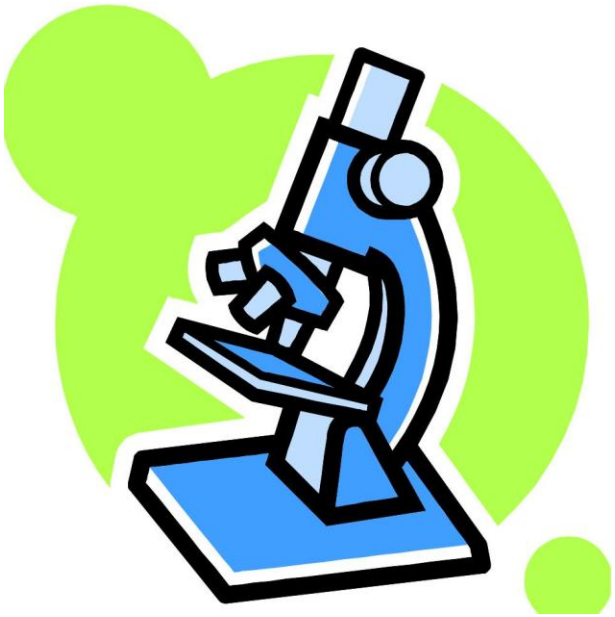
# Breast Cytopathology Review



Penny Barnes MD, FRCP(C)

June, 2016

# Breast FNA(C)

- Indications
- Adequacy
- Diagnostic terminology
- Liquid-based cytology
- Biomarker assessment
- Cases

# Indications for breast FNA

- Palpable mass
- Non-palpable breast lesions: image guided FNA
  - Lesions difficult to target by NCB
  - Breast implants

# FNA of Breast

- Safe, cost-effective procedure with few complications
- Primary indication is to determine if lump is benign or malignant
- Useful in evaluation of recurrence and metastasis of breast ca
- Assessment of lymph node status
- Diagnosis of inoperable tumors

# Important limitations

- Inability to discriminate in situ from invasive carcinomas
- Non-definitive diagnosis for many proliferative lesions, atypical hyperplasia, low grade neoplasms
- High rate of unsatisfactory results
- Largely replaced by core biopsy in many centres

# ‘Triple test’

- The triple test is the combination of results from CBE, imaging, and tissue sampling.
- When the three assessments are performed adequately and produce concordant results, the triple test diagnostic accuracy approaches 100%.
- Discordant results may indicate the need for excisional biopsy.

# FNA of Breast

- Sensitivity 92.5%
  - False negative rate 2-11%
- Specificity 99.8%
  - False positive rate <1%

# False Negatives

- Sampling errors
  - Incorrect localization
    - Small lesions
    - Large lesions
  - Fibrous/sparsely cellular lesions
- Interpretive errors
  - Infiltrating lobular carcinoma
  - Low grade ductal carcinomas
  - Mucinous carcinoma

# False Negatives

- Small subset of carcinomas probably cannot be diagnosed by FNAB (lesions with minimal atypia)
- A negative FNA cannot completely exclude malignancy

# False Positives

- Interpretation errors
  - Usual epithelial hyperplasia
  - Fibroadenomas
  - Papillary lesions
  - Atypical apocrine cells
  - Lactational changes
  - Gynecomastia with usual hyperplasia

# Specimen Adequacy

- An adequate specimen is one that leads to the resolution of a problem presented by a breast lesion
- Adequacy is determined by two judgments:

  1. Opinion of the aspirator that the cytologic findings are consistent with the clinical findings and that the lesion was adequately sampled.

  2. Opinion of the pathologist that the slides can be interpreted.

# Specimen Adequacy

- No specific requirement for a minimum # of ductal cells; mere presence of cells does not assure adequate sampling of a mass
- Description of specimen cellularity is recommended
  - Hypocellular (occasional clusters)
  - Moderately cellular (clusters easy to find)
  - Markedly cellular (epithelial cells in nearly every field)

# Diagnostic terminology

- Benign/negative
- Atypical
- Suspicious
- Malignant
- Unsatisfactory

# Positive for carcinoma

Features:

1. Hypercellularity
2. Discohesion – many single and loose groups of epithelial cells
3. Cytologic atypia – increased N/C, eccentric nuclei
4. Single cell population – no round-oval bipolar myoepithelial cells or benign ductal cells

# Suspicious of carcinoma

- 3 of 4 malignant features present
- Most cases will be malignant
- Further diagnostic procedures are indicated prior to definitive therapy: tissue biopsy

# Atypical

- Malignancy is not expected, but cannot be excluded
- Cellular
- Crowding / overlapping cells +/- 1 other feature of malignancy
- Tissue biopsy indicated

# Benign

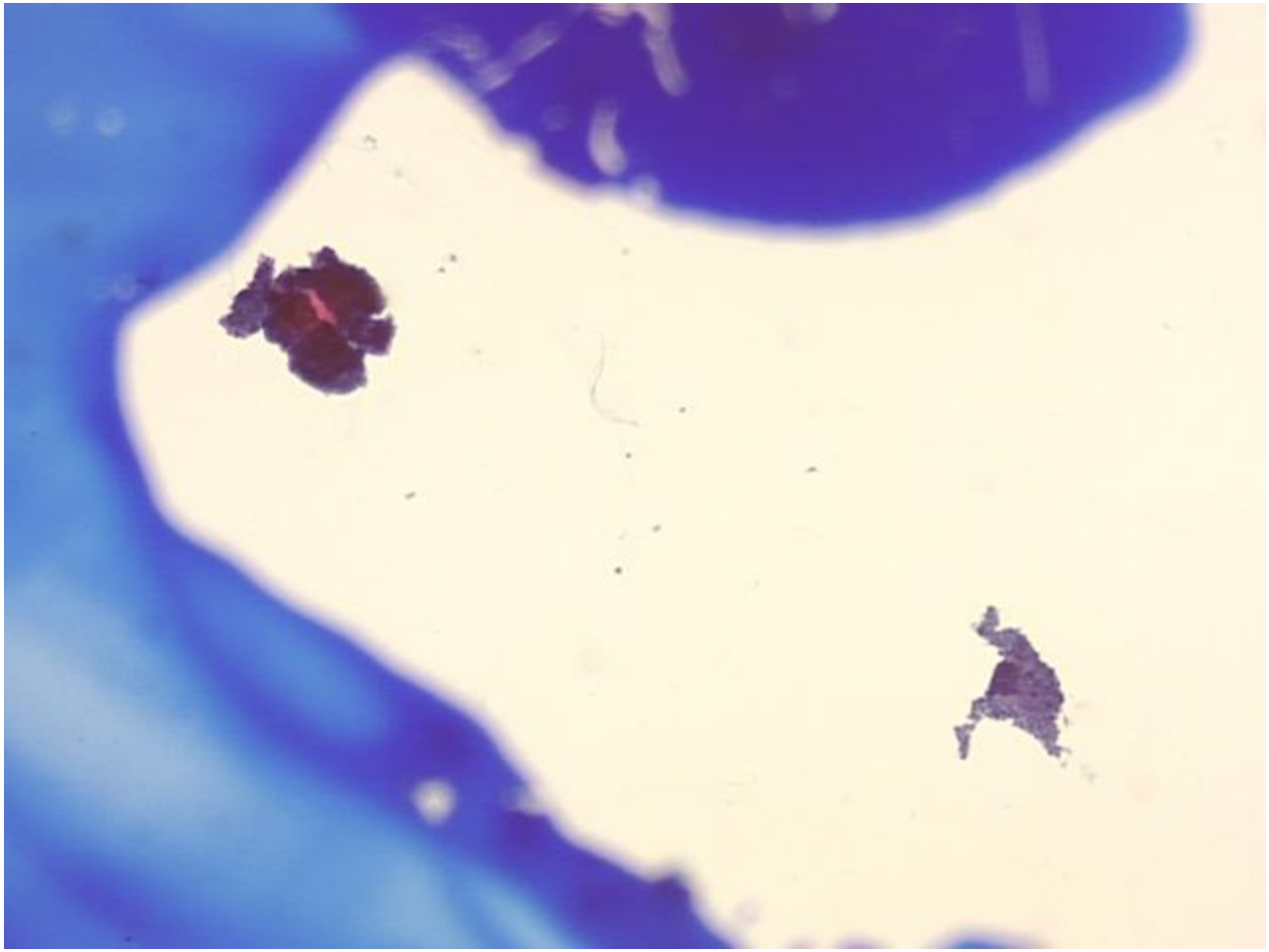
- Cellular
- No or mild crowding / overlapping
- Myoepithelial cells present
- Triple approach (biopsy versus mammographic follow-up)

