



# **Salivary Gland Tumors: Unknown Case Interactive Session**

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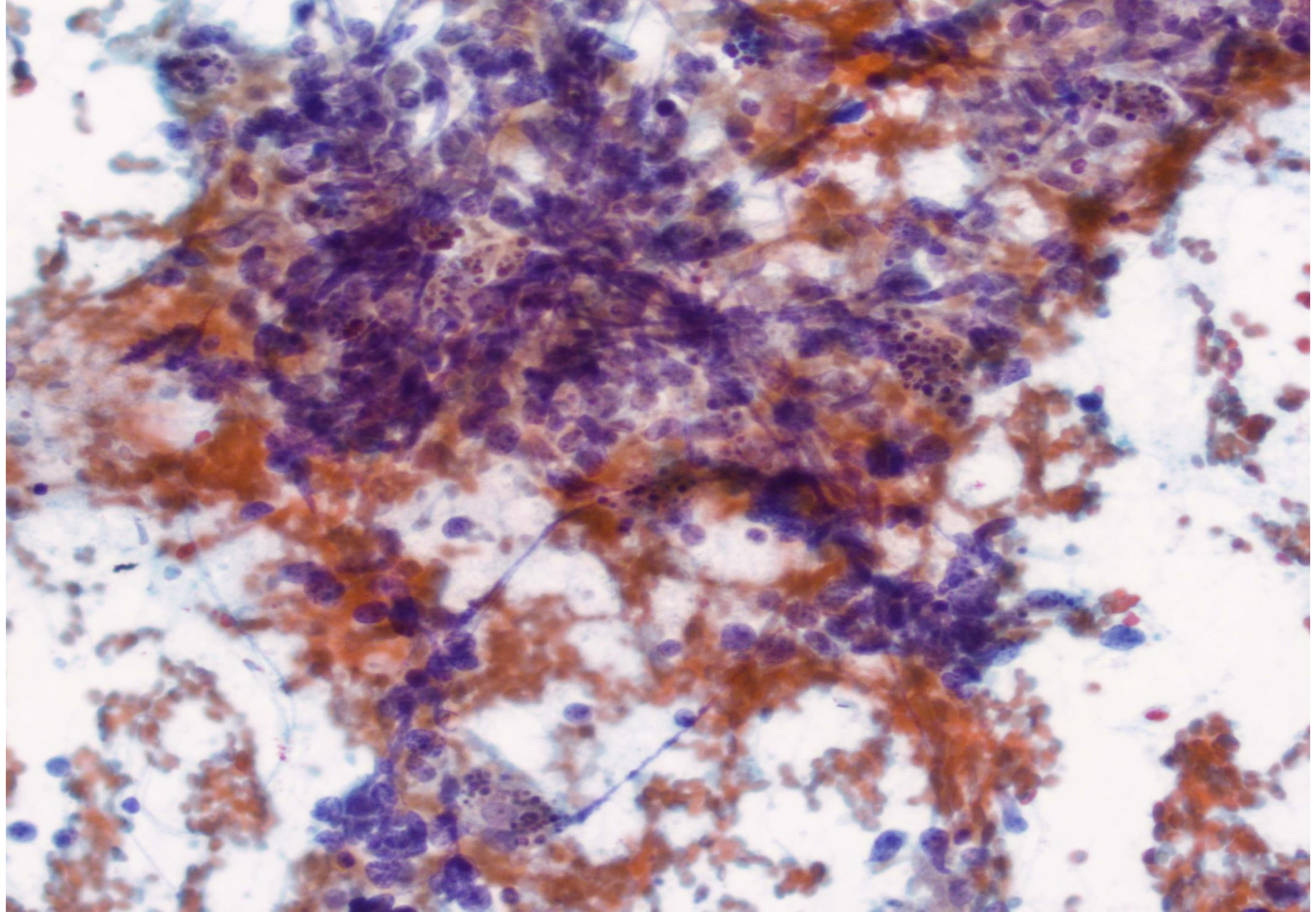
**Department of Pathology, Yale School of Medicine**

# Case 1

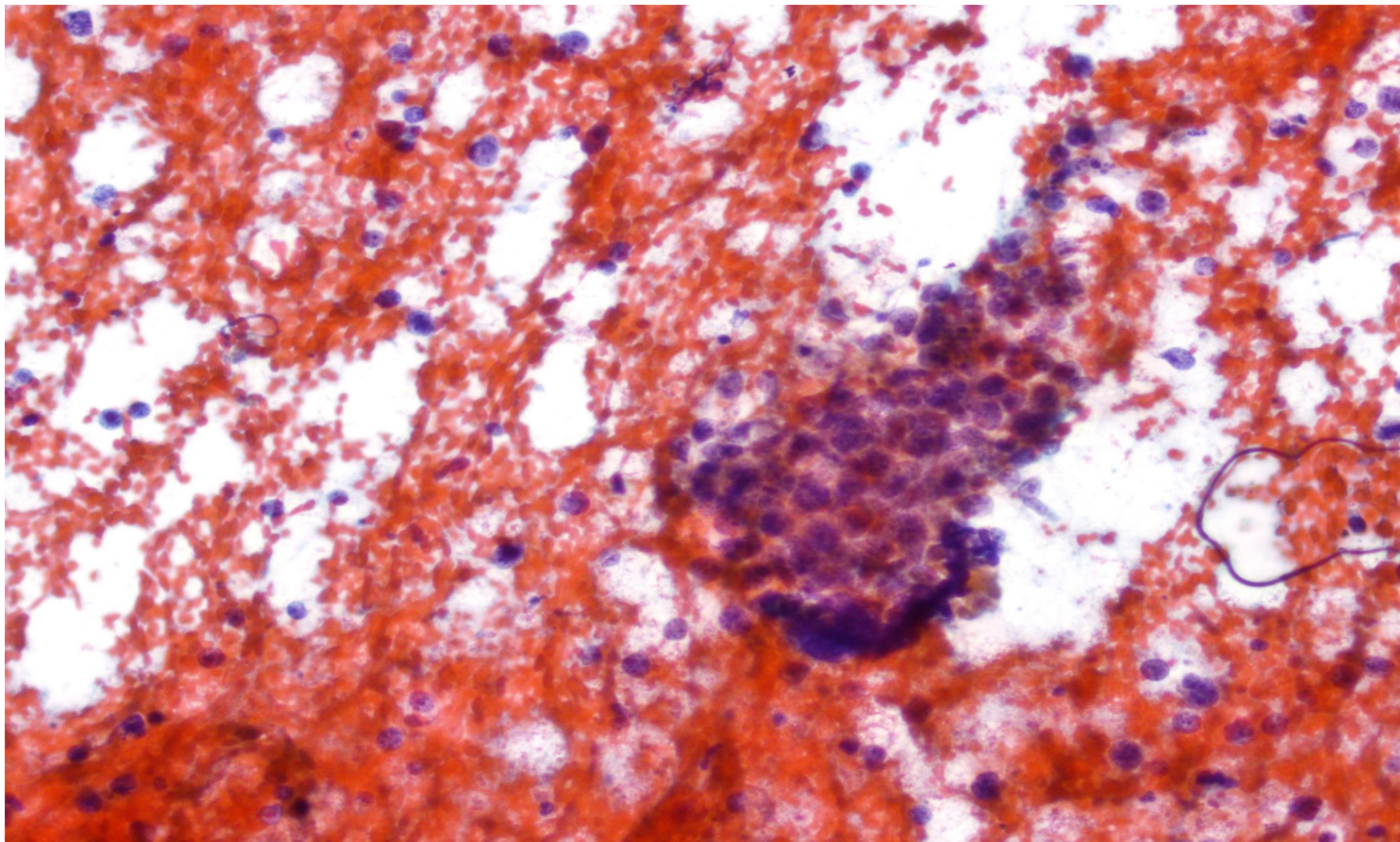
64-year-old female with right parotid mass

US Scan revealed a 2cm parotid mass and few borderline enlarged lymph nodes in the neck

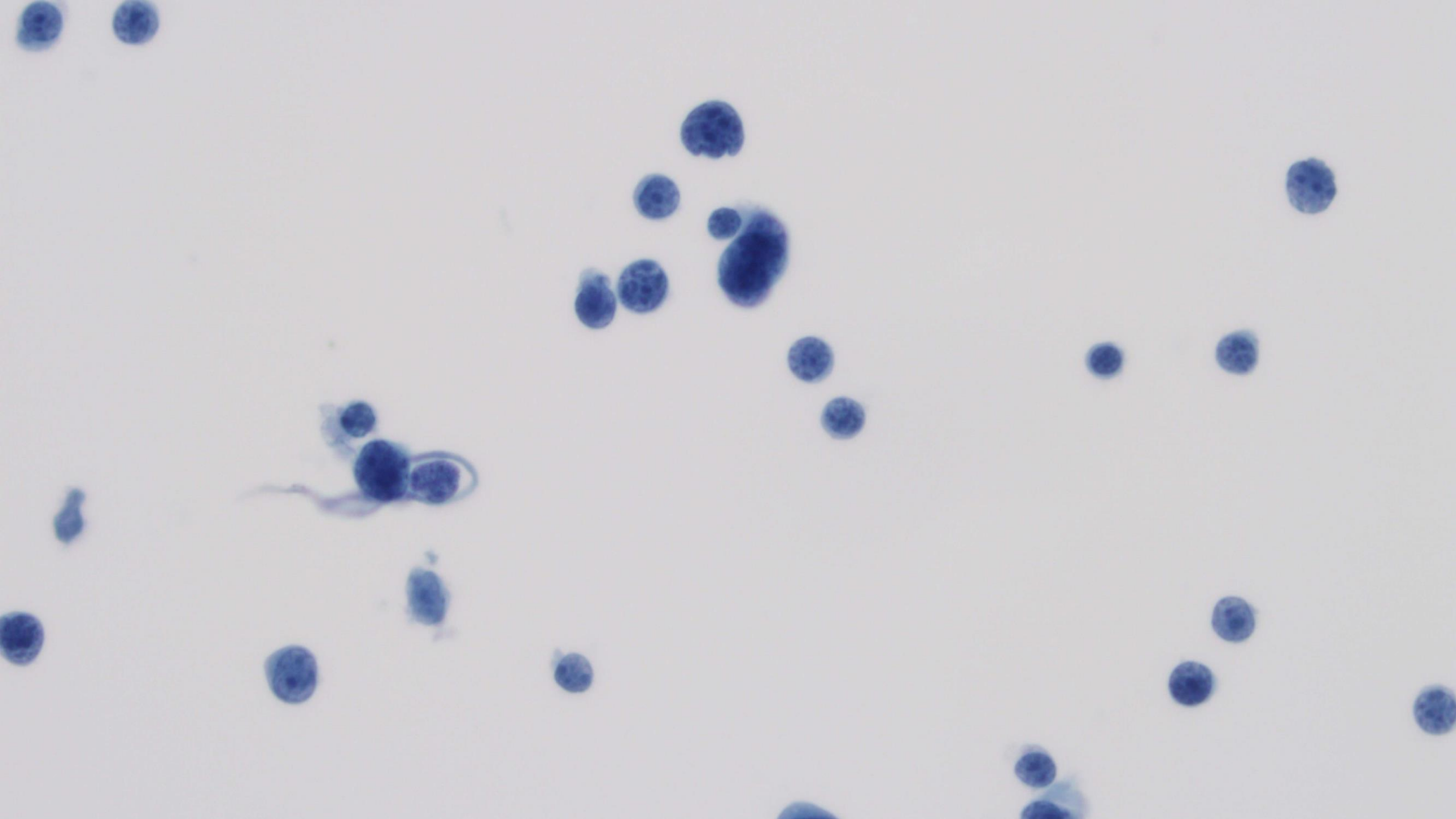


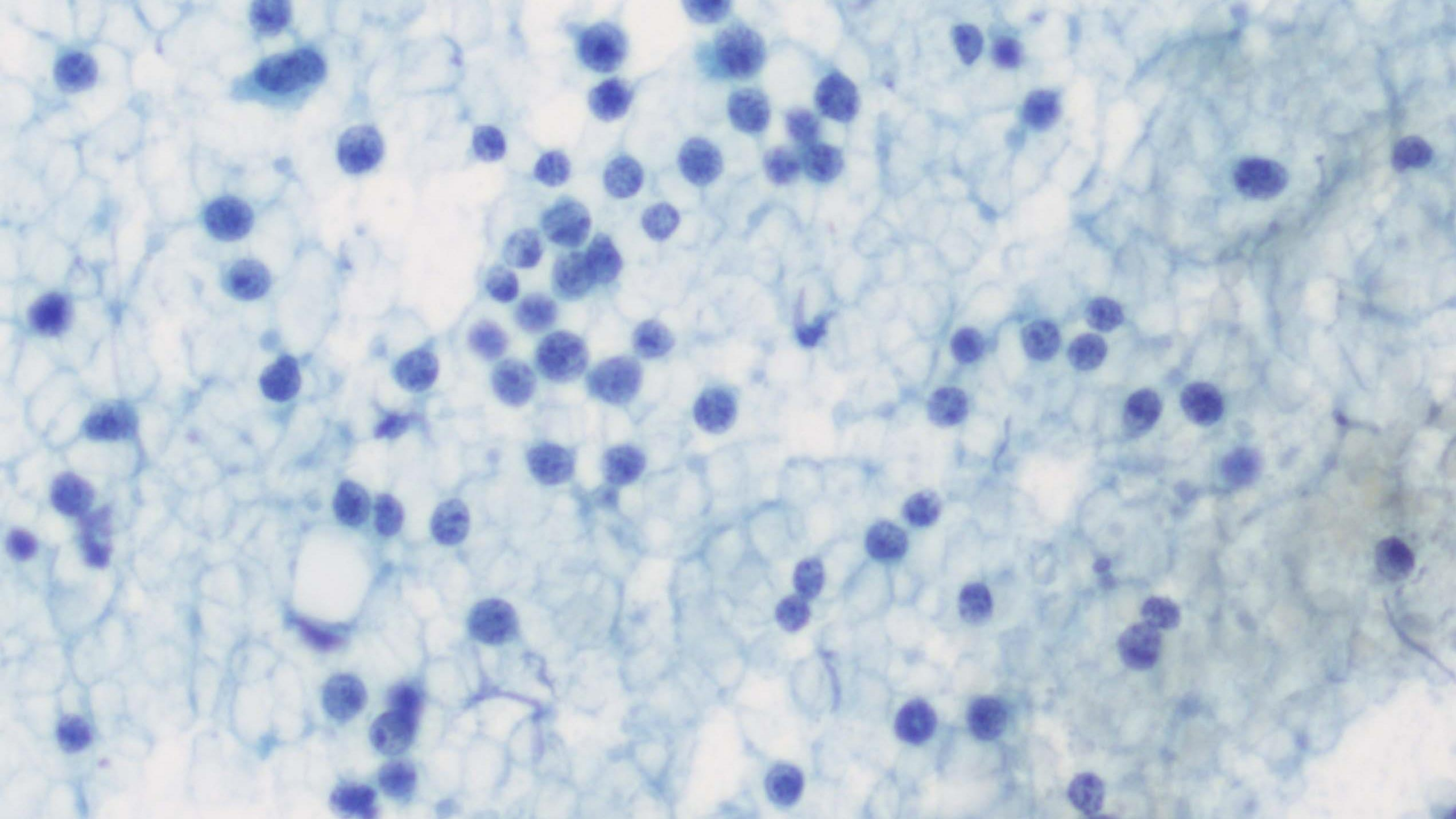




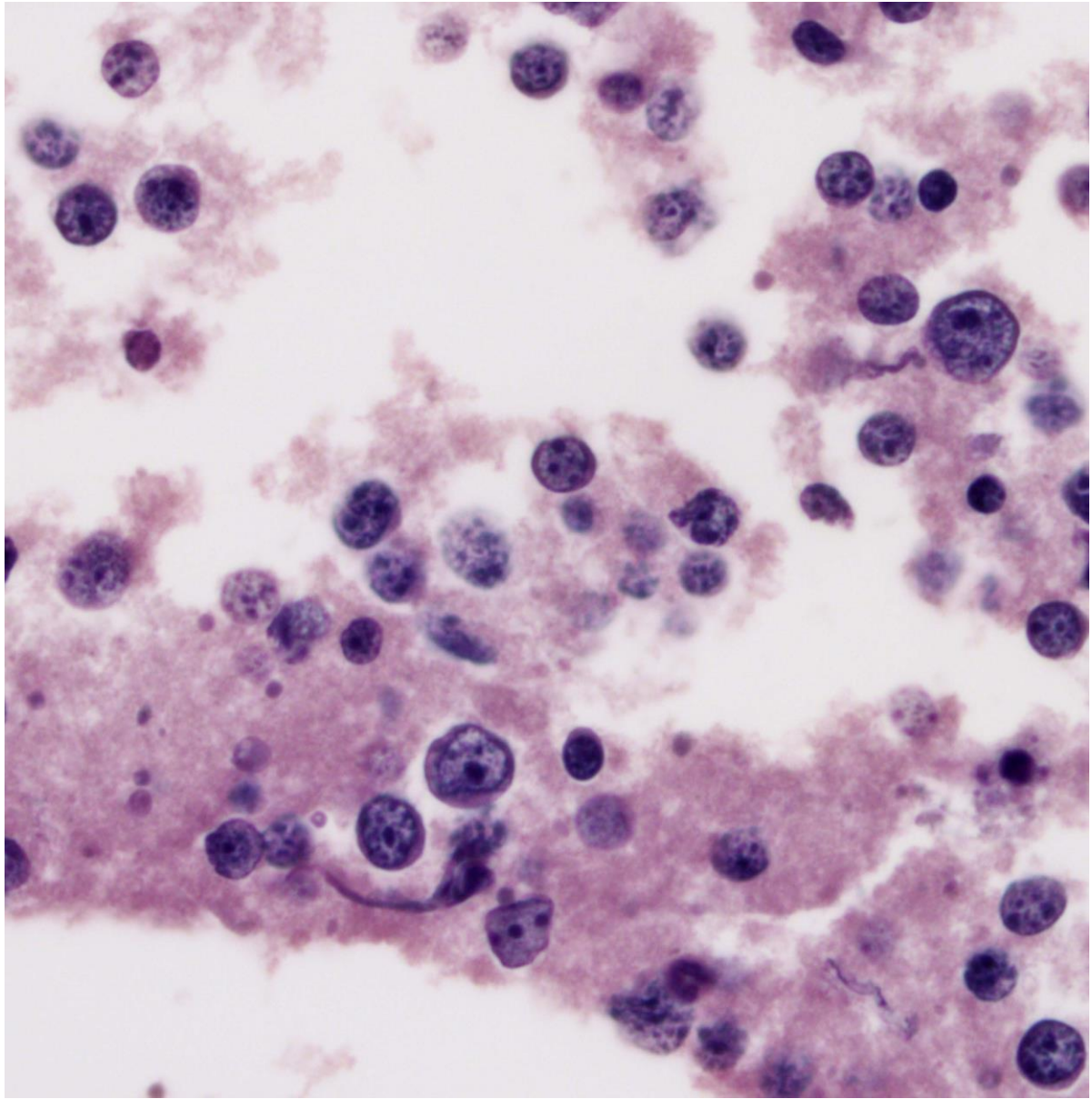
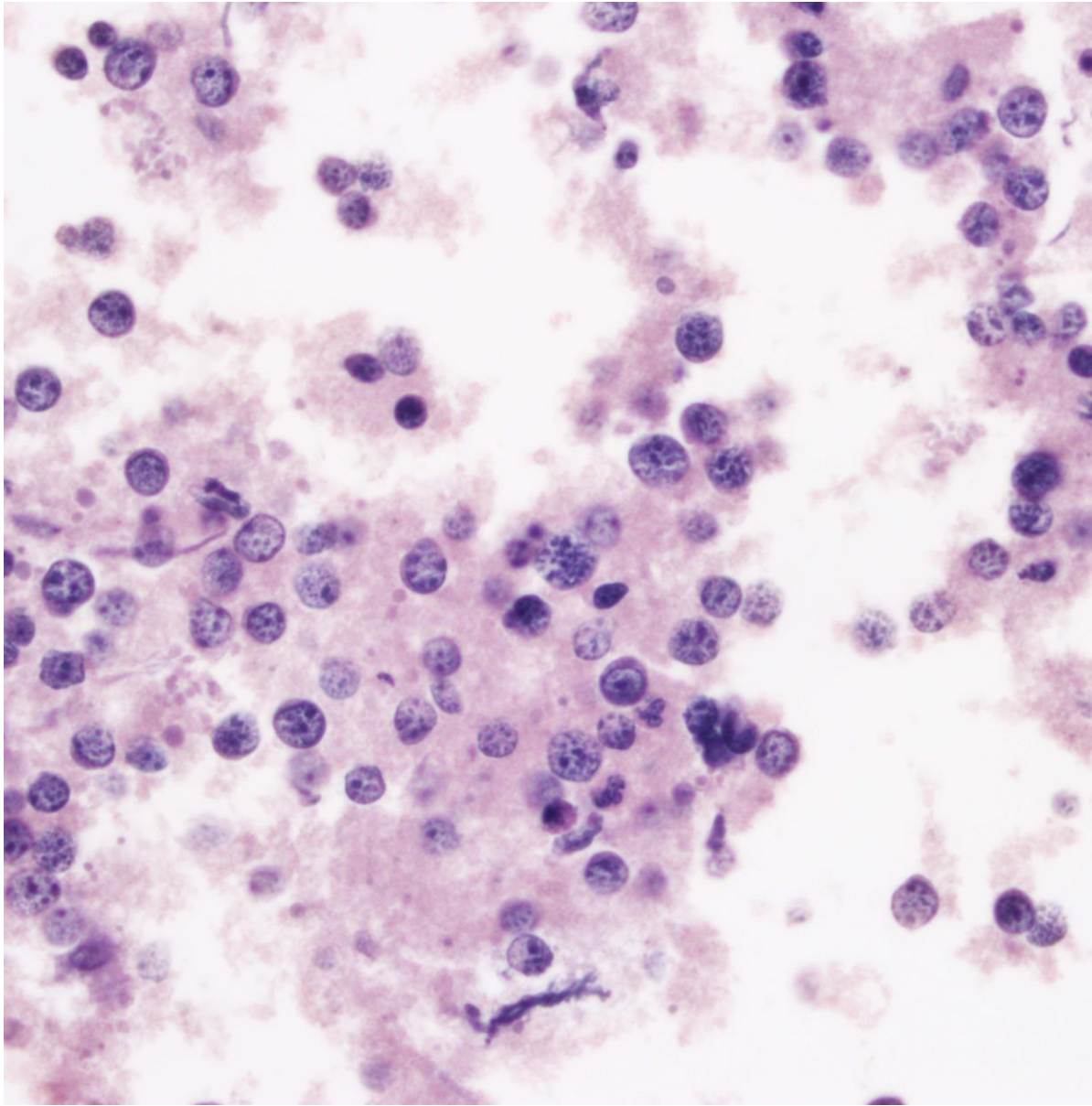






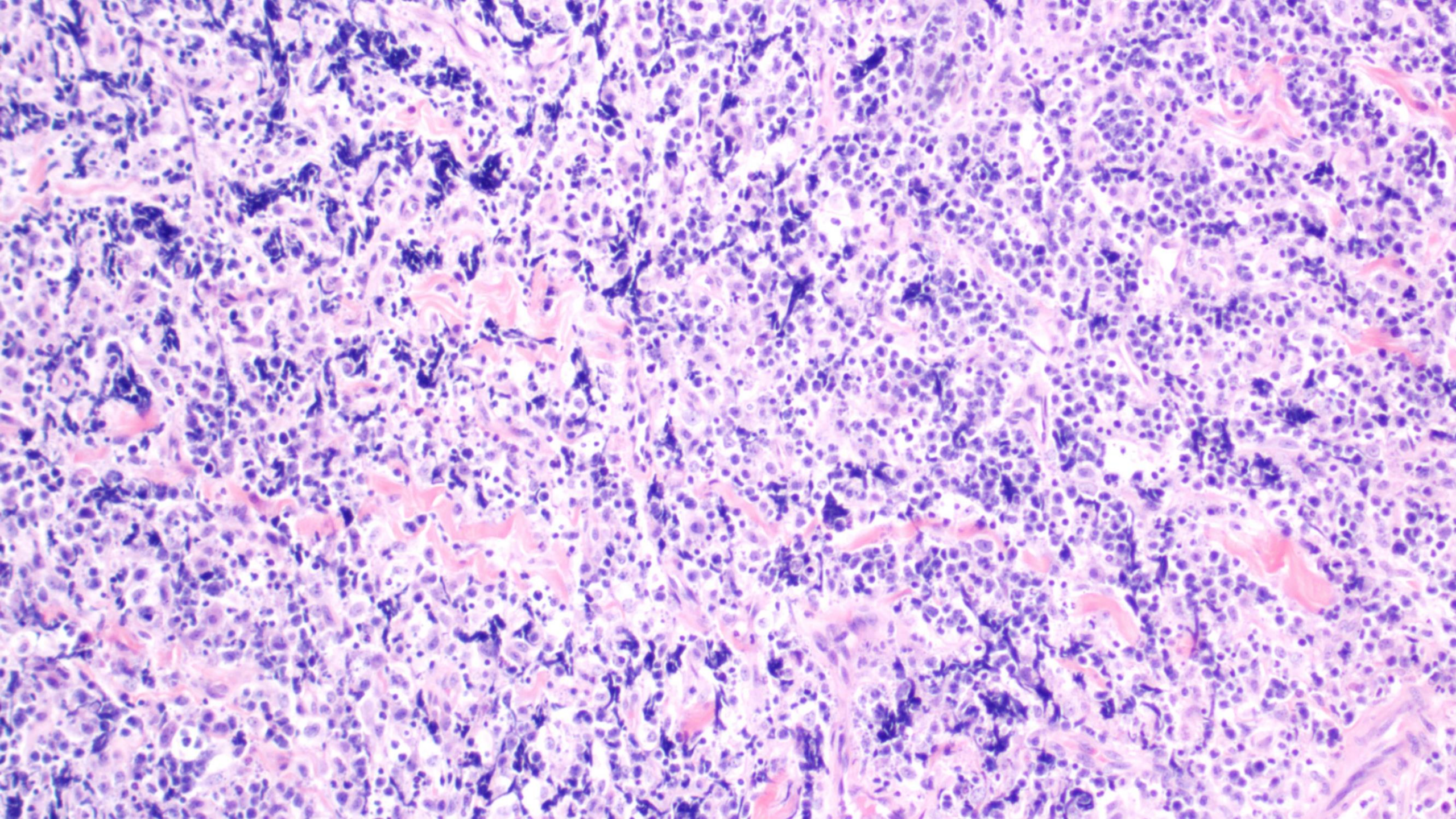




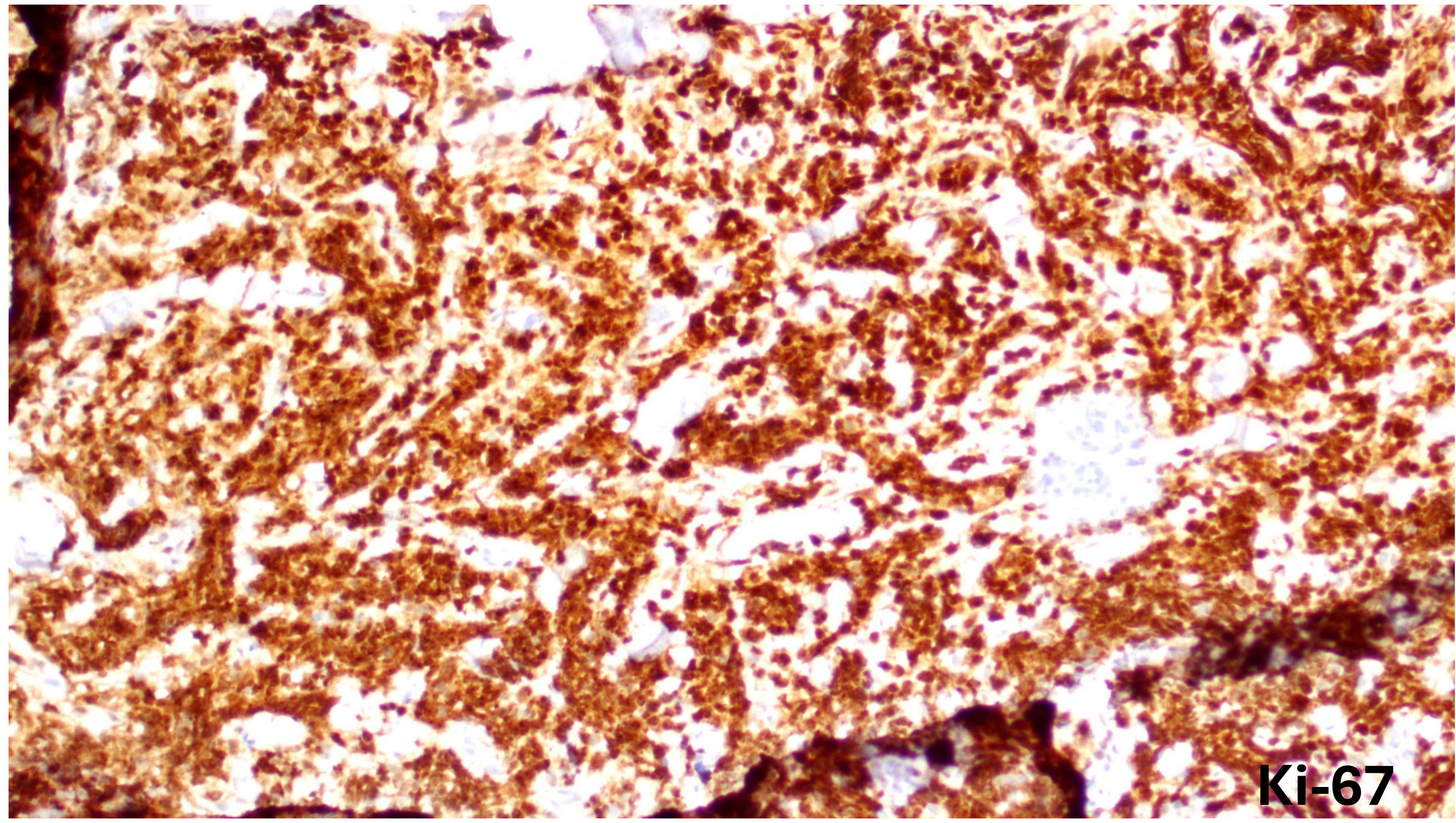


- IHC
  - CD20-positive B cells with co-expression of CD10, BCL-6 and c-Myc while negative for BCL-2
  - Tumor cells express kappa light chain restriction
- Tissue insufficient for molecular studies
- Diagnosis of large cell lymphoma, NOS was made
- Core biopsy obtained – Ki-67 proliferation index ~100%
- MYCC rearrangement demonstrated by FISH









**Ki-67**



What is the diagnosis?

