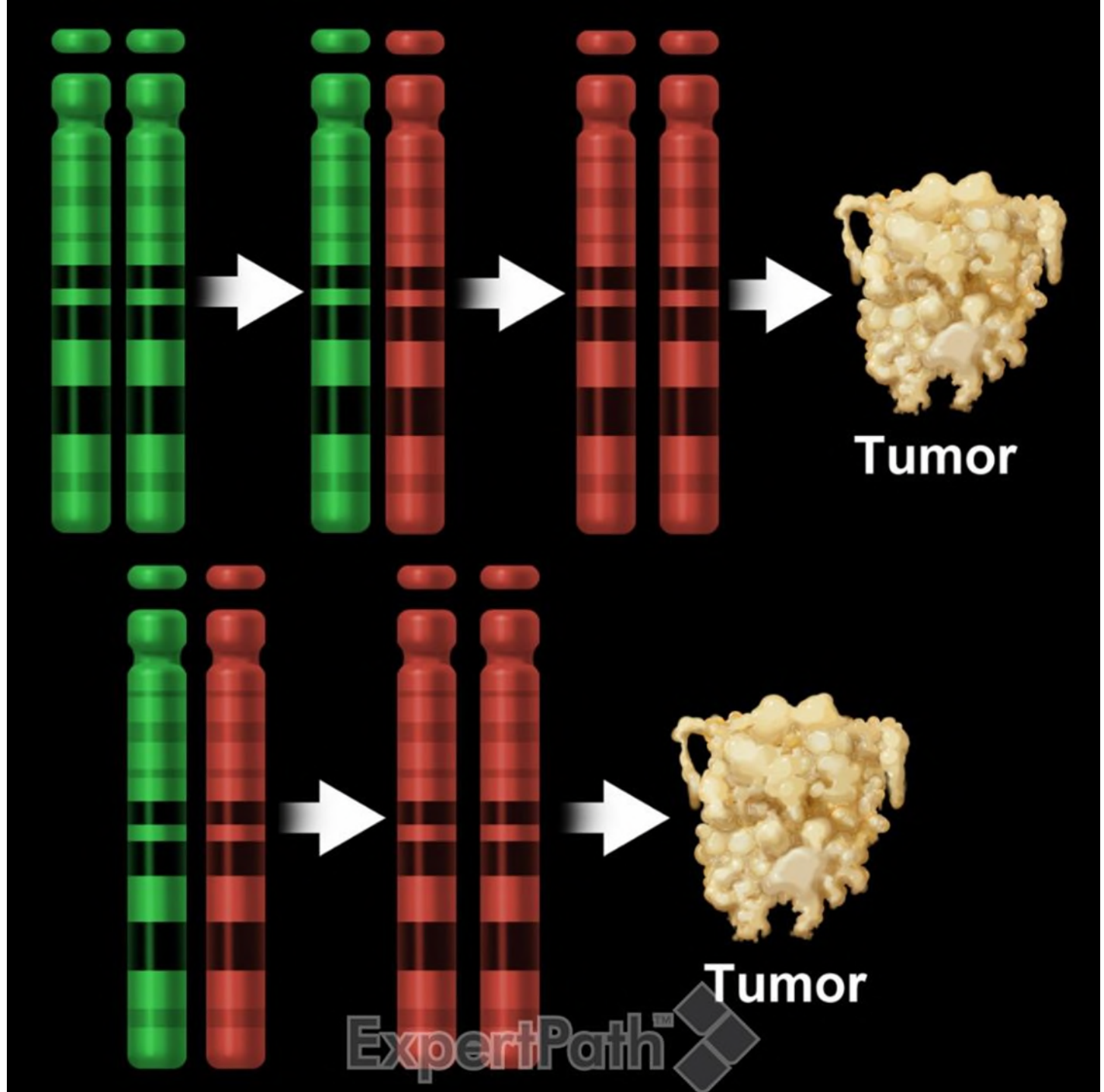
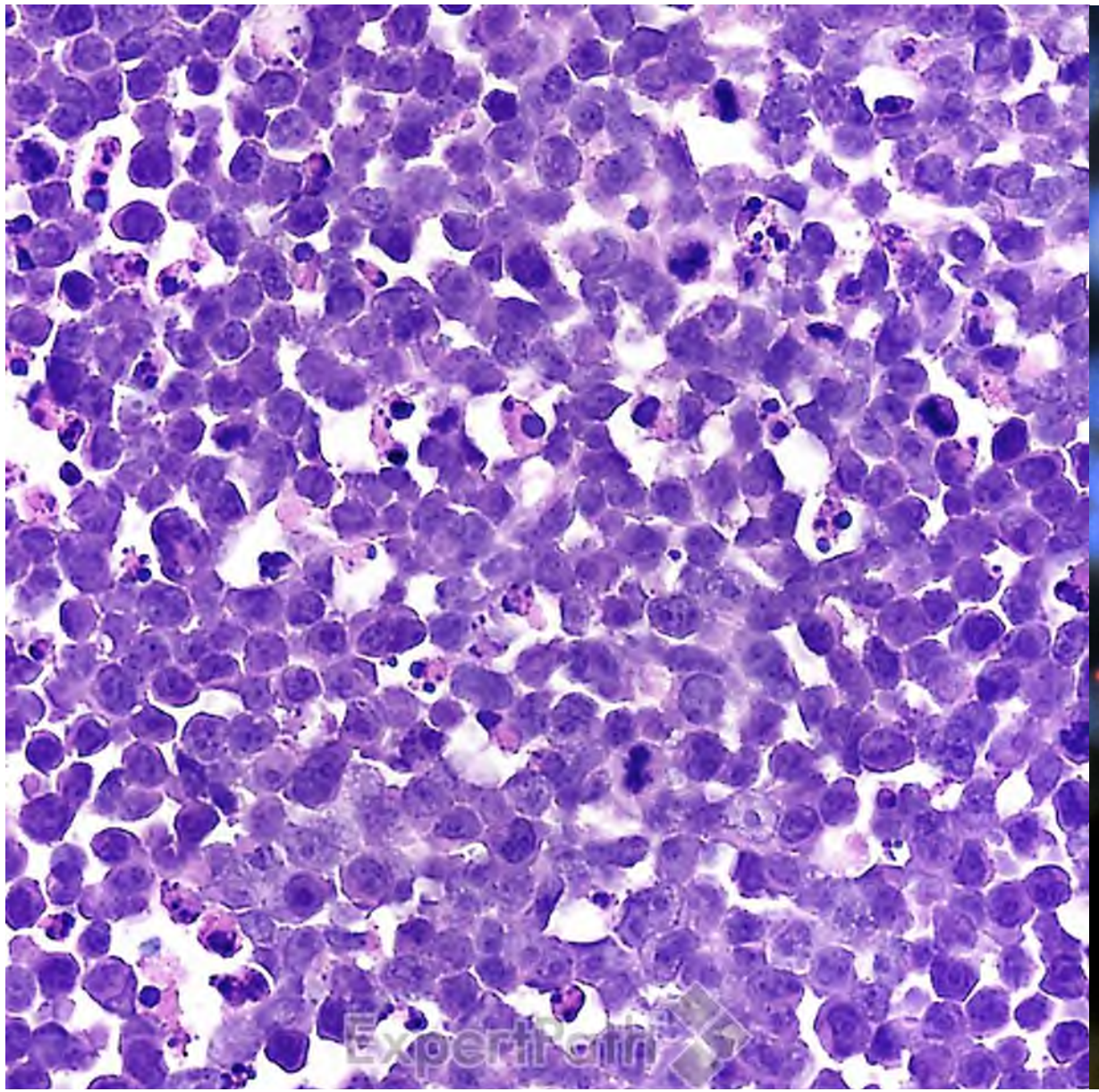