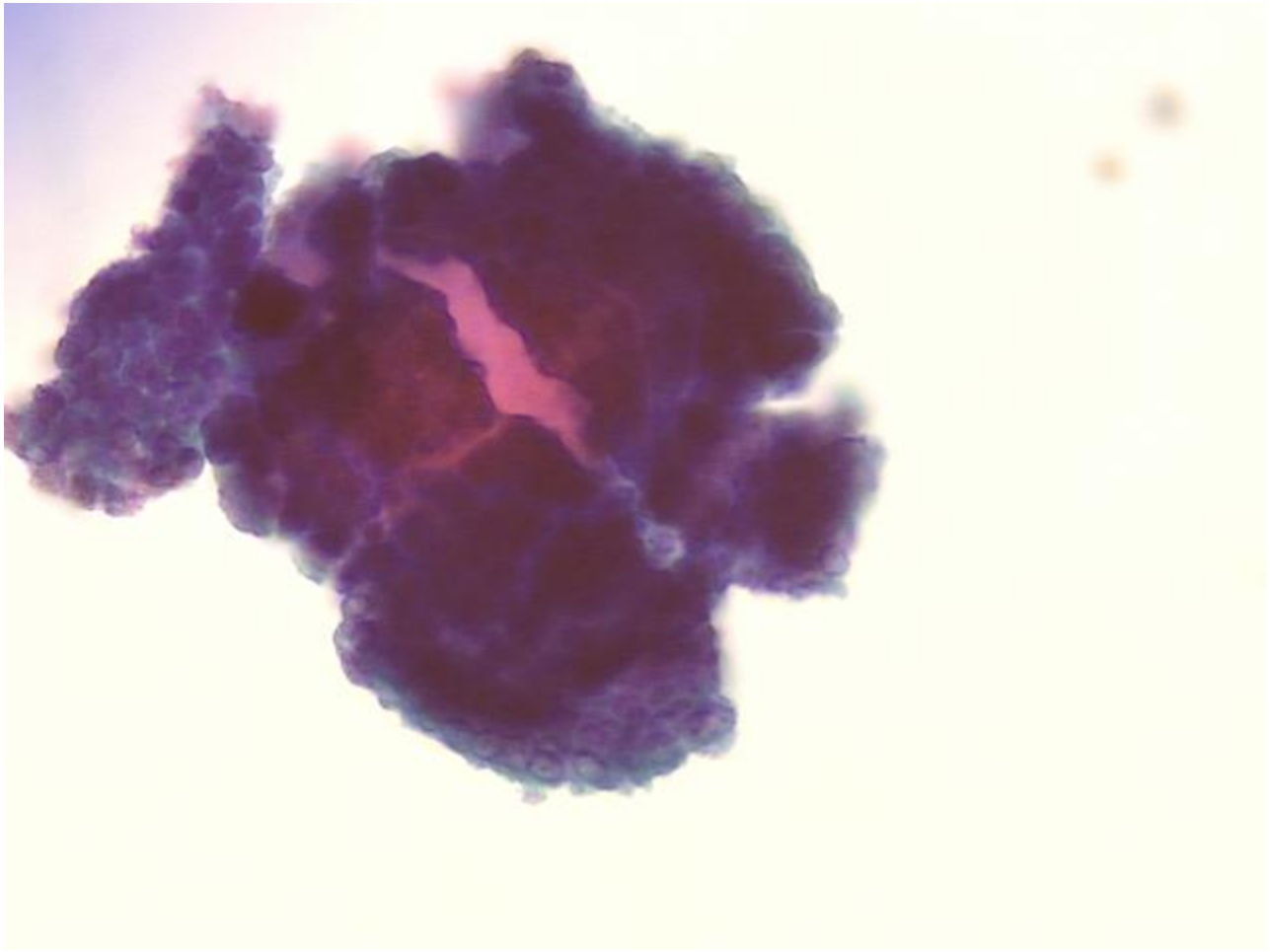
# Negative

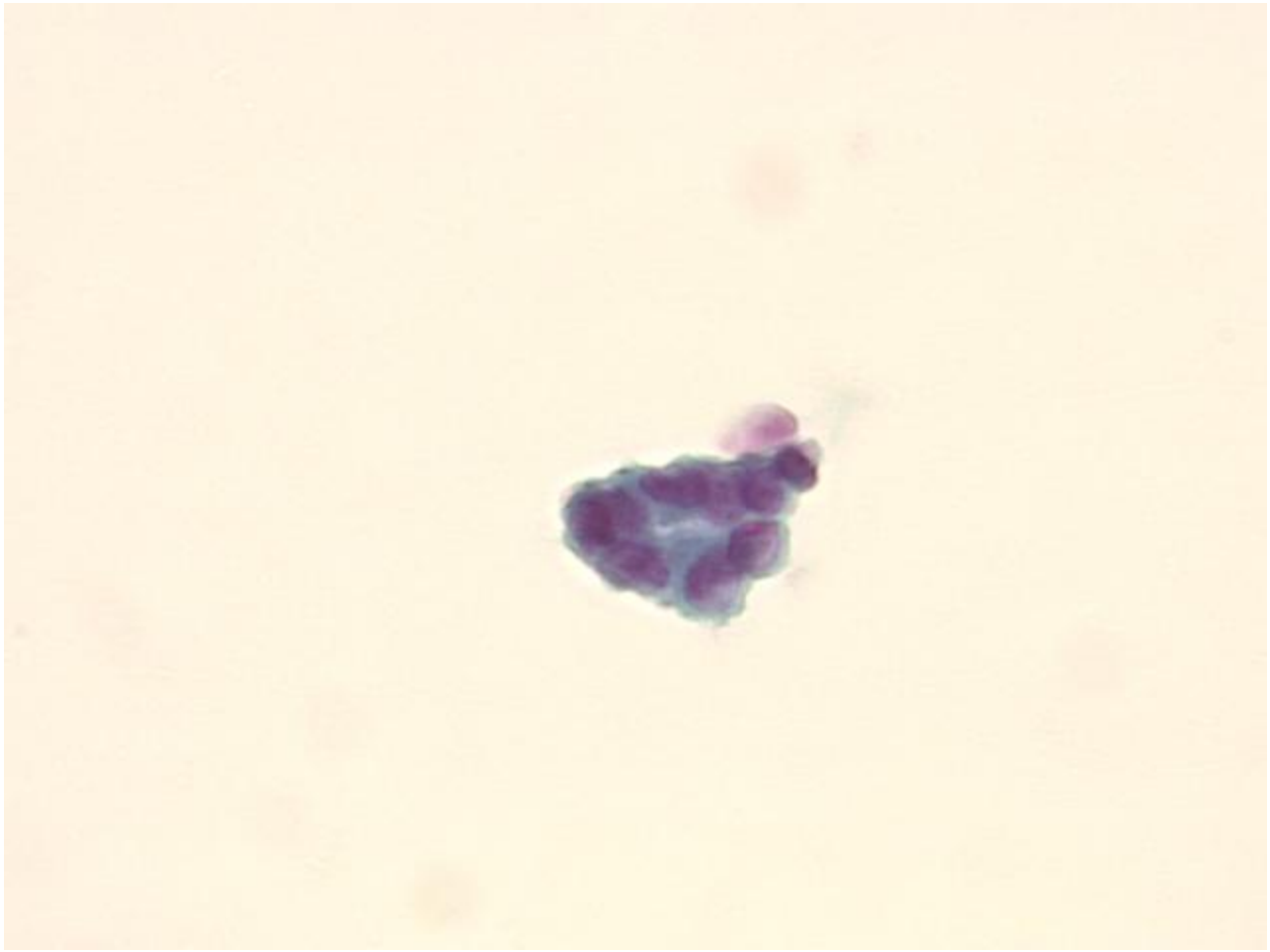
- No malignant features seen
- Triple approach (biopsy versus repeat FNA versus follow-up)