# Burkitt Lymphoma



# **Lymphoid-rich salivary lesions**

- Malignant lymphoma
- Reactive lymphoid hyperplasia– Intra/peri-salivary LNs
- Lymphoepithelial sialadenitis
- Chronic sialadenitis
- Warthin tumor
- Tumor associated lymphoid proliferation

# Malignant Lymphoma

- 2-5% of salivary gland neoplasms
- Primary, associated with
  - Lymphoepithelial sialadenitis
  - Warthin tumor
  - Intraparotid lymph node
- Secondary: part of generalized disease or leukemia
- Large B cell (35%), follicular (35%), low grade/MALT (30%)
- IHC, Flow cytometry, gene rearrangement

# Lymphoepithelial sialadenitis

- Associated autoimmune disorders (Sjogren syndrome)
- Parotid, Female, 5<sup>th</sup>-6<sup>th</sup> decade
- 44X risk of lymphoma (MALT)
- Difficult to distinguish from RLH
  - Polymorphous lymphoid cells
  - Rare ductal epithelial cells (lymphoepithelial islands)

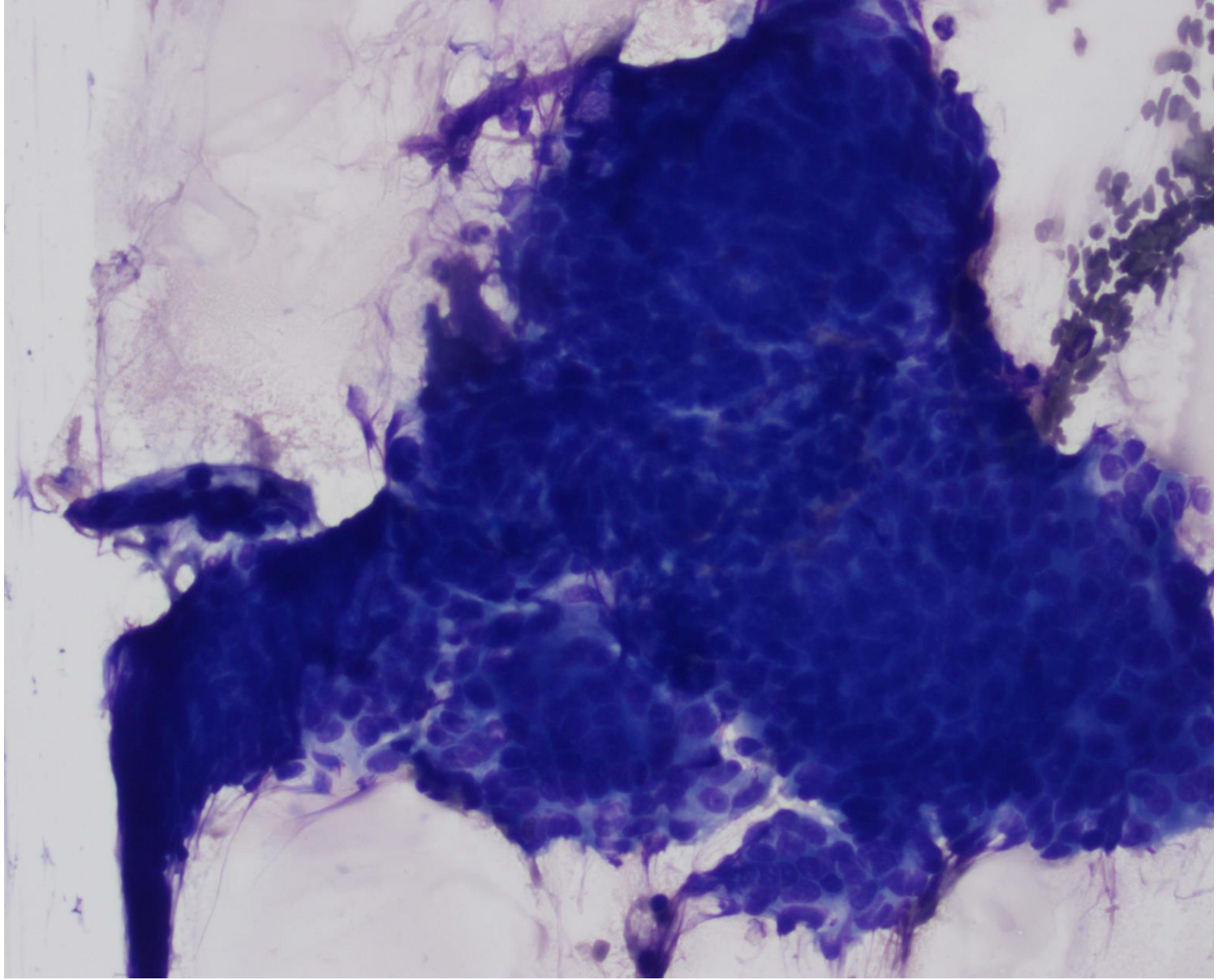
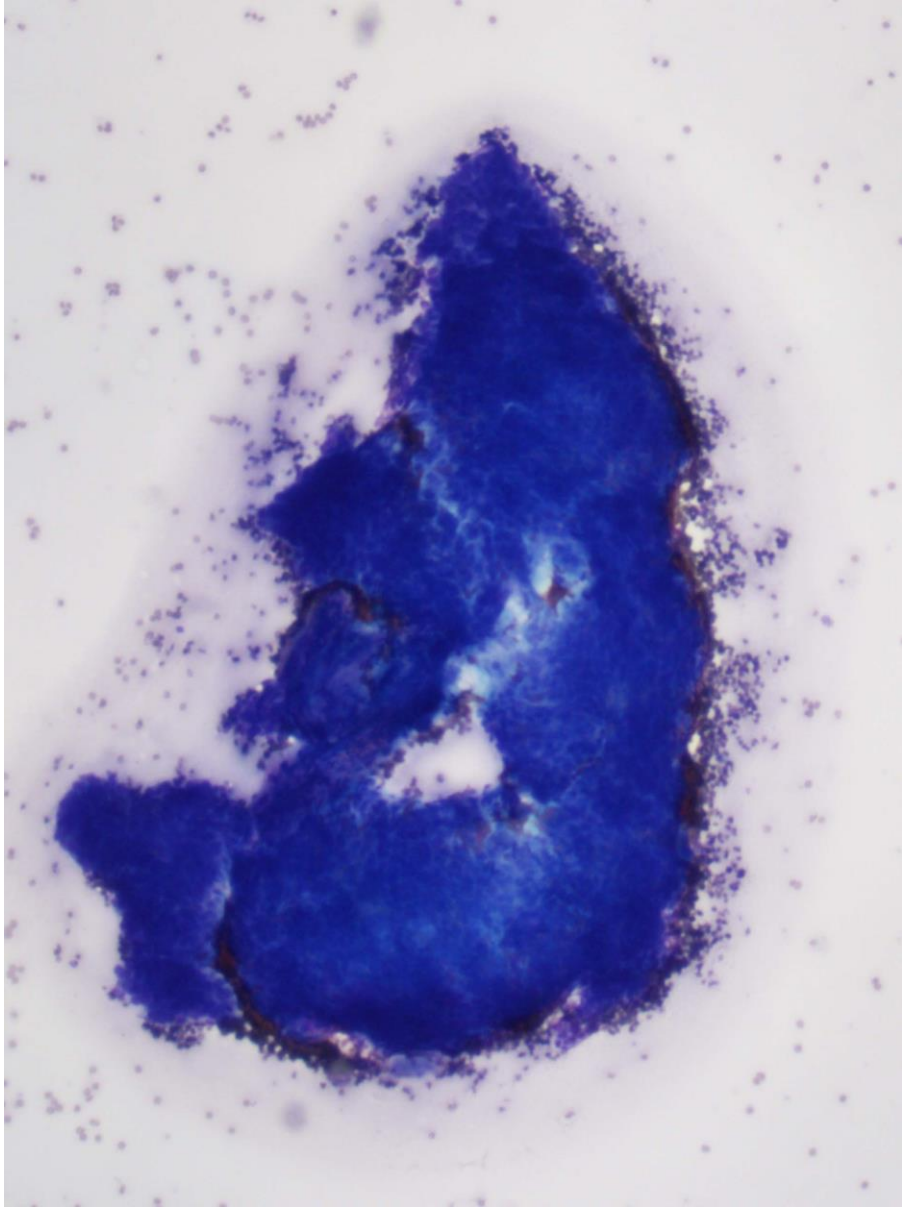


# Case 2

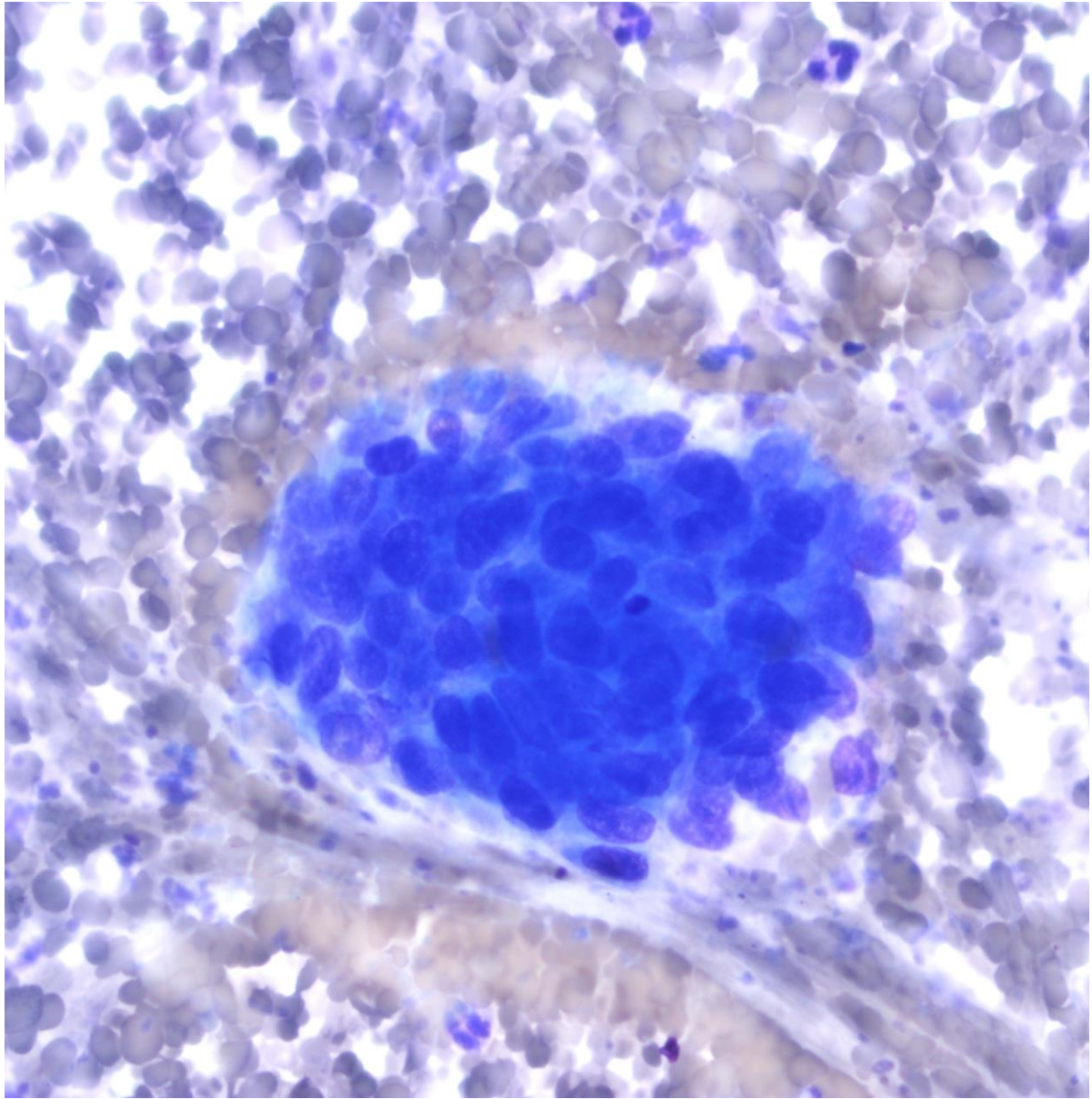
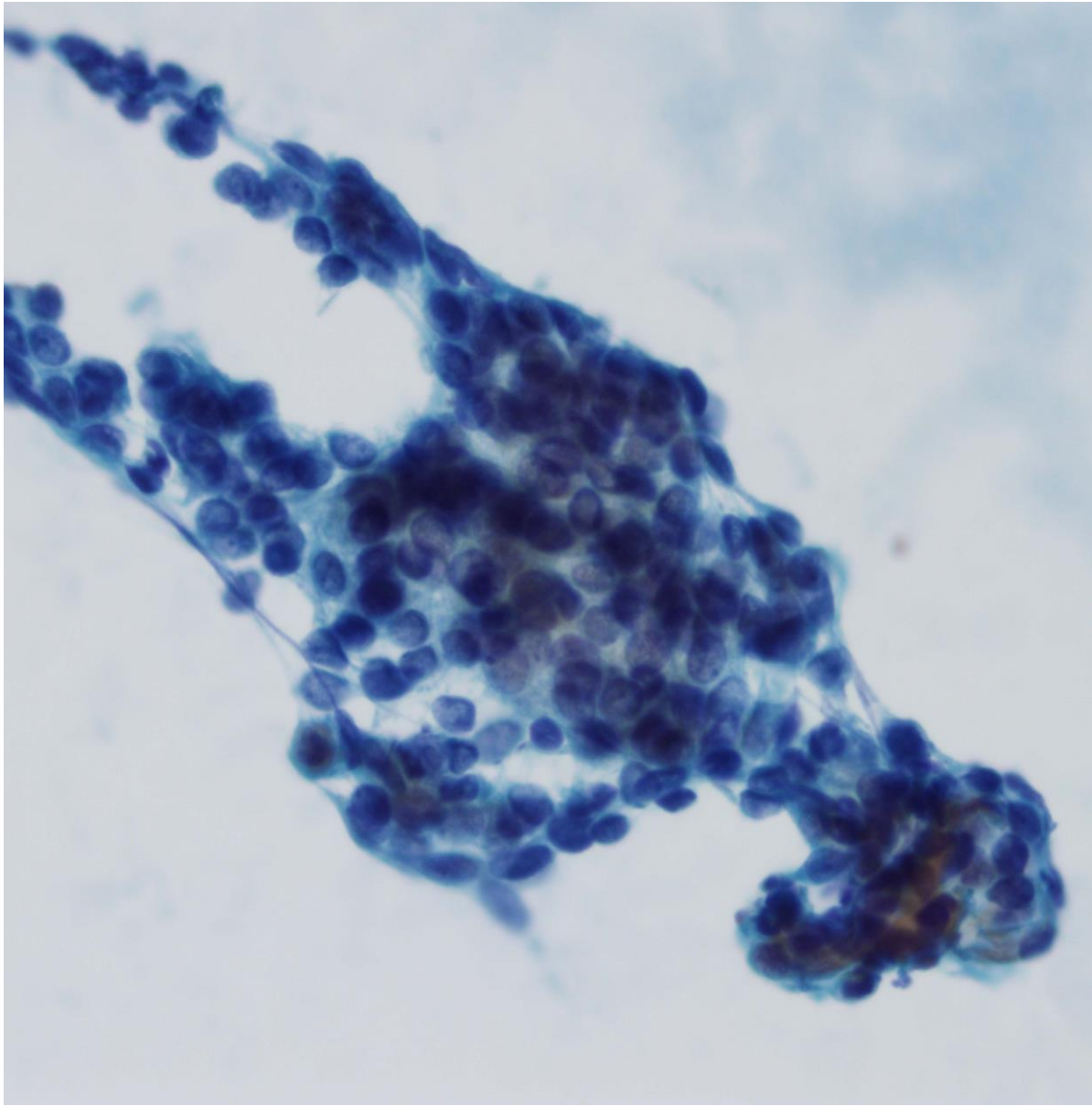
76-year-old male with 1 cm left parotid mass

History of Squamous cell carcinoma of the scalp

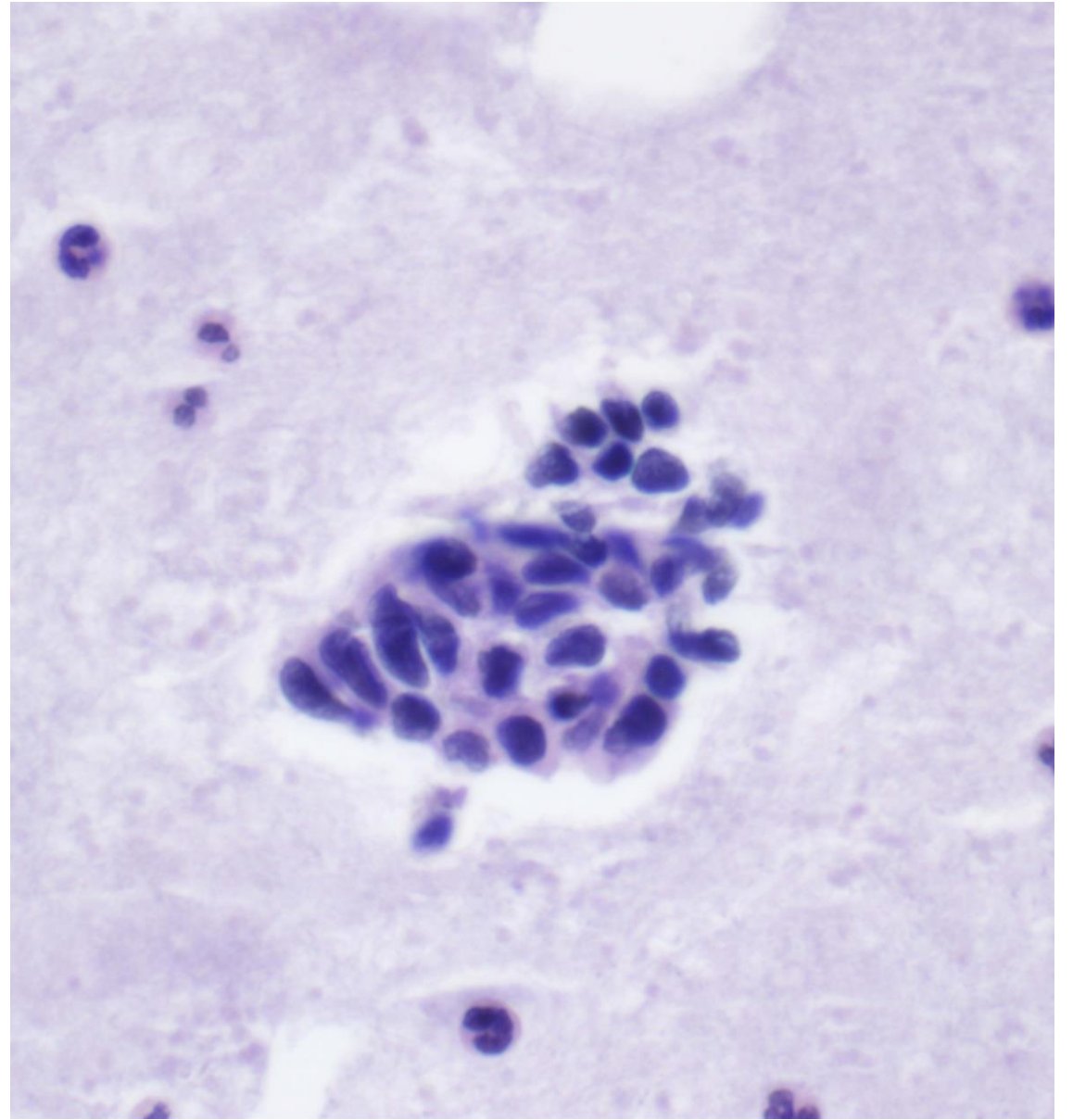
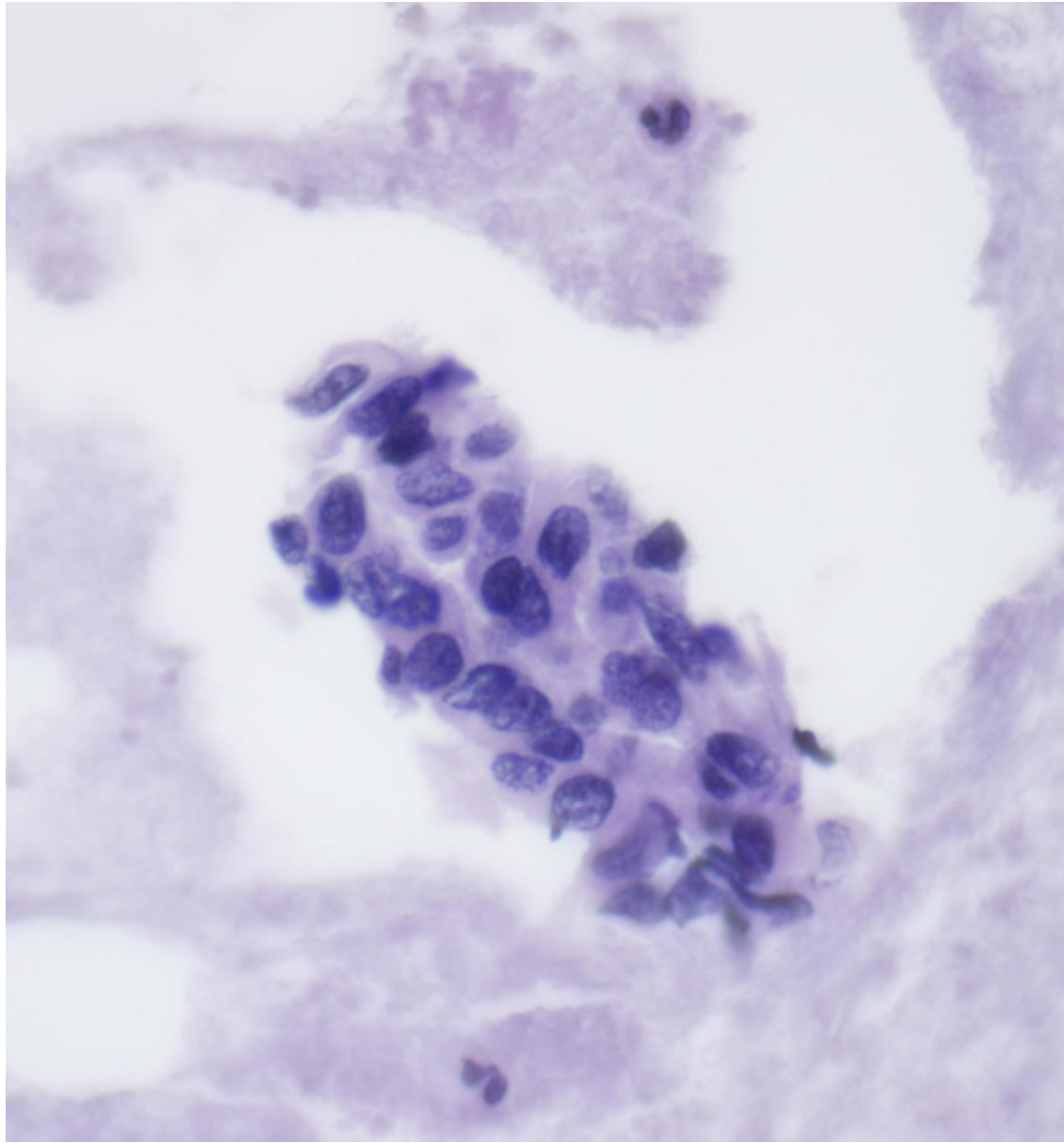
Referred to YNHH for radiation therapy

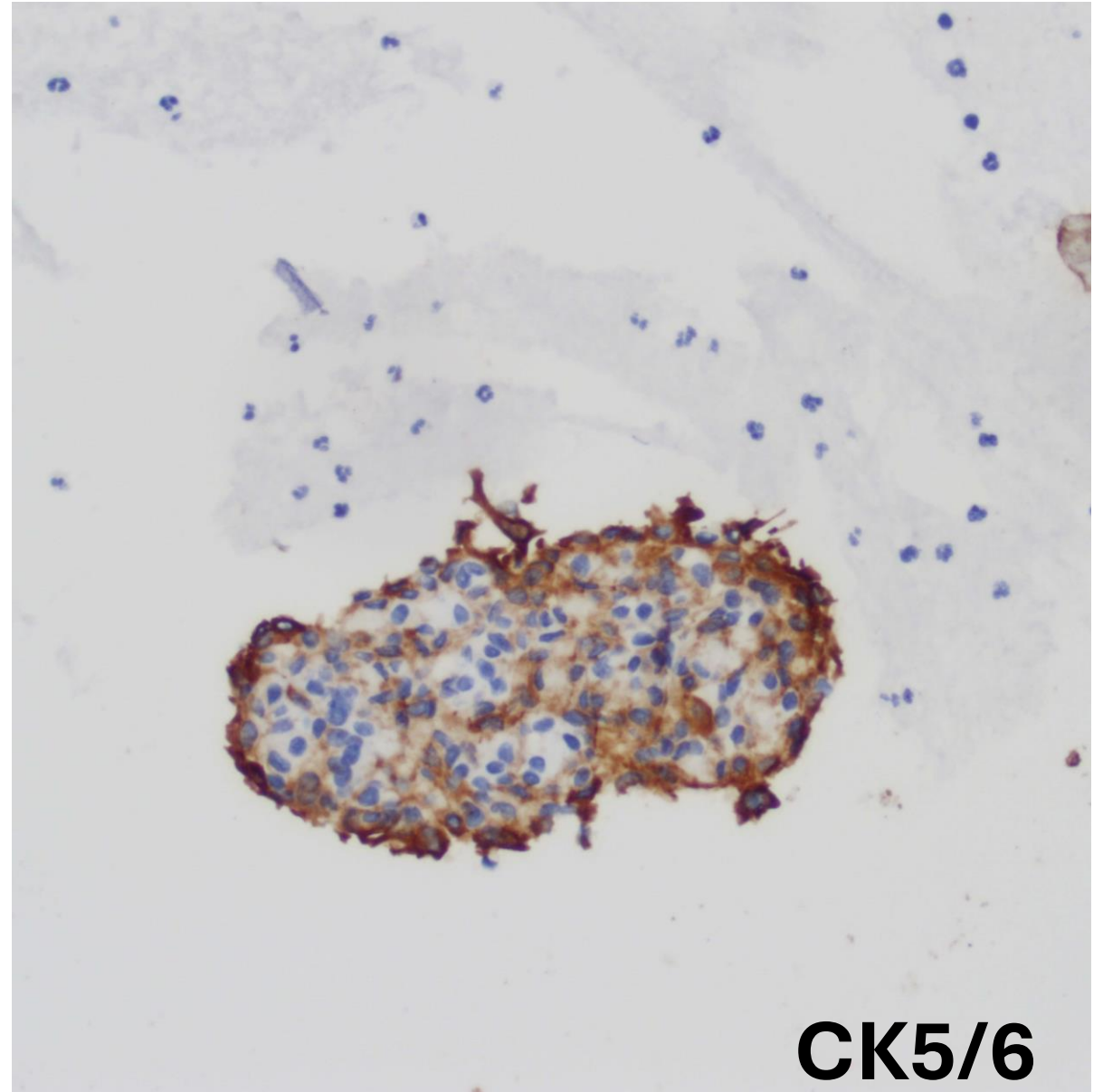
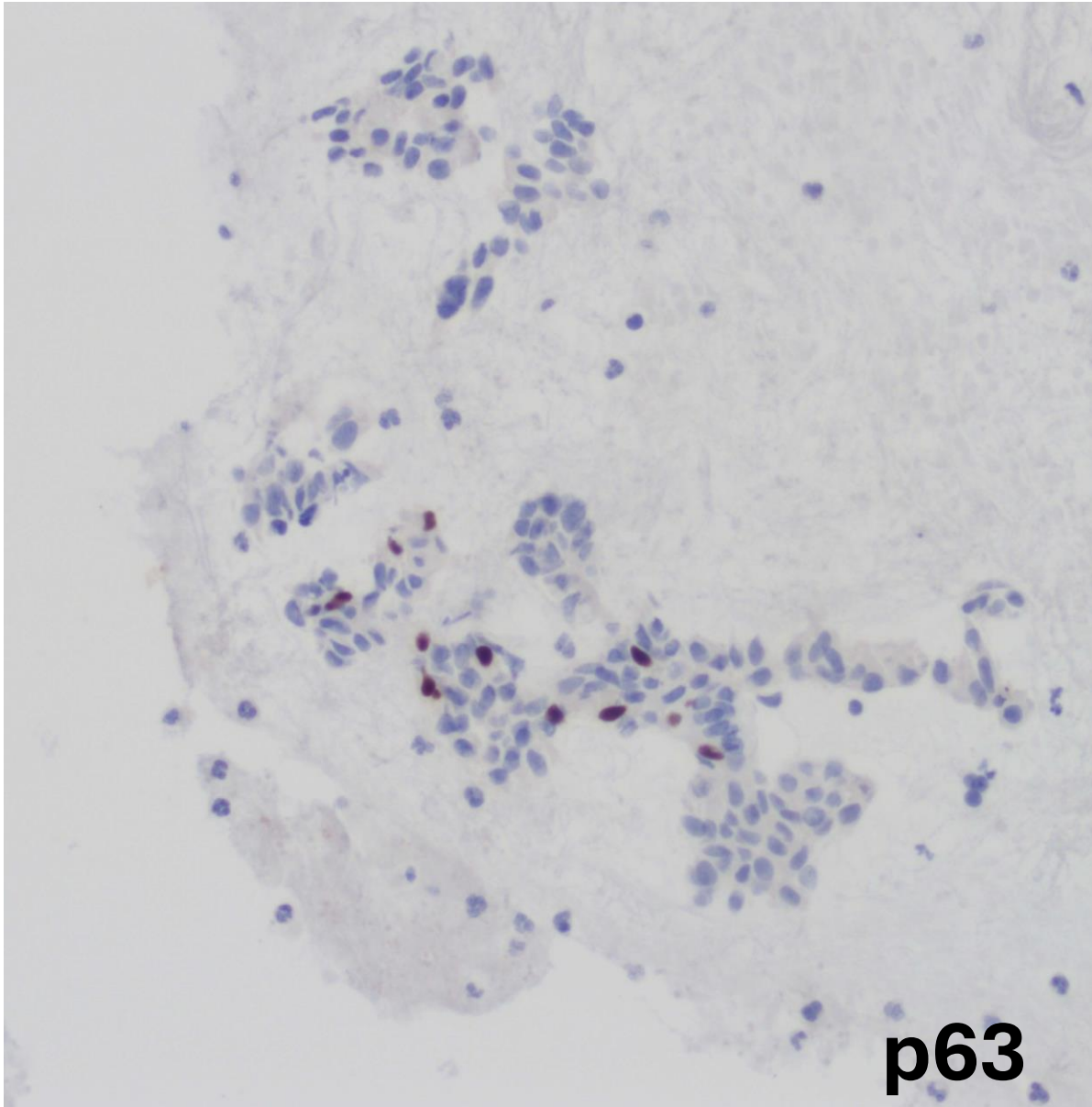












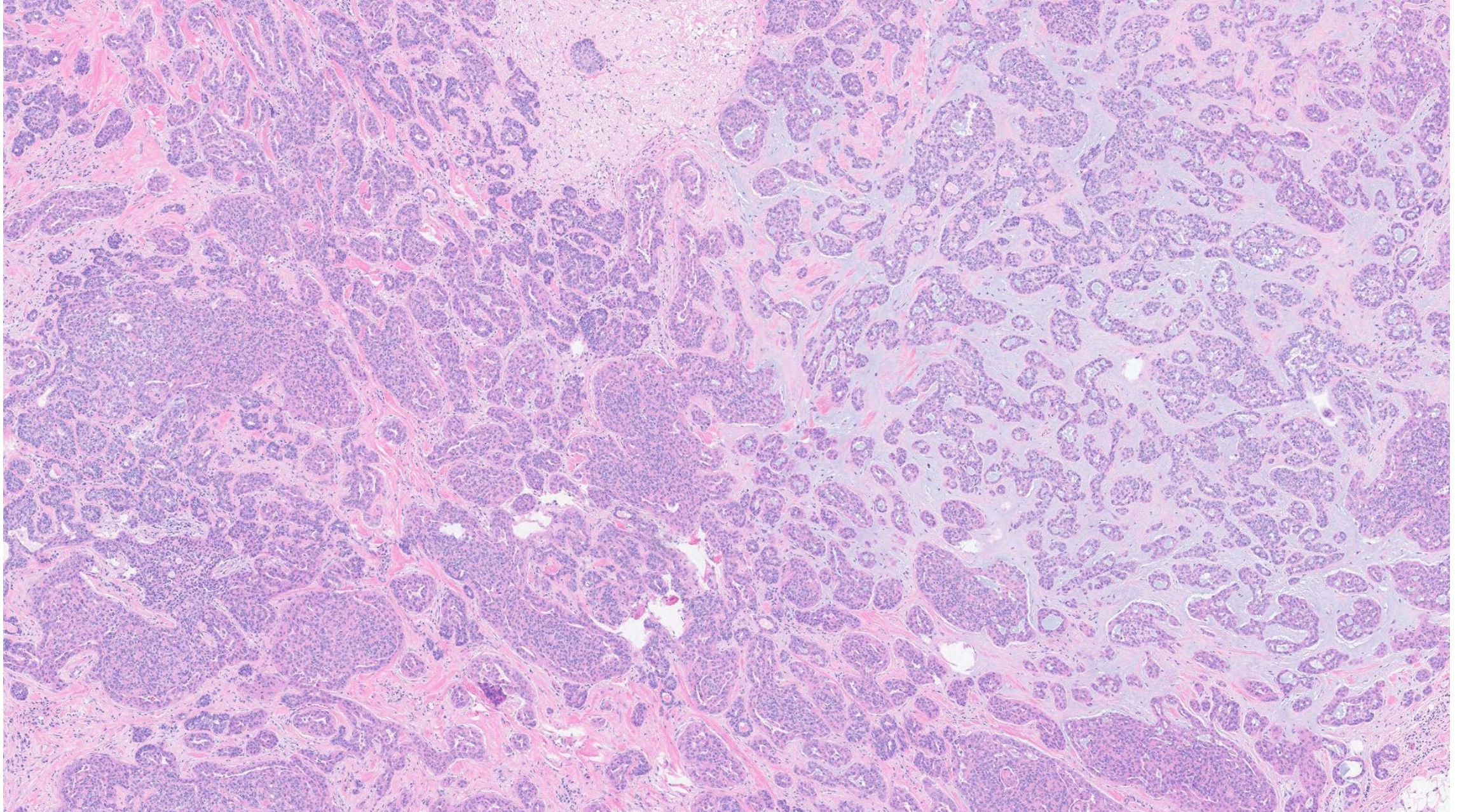


What is the diagnosis?