Tumor
Tumor
ExpertPath™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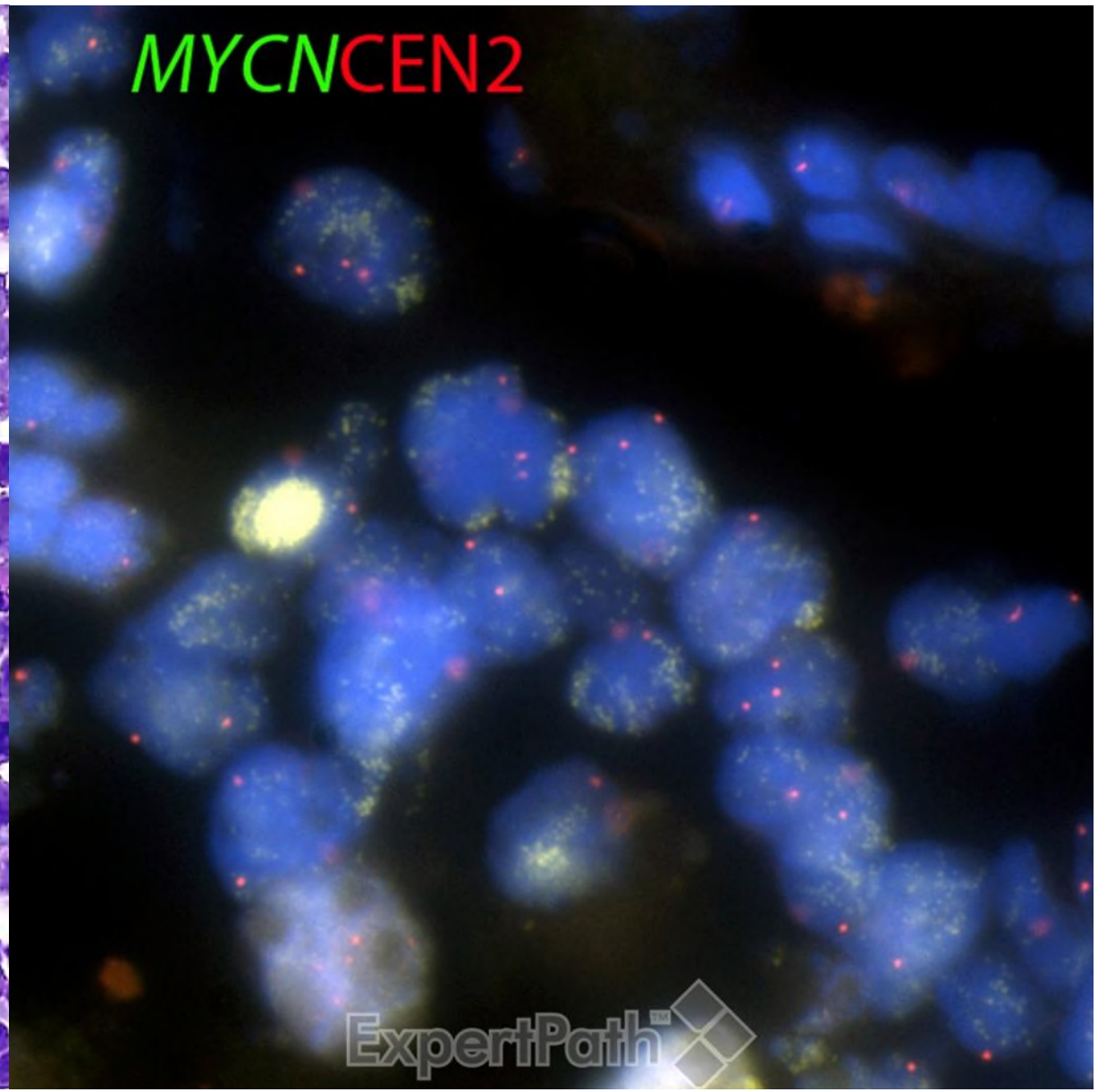

MYCNCEN2
ExpertPath

Characterisation of retinoblastomas without *RB1* mutations: genomic, gene expression, and clinical studies

Diane E Rushlow, Berber M Mol, Jennifer Y Kennett,* Stephanie Yee,* Sanja Pajovic, Brigitte L Thériault, Nadia L Prigoda-Lee, Clarellen Spencer, Helen Dimaras, Timothy W Corson, Renée Pang, Christine Massey, Roseline Godbout, Zhe Jiang, Eldad Zacksenhaus, Katherine Paton, Annette C Moll, Claude Houdayer, Anthony Raizis, William Halliday, Wan L Lam, Paul C Boutros, Dietmar Lohmann, Josephine C Dorsman, Brenda L Gallie*

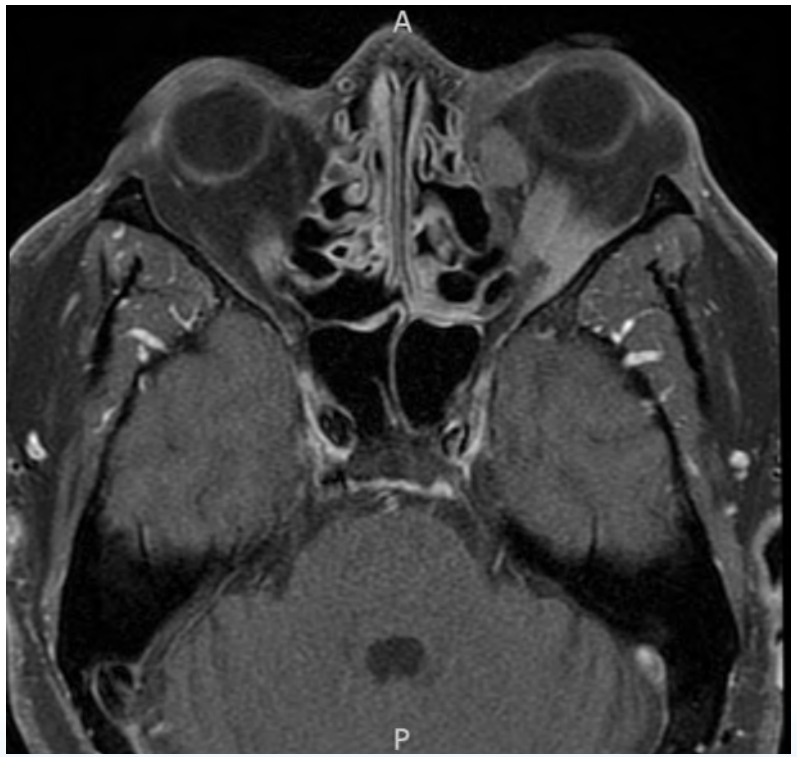
Lancet Oncol 2013

Case 4
Retinoblastoma with *MYCN* amplification

- Reported as occurring in a subset of *RB1* wildtype retinoblastomas
- Young age of onset (infants)
- Aggressive histology