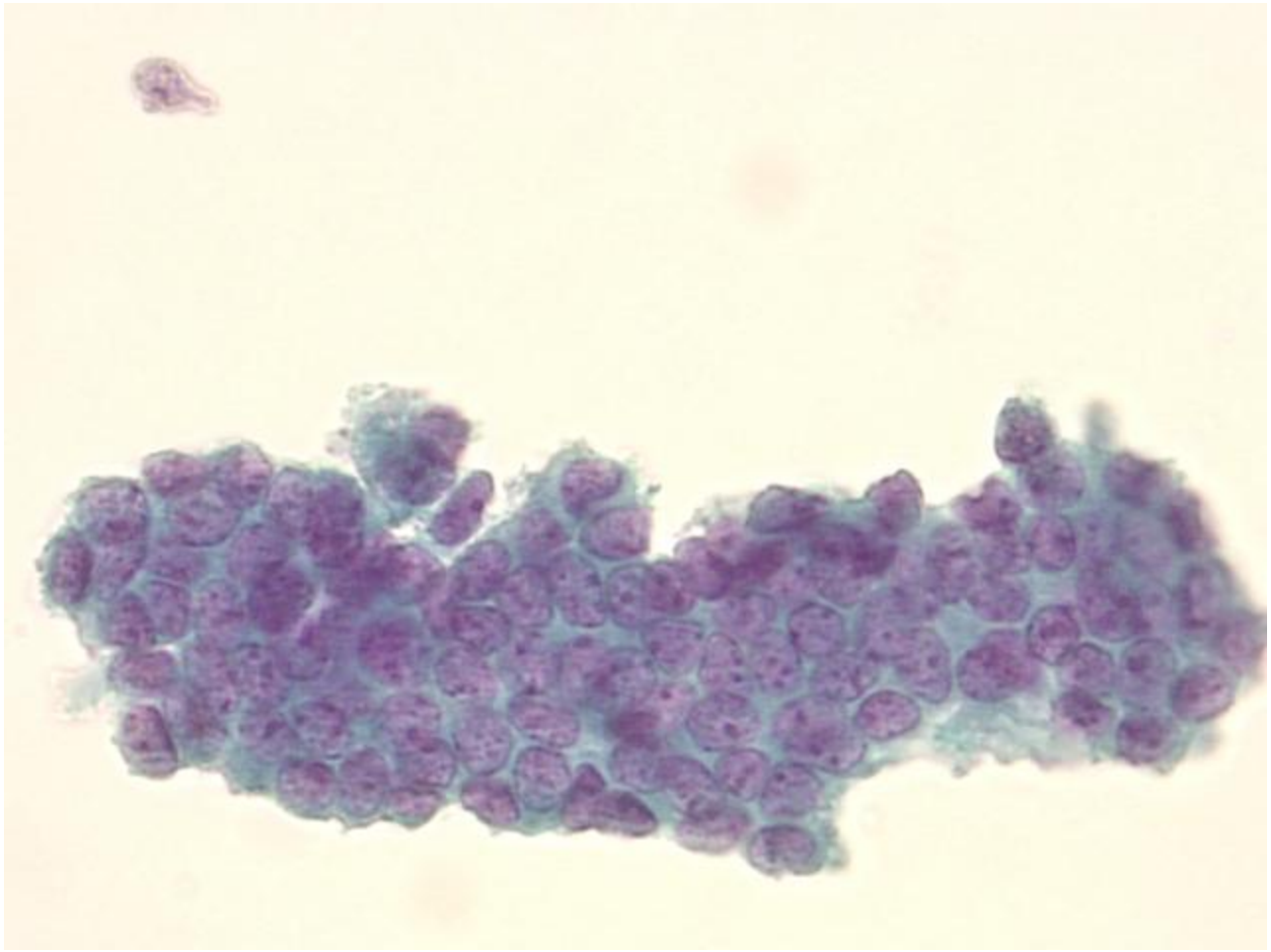
# Case 1

- 72 y.o. female with a palpable breast lump, LUOQ









# Cytological interpretation

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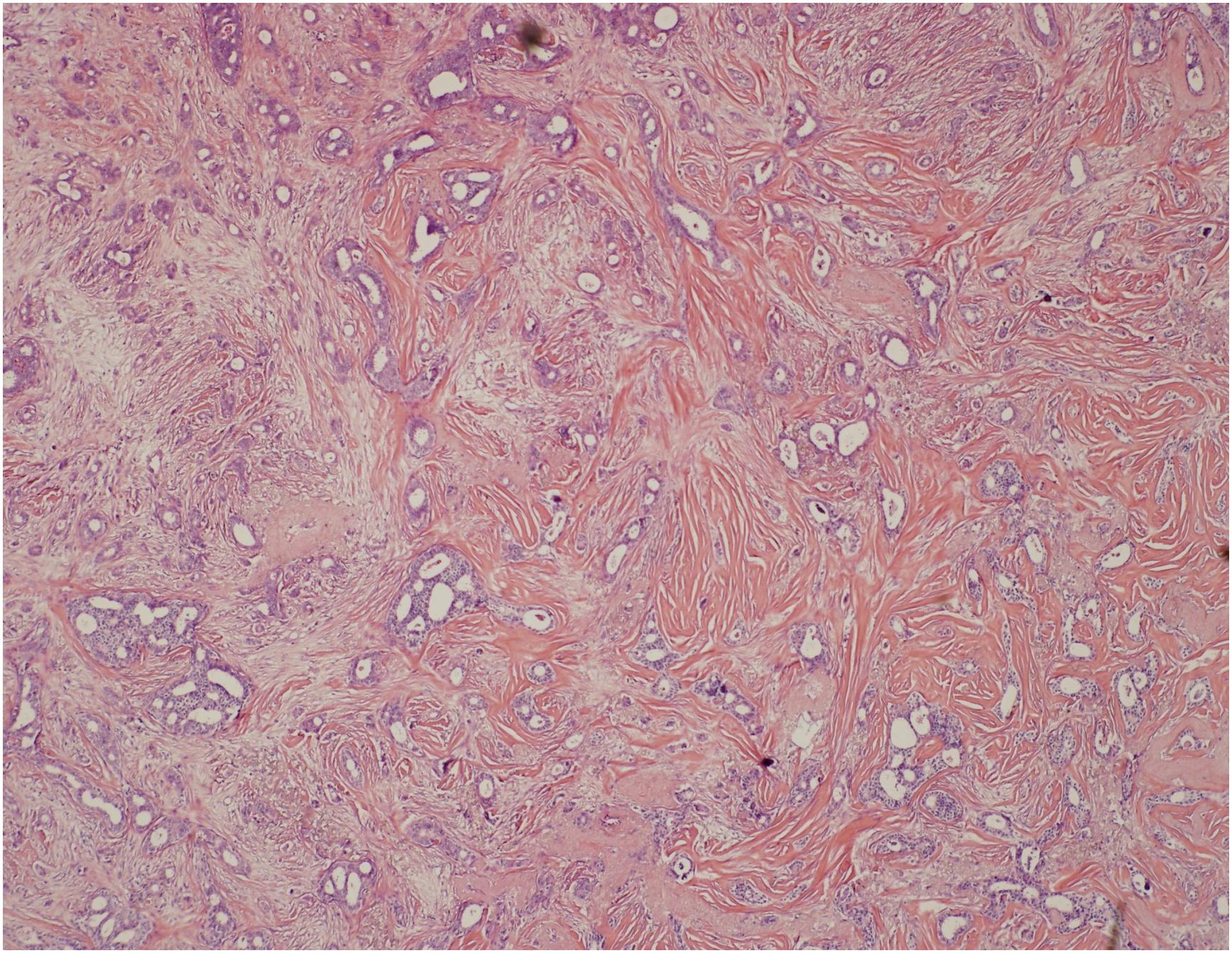
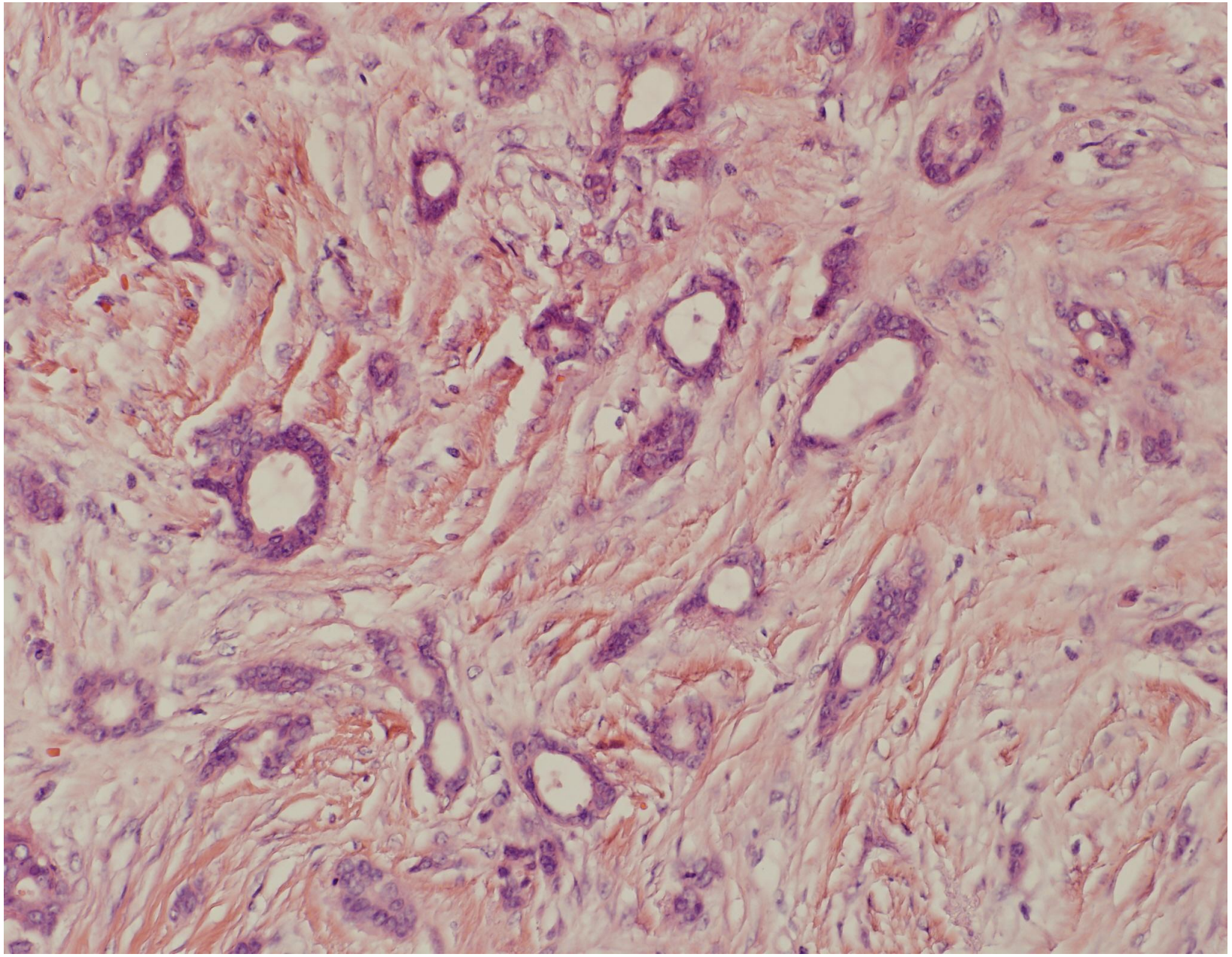




# Final histology

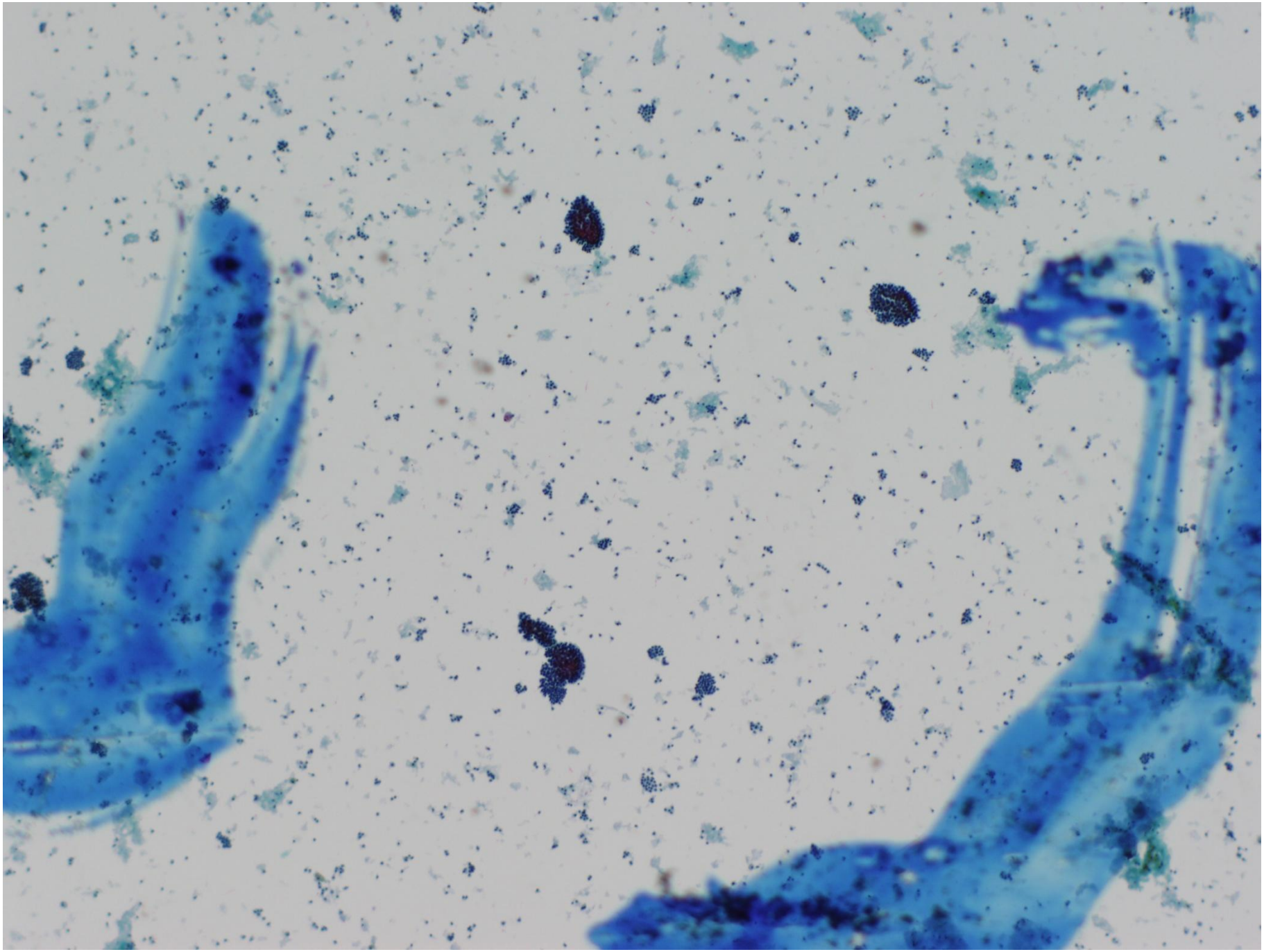
- Tubular mixed carcinoma
- Grade 1, 1 cm
- ER and PR positive
- 7/7 LNs negative