- Outside Cyto diagnosis: Malignant, metastatic squamous cell carcinoma
- Patient came to YNHH for radiation therapy
- Our revised Cyto diagnosis: Cellular neoplasm with atypia (SUMP)



## Follow-up resection





# Adenoid cystic carcinoma

# Adenoid Cystic Carcinoma

- Accounts for <10% of salivary gland neoplasms
- Presents in middle age, peak = 5<sup>th</sup> – 6<sup>th</sup> decades
- Prognosis - unfavorable



# Adenoid Cystic Carcinoma

- Monotonous cells characterized by high nuclear to cytoplasm ratio and round, hyperchromatic nuclei, which surround spherical hyaline matrix material
- Cells organized in sheets, clusters, or tubules, sometimes accompanied by background naked nuclei
- Hyaline globules:
  - Variable in size, usually larger than that seen in PA
  - Dense, homogeneous, round or tubular with sharp outlines
  - Magenta on Diff-Quik and green-gray on Pap stain

# Differential Diagnosis

- Pleomorphic adenoma
- Basal cell adenoma
- Myoepithelioma
- Lymphadenoma
- Cystadenoma



# Adenoid Cystic Carcinoma

- Usually positive for CD117
- Characterized by MYB gene fusion by IHC, FISH or RT-PCR

# Differential Diagnosis

- Basaloid neoplasms exhibit high N/C ratios and matrix material
- Basaloid neoplasms have demonstrated limited interobserver agreement and pose diagnostic challenges
- Basal cell adenoma:
  - Characterized by large fragments of cohesive basaloid cells surrounded by a rim of basement-like matrix
  - Peripheral palisading of cells surrounded by basement membrane material
- PA may resemble ADCa due to the presence of plasmacytoid or basaloid myoepithelial cells
- Fibrillary or chondromyxoid matrix in in PA, hyaline matrix in ADCa

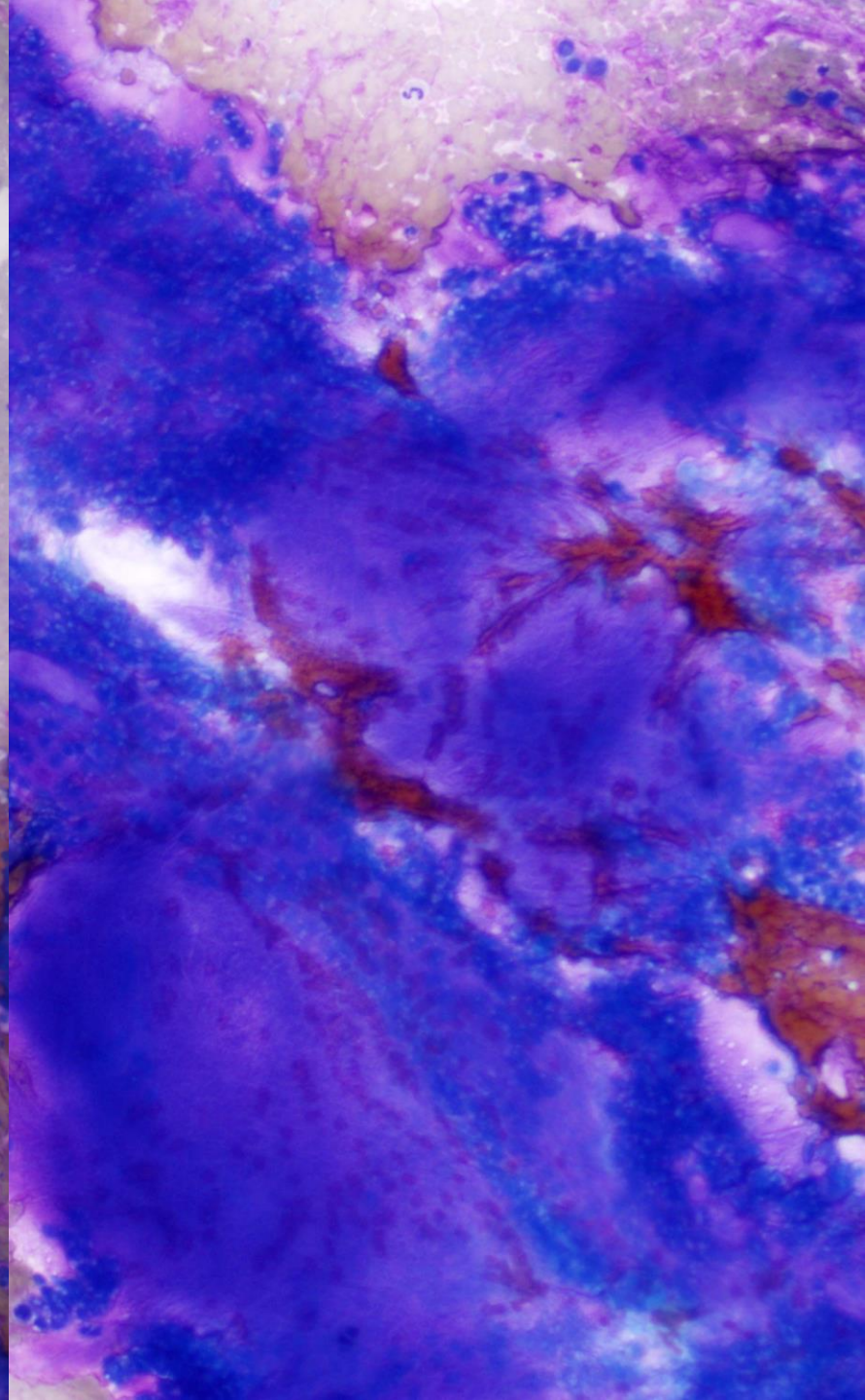
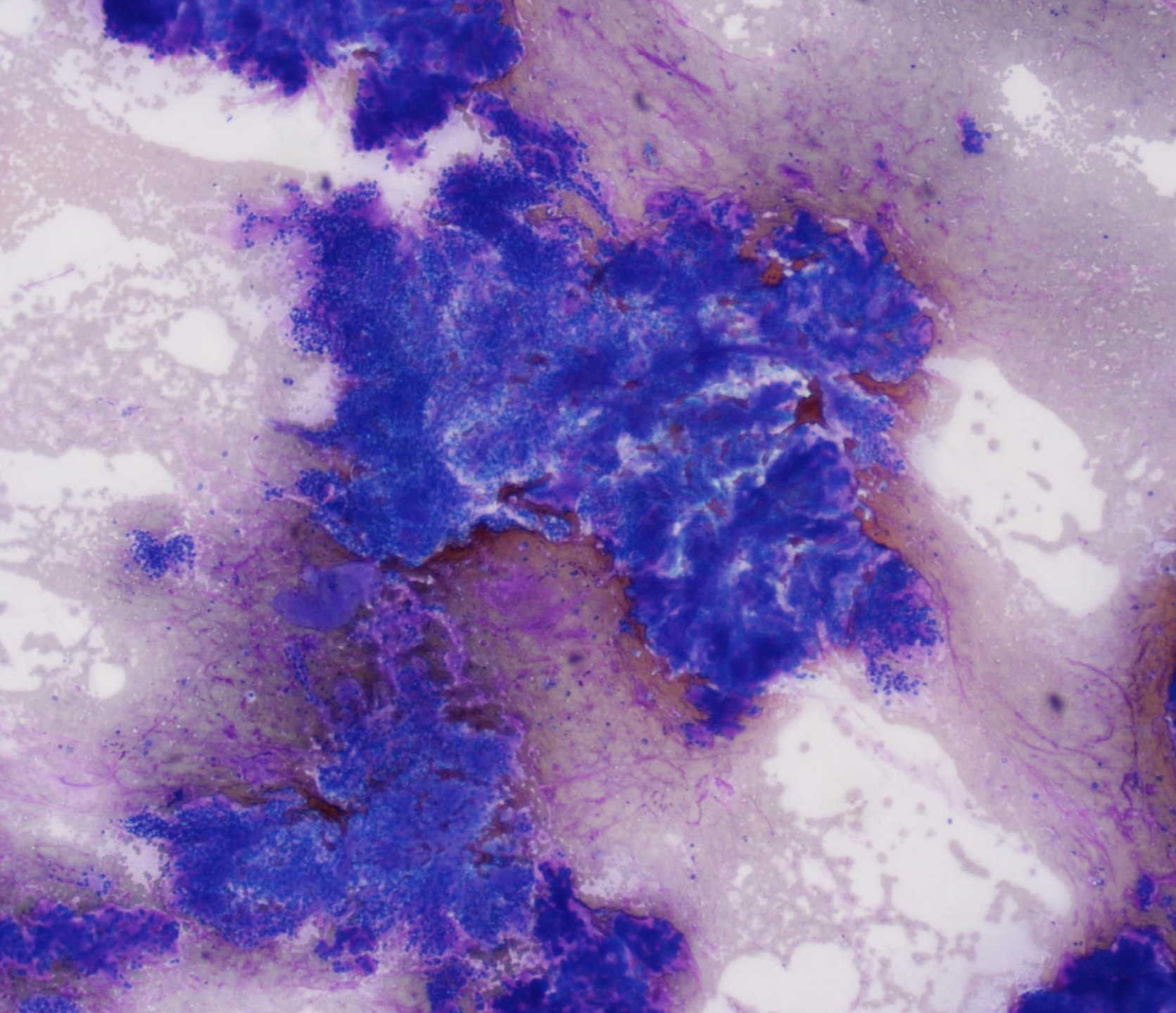


# Case 3

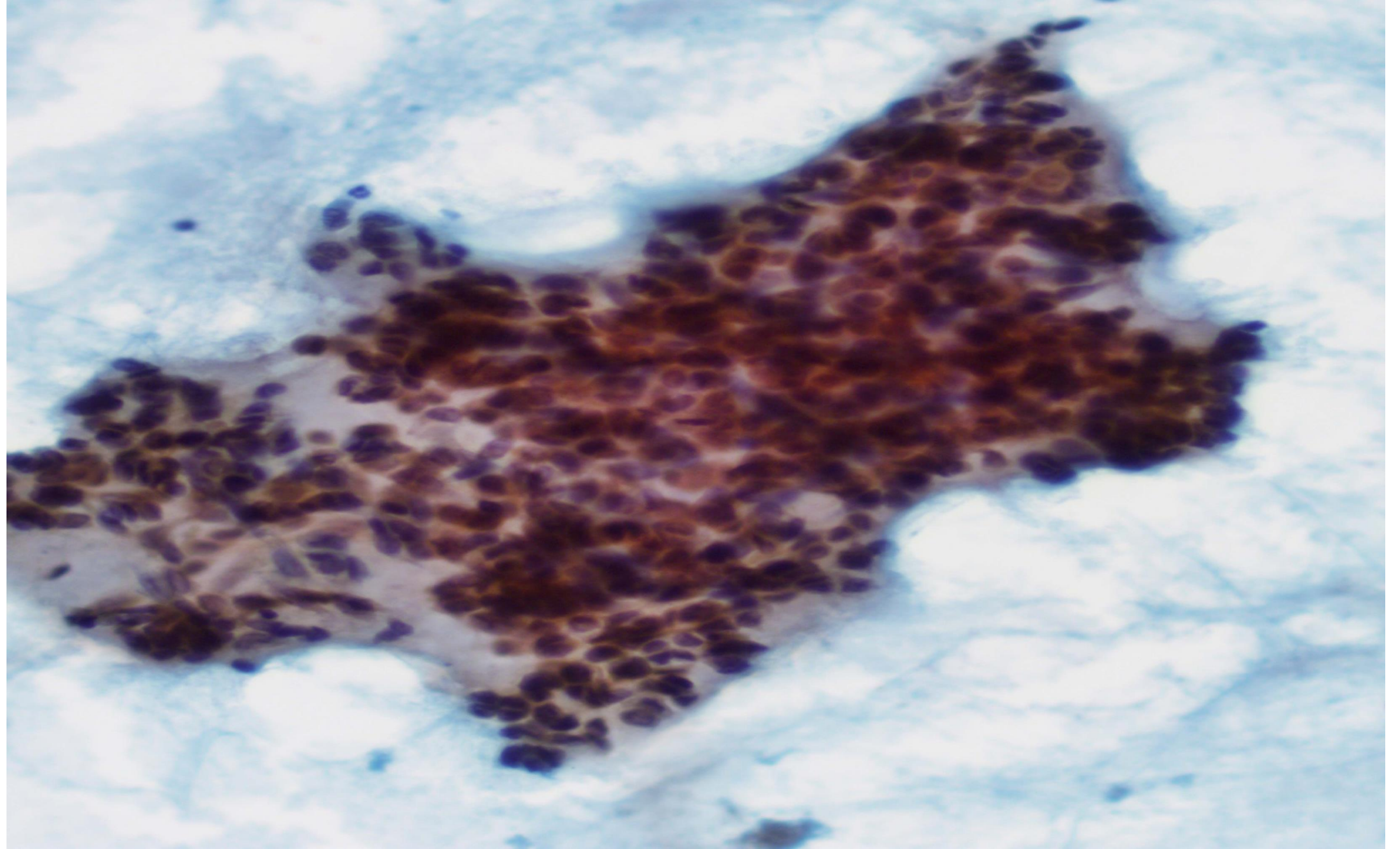
67-year-old female with 2.5 cm left parotid mass

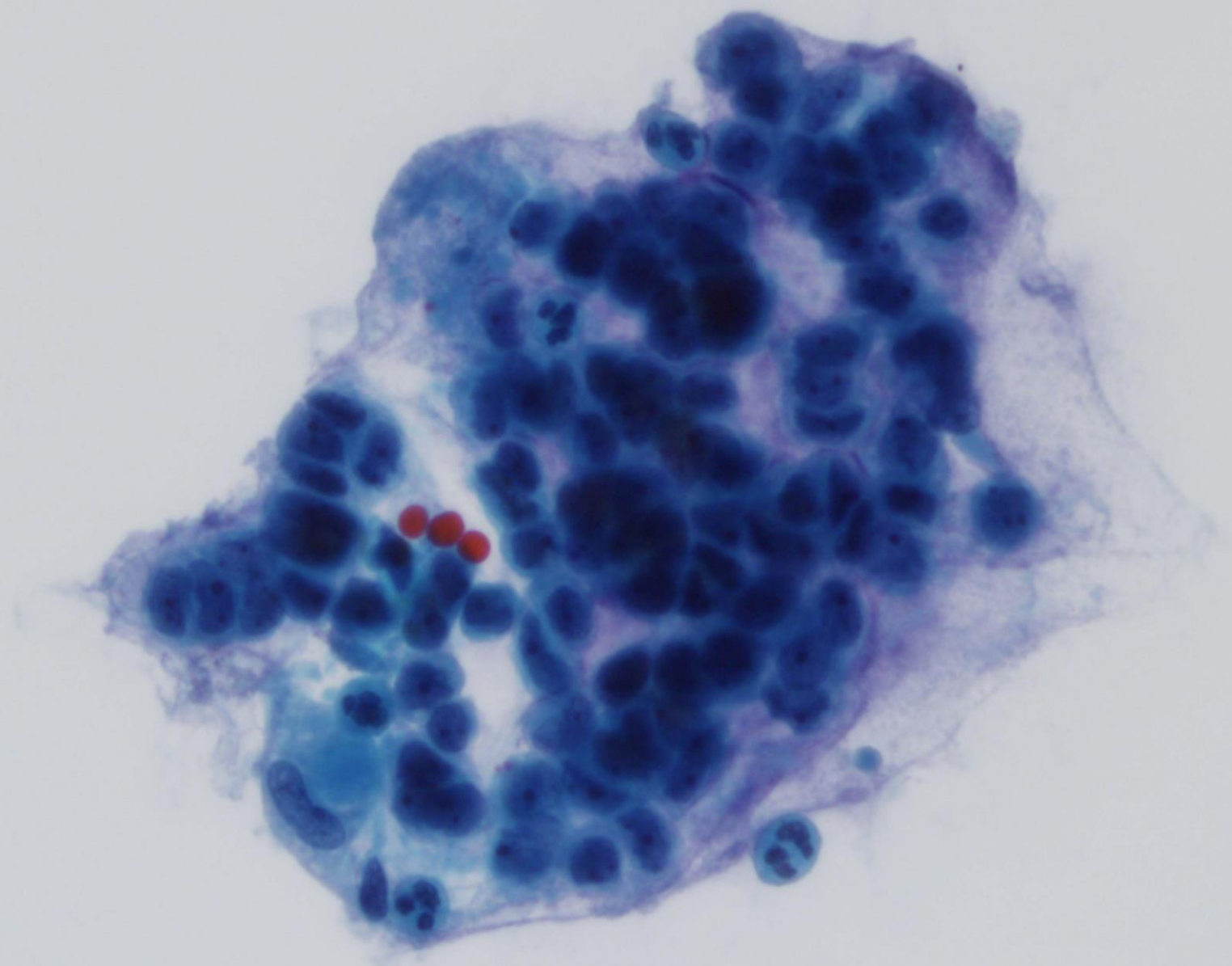
History of melanoma of the left cheek



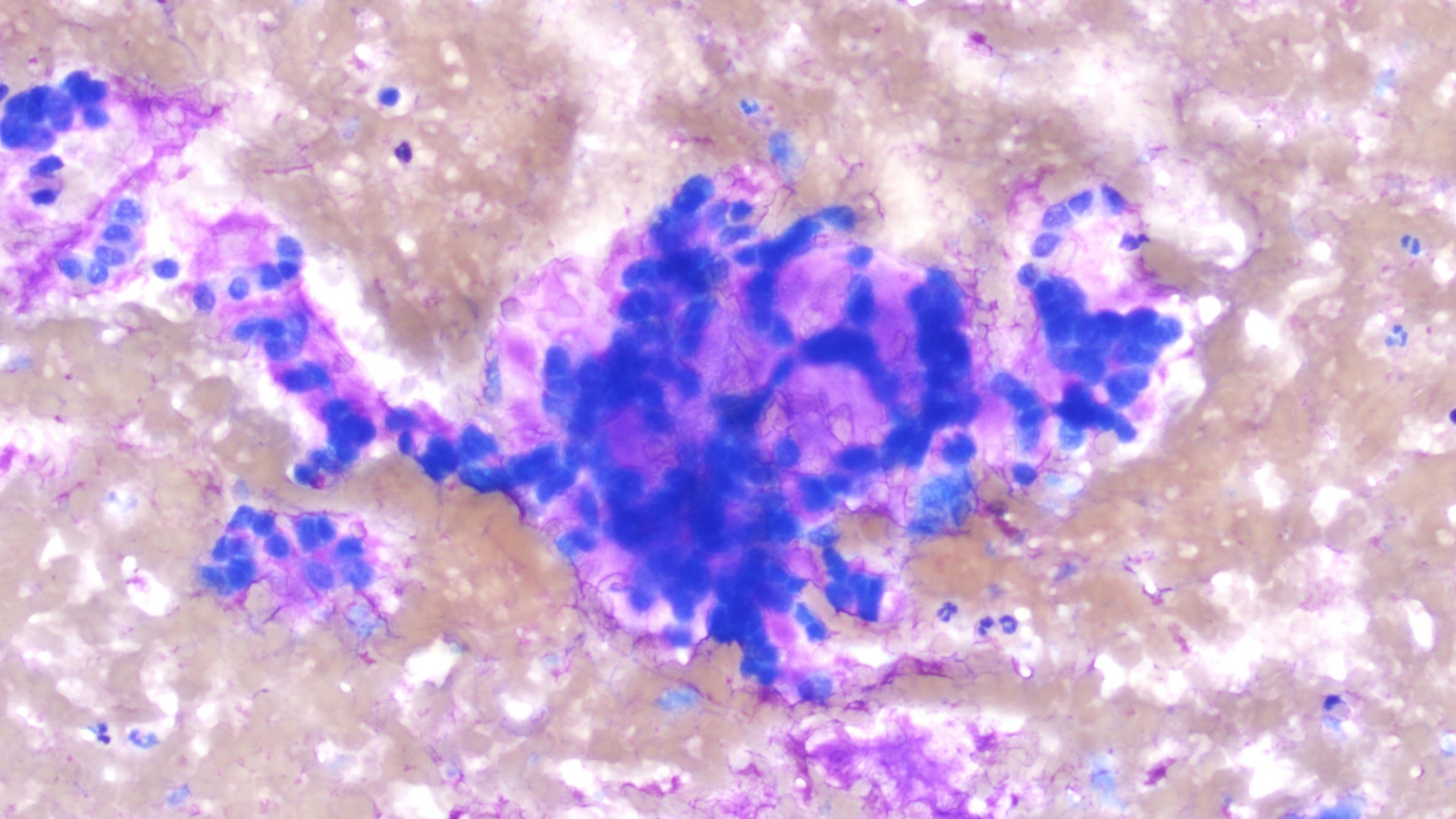










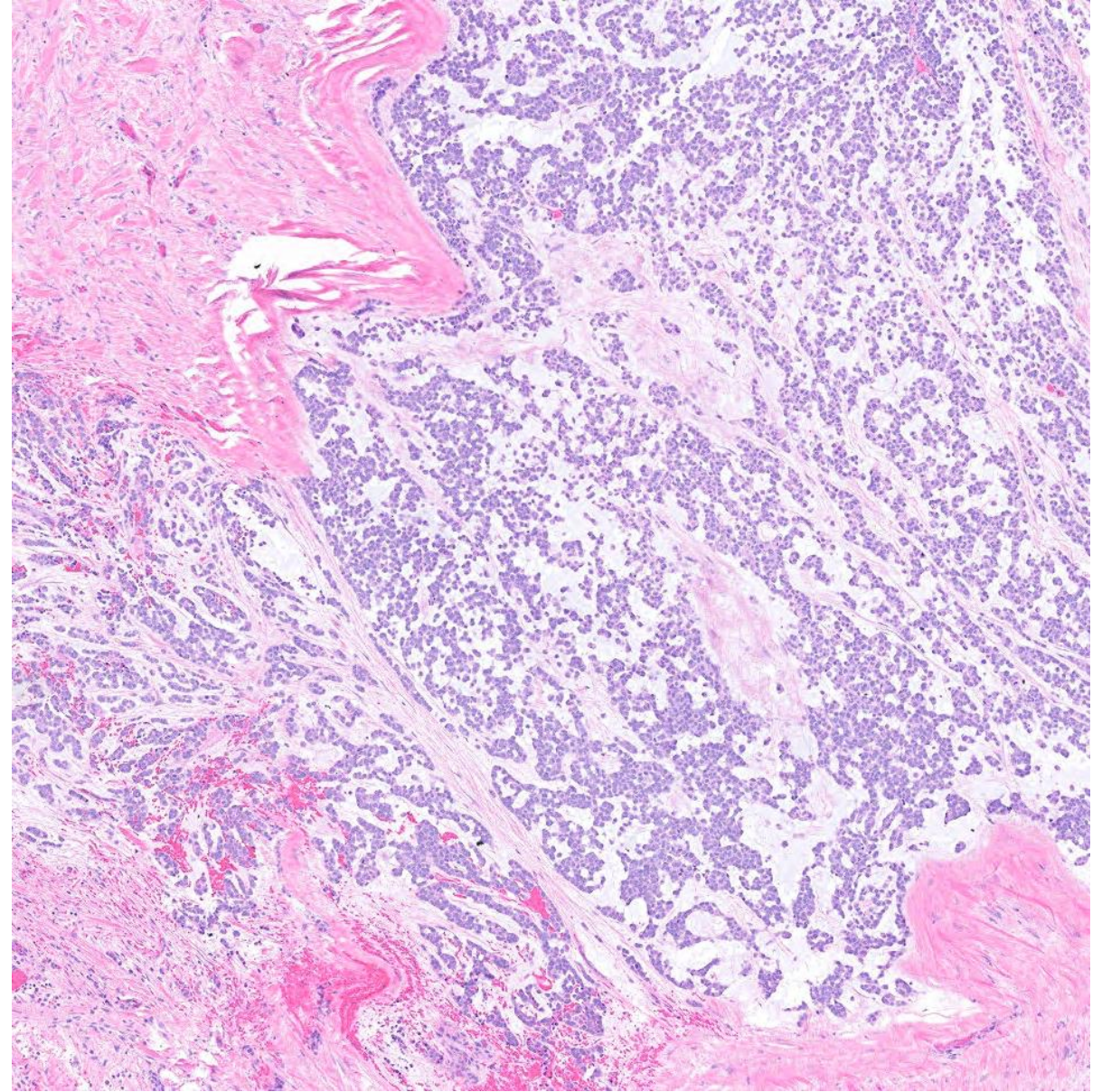
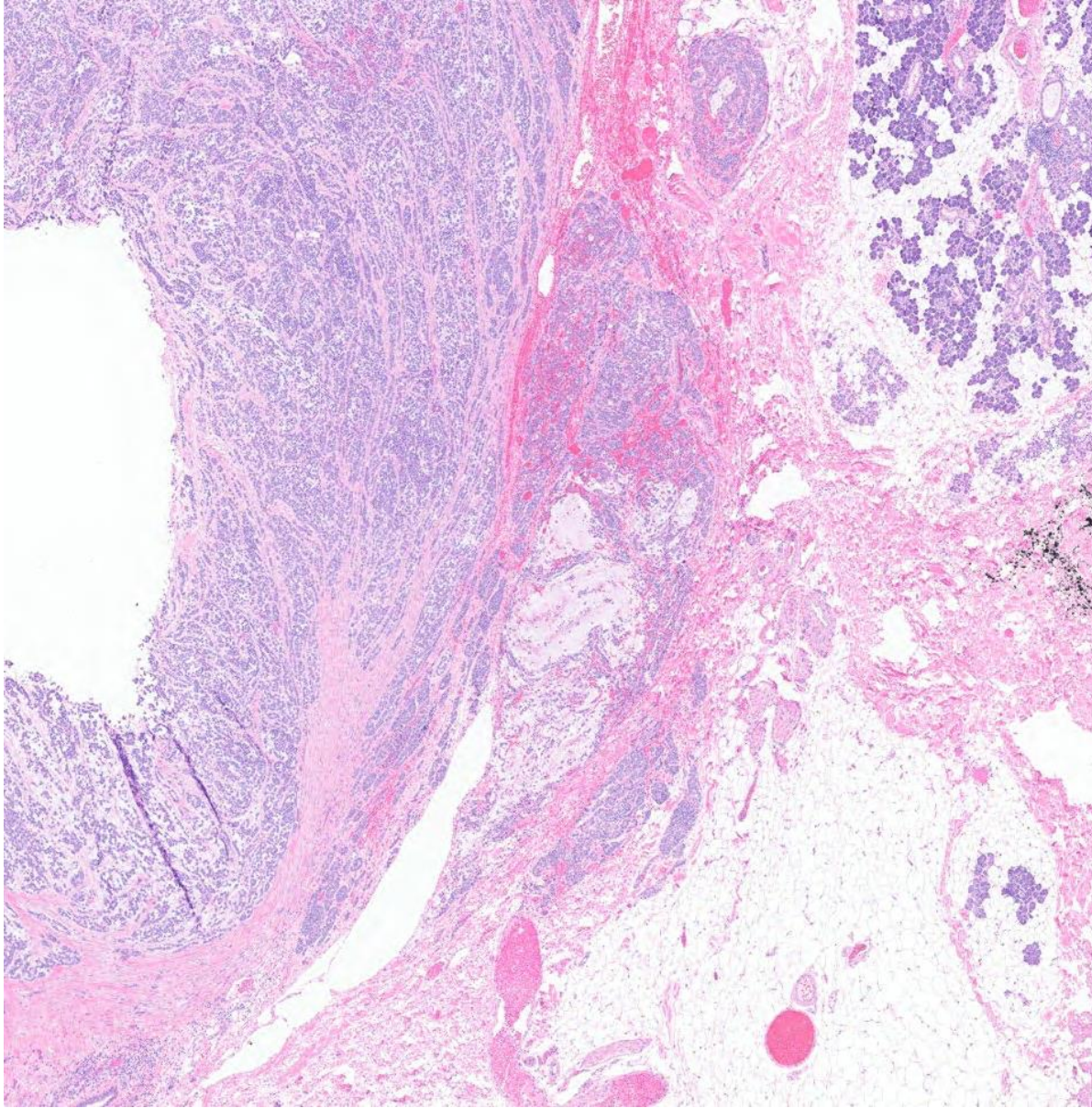