Case 5

- 63-year-old man
- Started experiencing tearing, swelling, pain and itching of left eye
- Progressive eye swelling over several months
- Left eye proptosis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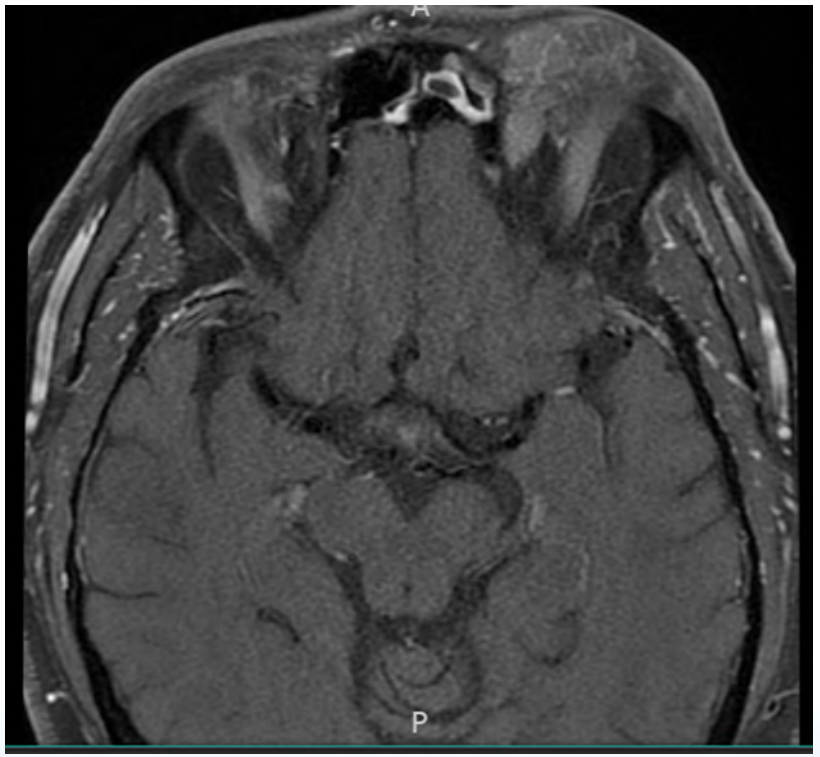
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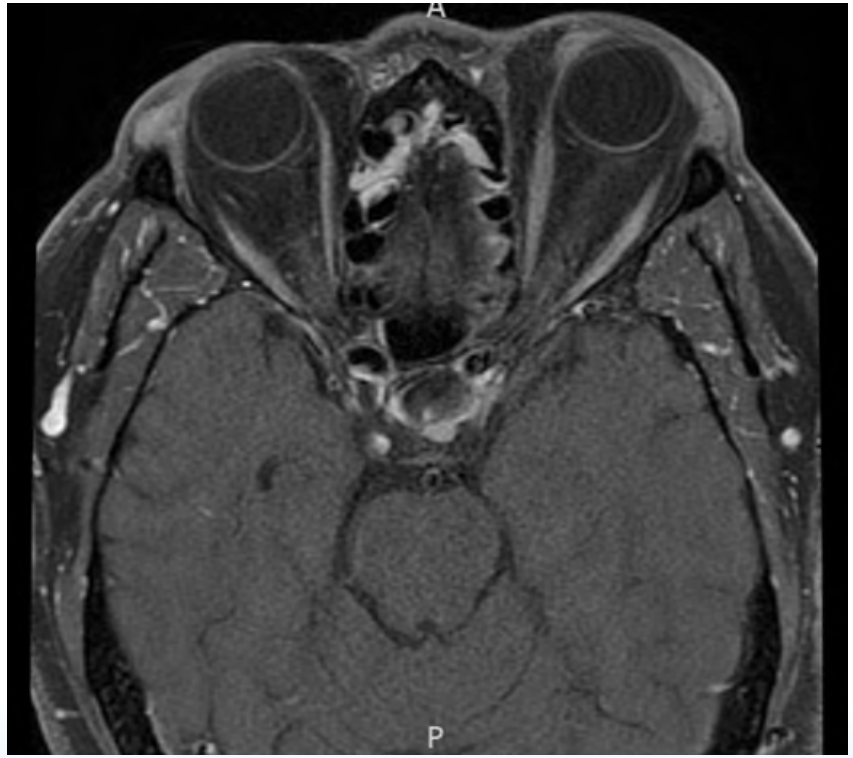
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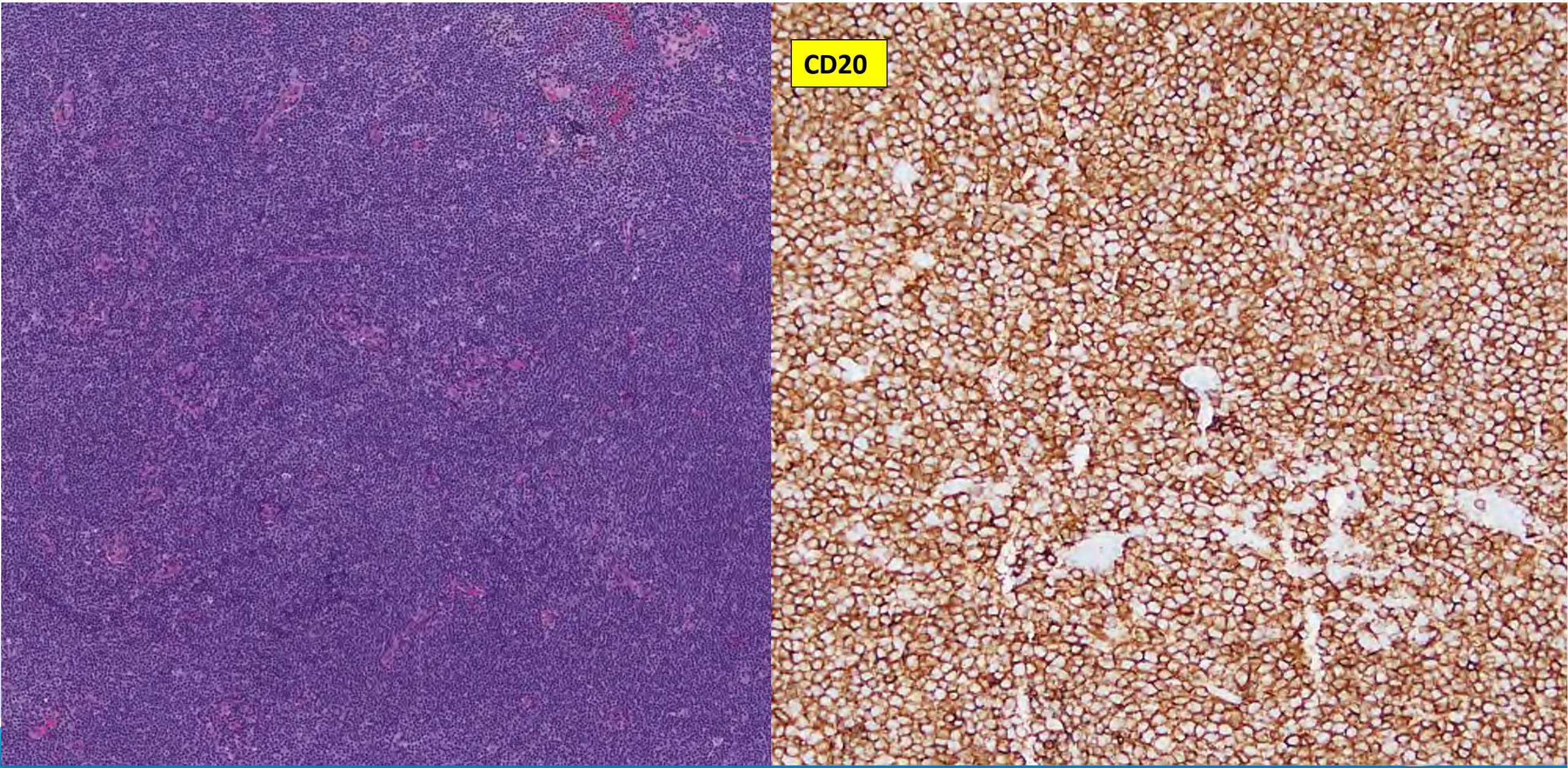
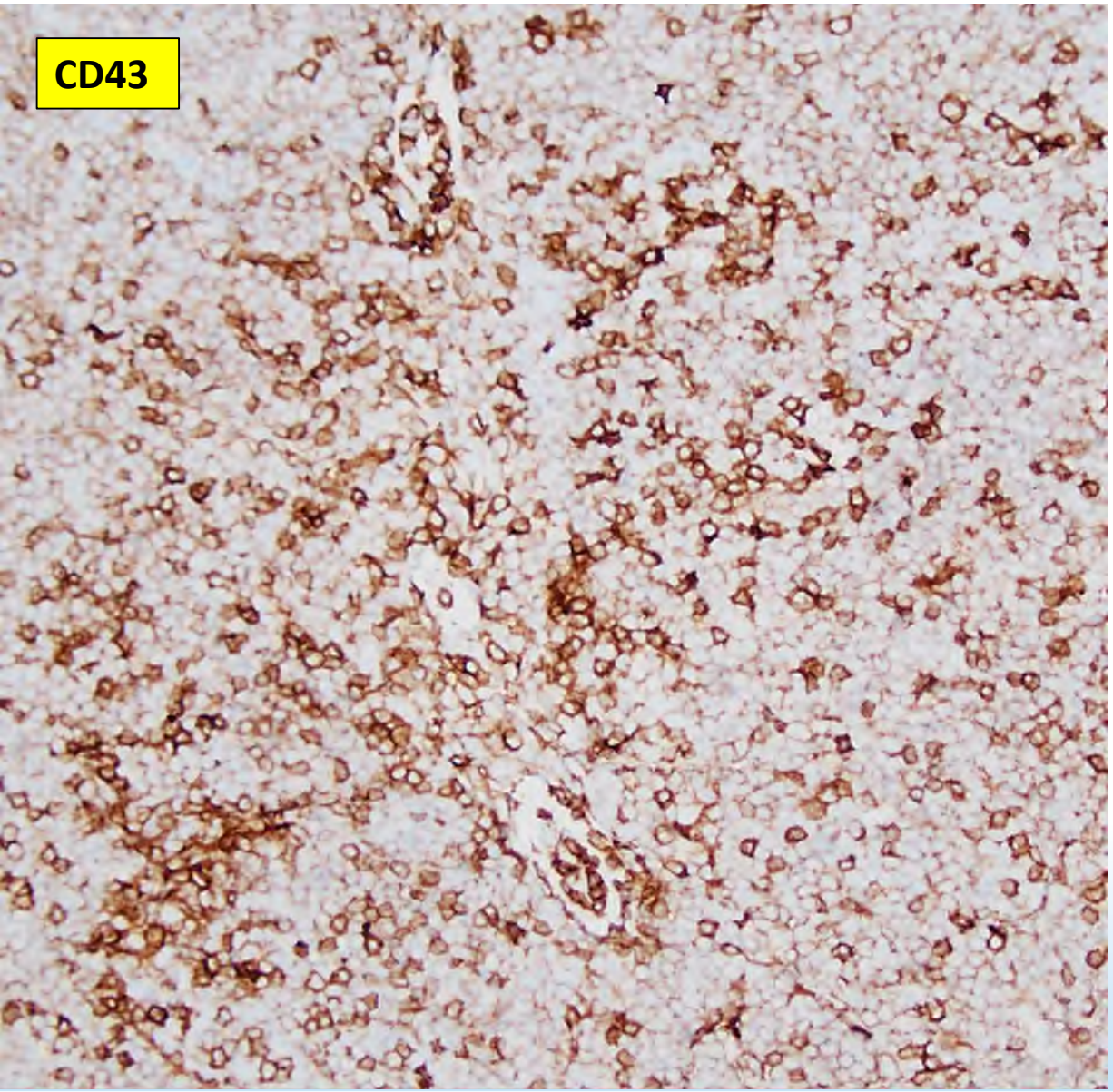
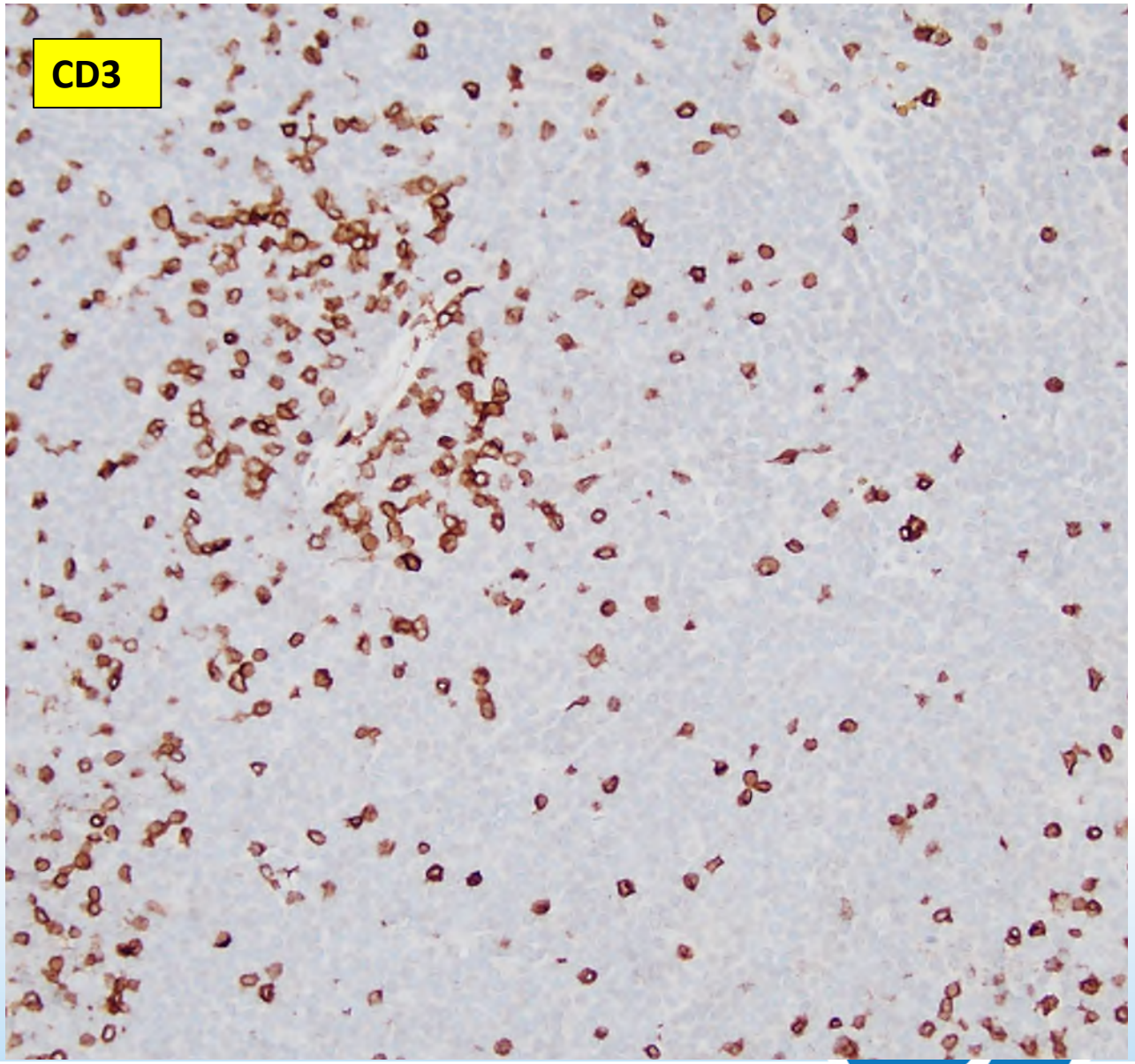