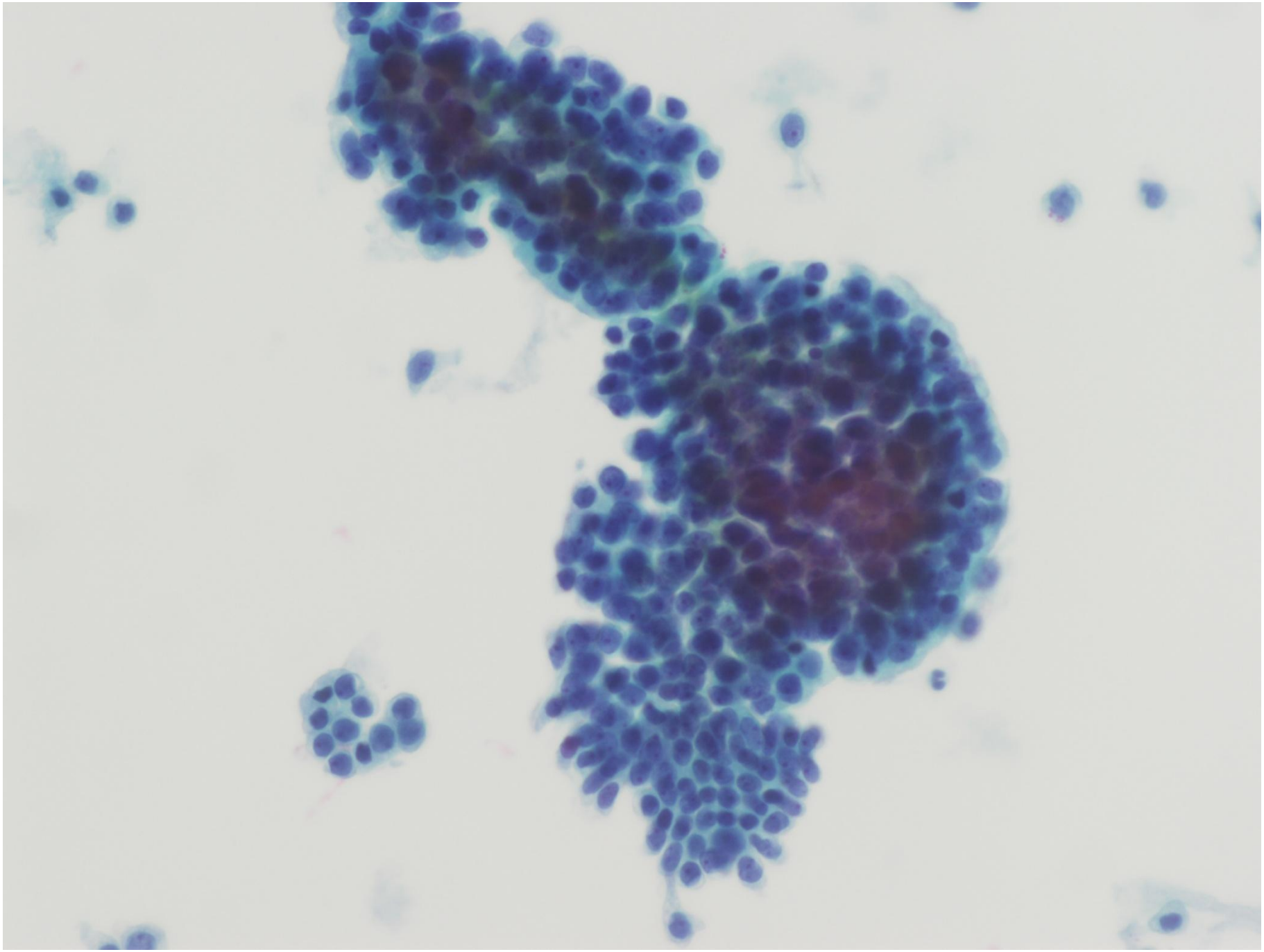
# Tubular carcinoma:cytologic features

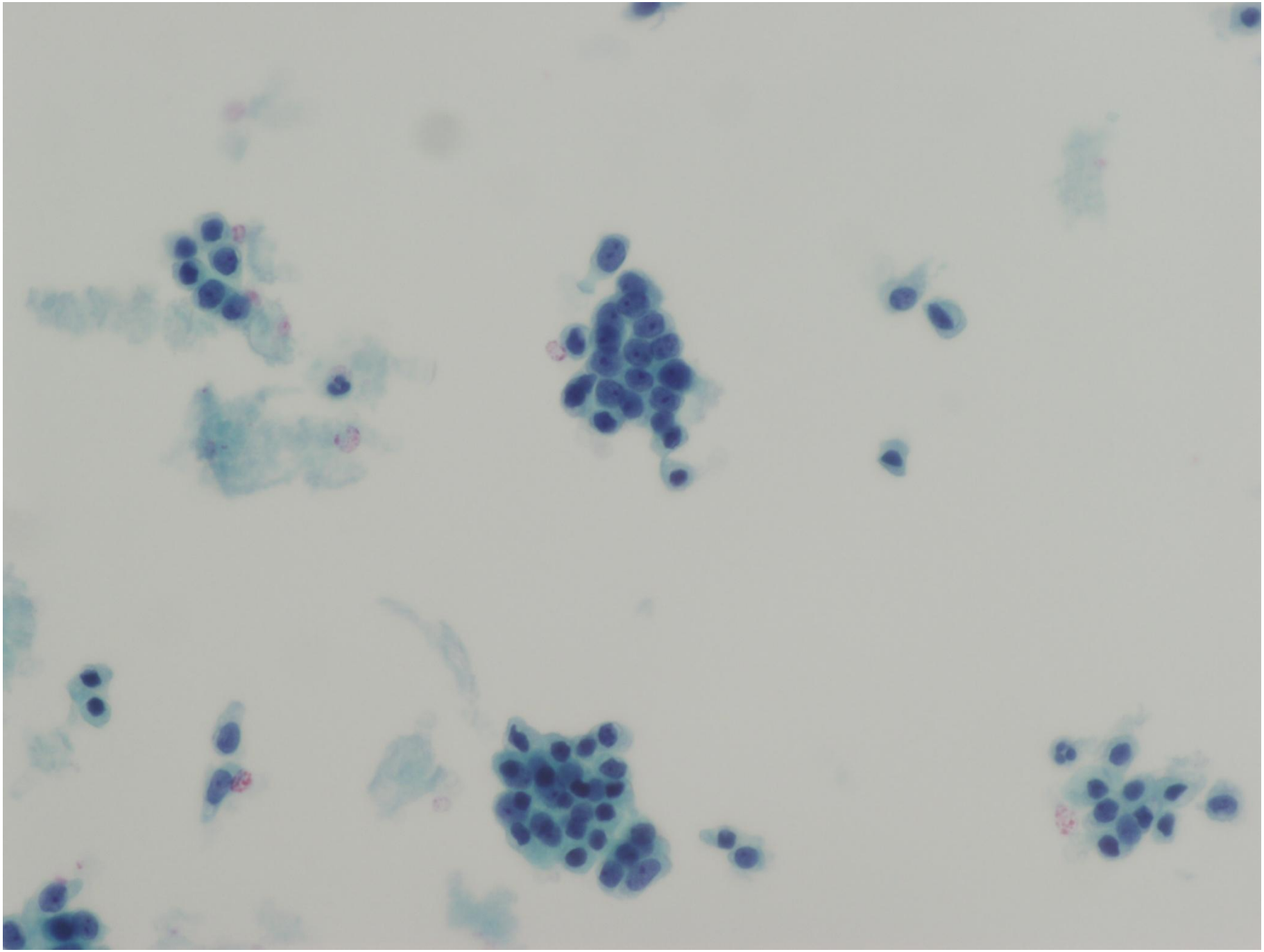
- Mild-moderate cellularity
- Compact clusters of monomorphic epithelial cells, multilayering; may see single epithelial cells
- Tubules with angulation
- Cells: moderate sized, scant cytoplasm, bland vesicular nuclei, even chromatin pattern
- Stripped bipolar nuclei
- Elastoid material