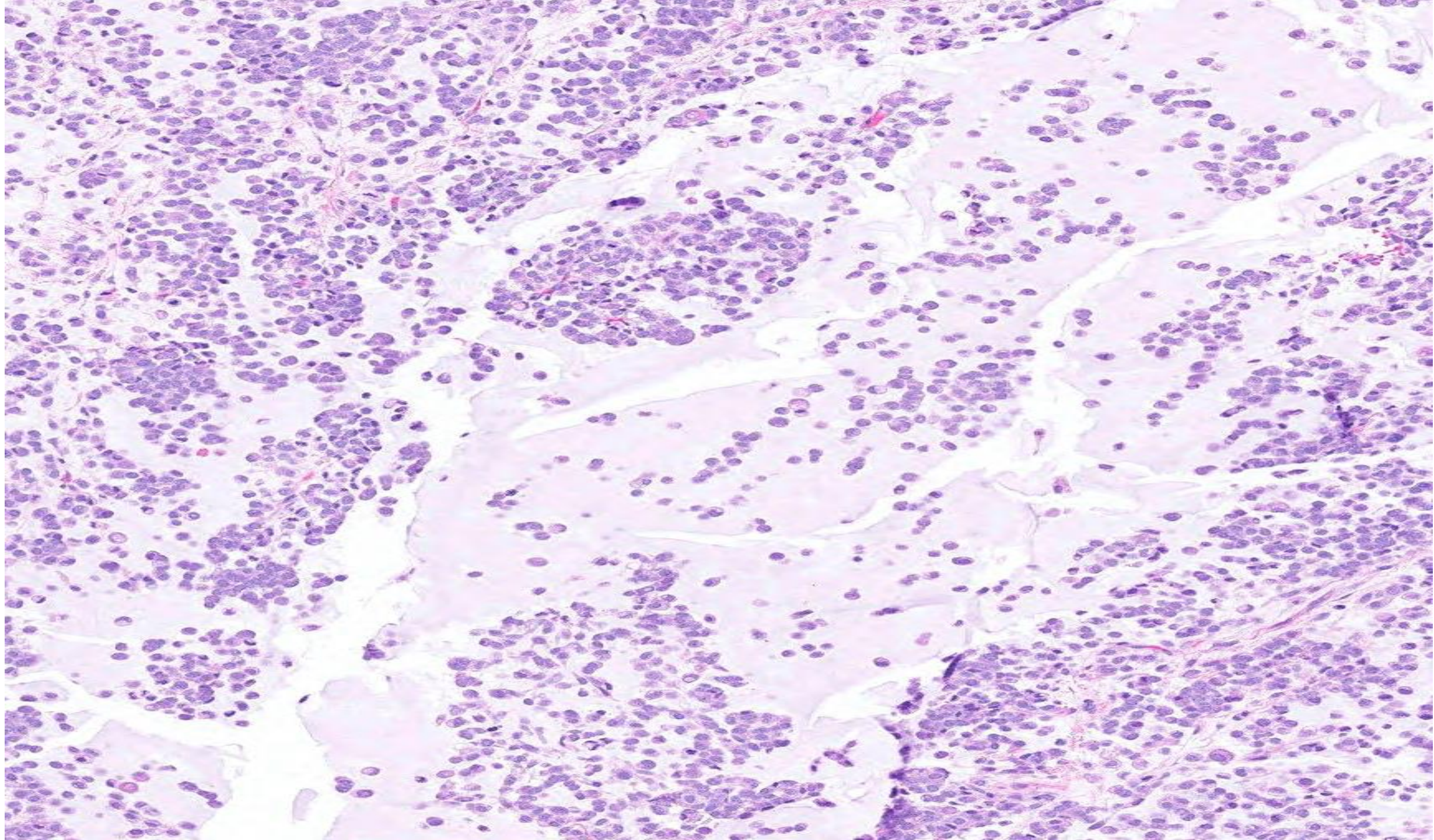
What is the diagnosis?



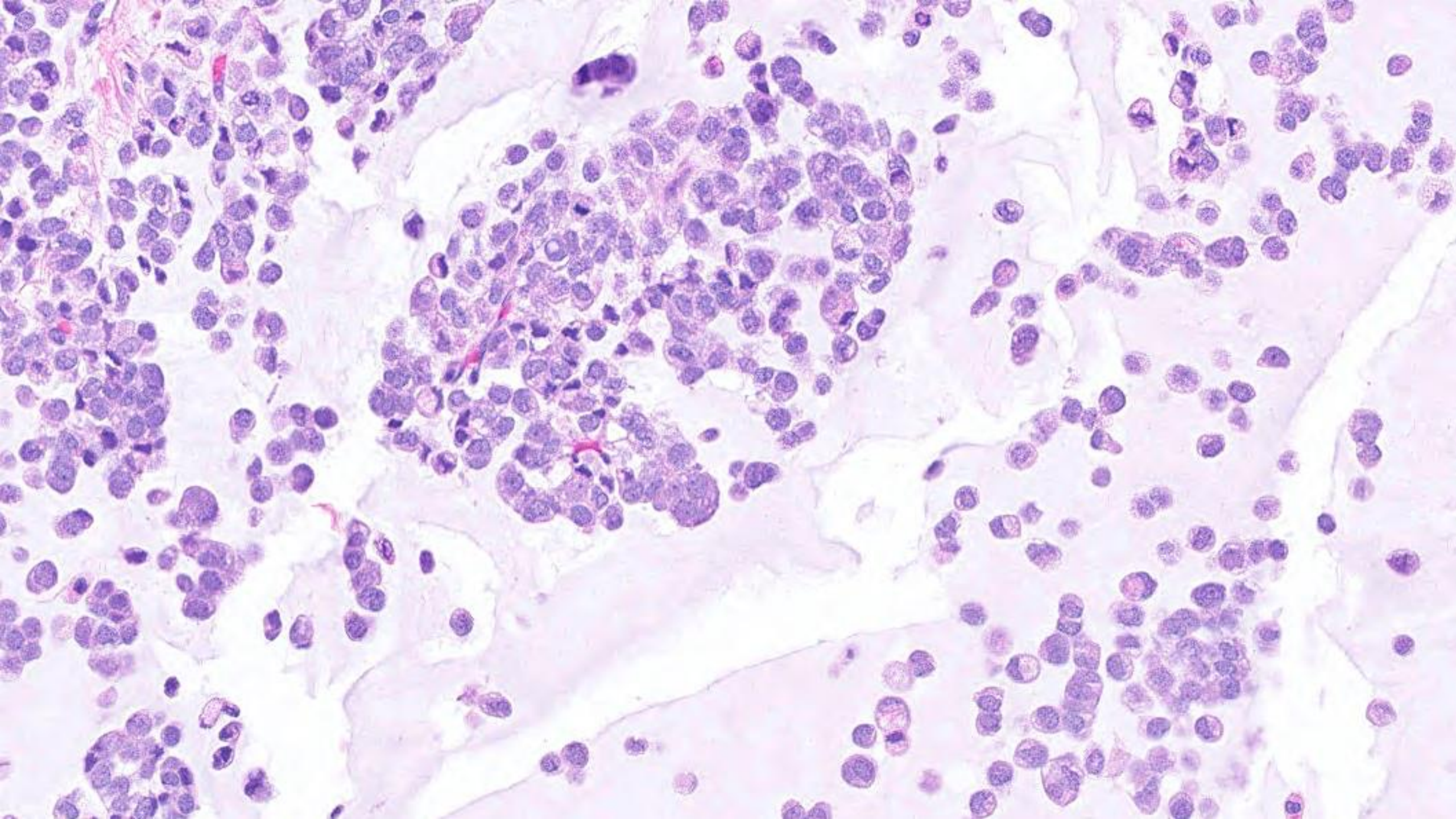
## Follow-up resection











# IHC

- Positive for S100, SOX10, PLAG1, p63, calponin
- Negative for HMB-45, Melan A

# Myoepithelial carcinoma

- Composed entirely of myoepithelial cells showing invasive growth
- May arise de novo or ex pleomorphic adenoma
- Accounts for 5% of all salivary gland neoplasms
- Frequency may be underestimated
- Median age of presentation, 6<sup>th</sup> decade
- Clinically aggressive, high propensity for distant metastases



# Myoepithelial carcinoma

- Hypercellular specimen composed entirely of myoepithelial cells
- Myoepithelial cells show a mixture of plasmacytoid, epithelioid or spindle morphology arranged as cords, small groups or single cells
- Metachromatic stroma, mitotic figures and nuclear pleomorphism may be present
- PLAG 1 fusion is the most common molecular event
- Clear cell myoepithelial carcinoma may show EWSR1 fusion

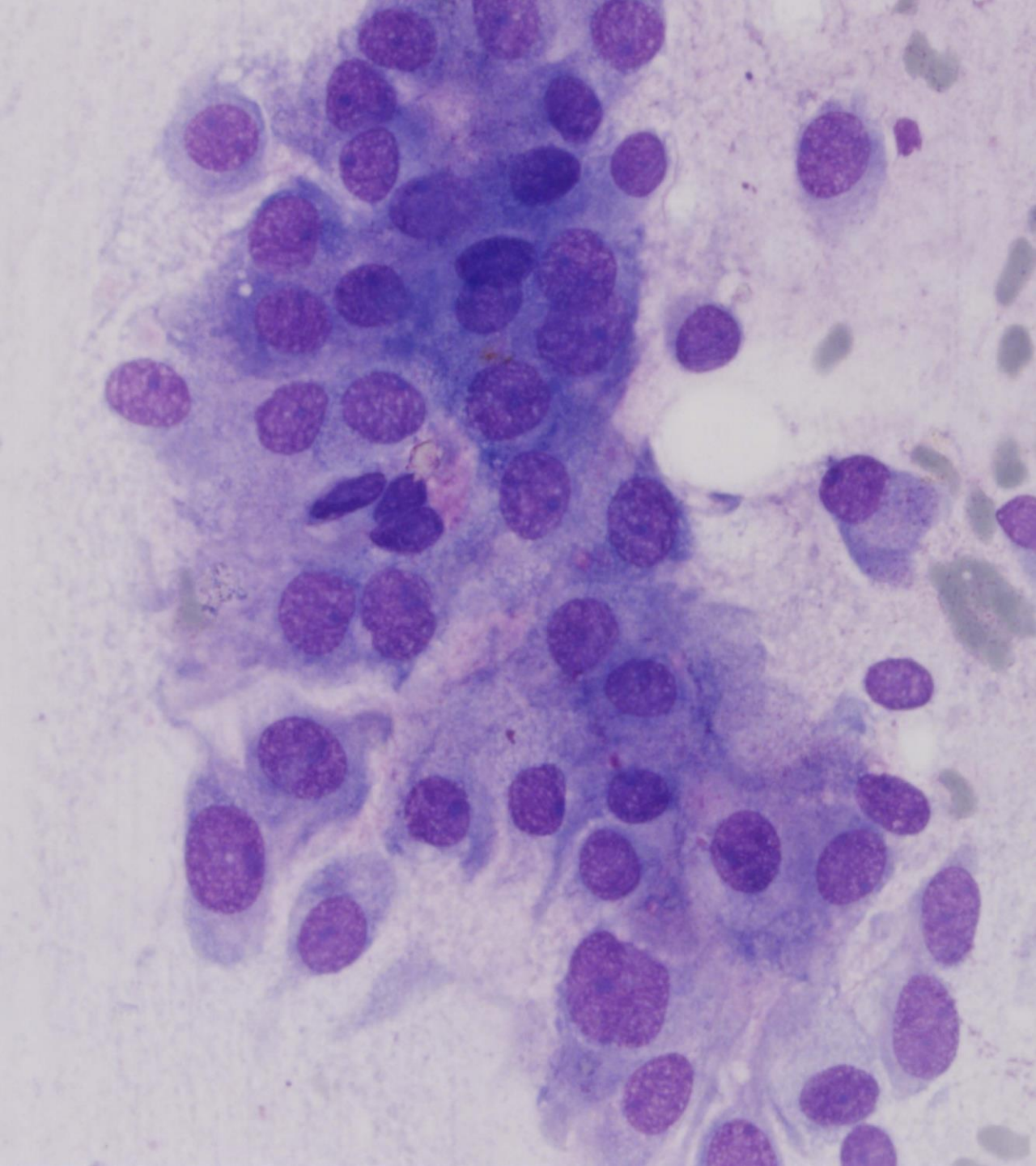
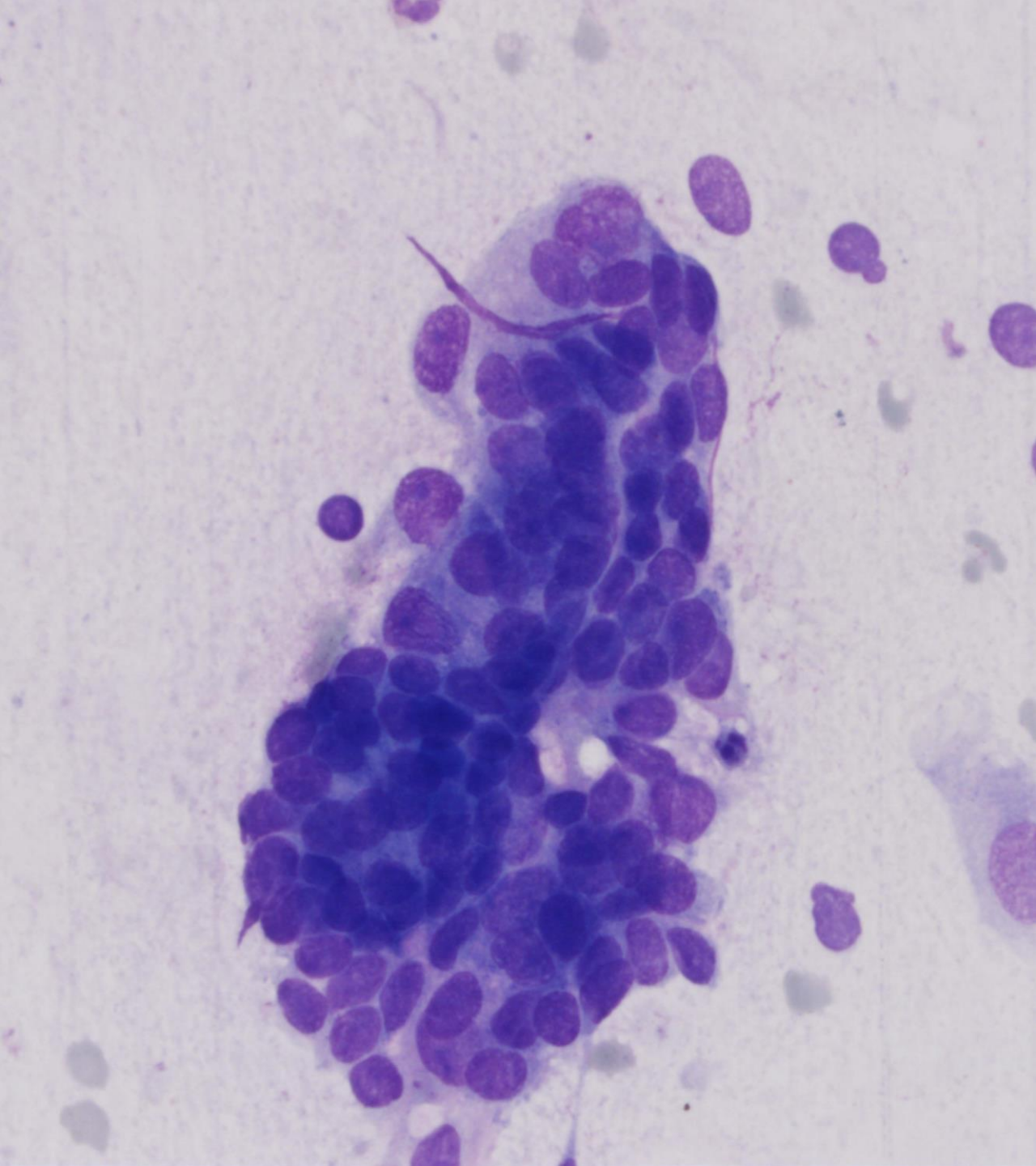
# Differential Diagnosis

- Myoepithelioma
  - Benign counterpart
  - Encapsulated without evidence of invasion
- Myoepithelial-rich pleomorphic adenoma
  - Lacks the multinodular/lobulated invasive growth pattern
- Polymorphous adenocarcinoma
  - Shows architectural diversity
  - Shows mutations/fusions involving PRKD genes

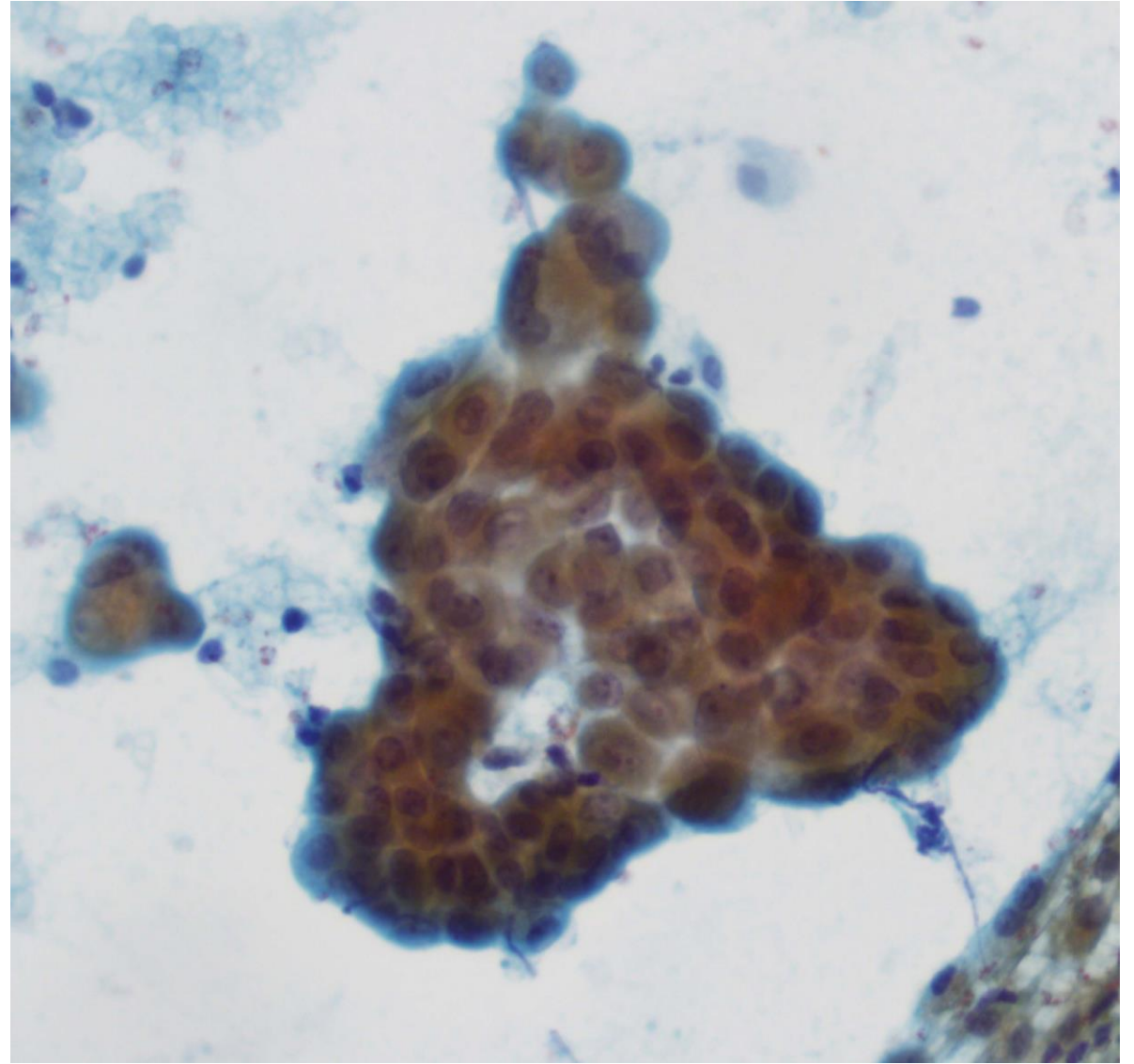
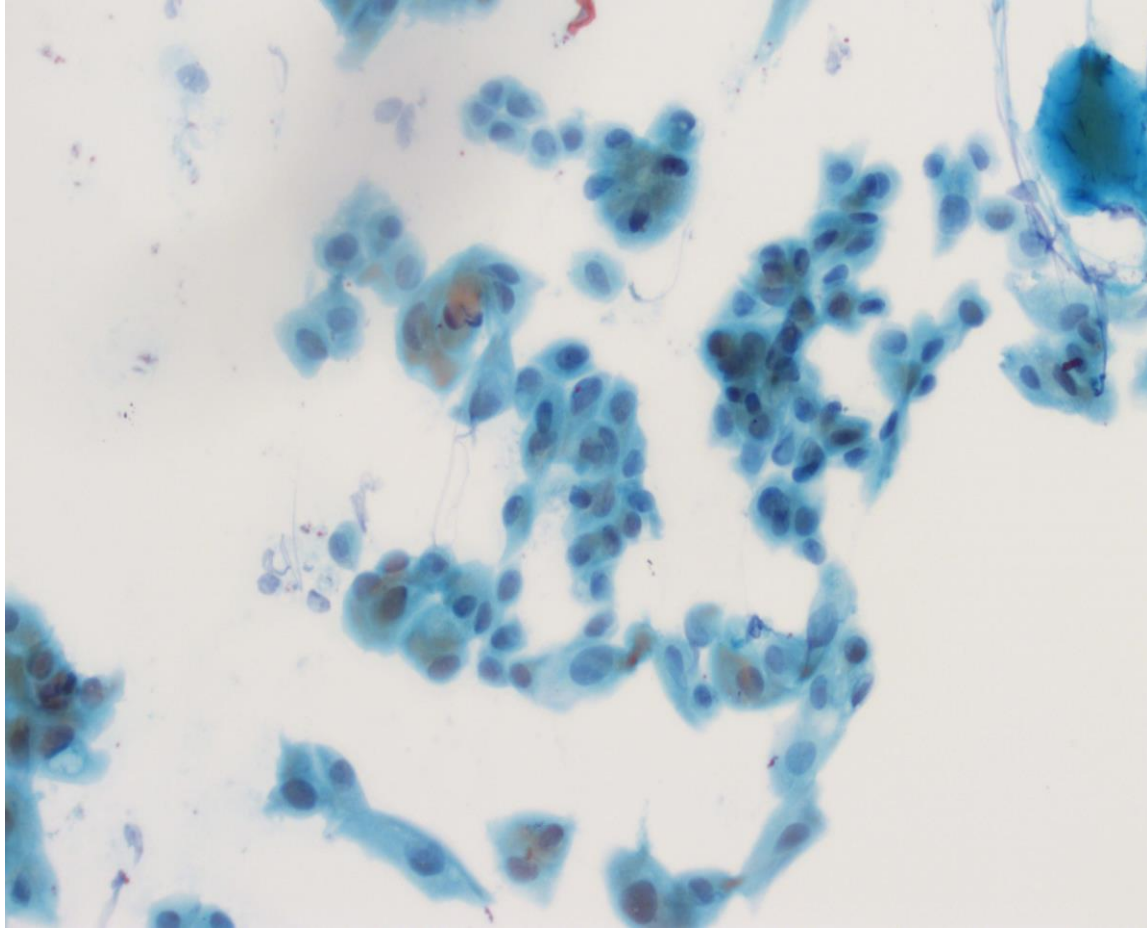


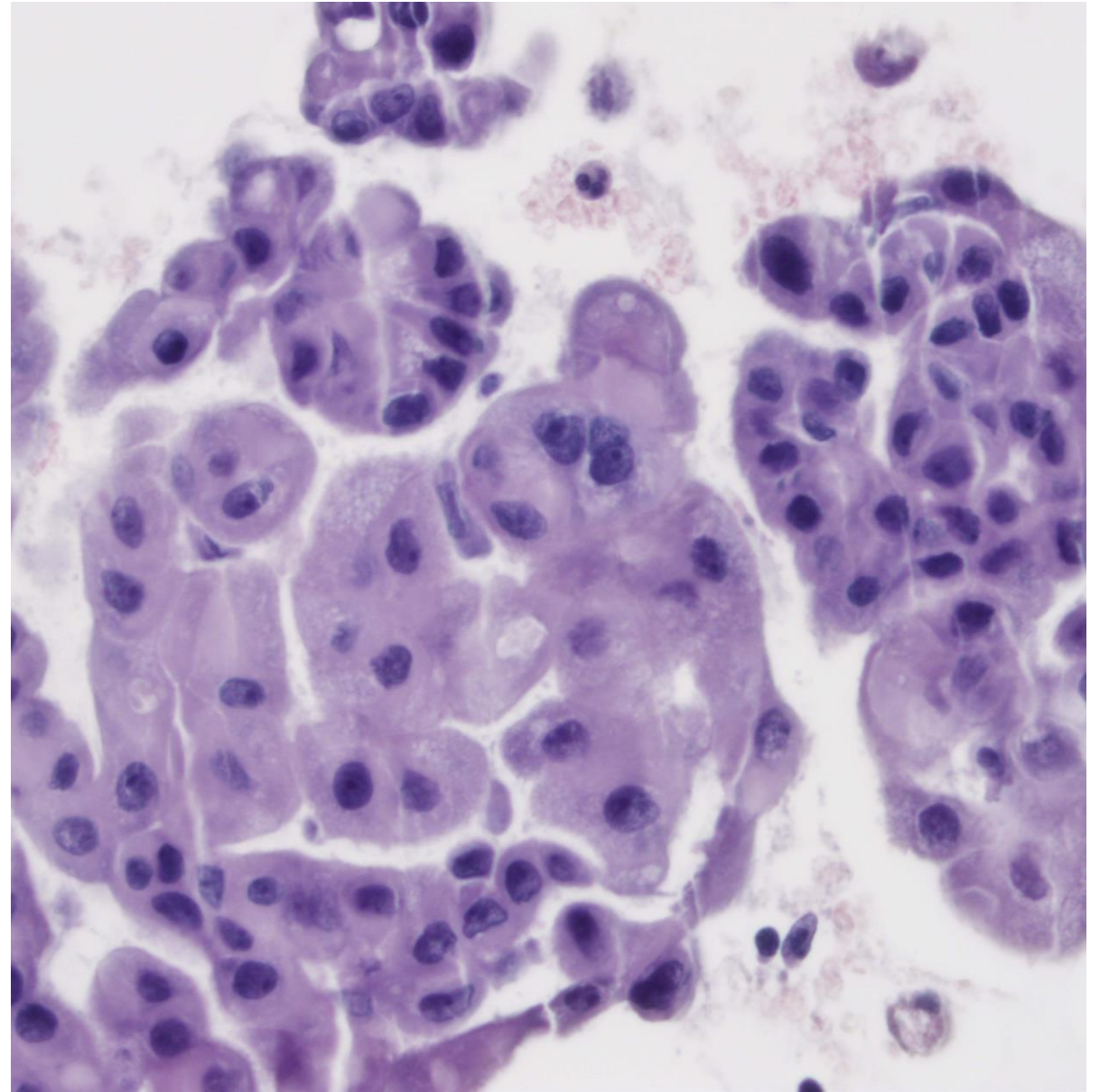
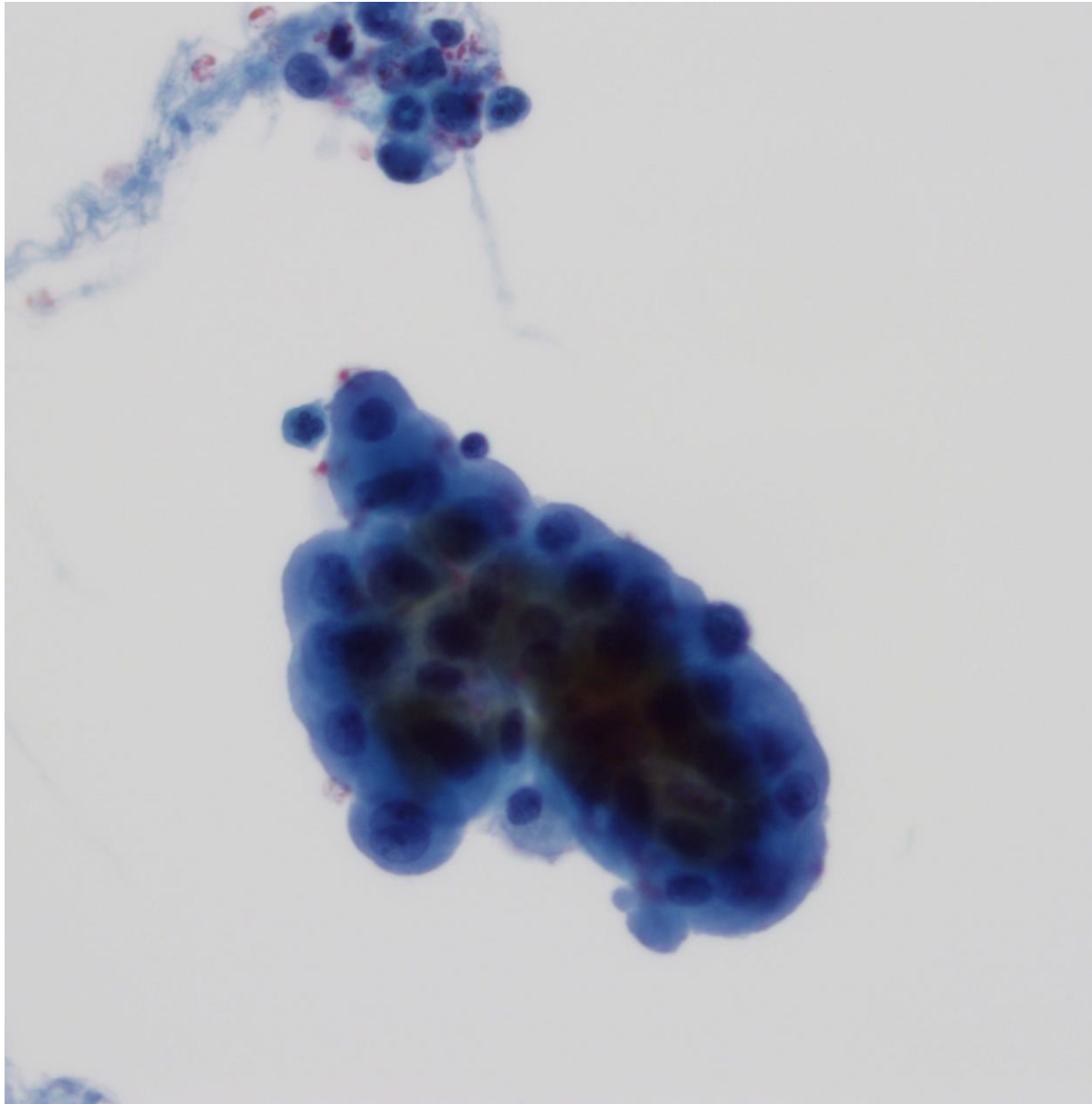
# Case 4