CD20


CD43


CD3

Case 5
Flow cytometry

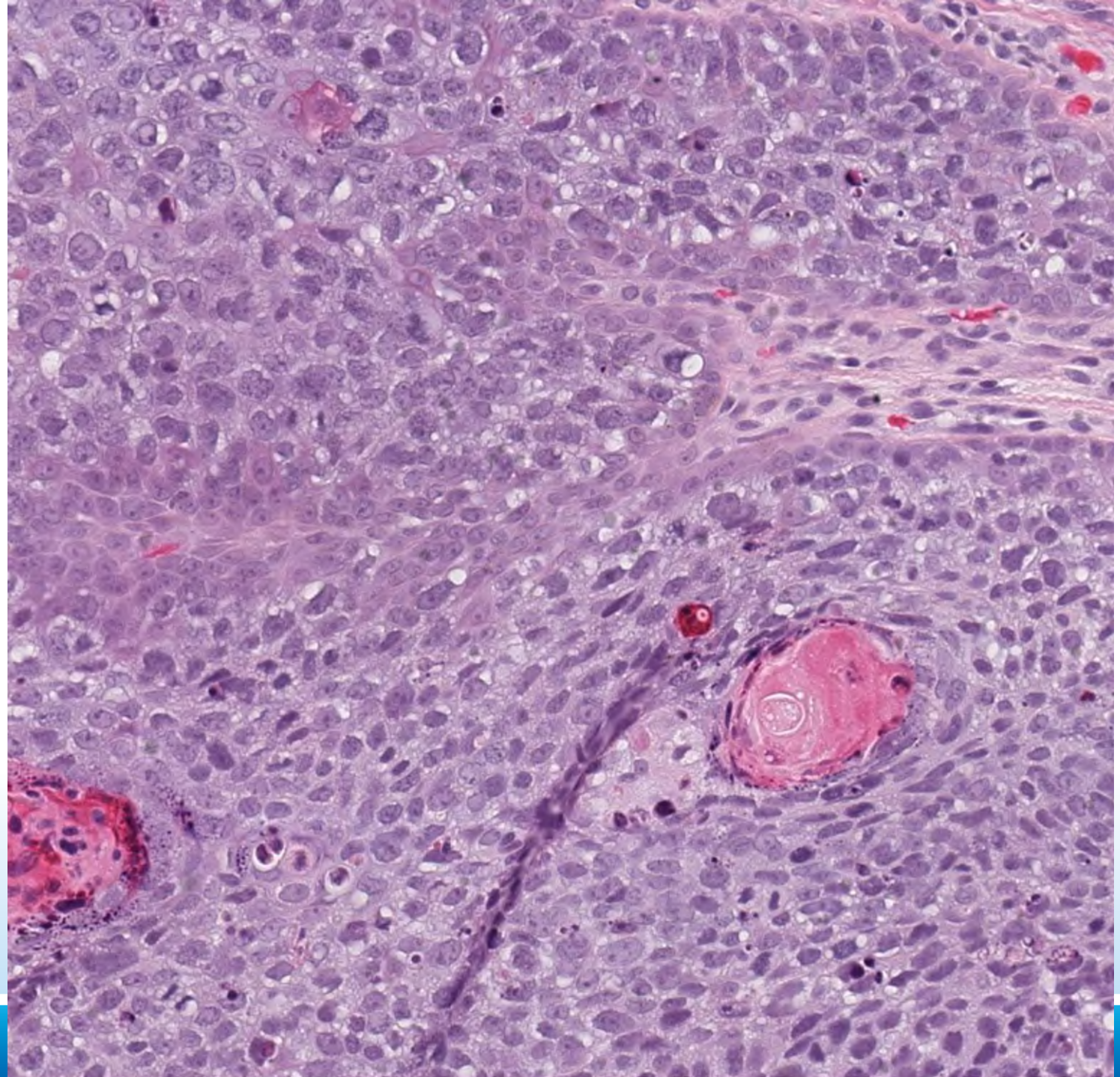
- “The majority of the B cells are phenotypically abnormal, accounting for 61% of total cells, and are small in size by forward light scatter.
- These show monoclonal expression of kappa light chain and also express CD19 and brighter than normal CD20 but lack CD5, CD10, CD200 and CD38.”