# Case 2

- 79 year old female
- Right breast mass and bloody nipple discharge







# Cytological interpretation?

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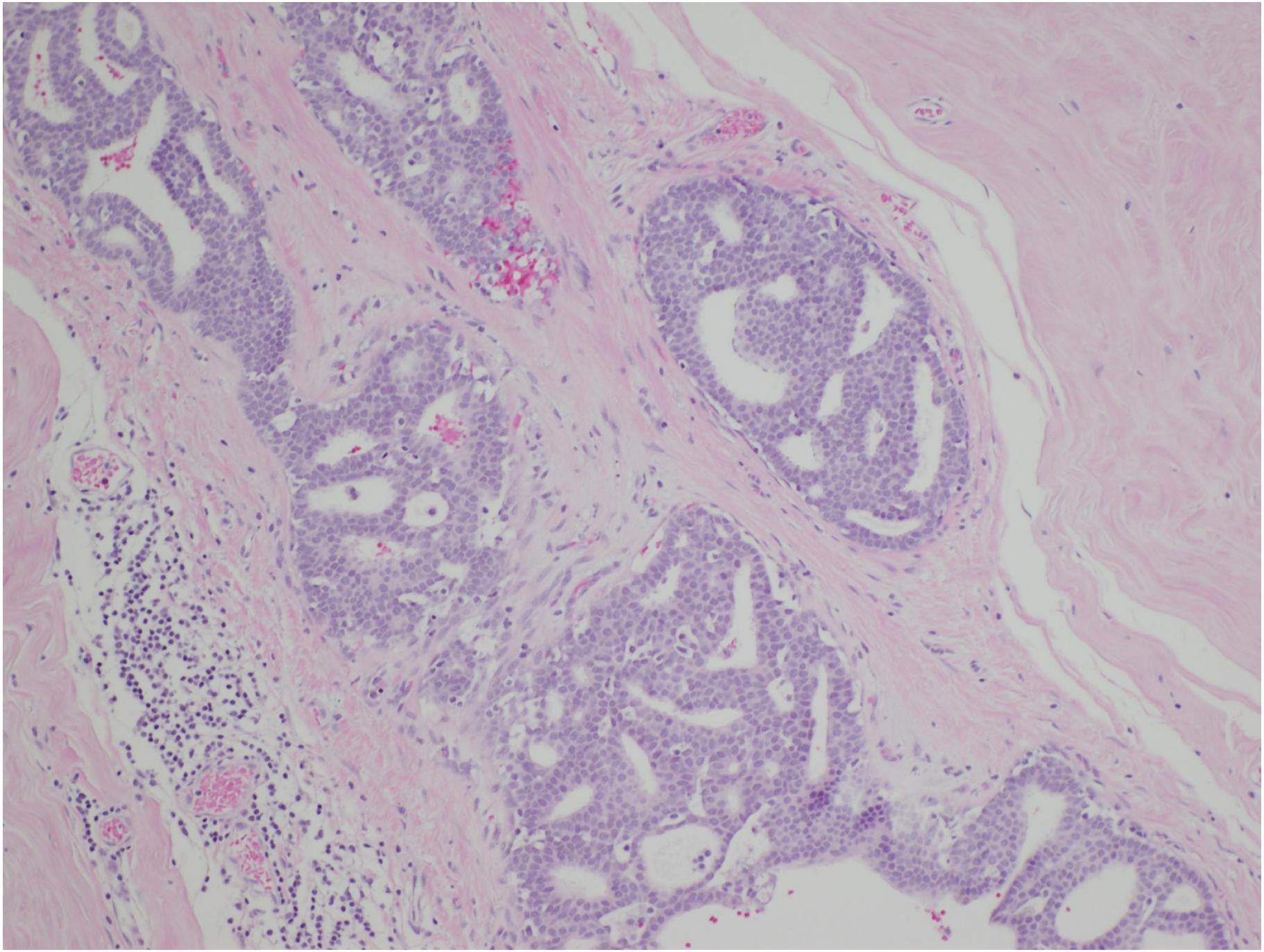


# Case 2

- Ductal carcinoma in situ, low-intermediate grade, ~6.0 cm in extent
- No invasive component
- 2/2 SLNs negative

# Liquid-based cytology in breast FNA

- Designed to improve the conventional cytological preparations by avoiding limiting factors:
  - Obscuring material
  - Air-dried artifacts
  - Irregular thickness of smears

# Liquid-based cytology in breast FNA

- Disadvantages:
  - Loss of informative background: stromal cells, extracellular material
  - Alterations in architecture: fragmentation of epithelial groups, loss of cohesion

# LBC: Fibroadenoma

- Some studies report lower diagnostic rate with LBC
- Smaller aggregates vs large branching sheets
- Decreased myoepithelial cells in BG
- Increased cellular dyshesion and prominent nucleoli, therefore more cases classified as atypical

# Fibroadenoma

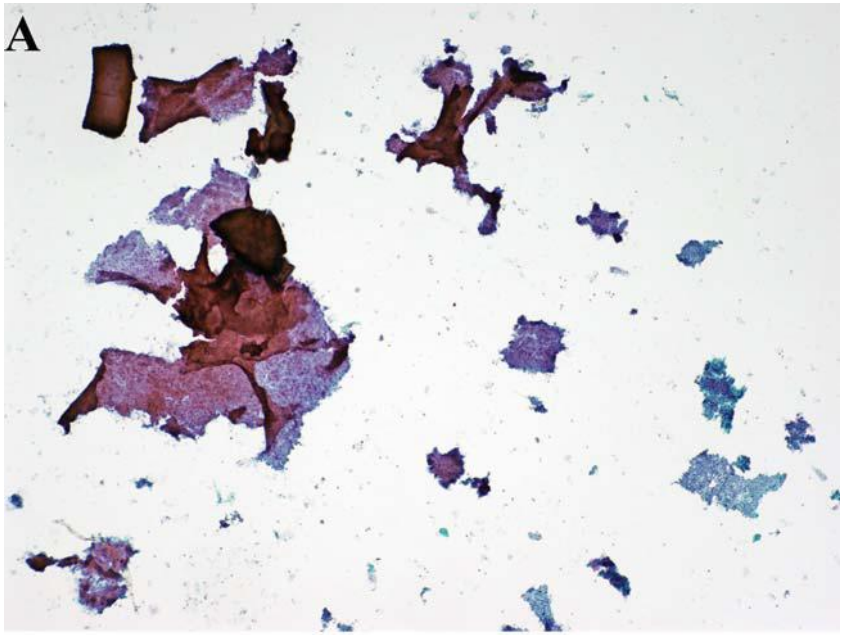
- Cellular
- Large cohesive branching sheets of ductal cells
- Numerous myoepithelial cells (bipolar cells)
- Fragments of fibromyxoid stroma

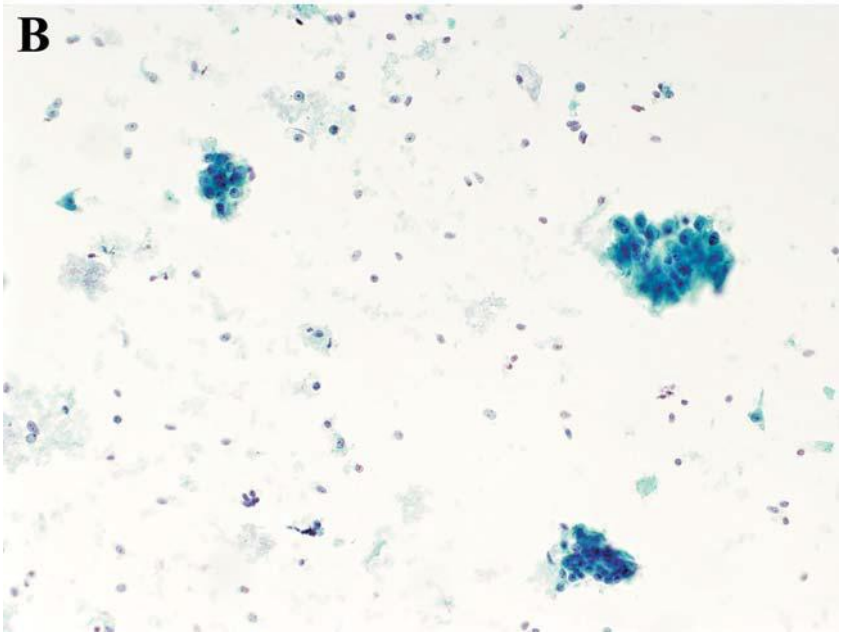
# Fine-Needle Aspiration Cytology of Mammary Fibroadenoma: A Comparison of ThinPrep® and Cytospin Preparations

Thai Yen Ly, M.D., Penny J. Barnes, M.D., and Rebecca F. MacIntosh, M.D.*

Diagnostic Cytopathology 2011;39(3): 181-187.

Cytospin case



ThinPrep® case

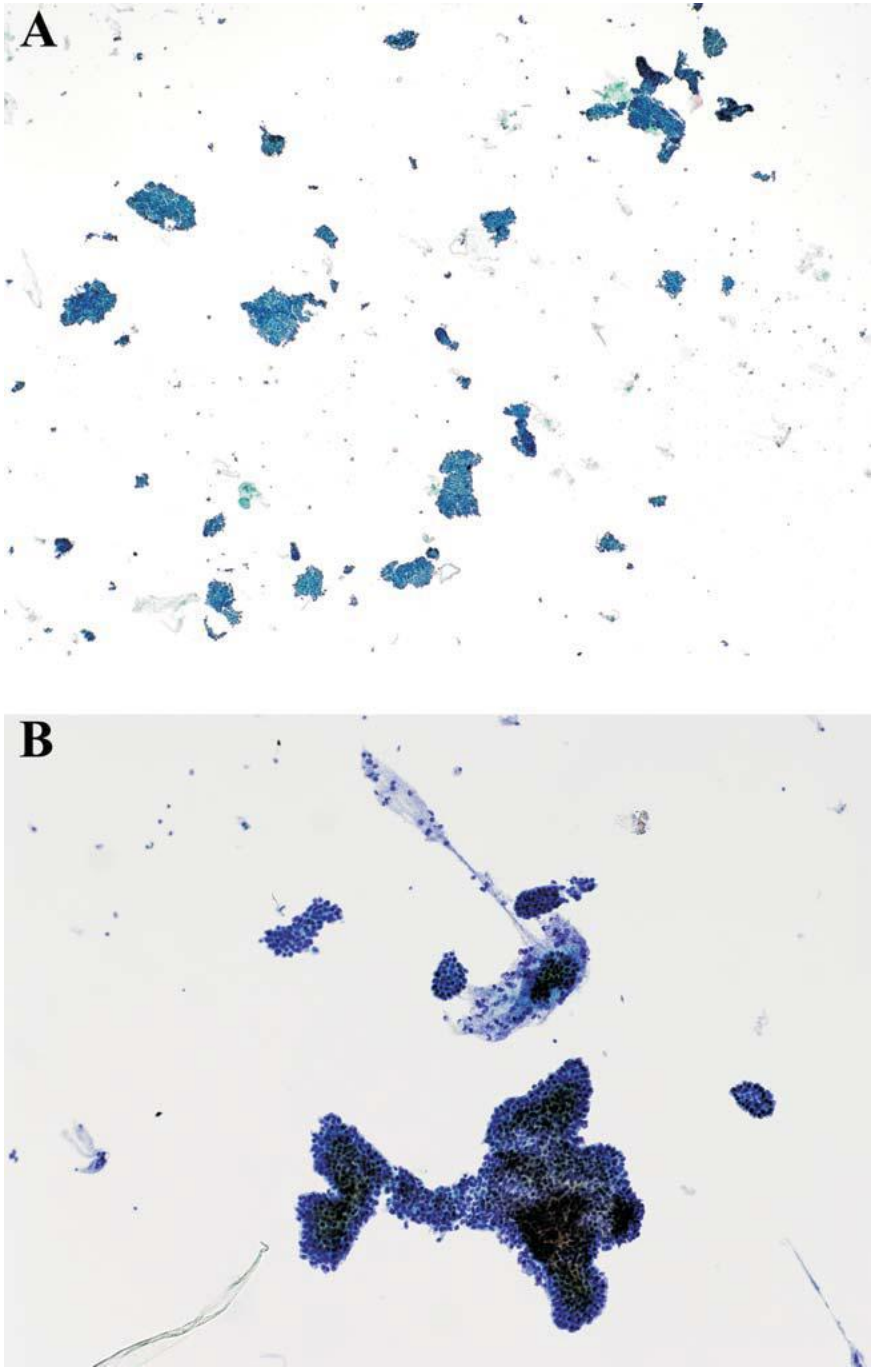


**Table I.** Performance Characteristics of CyS and TP for FNA Diagnosis of FA

| *Preparation* | *Sensitivity (%)* | *Specificity (%)* | *PPV (%)* | *NPV (%)* |
|---|---|---|---|---|
| Cytospin | 68 | 96 | 75 | 95 |
| ThinPrep® | 94 | 96 | 71 | 99 |