66-year-old female with 2.1 cm left parotid mass

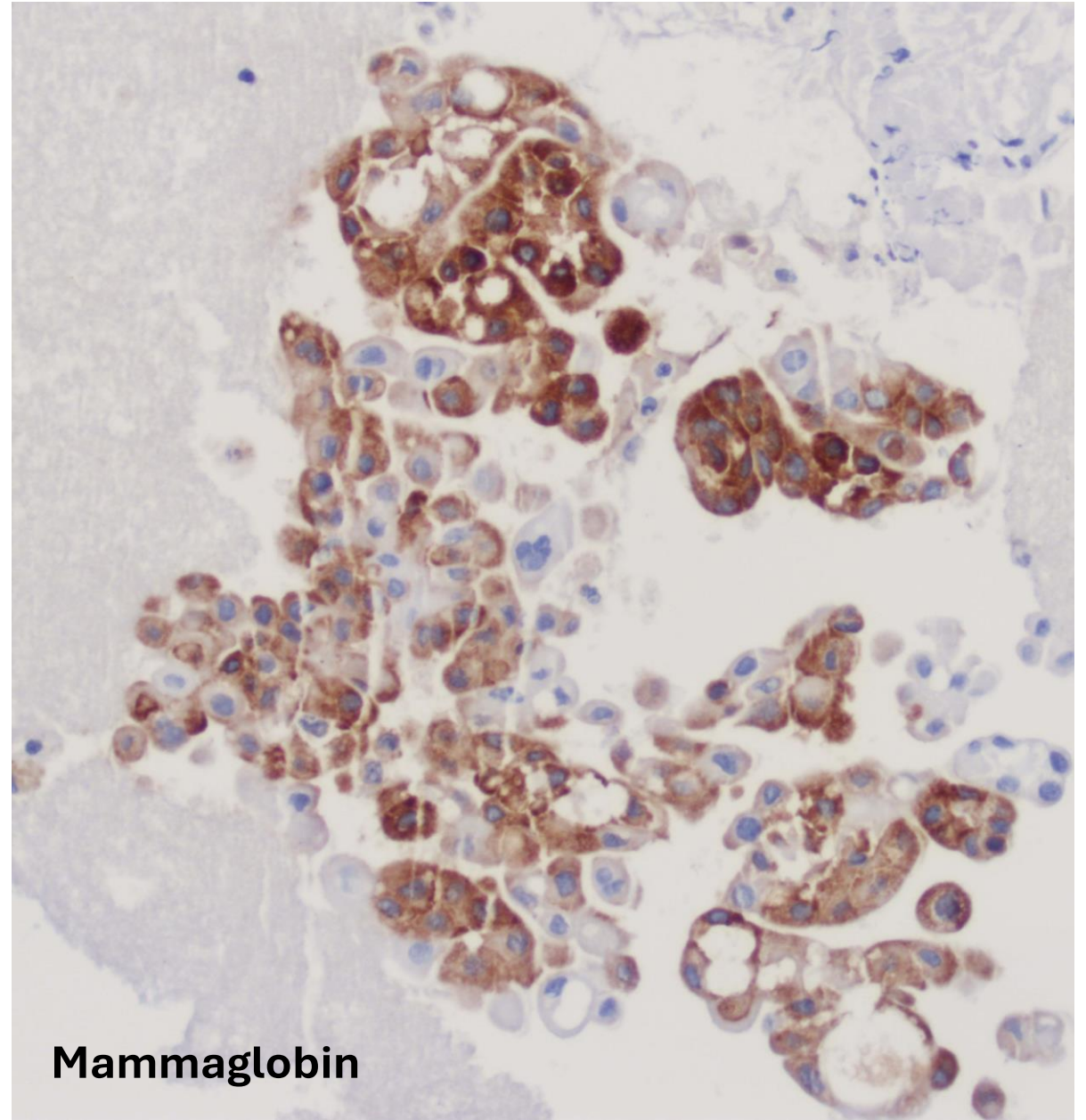
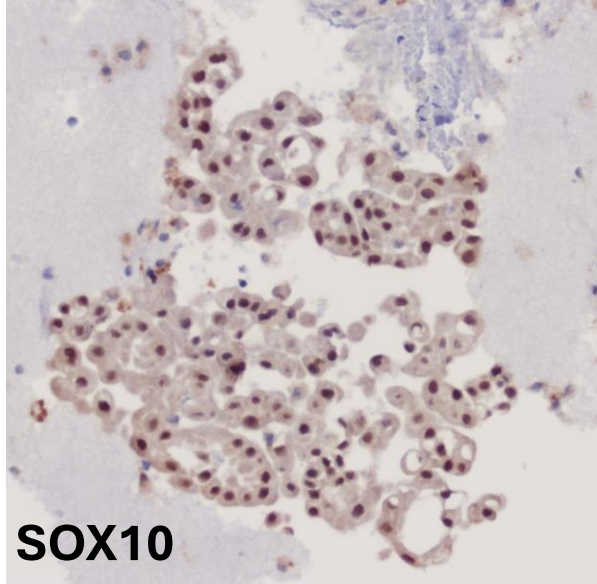
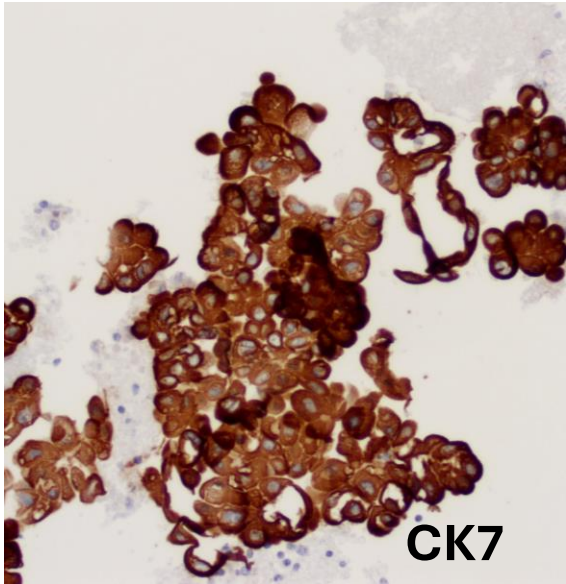
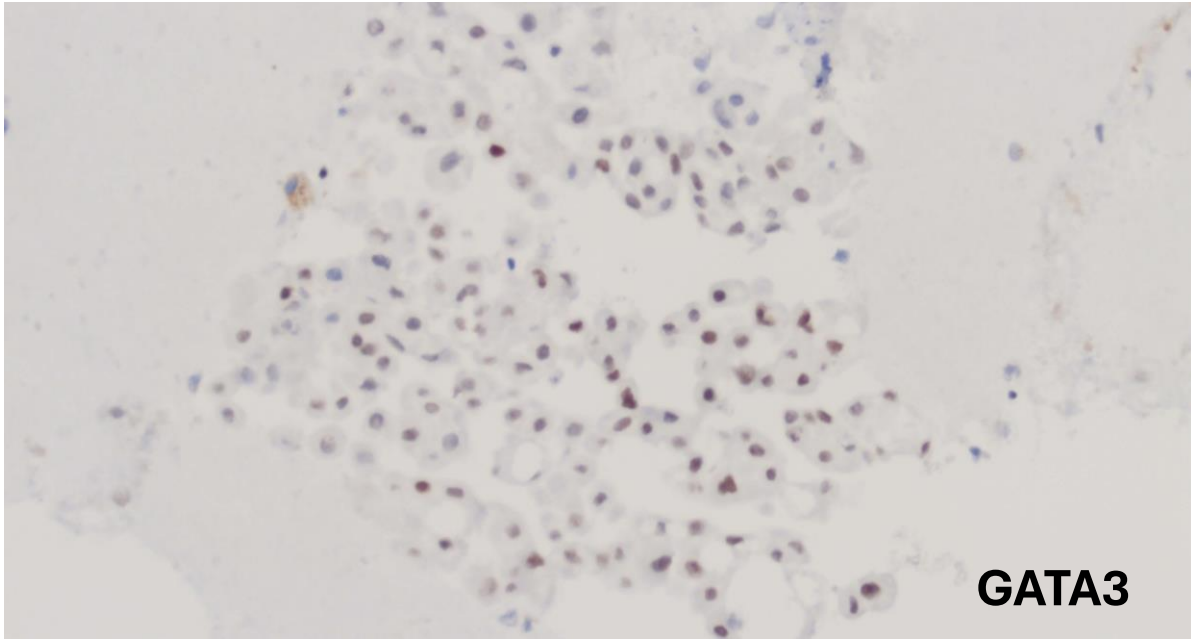








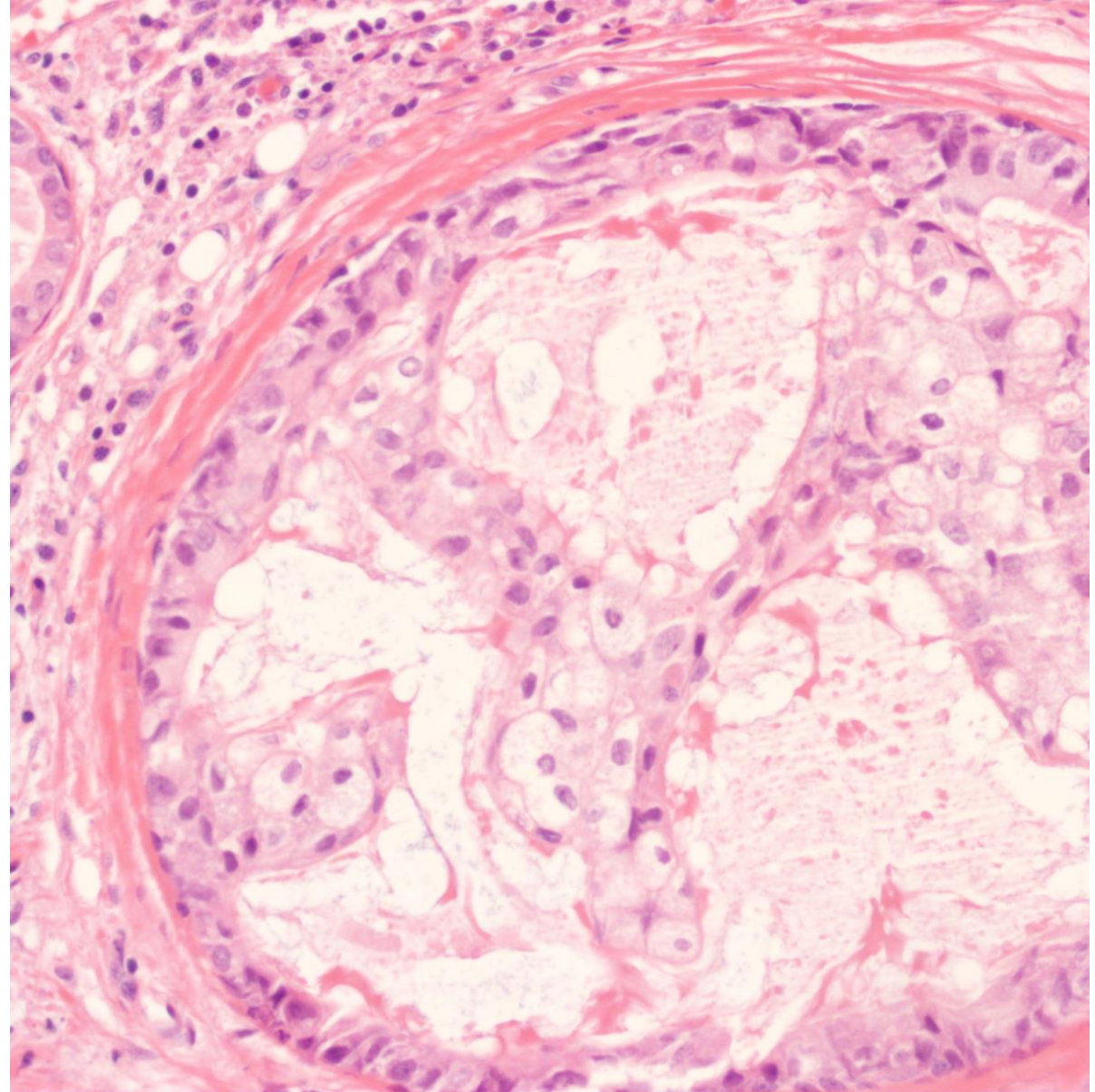
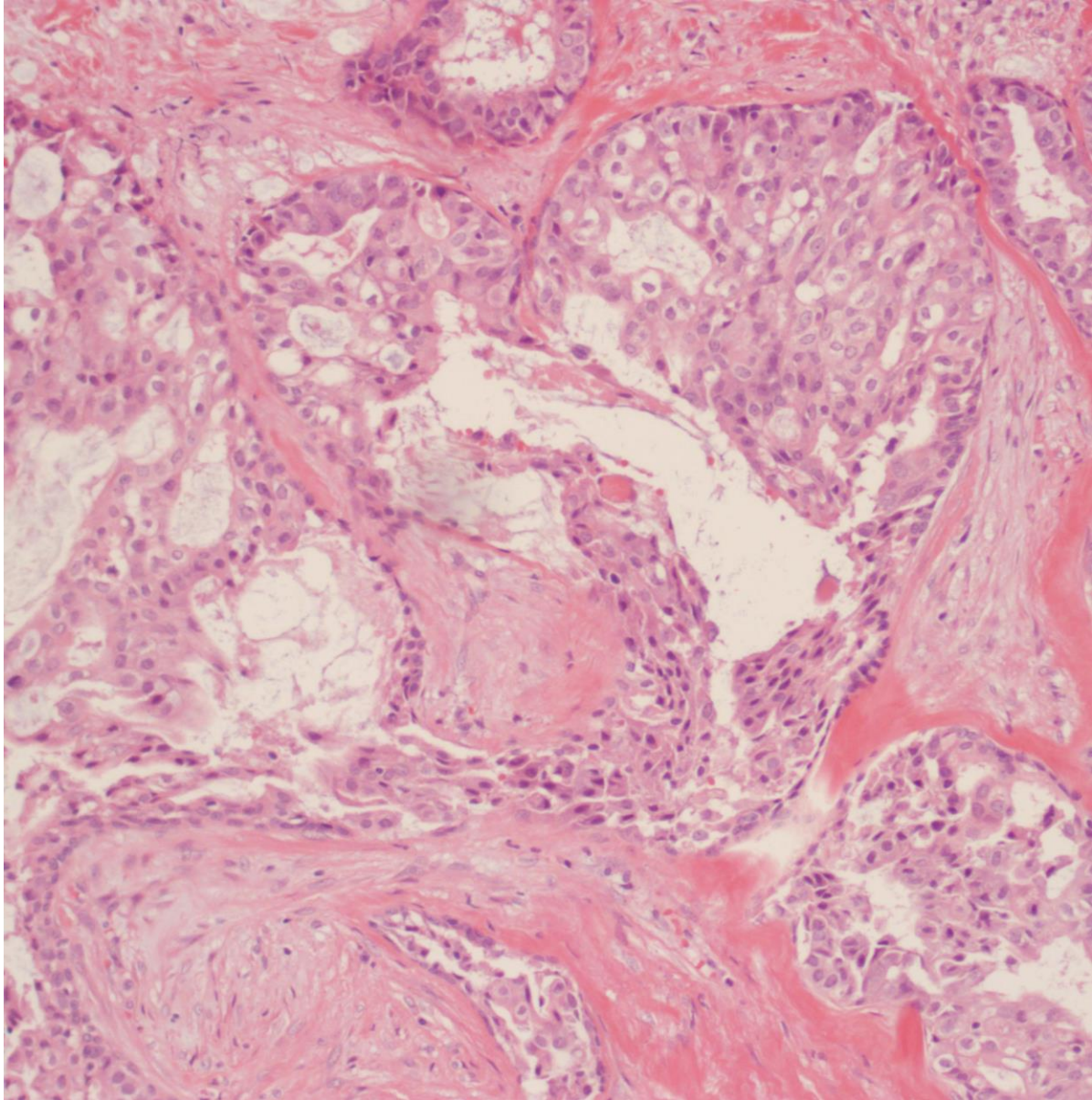




What is the diagnosis?



## Follow-up resection



# Secretory carcinoma

- Rare salivary gland neoplasm
- Resembles breast secretory carcinoma
- More common in the parotid in middle aged and older patients
- Prognosis similar to other low-grade SG tumors
- High-grade variant less frequent



# Secretory carcinoma

- Crowded cell clusters, papillary groups and isolated cells
- Large polygonal cells
- Abundant vacuolated cytoplasm
- Absence of cytoplasmic zymogen granules
- Indistinct cell borders
- Bland round nucleus with distinct nucleolus
- Usually positive for mammaglobin, GATA-3 and S-100
- ETV6-NTRK3 gene fusion is characteristic

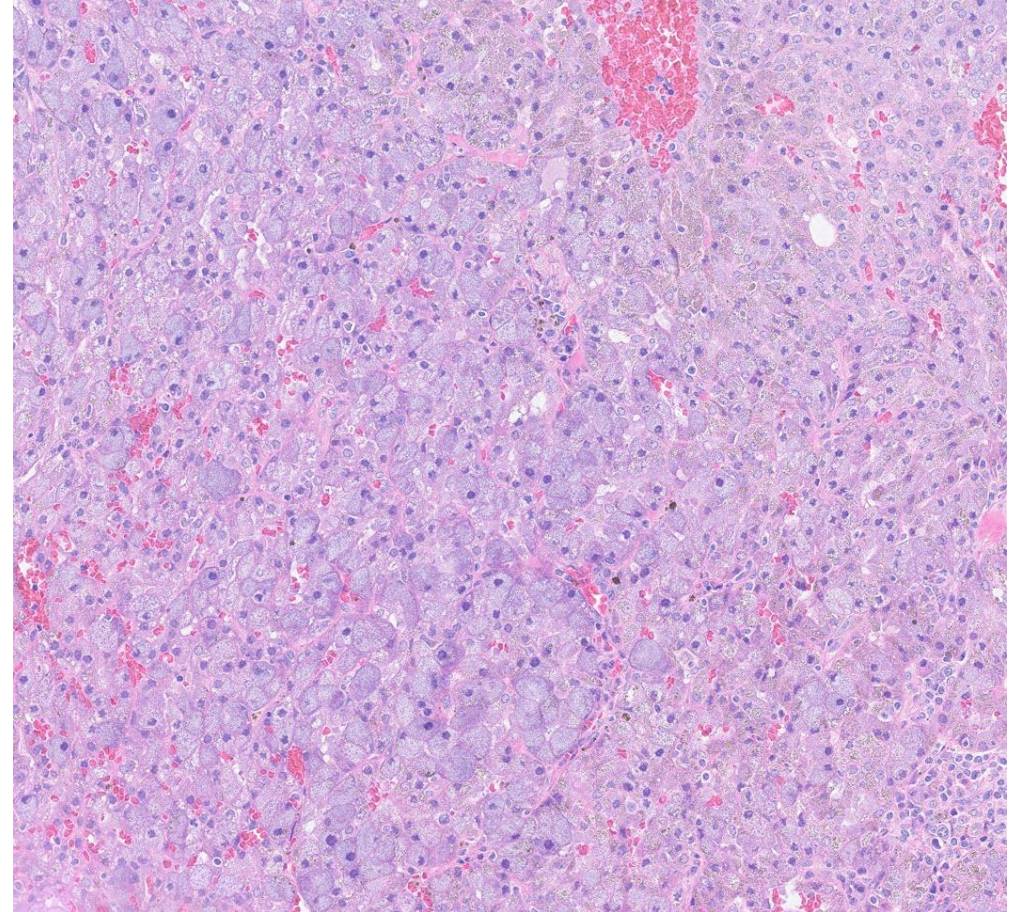
# Differential Diagnosis

- Acinic cell carcinoma
- Mucoepidermoid carcinoma
- Sebaceous neoplasms
- Clear cell neoplasms
- Salivary duct carcinoma
- Adenocarcinoma NOS



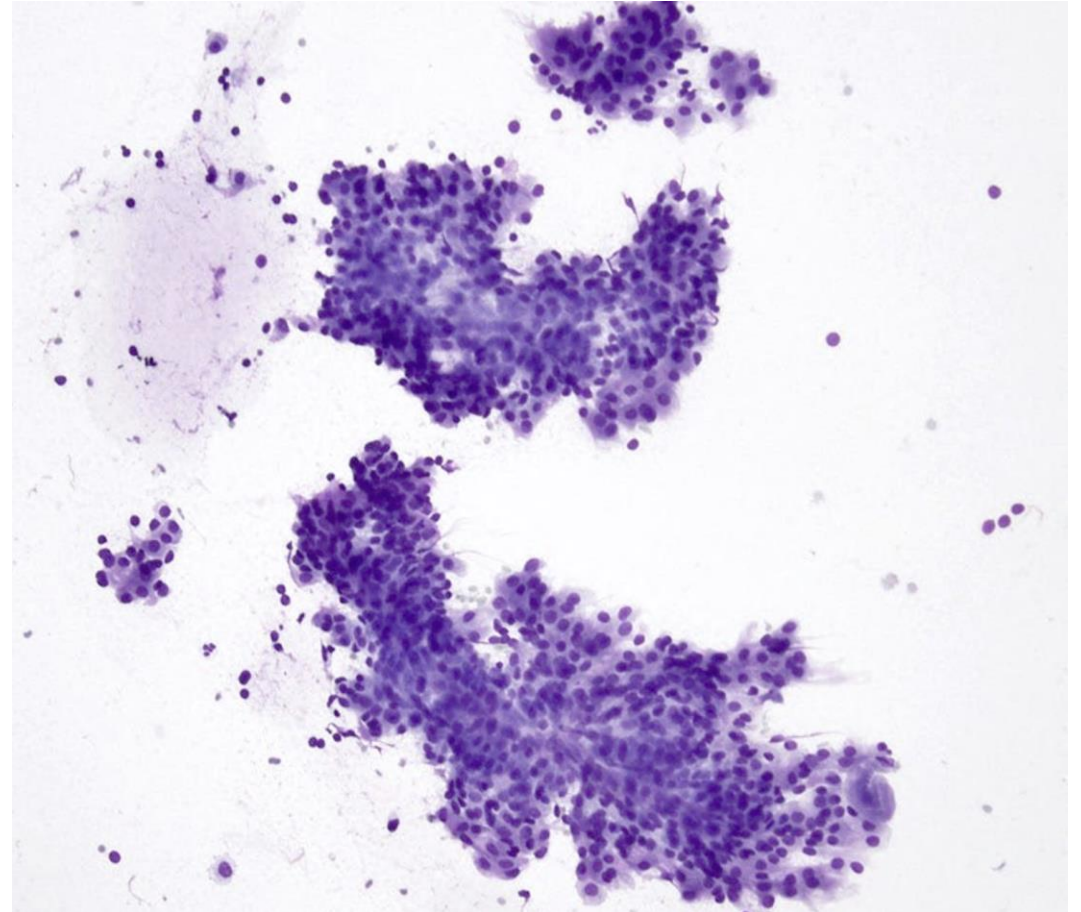
# Acinic Cell Carcinoma

- Contains cytoplasmic PAS positive-diastase resistant zymogen granules
- Strongly immunoreactive for SOX10 and DOG1.



# Mucoepidermoid carcinoma

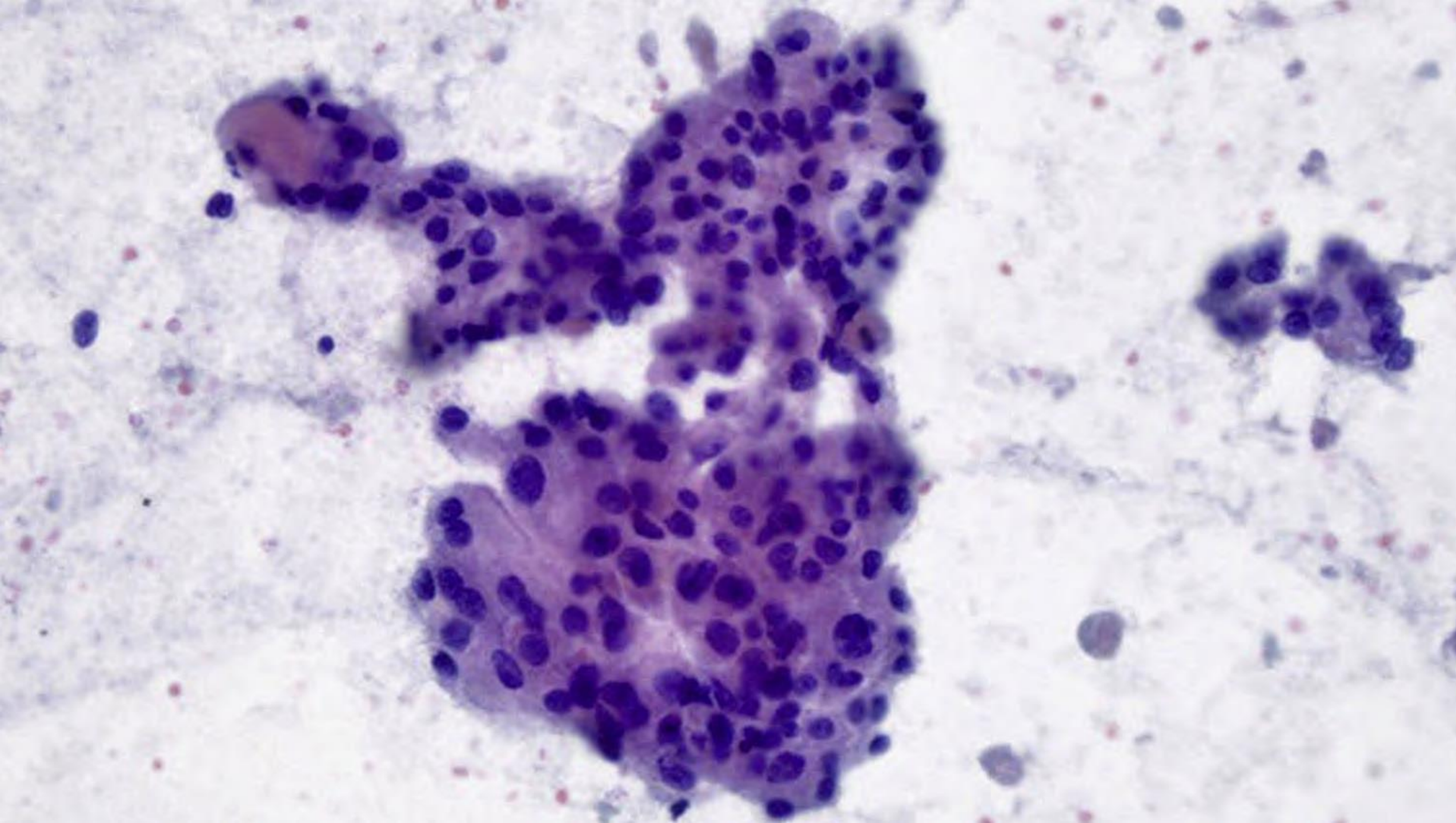
- Goblet cells with intracytoplasmic mucin among squamoid intermediate cells
- Lacks the multivacuolated cells
- Diffusely positive for p40 and p63
- *MAML2-CRTC1* translocations in the majority of tumors