Case 5
Extranodal Marginal Zone B-cell Lymphoma

- Most common lymphoma of the ocular adnexa
- In contrast Large B-cell lymphoma most common primary intraocular type
- Flow cytometry very useful in diagnosis
- Indolent clinical course

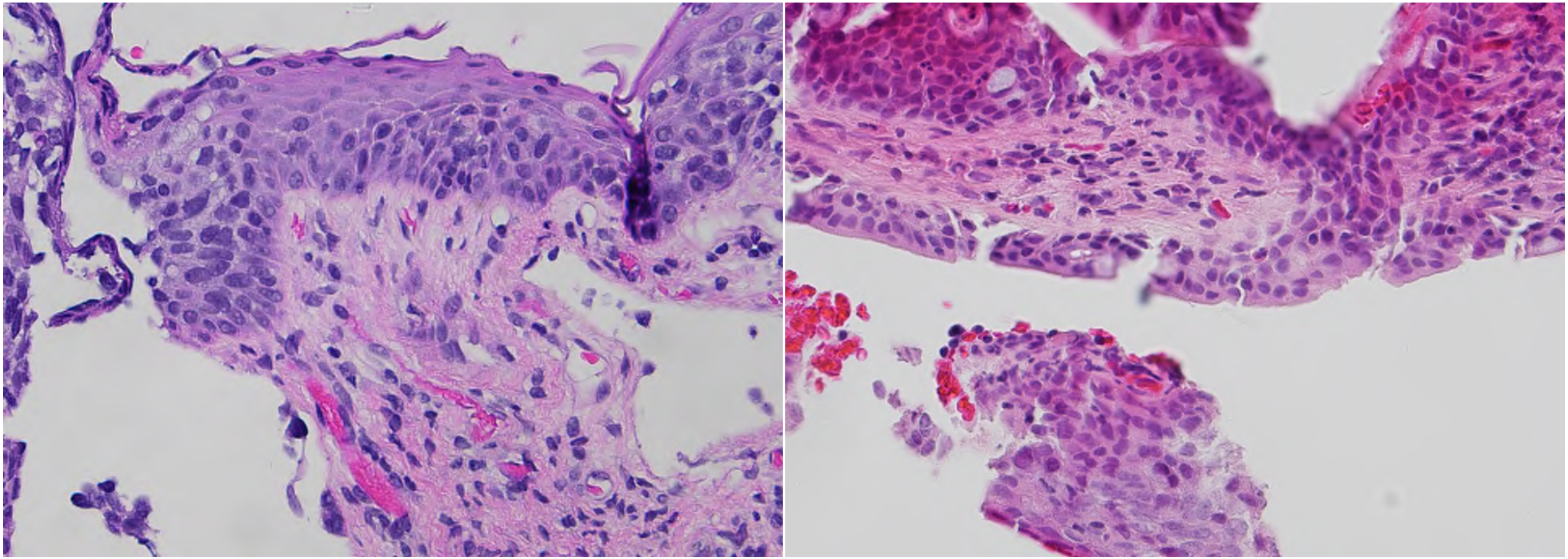
Case 6

- 54-year-old man with lesion of the right eyelid
- Painful and itchy
- Appearance consistent with chalazion