PPV, positive predictive value; NPV, negative predictive value.

**Table II.** Frequency of Cytomorphologic Features of FA in Histologically Concordant CyS and TP Cases

| *Feature* | *CyS (n = 21)* | *TP (n = 15)* |
|---|---|---|
| Marked cellularity | 3 (14%) | 14 (93%) |
| High cellularity | 12 (57%) | 1 (7%) |
| Moderate cellularity | 5 (24%) | 0 (0%) |
| Hypocellular | 1 (5%) | 0 (0%) |
| Large epithelial cell groups | 20 (95%) | 15 (100%) |
| Staghorn configurations | 21 (100%) | 13 (87%) |
| Stroma | 14 (67%) | 15 (100%) |
| Stripped nuclei | 21 (100%) | 15 (100%) |
| Mean number of stripped nuclei | 33/HPF | 15/HPF |

# Fibroadenoma

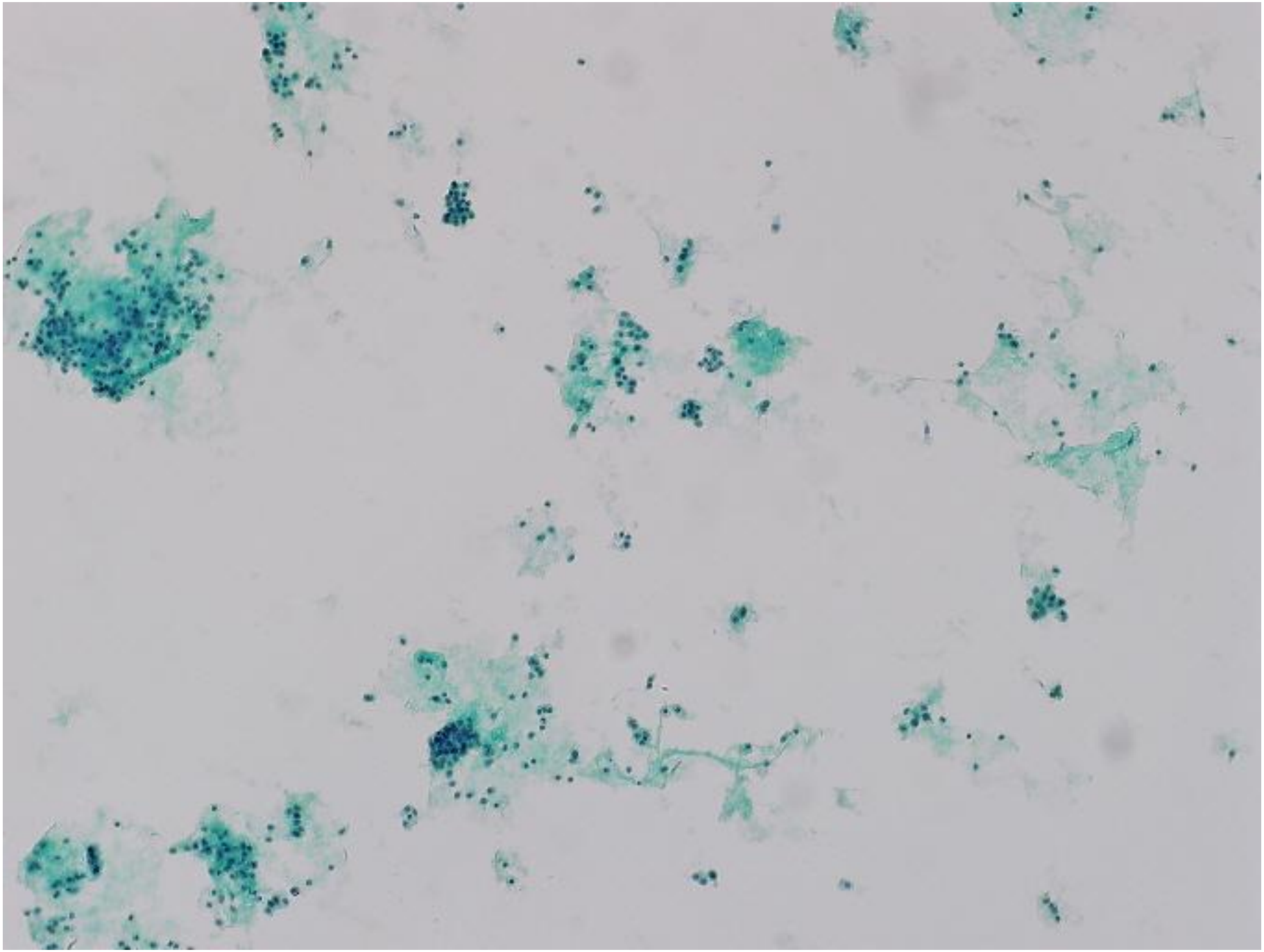
- Ly et al. Cytohistologic correlation rates for FA diagnosis on FNA were higher for ThinPrep (68%) compared with Cytospin (55%)