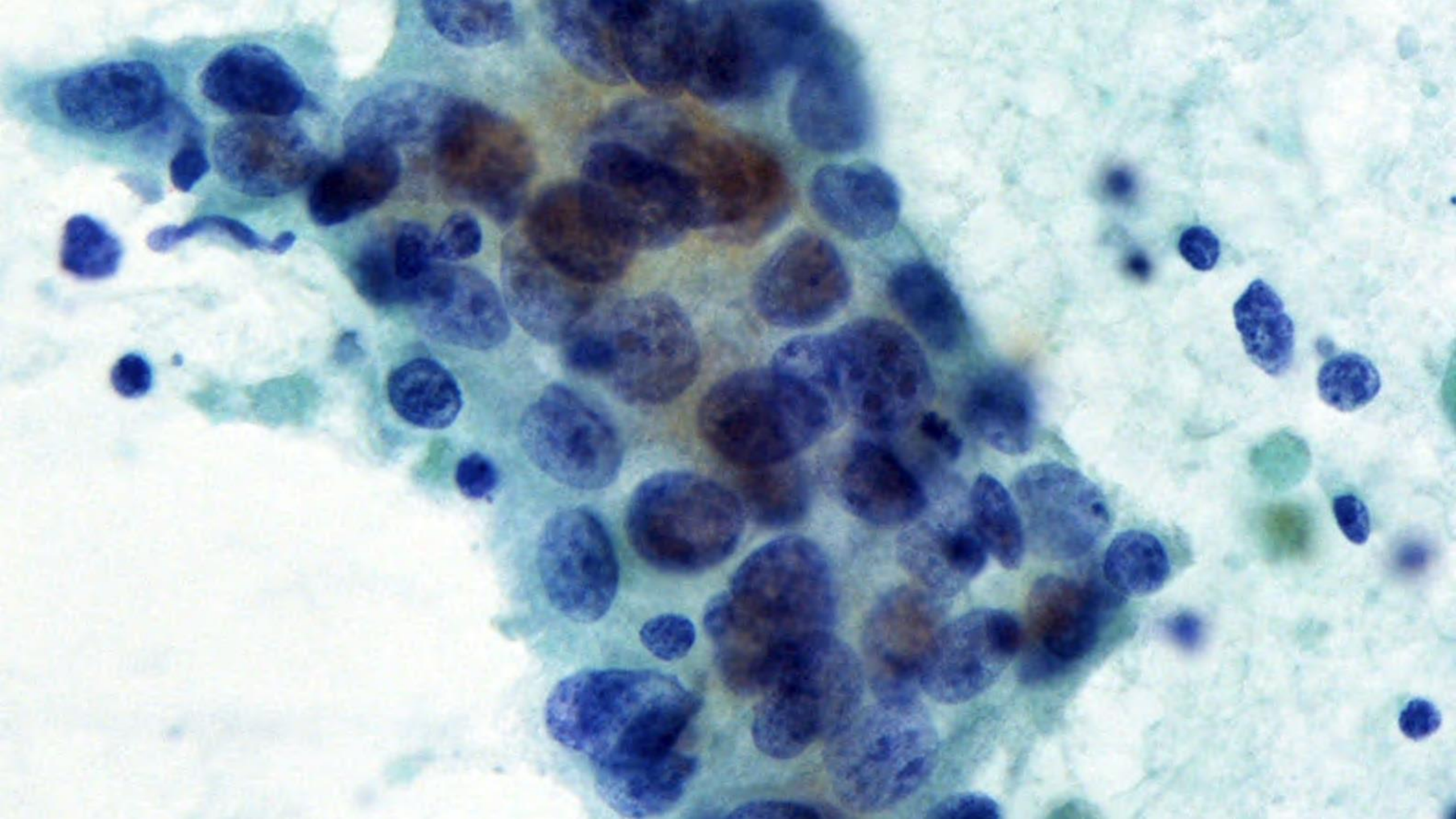


# Case 5

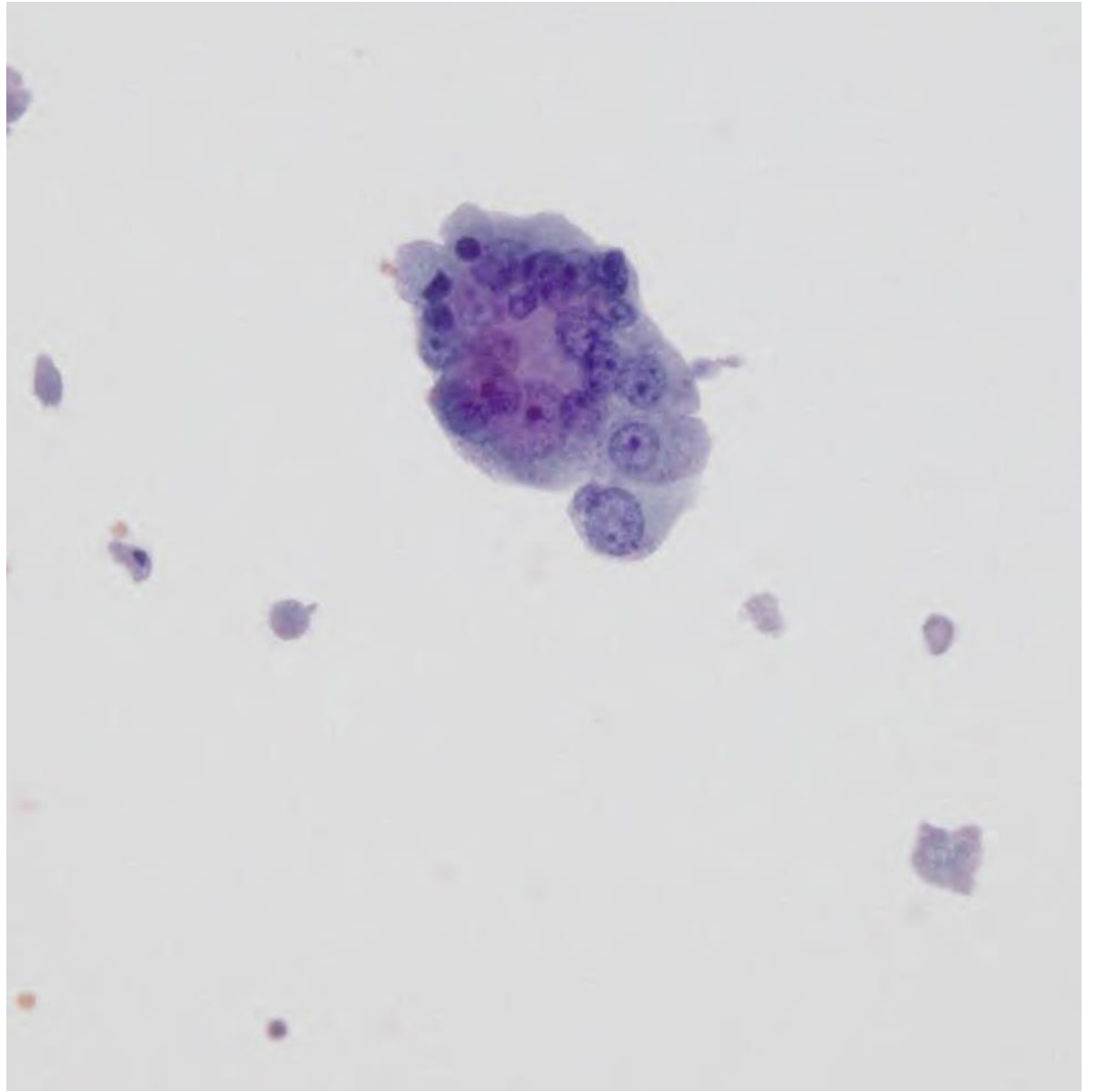
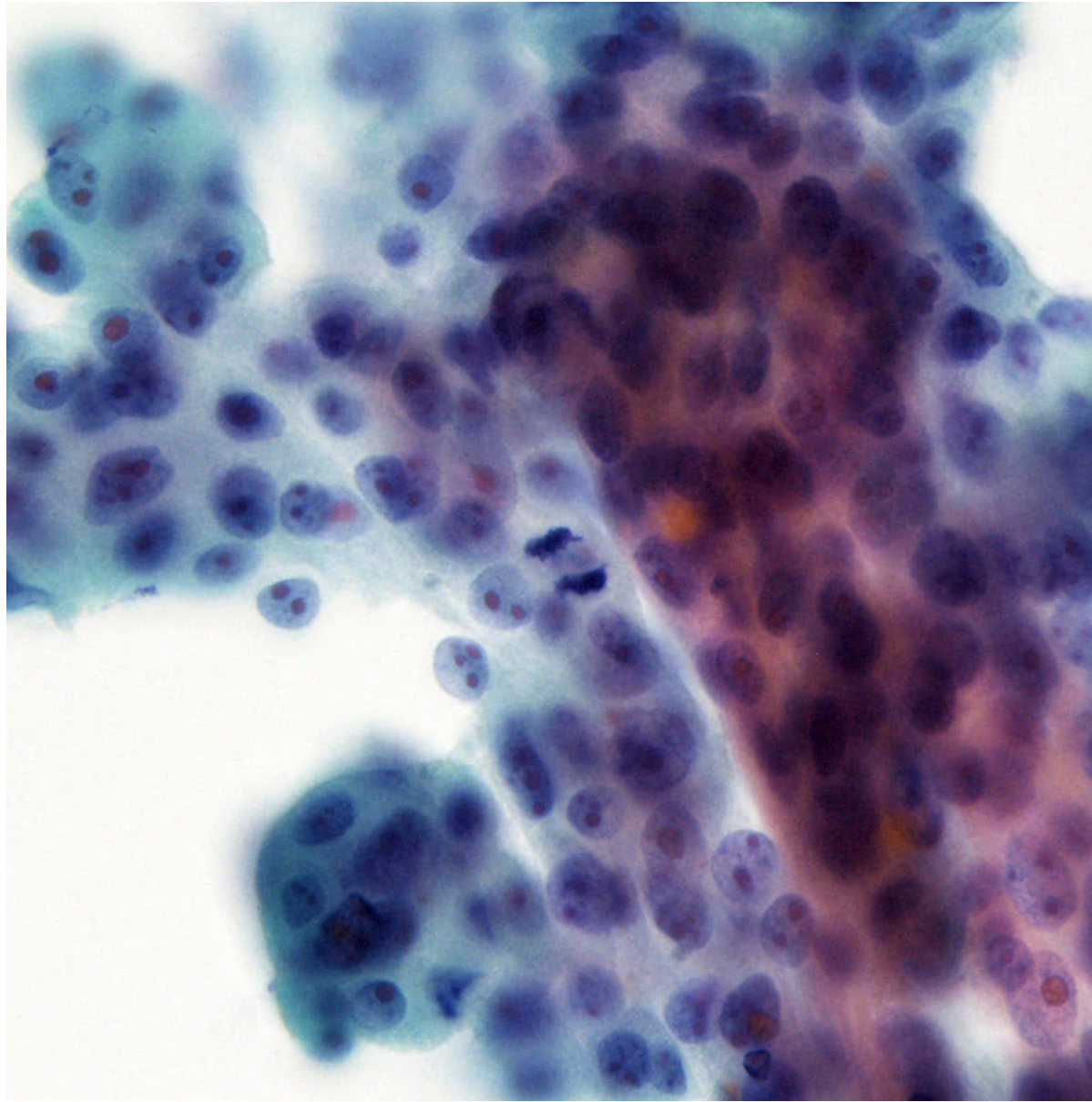
58-year-old female with 2.7 cm left parotid mass









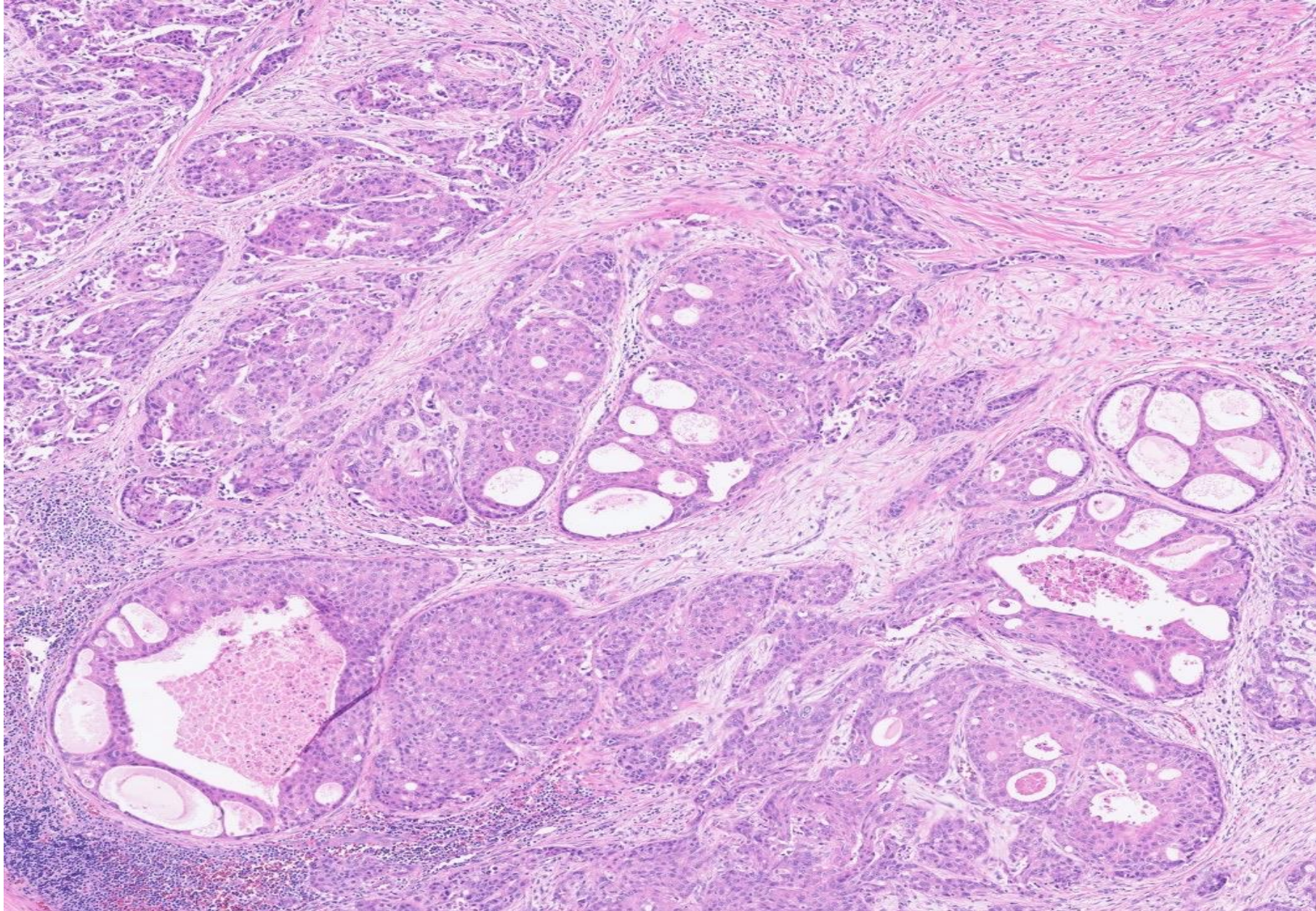




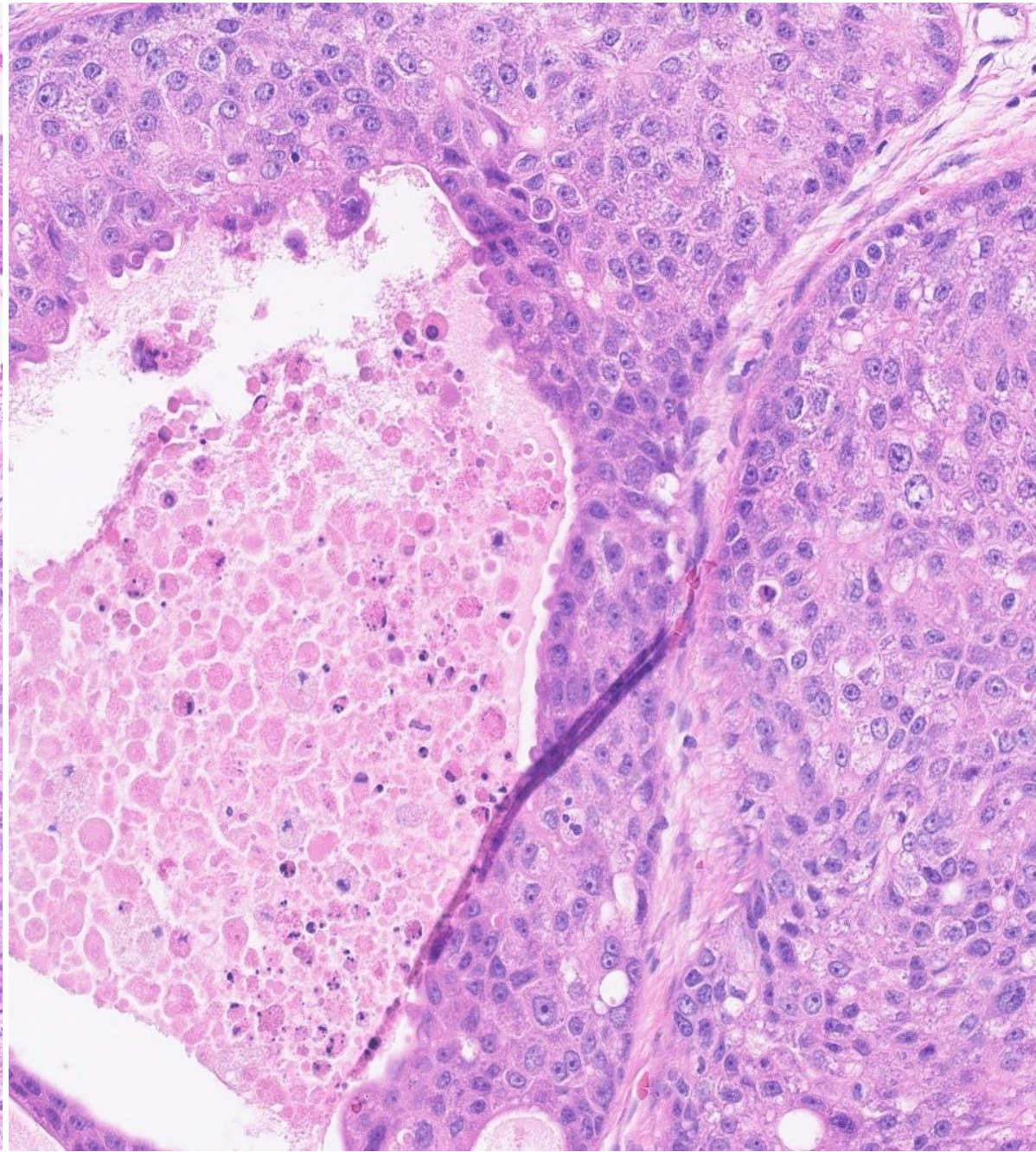
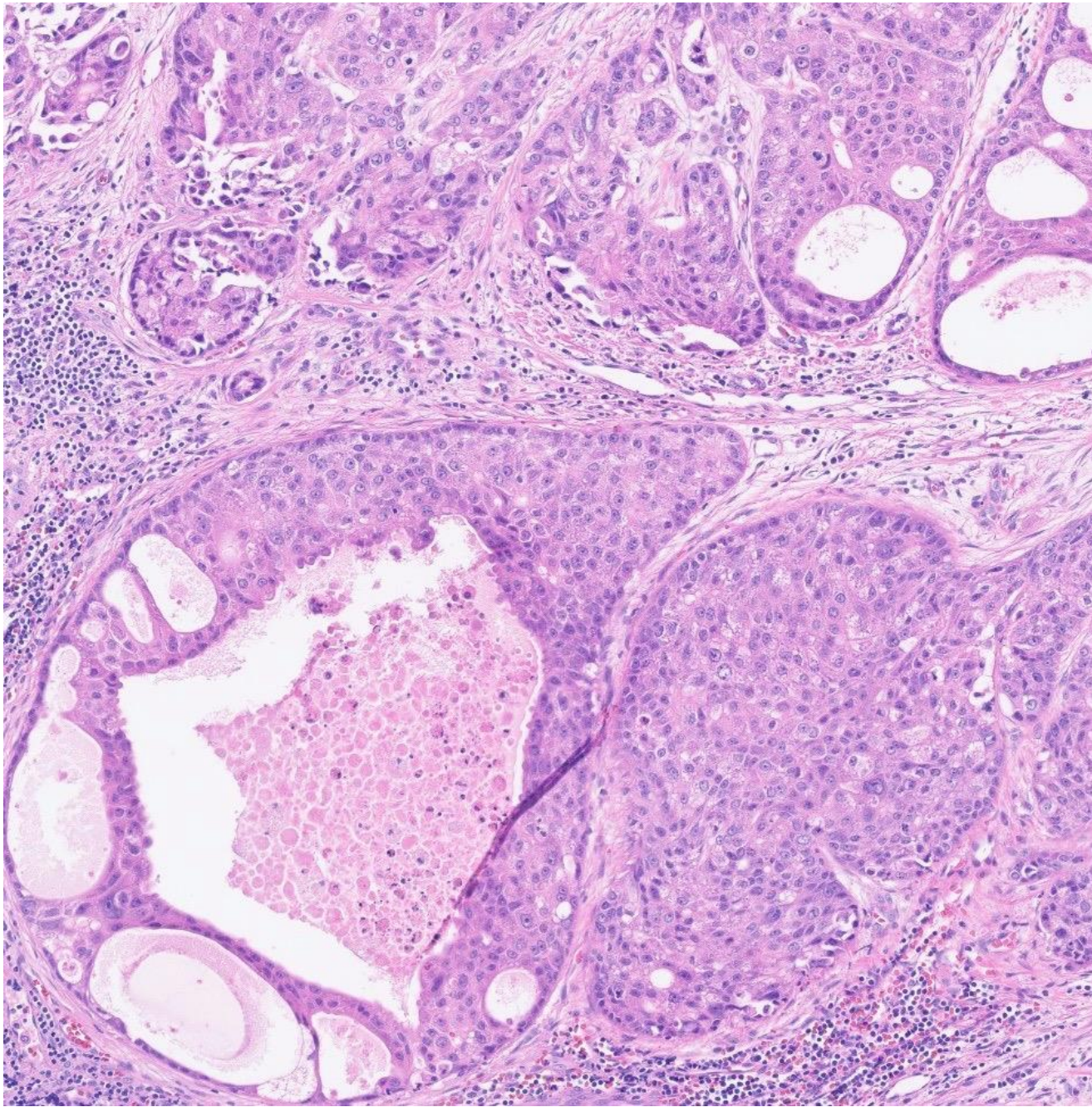
**What is the diagnosis?**



## Follow-up resection





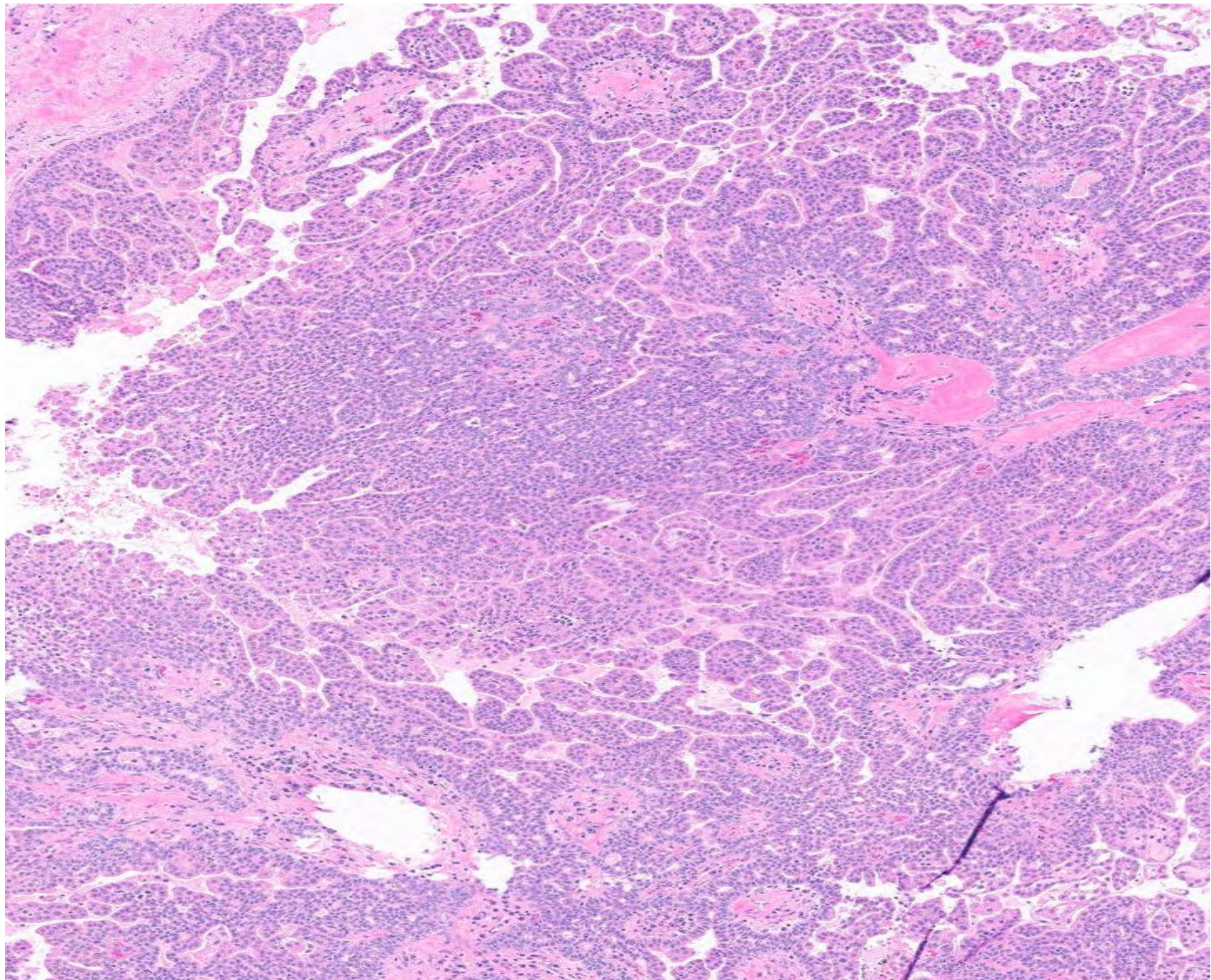




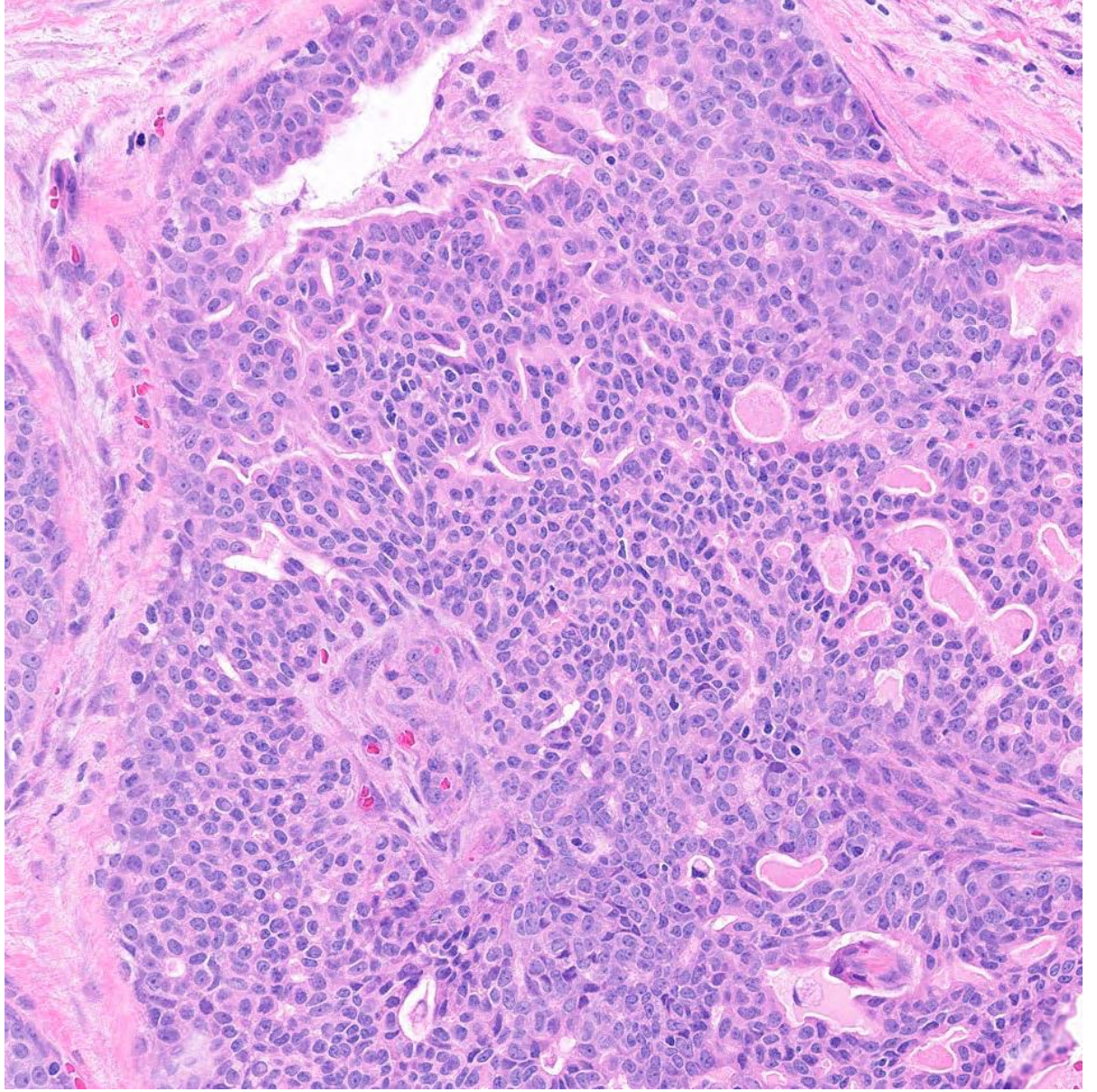
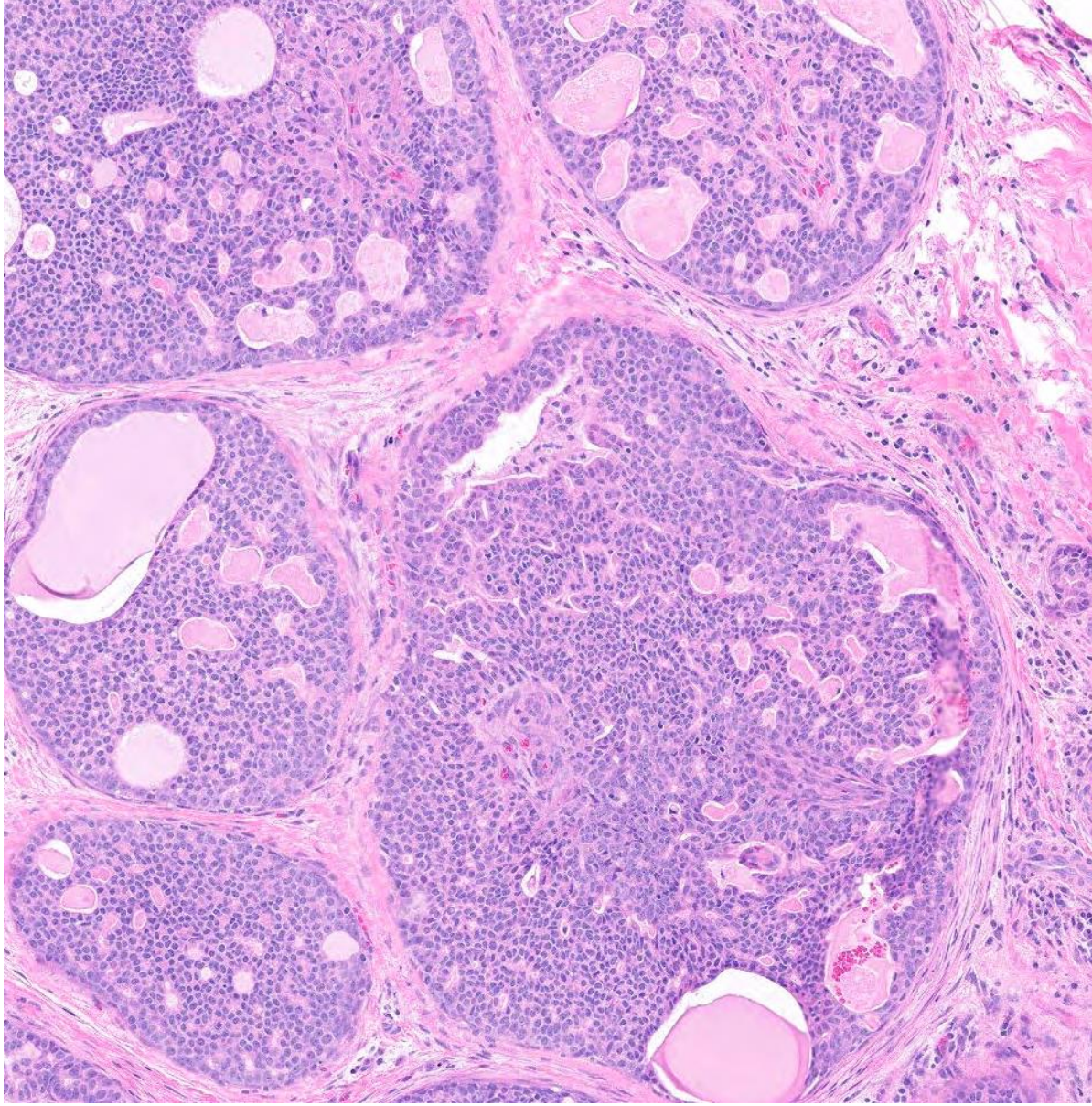
# Salivary Duct Carcinoma