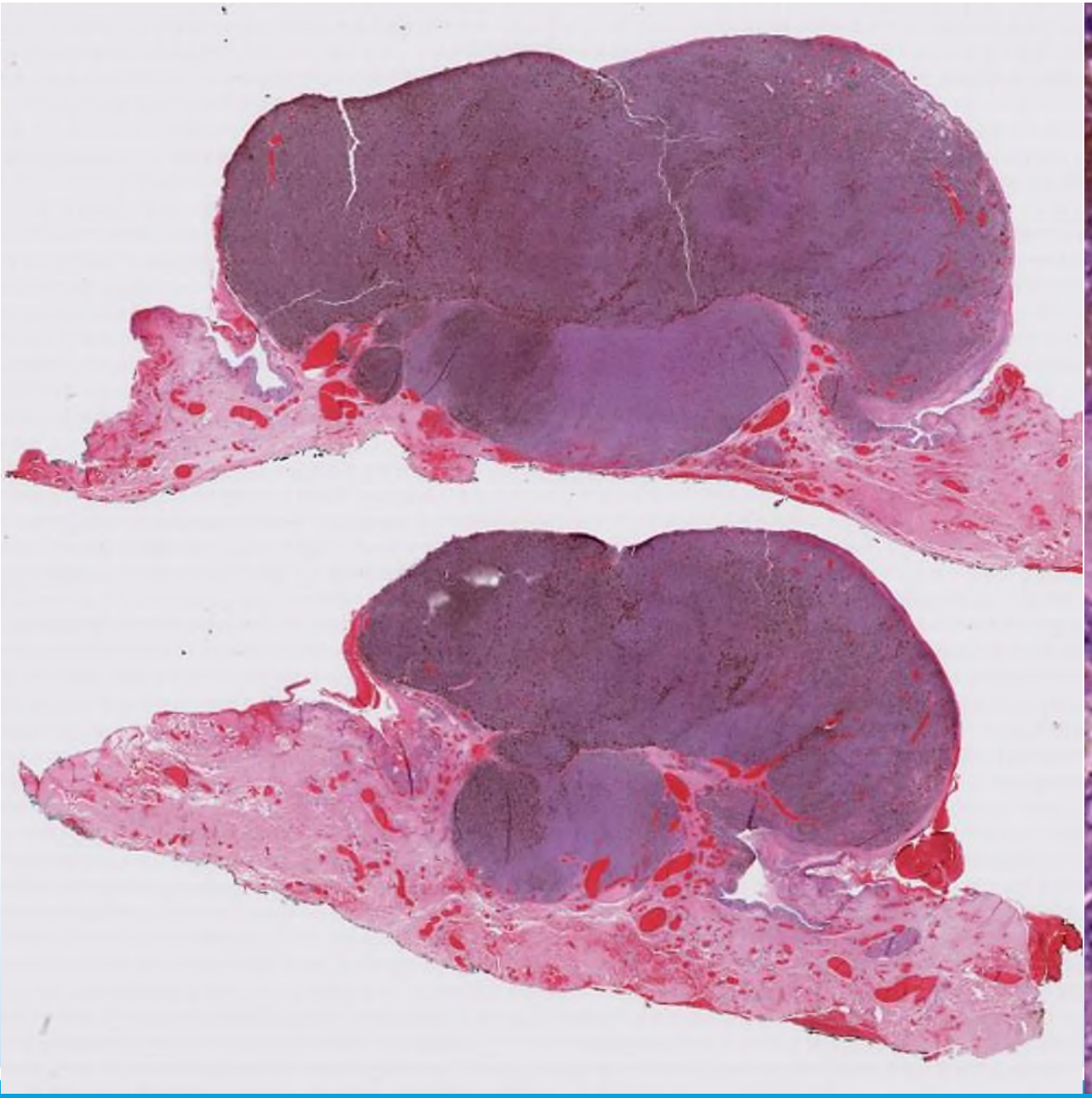
Case 6
Sebaceous Carcinoma

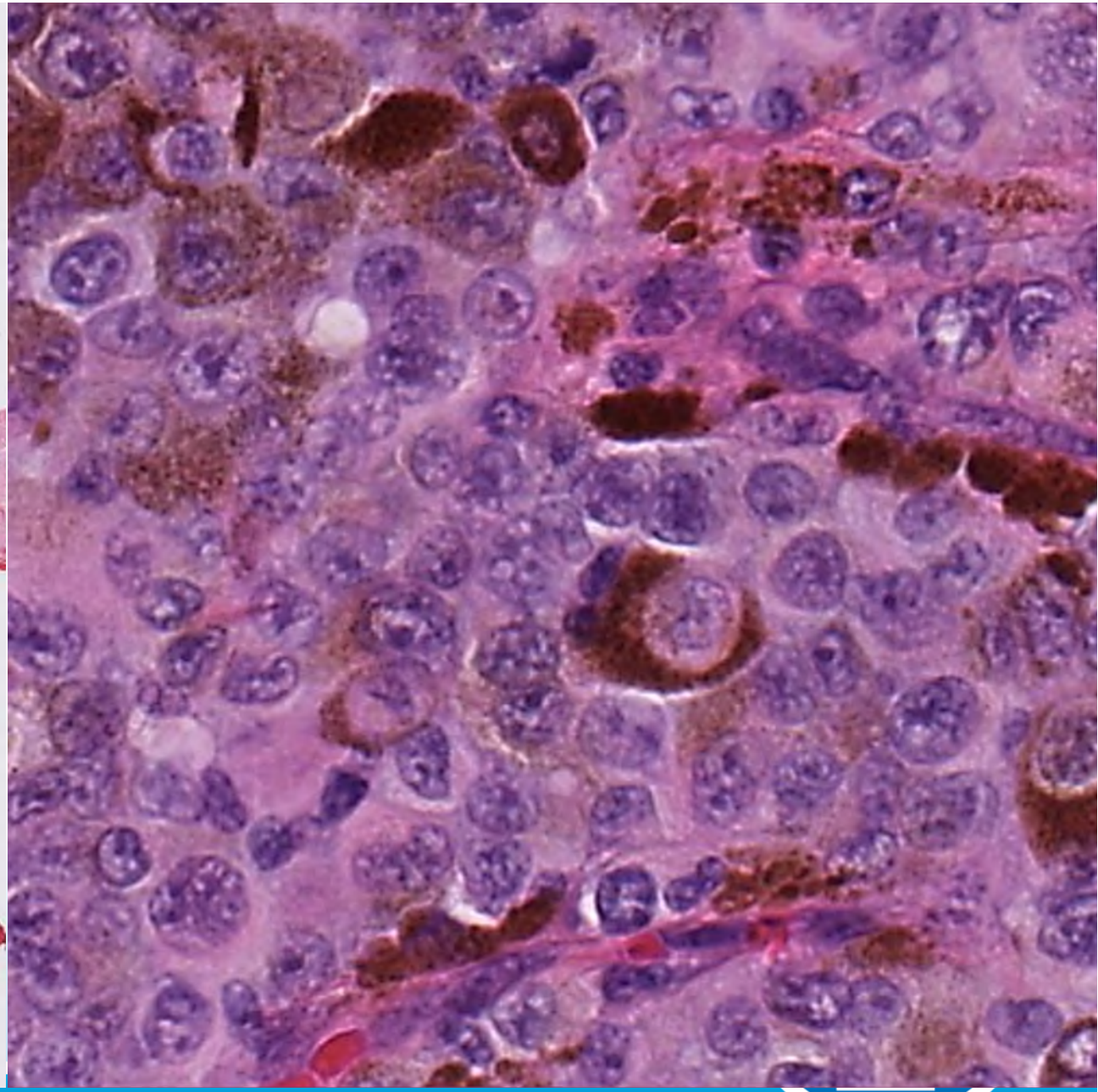
- Usually affect elderly patients
- Predilection for the eyelids
- Presentation as a chalazion typical
- Diagnostic morphologic features usually present
- Minimal involvement, pagetoid spread more challenging to diagnose

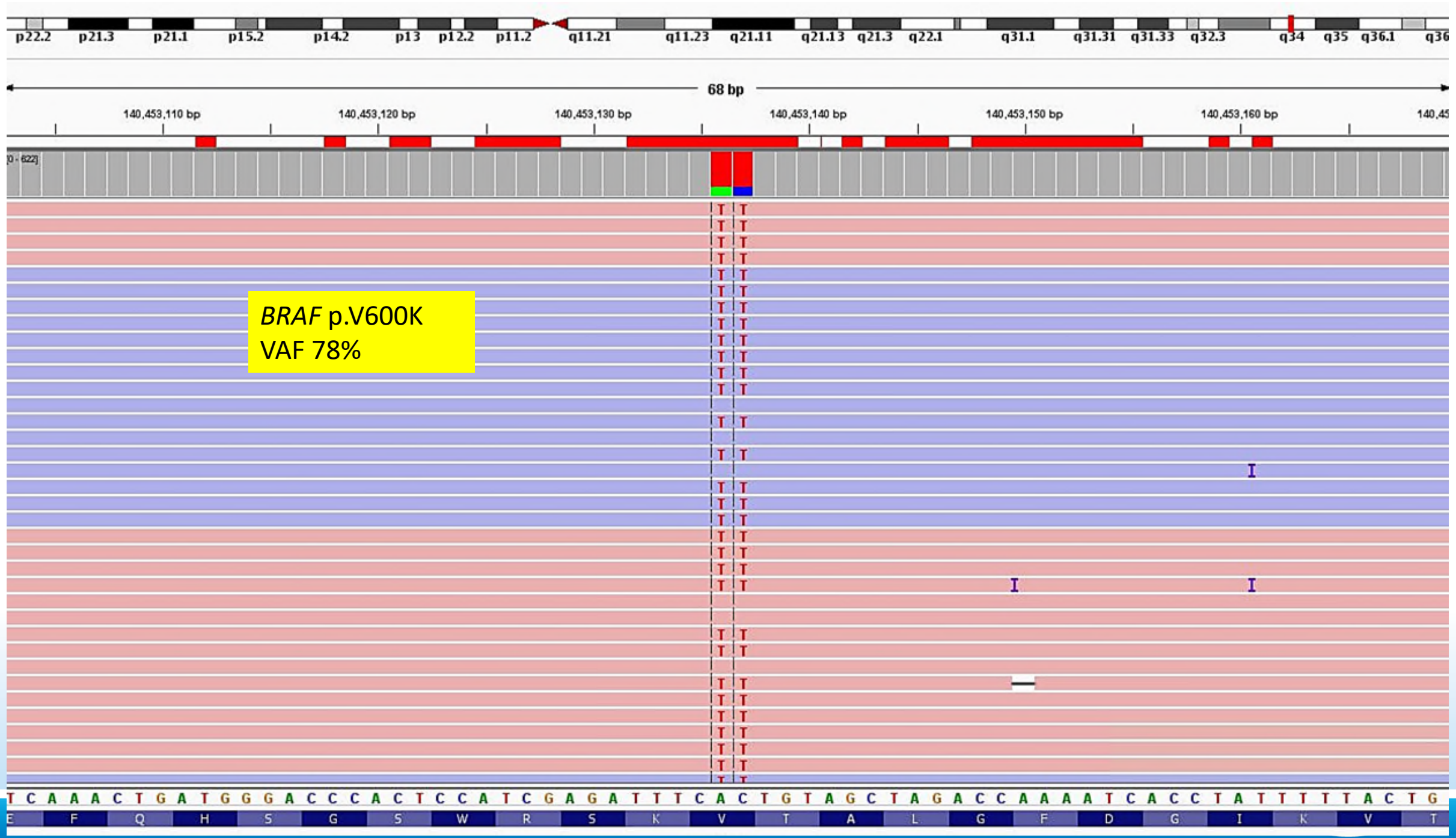


Case 7

- 68-year-old woman
- Mass on the right nasal bulbar conjunctiva extending from the caruncle to the limbus 12 x 4.5 mm






p22.2 p21.3 p21.1 p15.2 p14.2 p13 p12.2 p11.2 q11.21 q11.23 q21.11 q21.13 q21.3 q22.1 q31.1 q31.31 q31.33 q32.3 q34 q35 q36.1 q36
68 bp
140,453,110 bp
140,453,120 bp
140,453,130 bp
140,453,140 bp
140,453,150 bp
140,453,160 bp
BRAF p.V600K
VAF 78%
T C A A A C T G A T G G G A C C C A C T C C A T C G A G A T T T C A C T G T A G C T A G A C C A A A A T C A C C T A T T T T T A C T G
E F Q H S G S W R S K V T A L G F D G I K V T

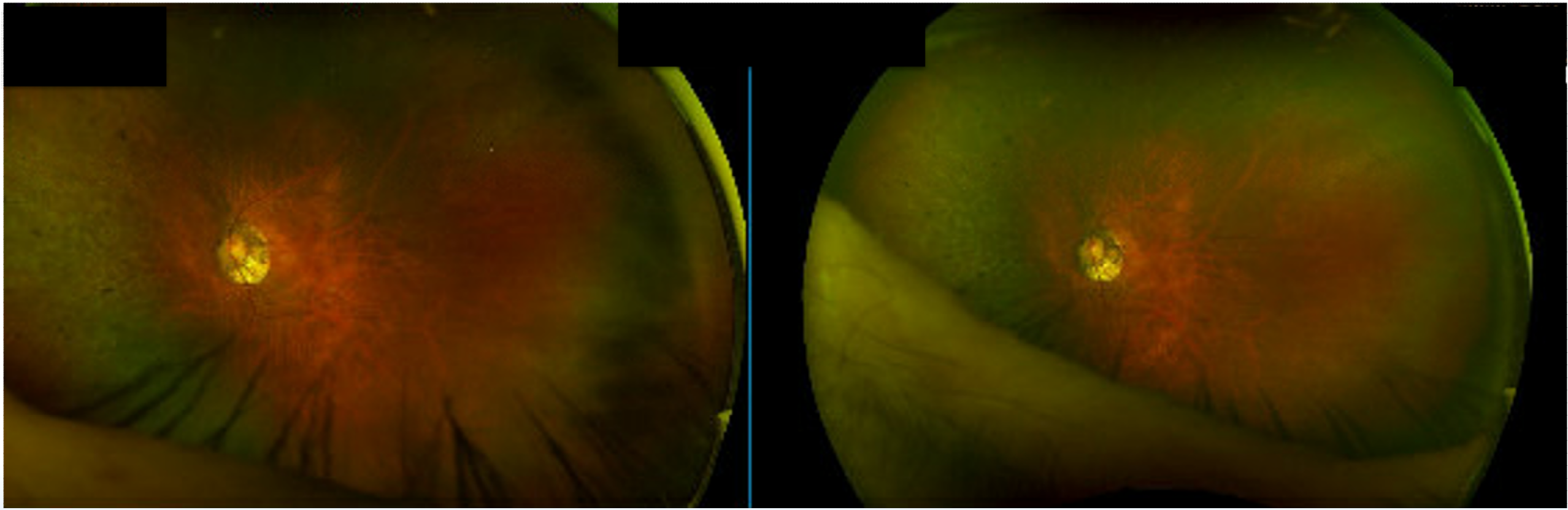
Case 7
Conjunctival melanoma

- Relatively rare compared to uveal melanoma
- Primary acquired melanosis (PAM) with atypia known precursor
- Lymphatic spread in advance cases
- Exenteration performed in cases with recurrence/orbital involvement
- Alterations in MAPK pathway components (BRAF, RAS, etc)