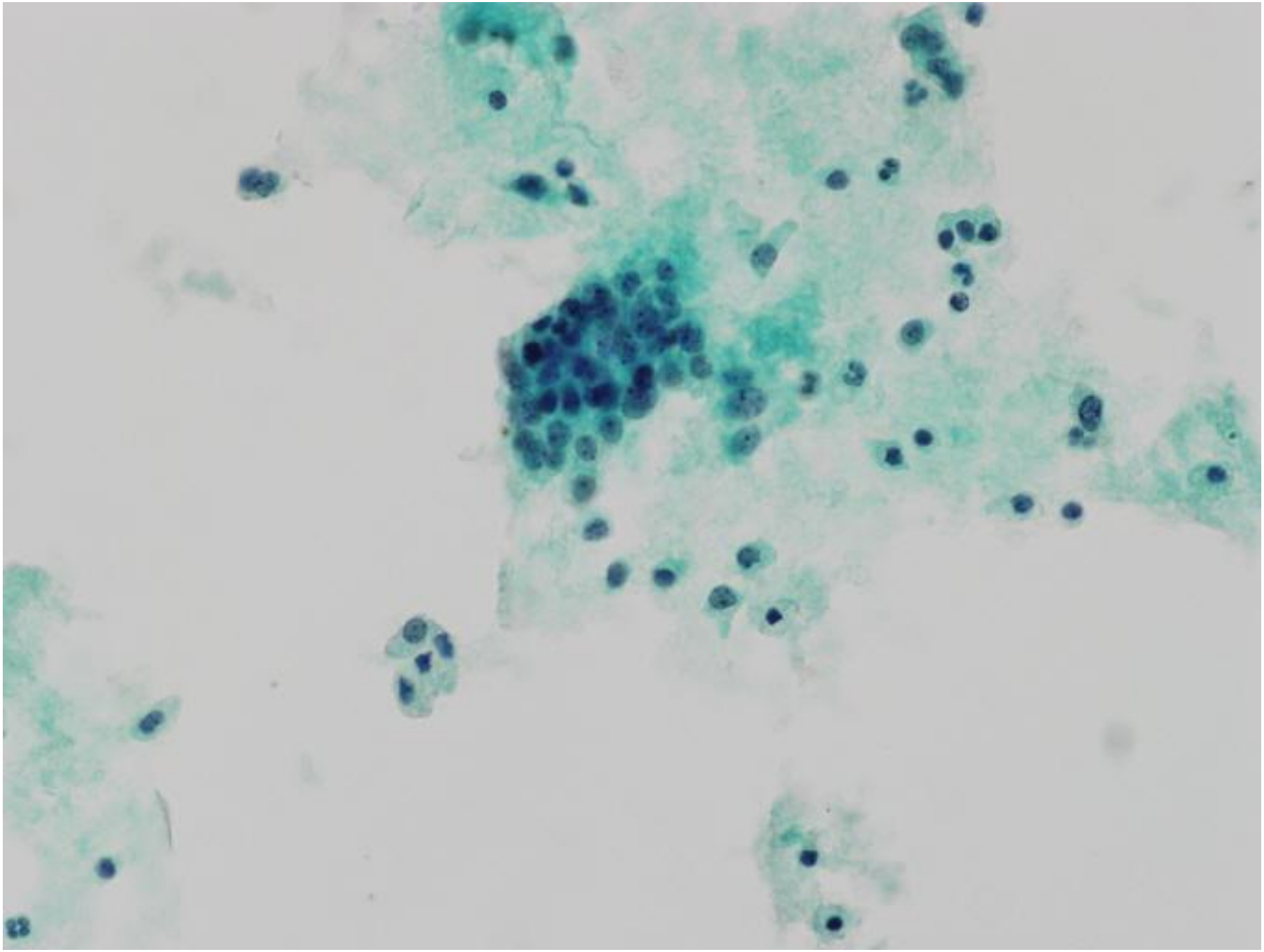
# Papillary lesions

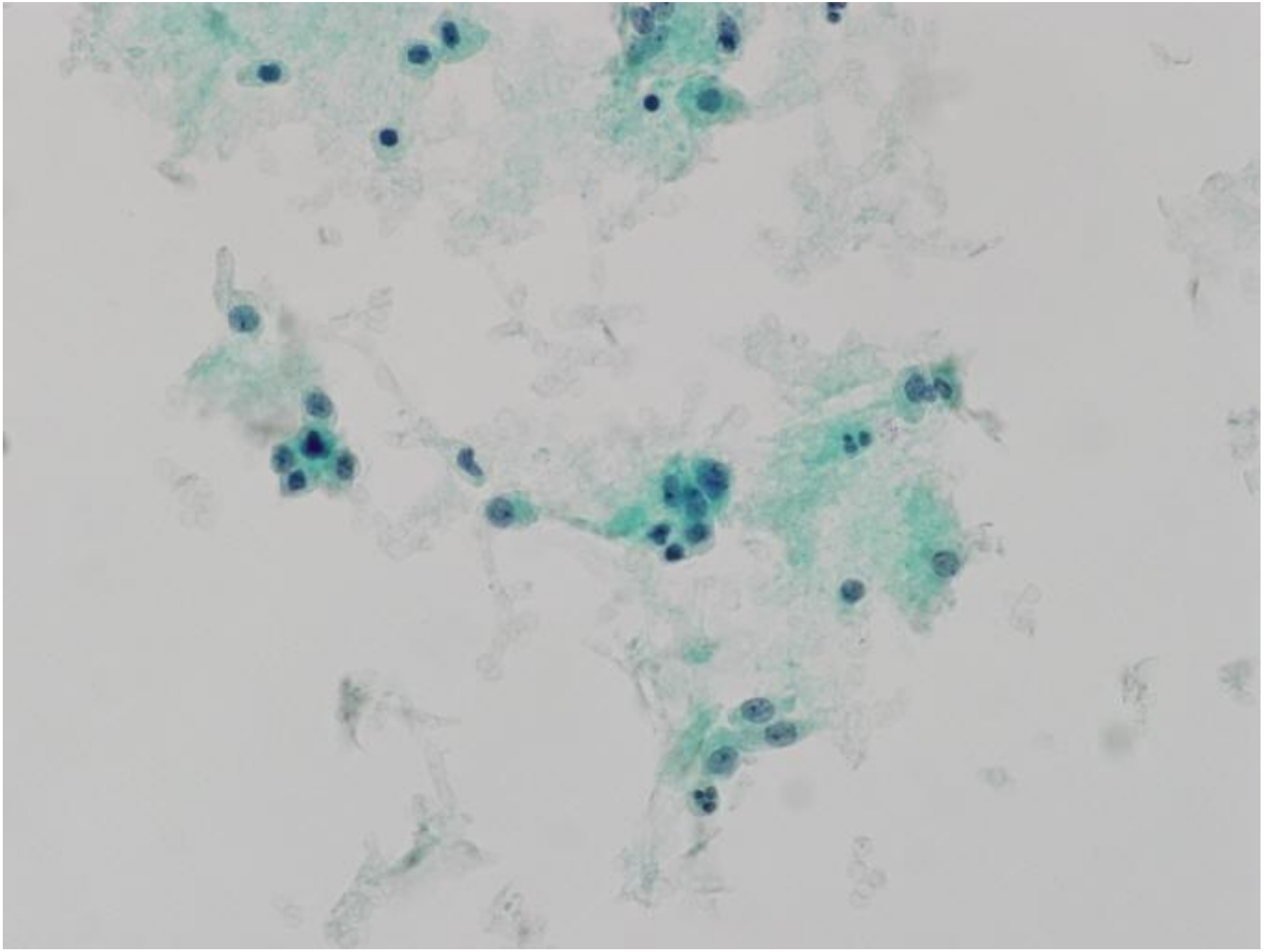
- Papillary clusters
- Single columnar cells
- Difficult to identify on FNA
- No studies of papillary breast lesions using LBC preparations