- Highly aggressive malignancy
- Occurs primarily in middle aged men
- Resembles ductal carcinoma of the breast
- Exhibits varying patterns of disorganized 3-dimensional clusters of malignant epithelial cells
- Large, polygonal cells with granular to vacuolated oncocytic cytoplasm
- Nuclear hyperchromasia, nucleomegaly, nuclear pleomorphism with prominent nucleoli











# Salivary duct Carcinoma

- Most exhibit nuclear staining for AR
- About 30% express HER2
- A small subset demonstrates mammaglobin immunoreactivity
- Negative for p63, S100 and SOX10
- Alterations of PLAG1 and HMGA2 in CXPA

# Salivary duct Carcinoma

- Diagnostic challenges
  - Basal cytomorphology
  - Hyalinized stroma of SDC can be mistaken for chondromyxoid matrix of PA
  - When lacking cribriform architecture, may be confused with adenocarcinoma NOS or high-grade MEC



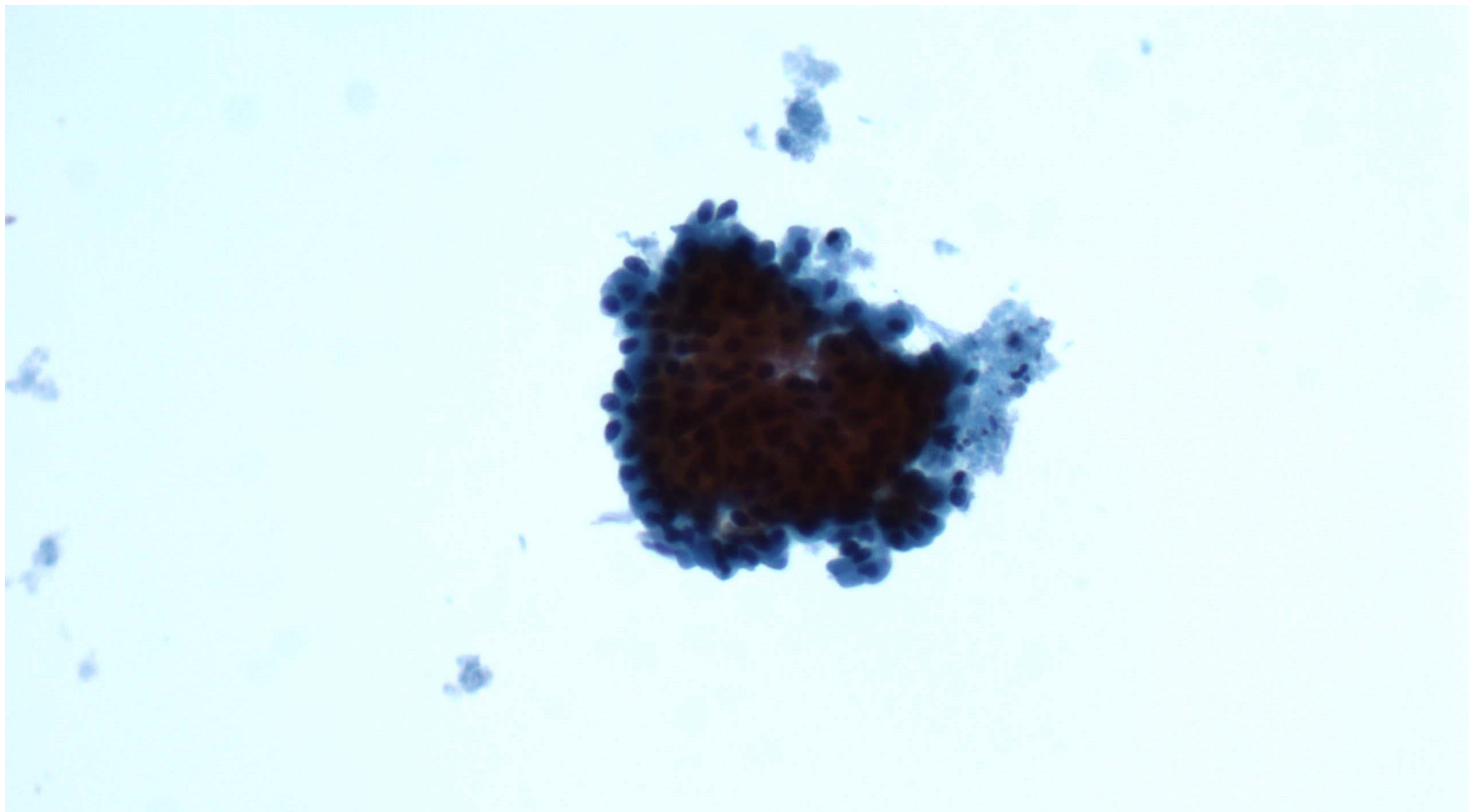
# Differential Diagnosis

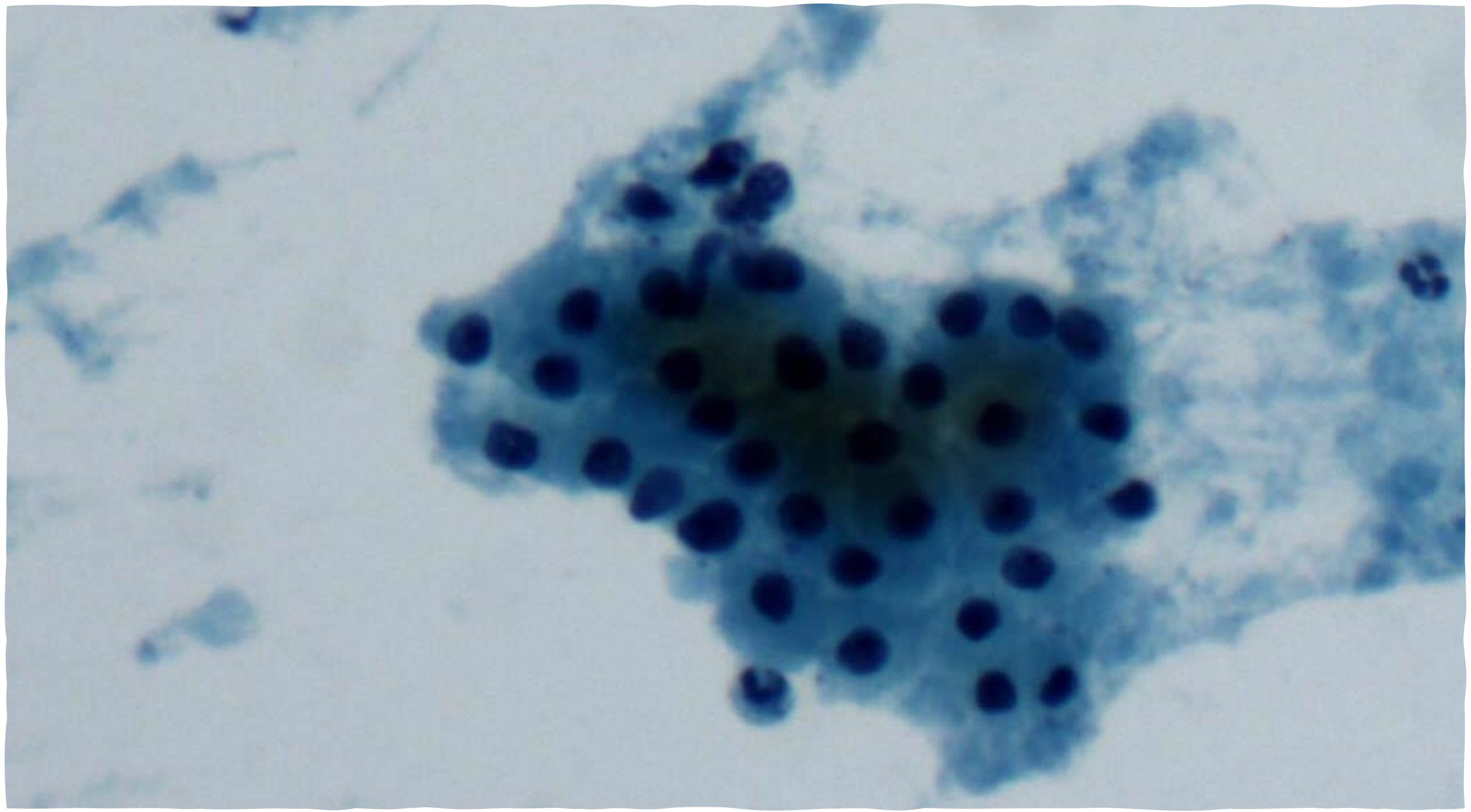
- Other salivary gland malignancies with high-grade transformation
  - Adenoid cystic carcinoma
  - Mucoepidermoid carcinoma
  - Epithelial-myoepithelial carcinoma
  - Acinic cell carcinoma
- Metastatic carcinoma

# Case 6

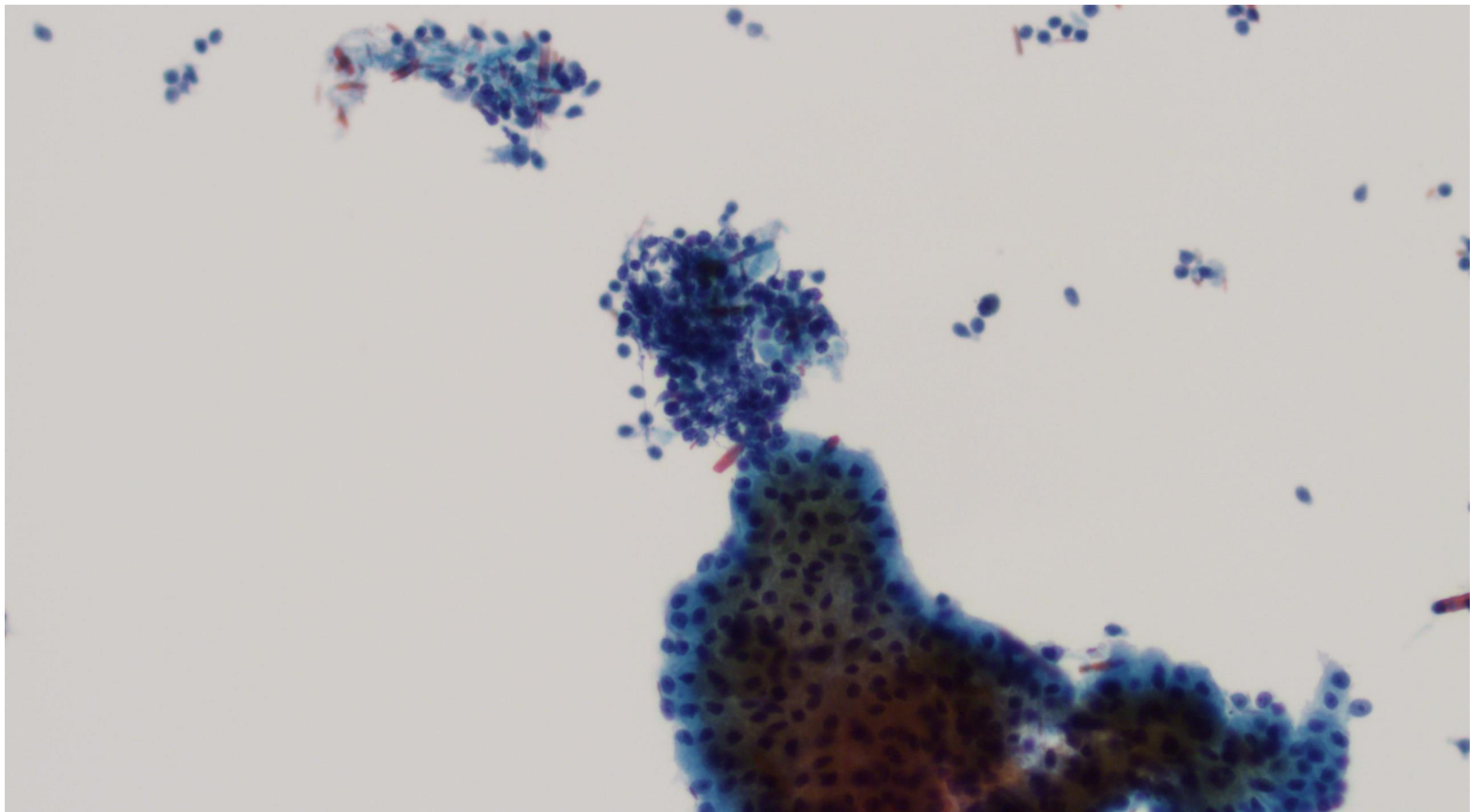
74-year-old male with 3 cm right parotid mass



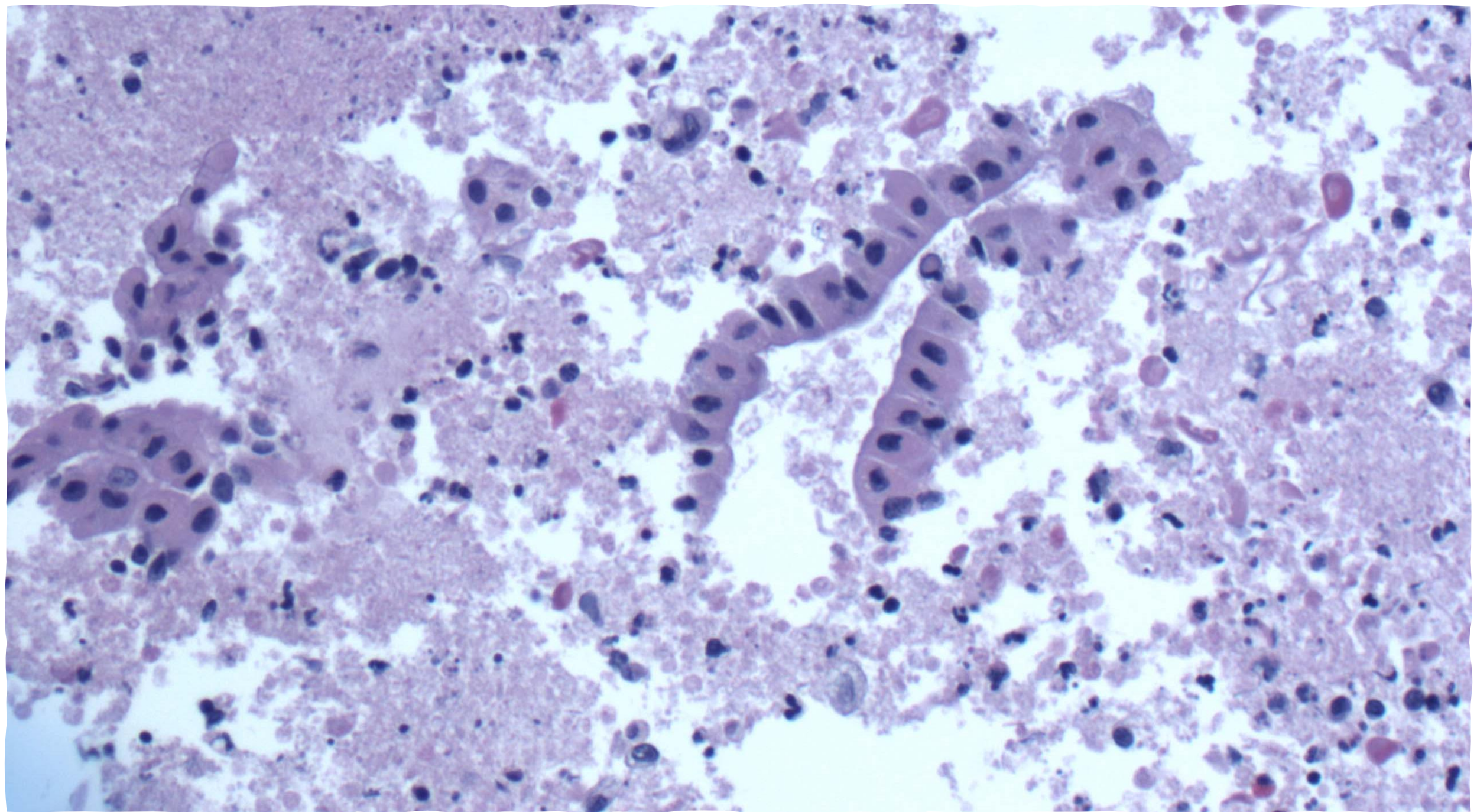










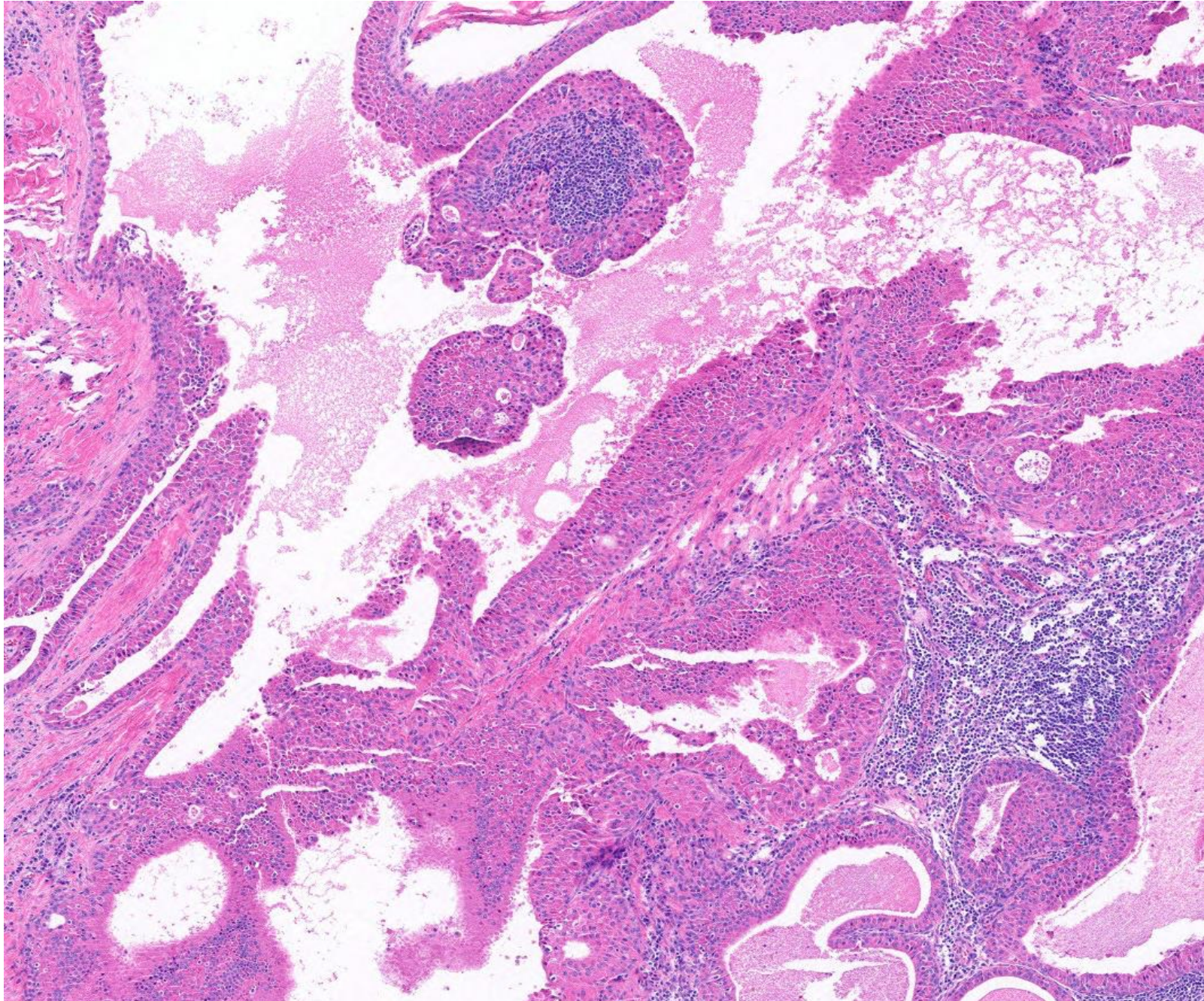




**What is the diagnosis?**



## Follow-up resection





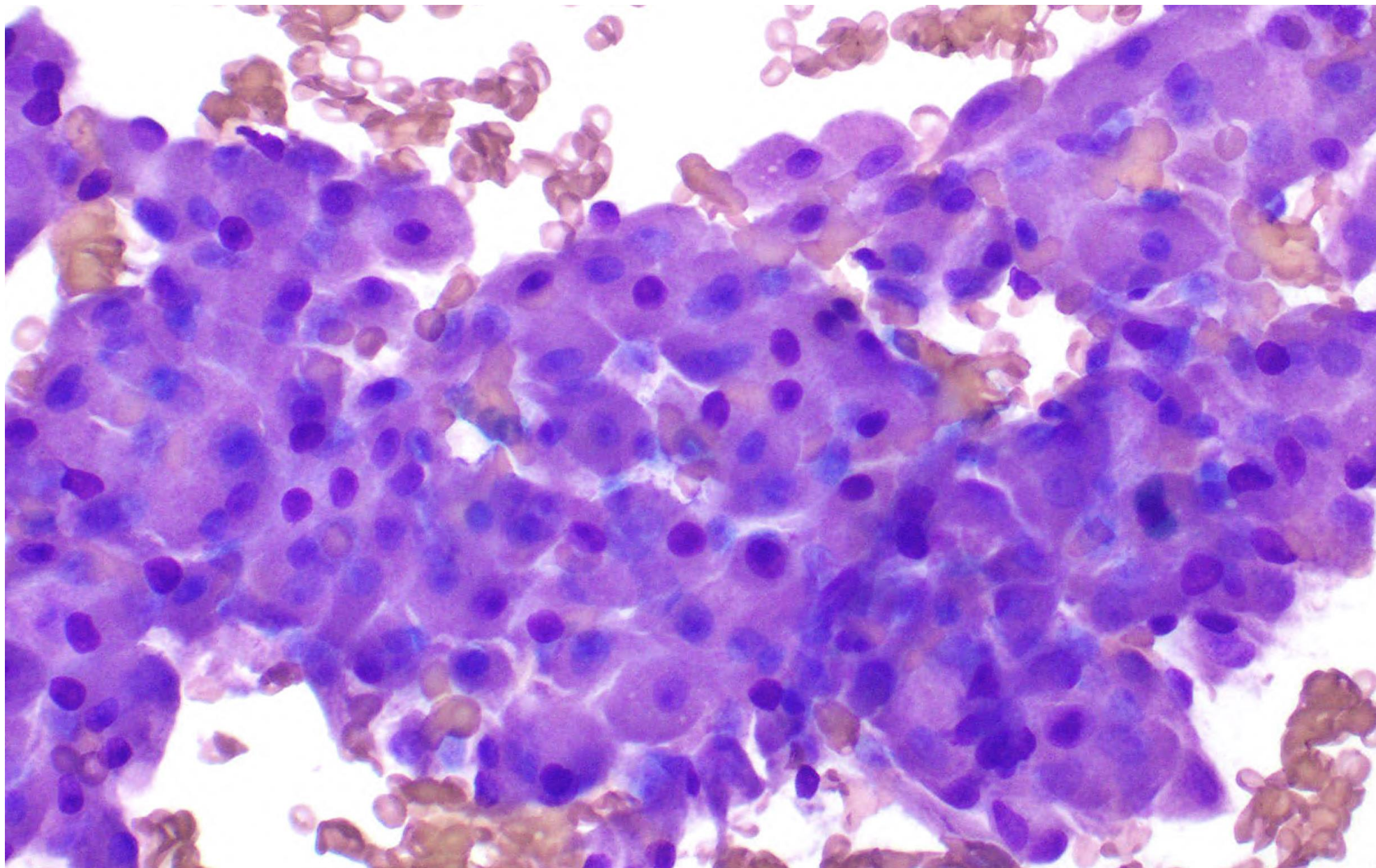
# Warthin Tumor

- Benign salivary gland neoplasm
- Oncocytic epithelial cells arranged in ductal, papillary, or cystic patterns within a lymphoid stroma
- Smears show cohesive fragments of oncocytic cells interspersed with numerous lymphocytes amidst granular and proteinaceous debris
- Risk factors: Smoking, EBV virus, autoimmune disorders
- Differential diagnosis: Oncocytoma, oncocytosis, oncocytic metaplasia

# Warthin Tumor – Differential diagnosis

- In Warthin tumor, oncocytic cells exhibit minimal pleomorphism, monotonous appearance and centrally located round nuclei
- Monolayered sheets vs. 3-dimensional clusters in oncocytoma
- Oncocytosis is generalized hyperplasia without mass formation or encapsulation





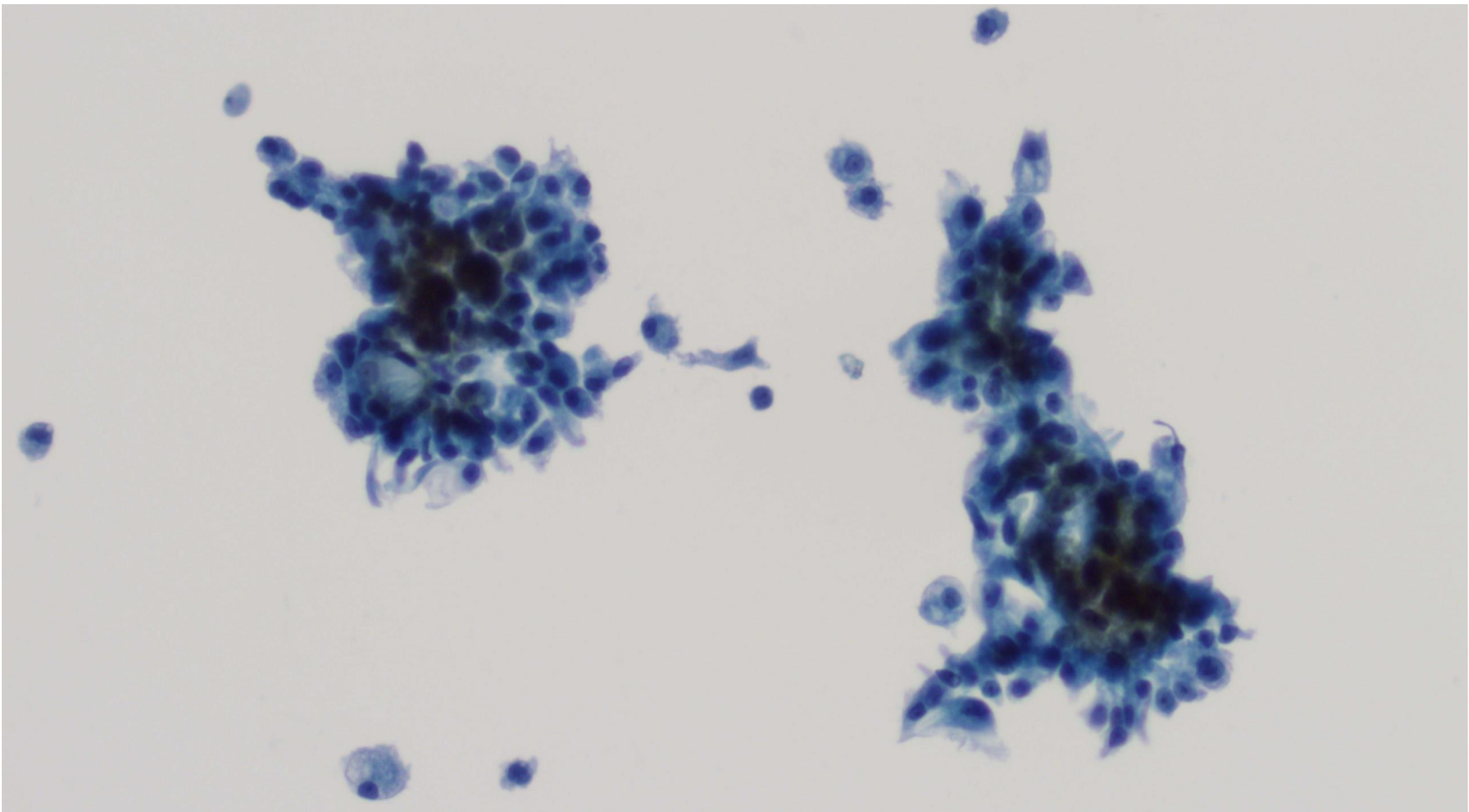
# Pitfalls

- Squamous and mucinous metaplasia can be confused with Warthin-like mucoepidermoid carcinoma
- Squamous metaplasia can be mistaken for squamous cell carcinoma
- Lymphoepithelial cyst may overlap with WT