Case 7-
Follow-up

- Treated with I-125 plaque, cryo
- Orbital exentration 8 months later
- Right orbit-no evidence of recurrence 2 years later

Left eye-choroidal melanocytosis stable

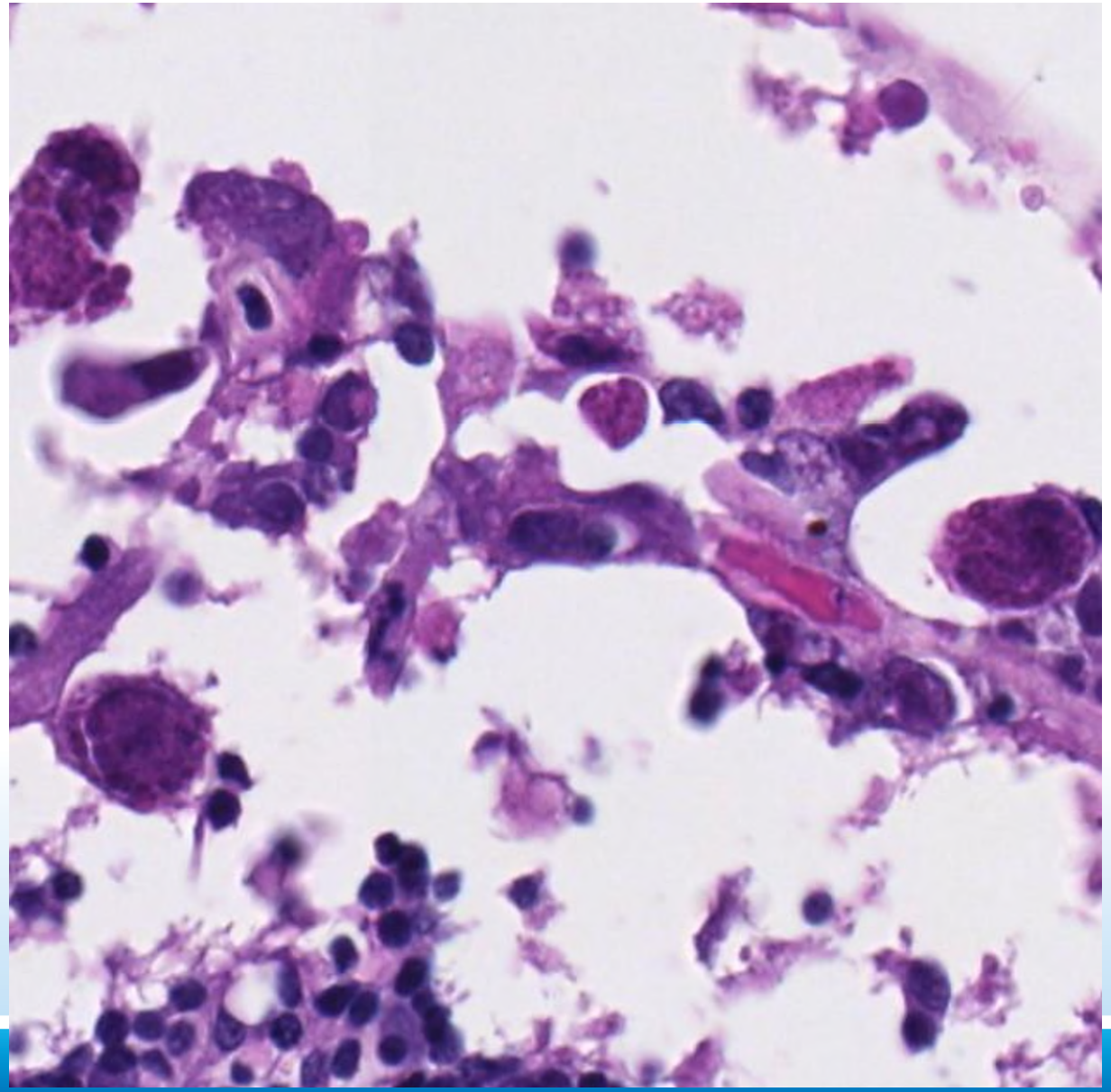


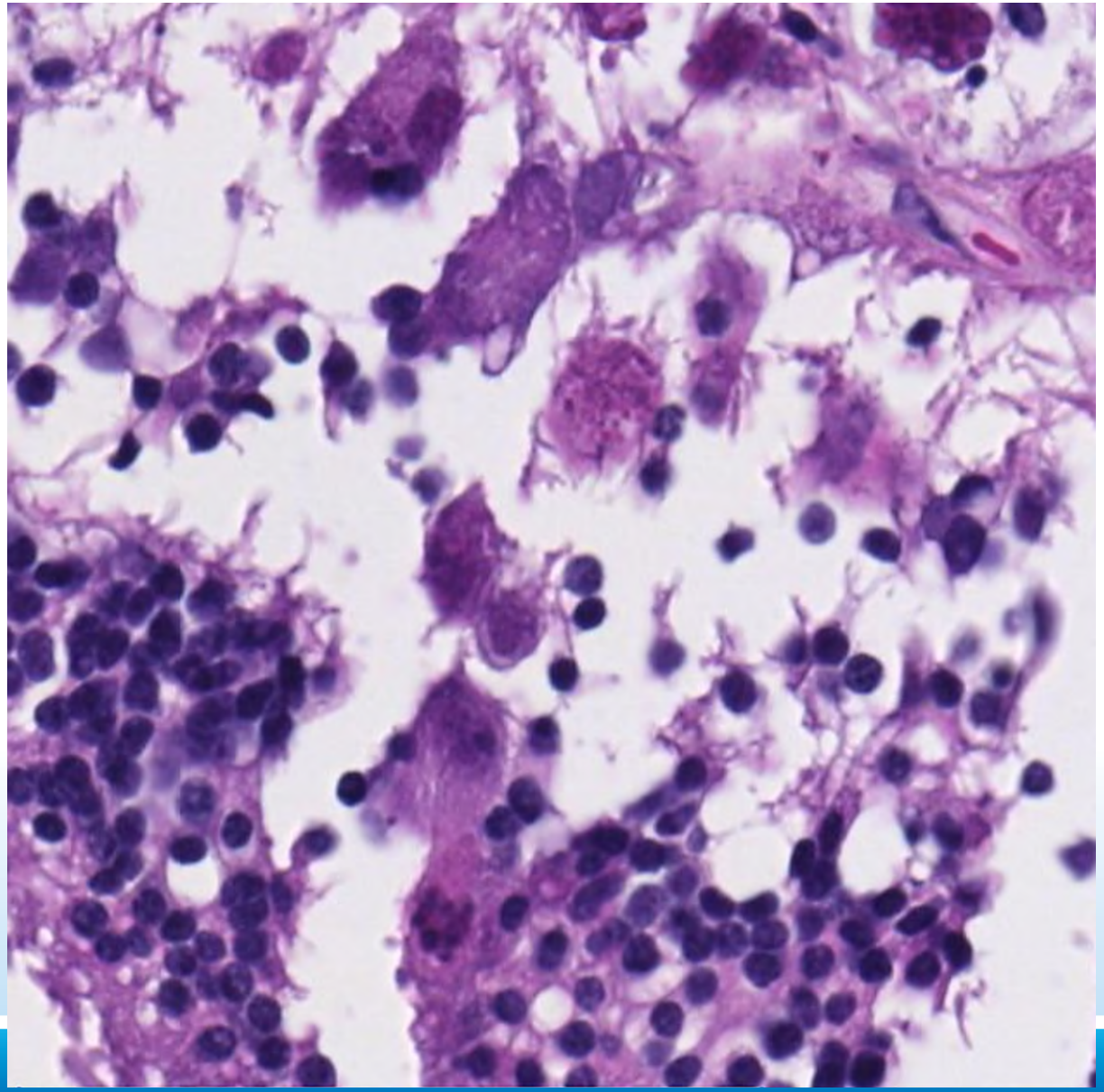
Case 8

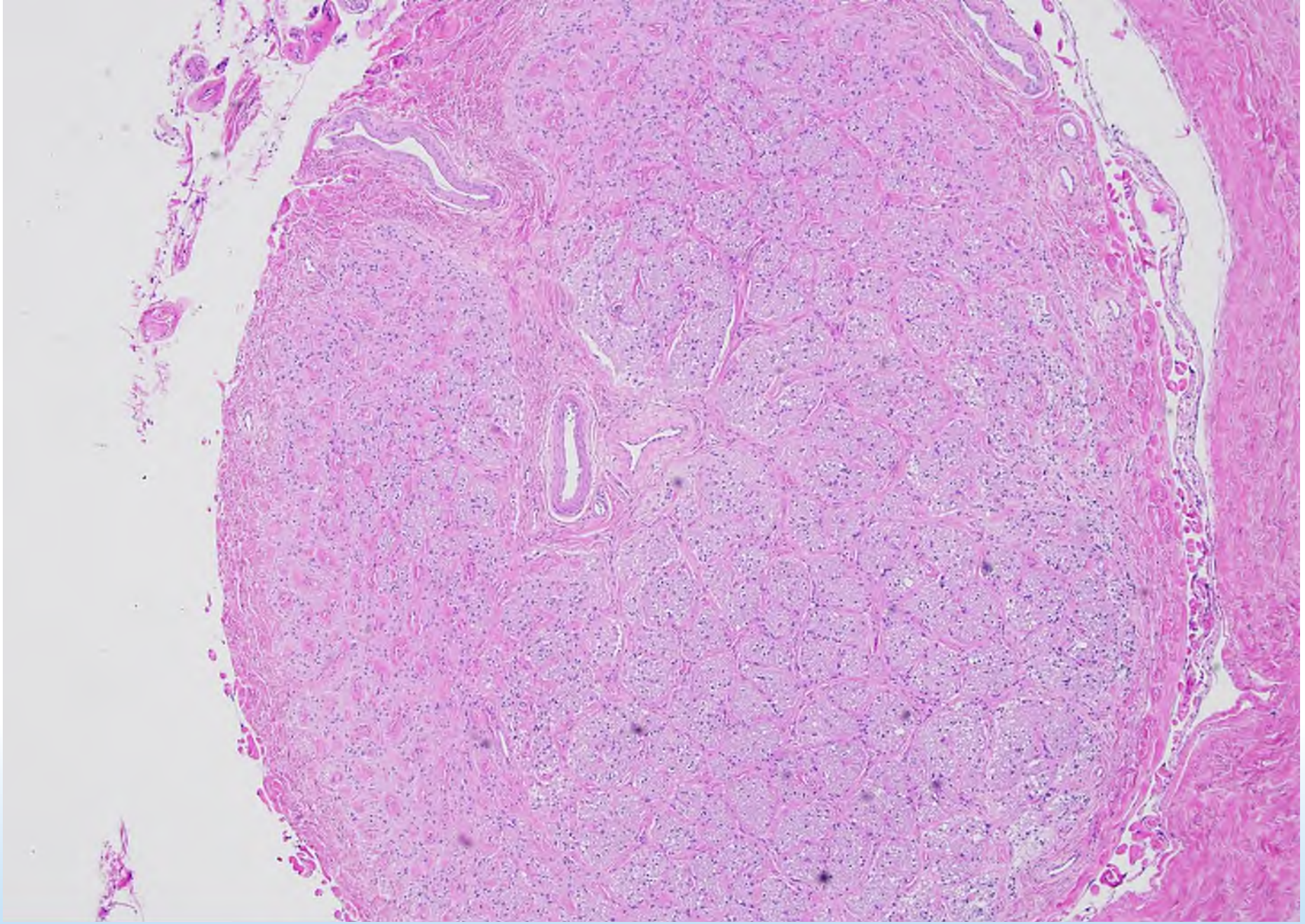
- 72-year-old man with complicated past medical history including sarcoidosis
- Sudden loss of vision in right eye
- Blindness
- Progressive decline, weakness, fatigue and mental fogginess
- Admitted for progressive hypoxemia, eventually shock and metabolic acidosis.

Autopsy

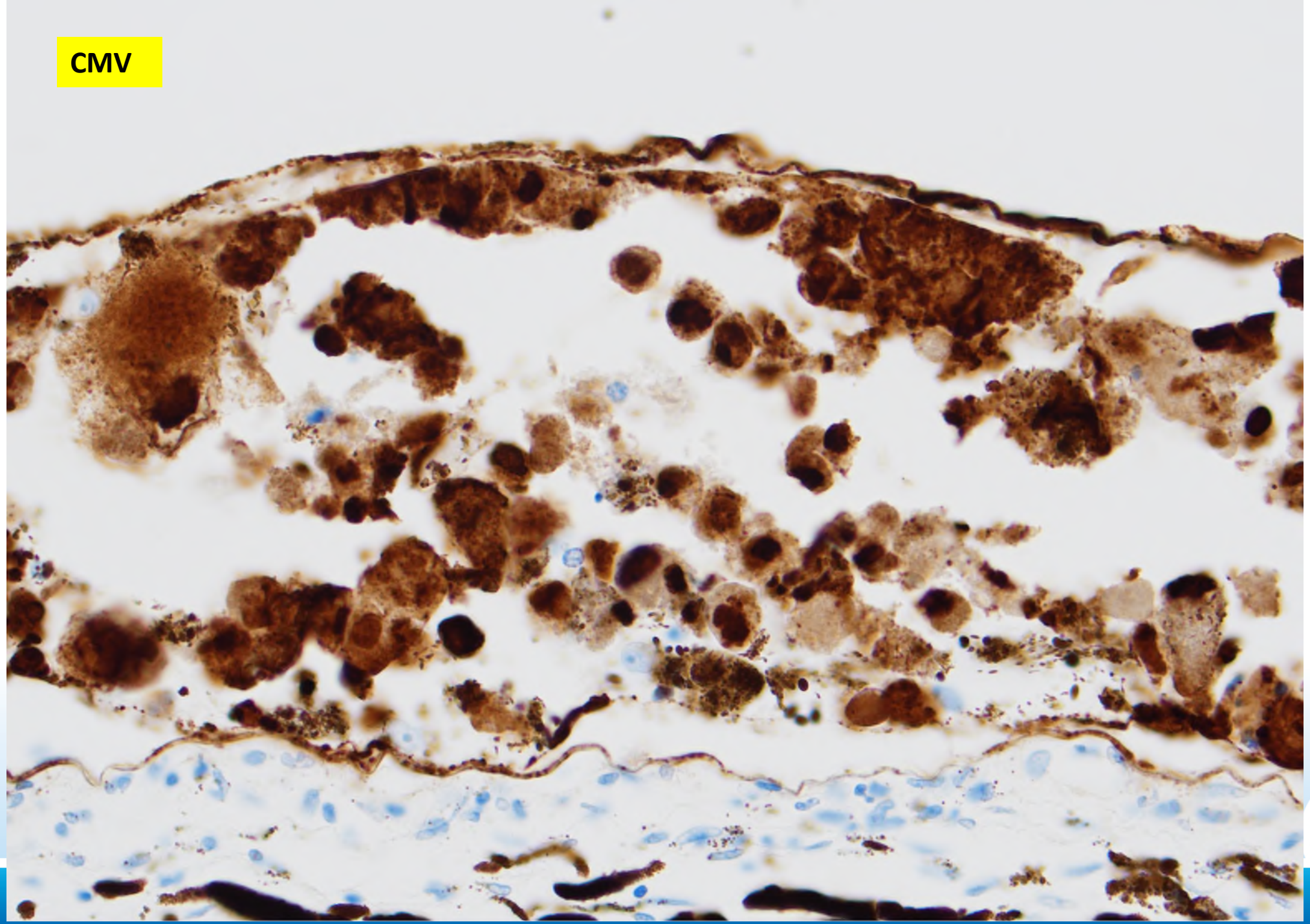
- Organizing pneumonia and hemophagocytic histiocytosis







CMV



Case 8: CMV retinitis

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- Afshar AR. Next-Generation Sequencing of Retinoblastoma Identifies Pathogenic Alterations beyond *RB1* Inactivation That Correlate with Aggressive Histopathologic Features. Ophthalmology 2020 Jun;127(6):804-813
- Pacheco R. Conjunctival melanoma: outcomes based on tumour origin in 629 patients at a single ocular oncology centre. Eye (Lond) 2021.

Questions?

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3. Ahmed OM. Epidemiology, outcomes, and prognostic factors of orbital lymphoma in the United States. Orbit 2020 Dec;39(6):397-402
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