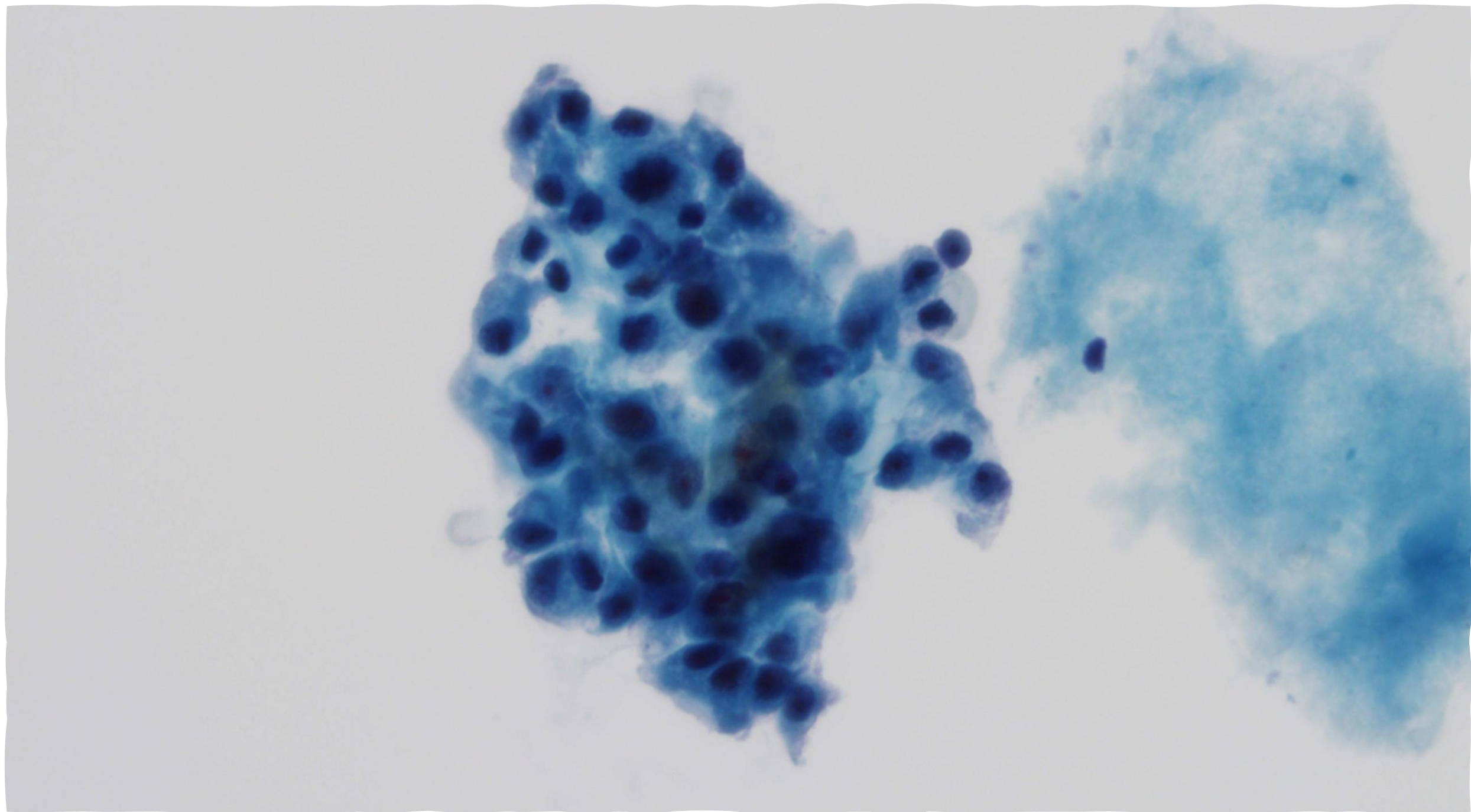


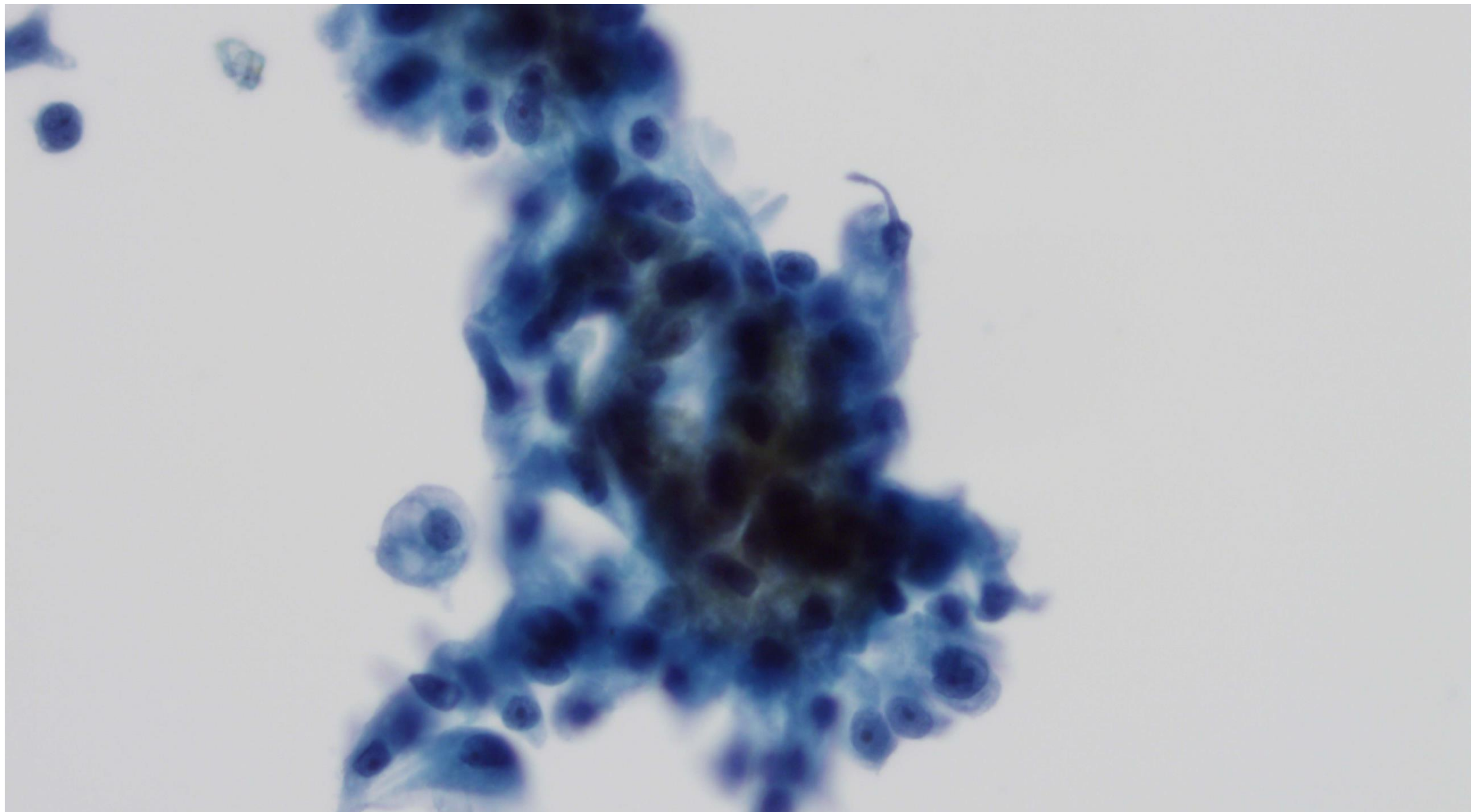
# Case 7

69-year-old female with 1.3 cm right buccal mucosa mass

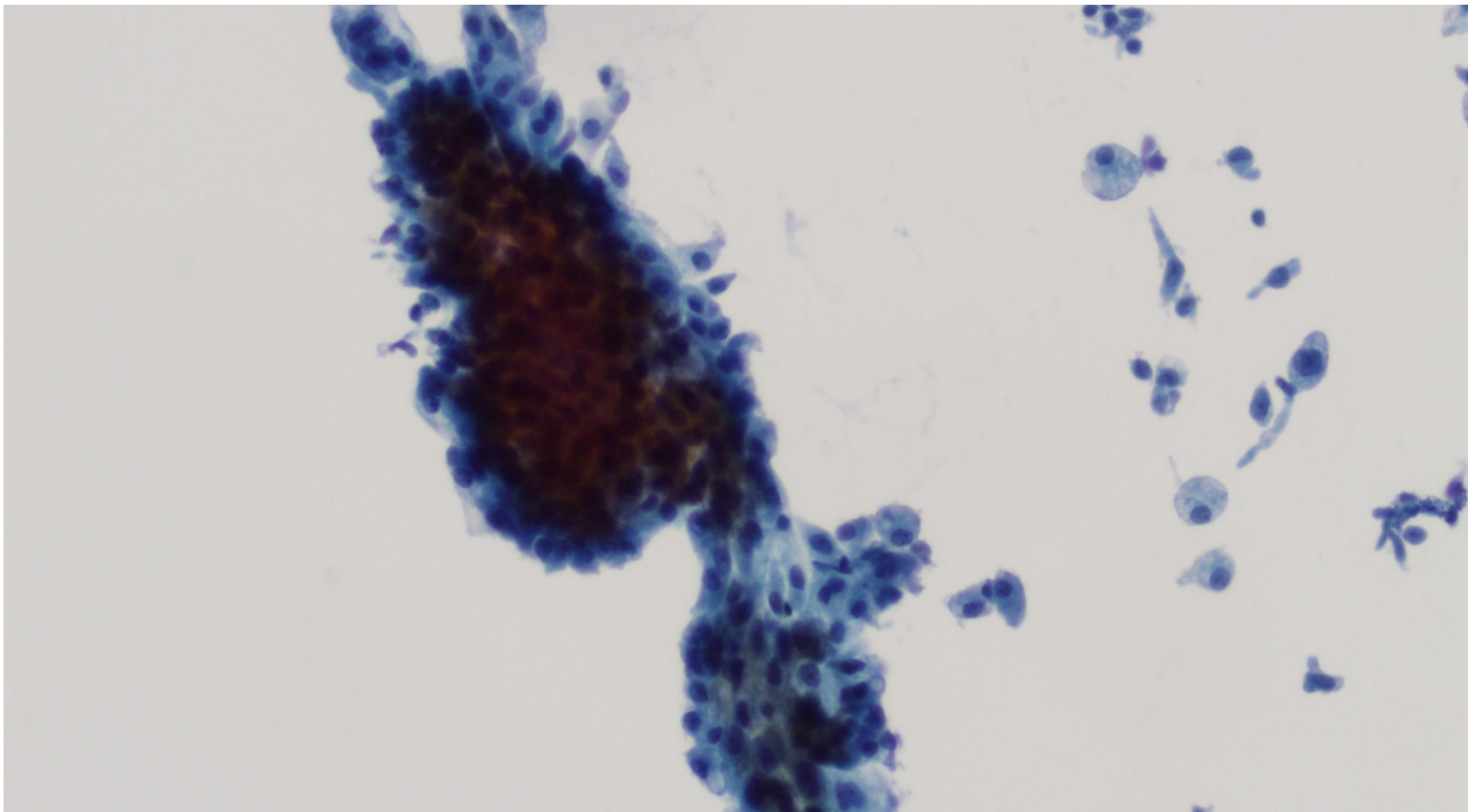


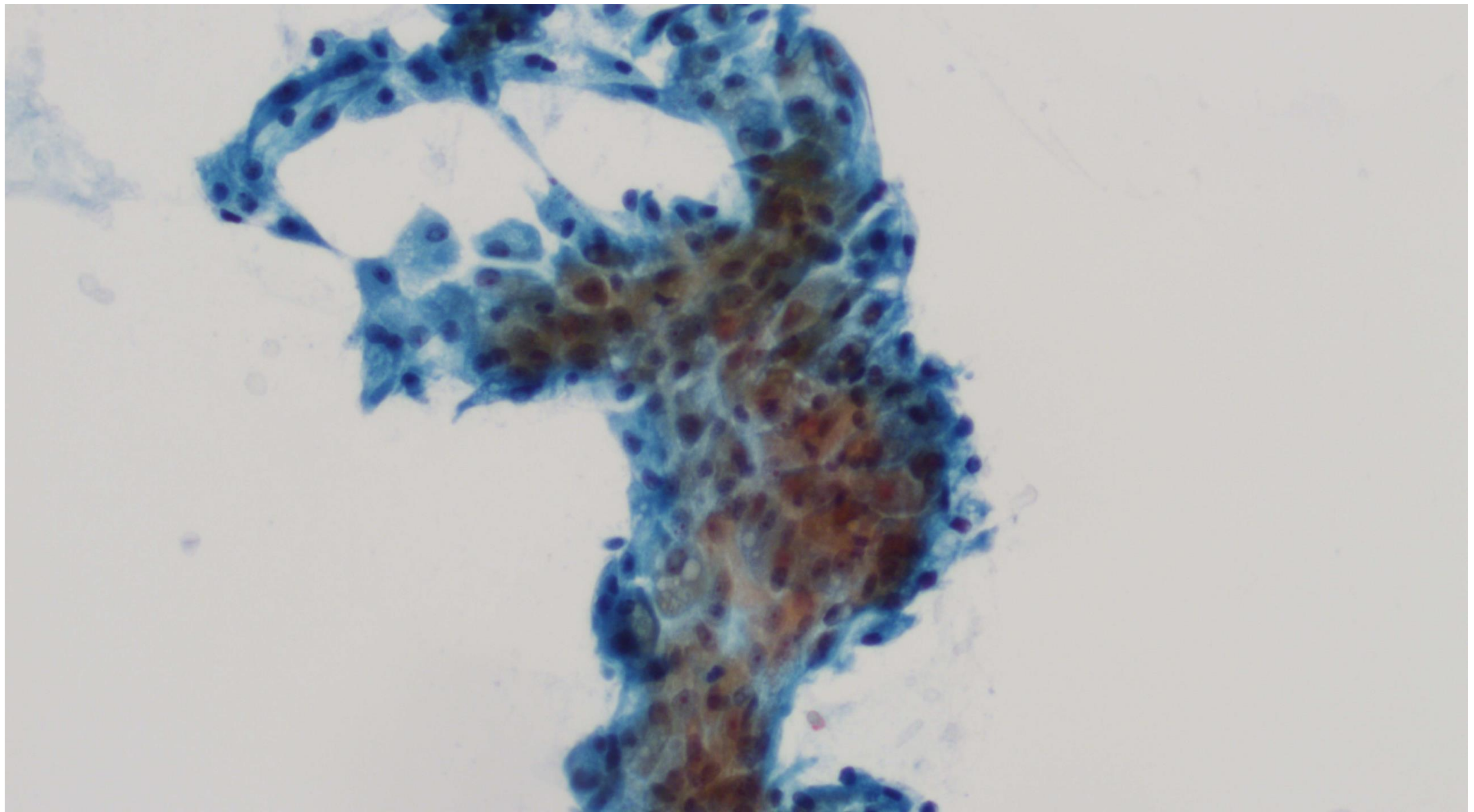








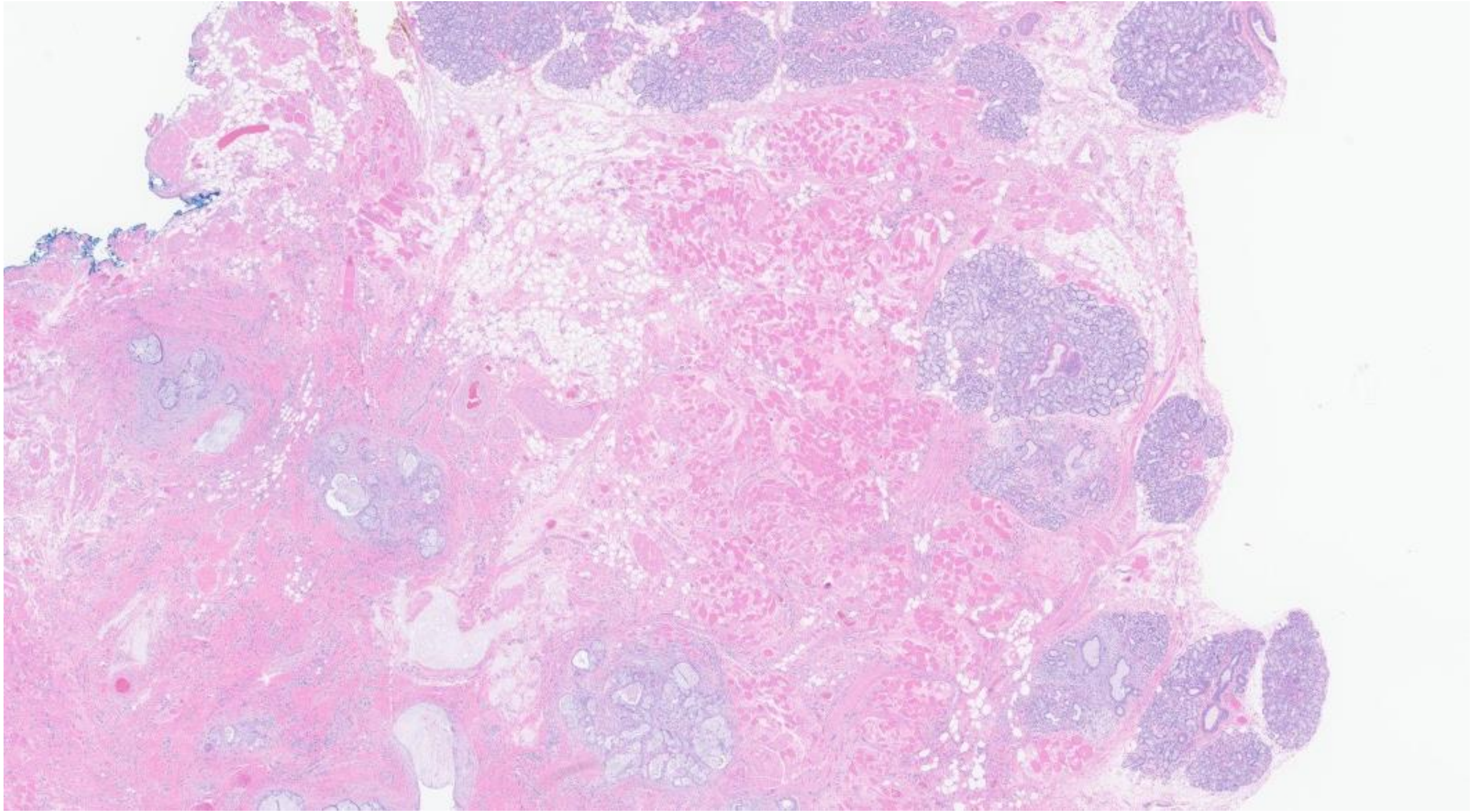




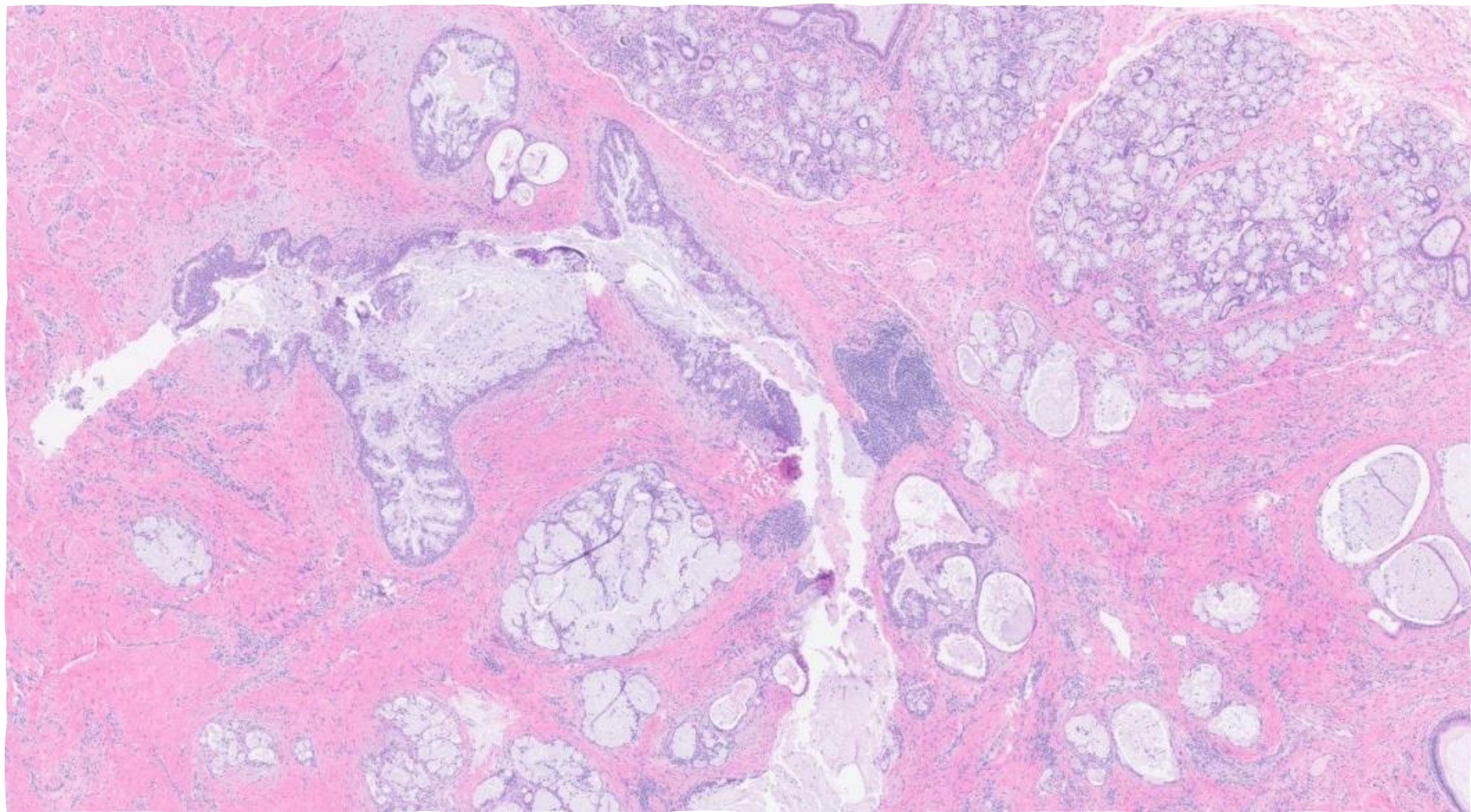


**What is the diagnosis?**

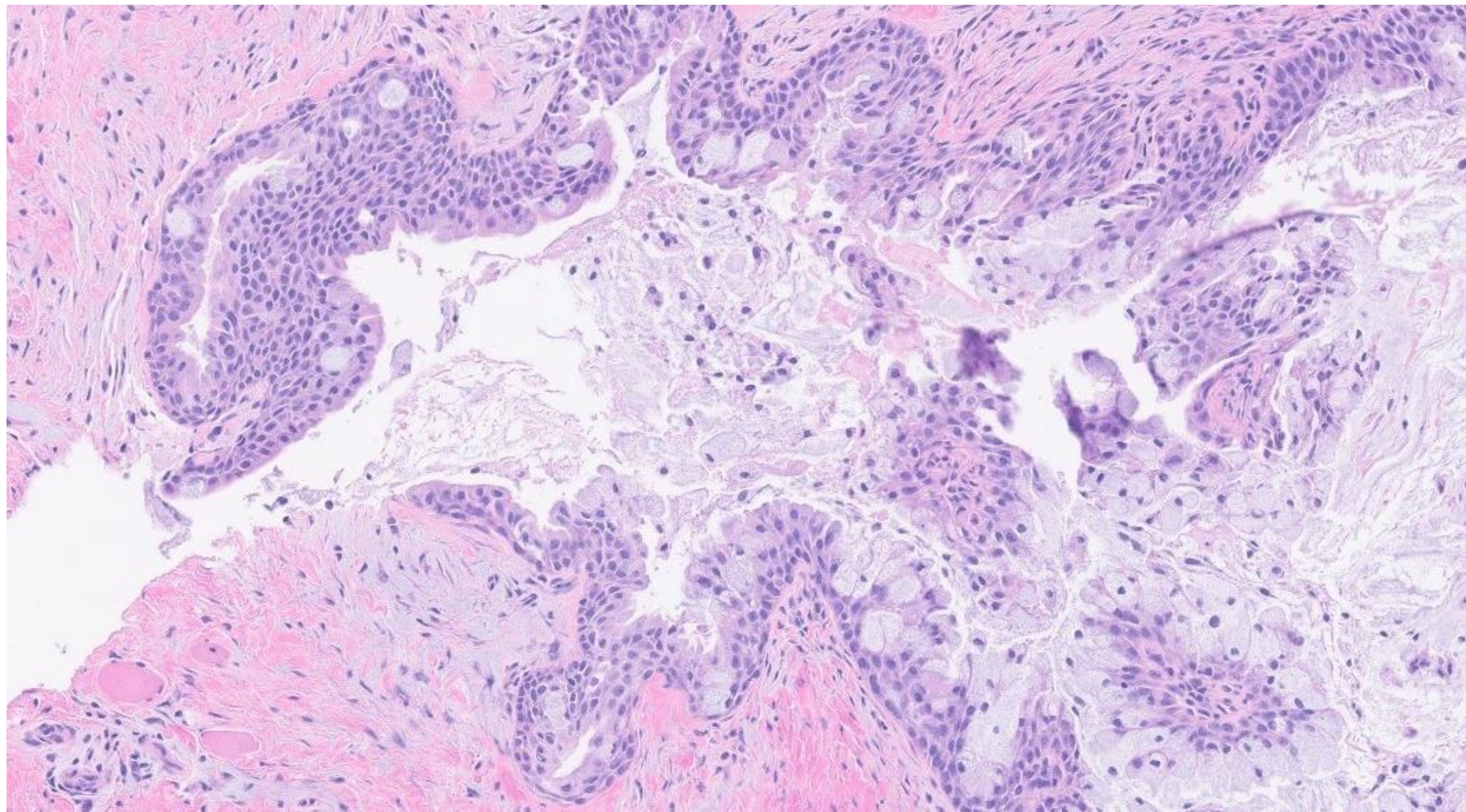
## Follow-up resection



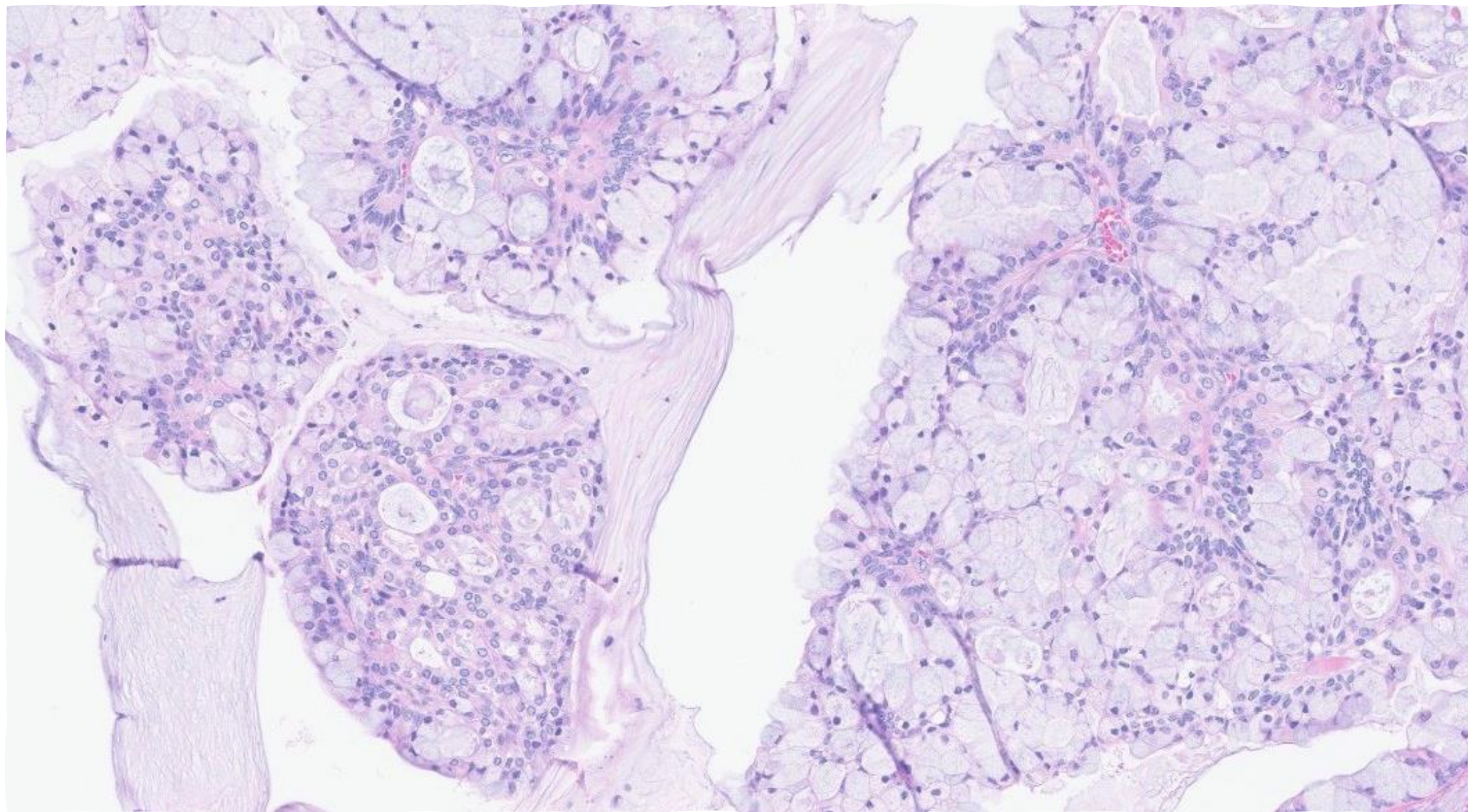












# Mucoepidermoid carcinoma

- Most common salivary gland malignancy
- Highest incidence during 5<sup>th</sup> decade
- Primarily affects major salivary glands
- 3 distinct cell types: epidermoid, intermediate and mucous cells with variable amount of mucin
- Categorized into 3 histologic grades based on cystic component proportion, perineural invasion, necrosis, mitotic activity and nuclear atypia



# Mucoepidermoid carcinoma

- Low grade MEC exhibit low cellularity has infrequent epithelial fragments, abundant extracellular mucin, with cystic muciphages
- Cyst content in LGMEC can lead to false negative diagnosis
- LGMEC can be mistaken for mucocele
- MSRSGC has suggested categorizing cases with predominantly mucinous cyst content as AUS (category III)
- Poses more diagnostic challenges than HG

# Mucoepidermoid carcinoma

- MEC with prominent tumor-associated lymphoid proliferation can be confused with Warthin tumor
- High-grade MEC can be mistaken for squamous cell carcinoma
- MEC is defined by rearrangement of the *MAML2* gene



# Differential Diagnosis

- Mucocele
- Chronic sialadenitis with mucinous metaplasia of ducts
- Pleomorphic adenoma
- Secretory carcinoma

**THANK YOU!**