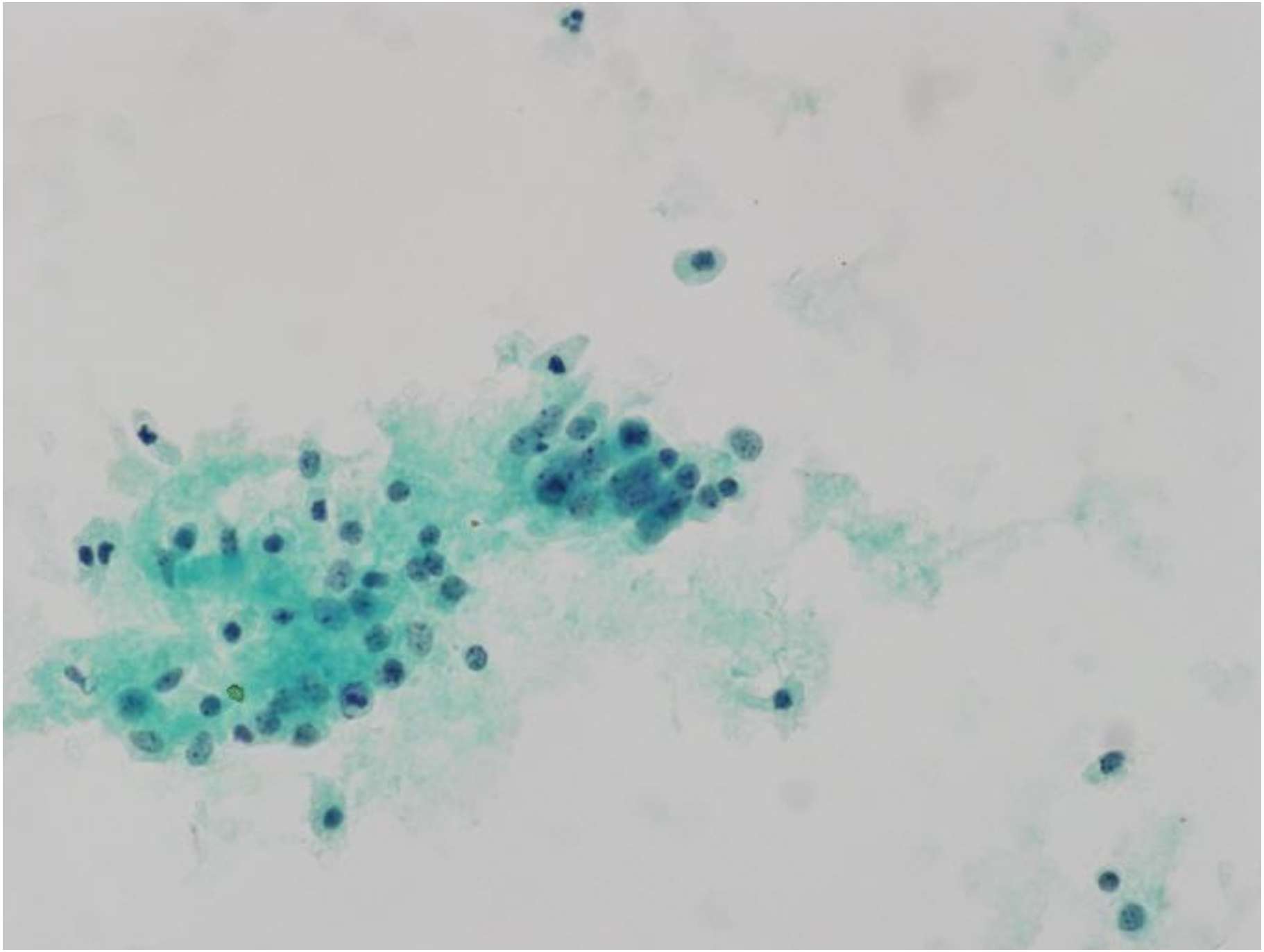
# Case 3

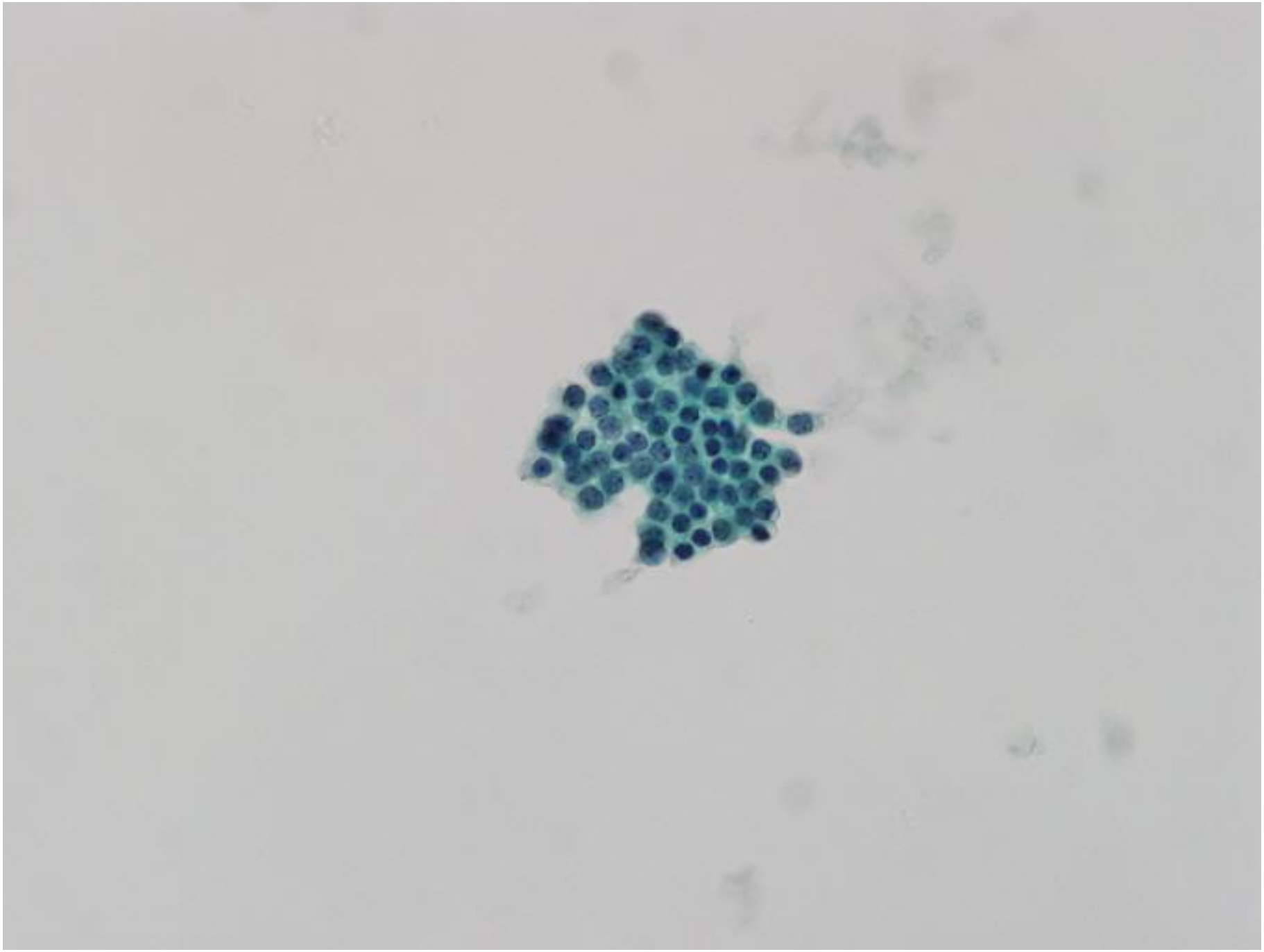
- 67 year old female
- Mass in breast





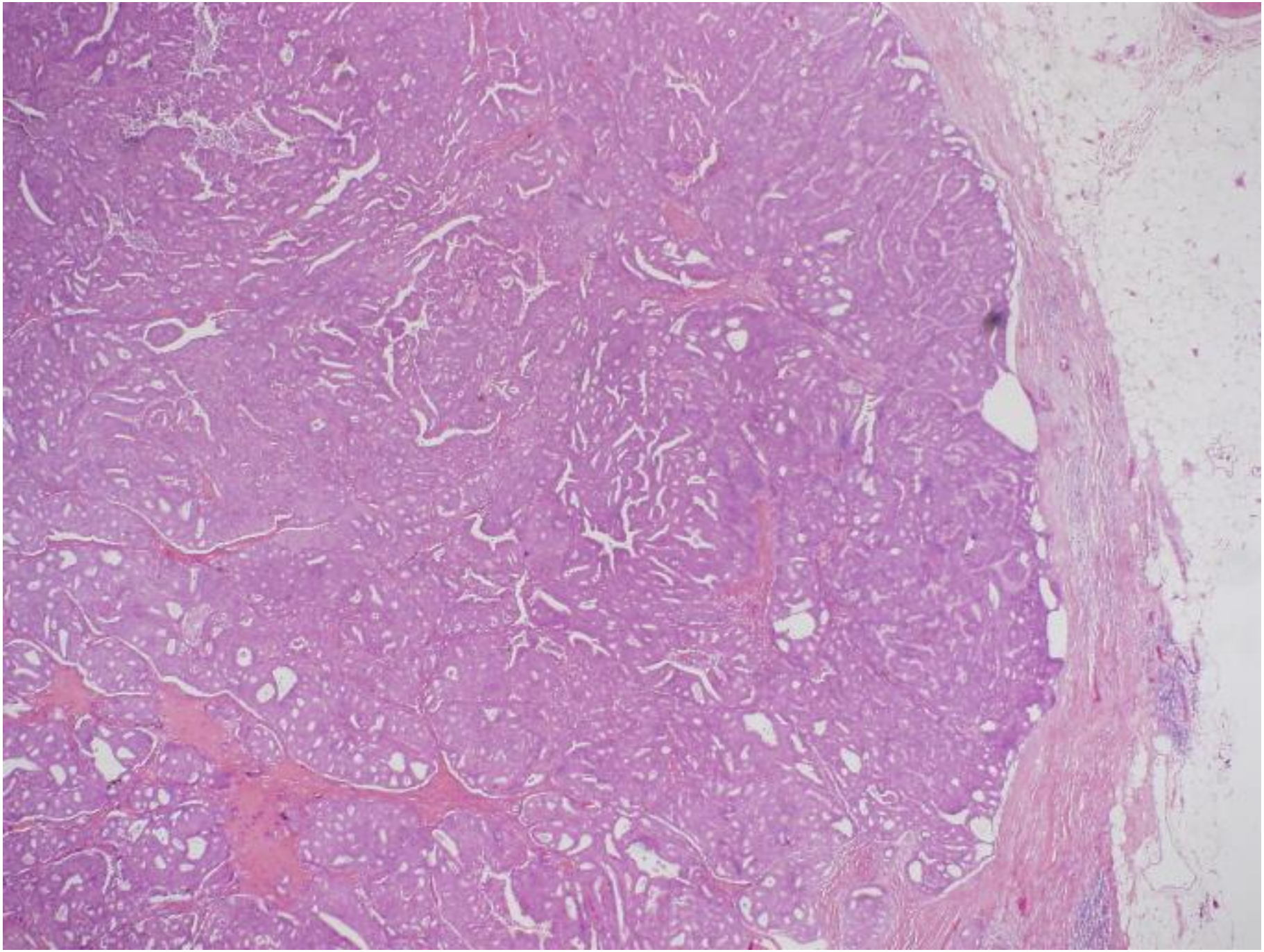


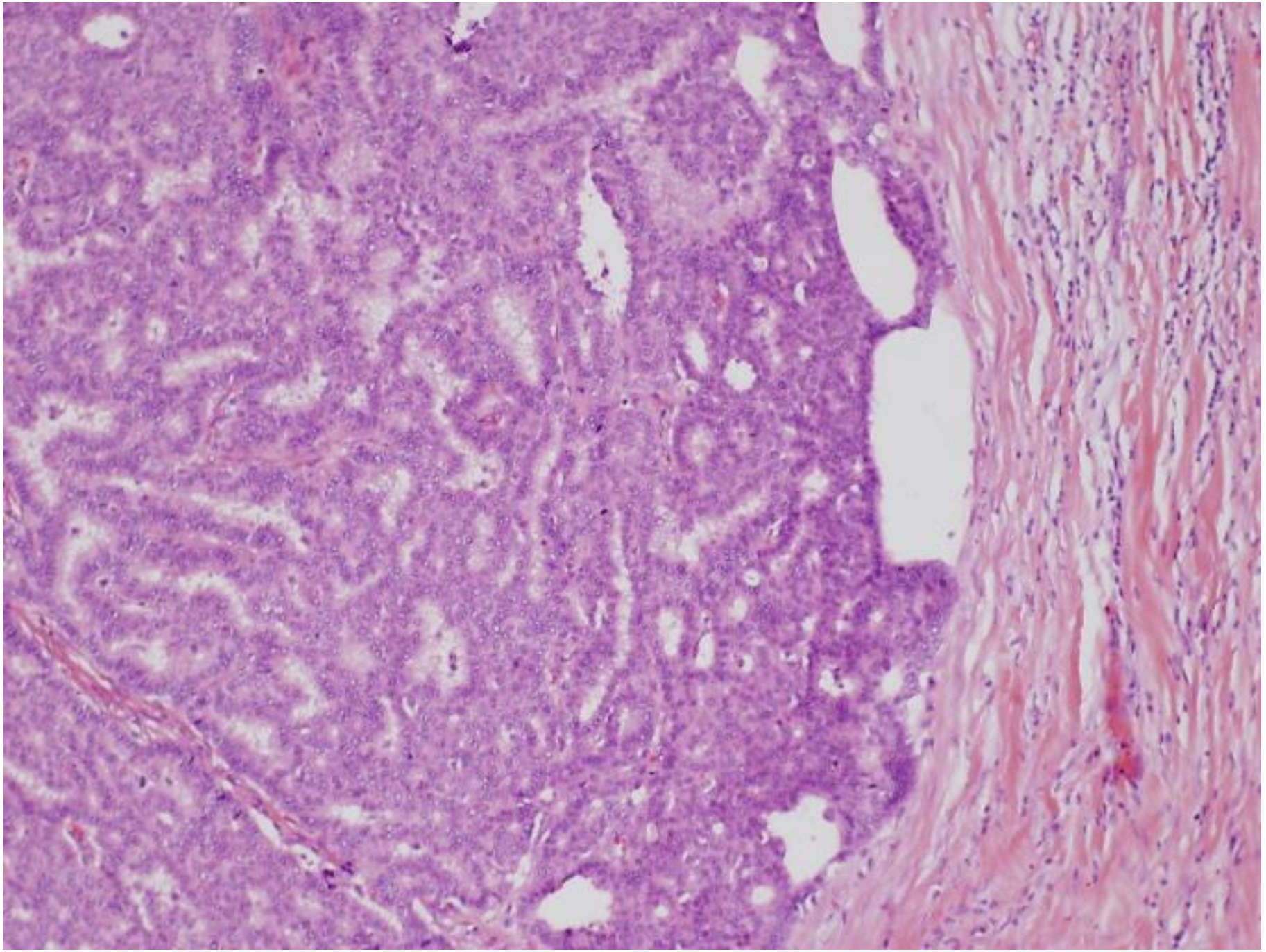




# Cytological Diagnosis

- Abnormal
- Moderately cellular specimen consisting of ductal cells with minimal nuclear atypia. Single cells and small clusters are present in the background. A low grade ductal carcinoma cannot be excluded.





# Histological Diganosis

- Breast, wide local excision (right) – Encapsulated papillary carcinoma, low grade

# Encapsulated Papillary Carcinoma

- Cytological Features
  - No single feature distinguishes EPC from papilloma
  - Cyst contents may be main finding
  - Papillary cores covered by columnar cells are diagnostic of papillary lesion
  - Rounded cell clusters of small hyperchromatic cells with “mulberry-like” appearance
  - Detached columnar cells may be prominent

# Breast carcinoma

- LBC:
  - Loss of background material: necrotic debris, blood, mucin
  - More prominent nucleoli, hyperchromasia, less coarse chromatin (SurePath vs CS)
  - Flattened cell aggregates (TP vs CS)

# Diagnostic performance

- Very similar LBC or CS
- Sensitivity: 84% CS, 86% TP
- Specificity: 98.6% CS, 96.5% TP
- PPV: 96.5% CS, 95% TP
- NPV: 91% CS, 88% TP

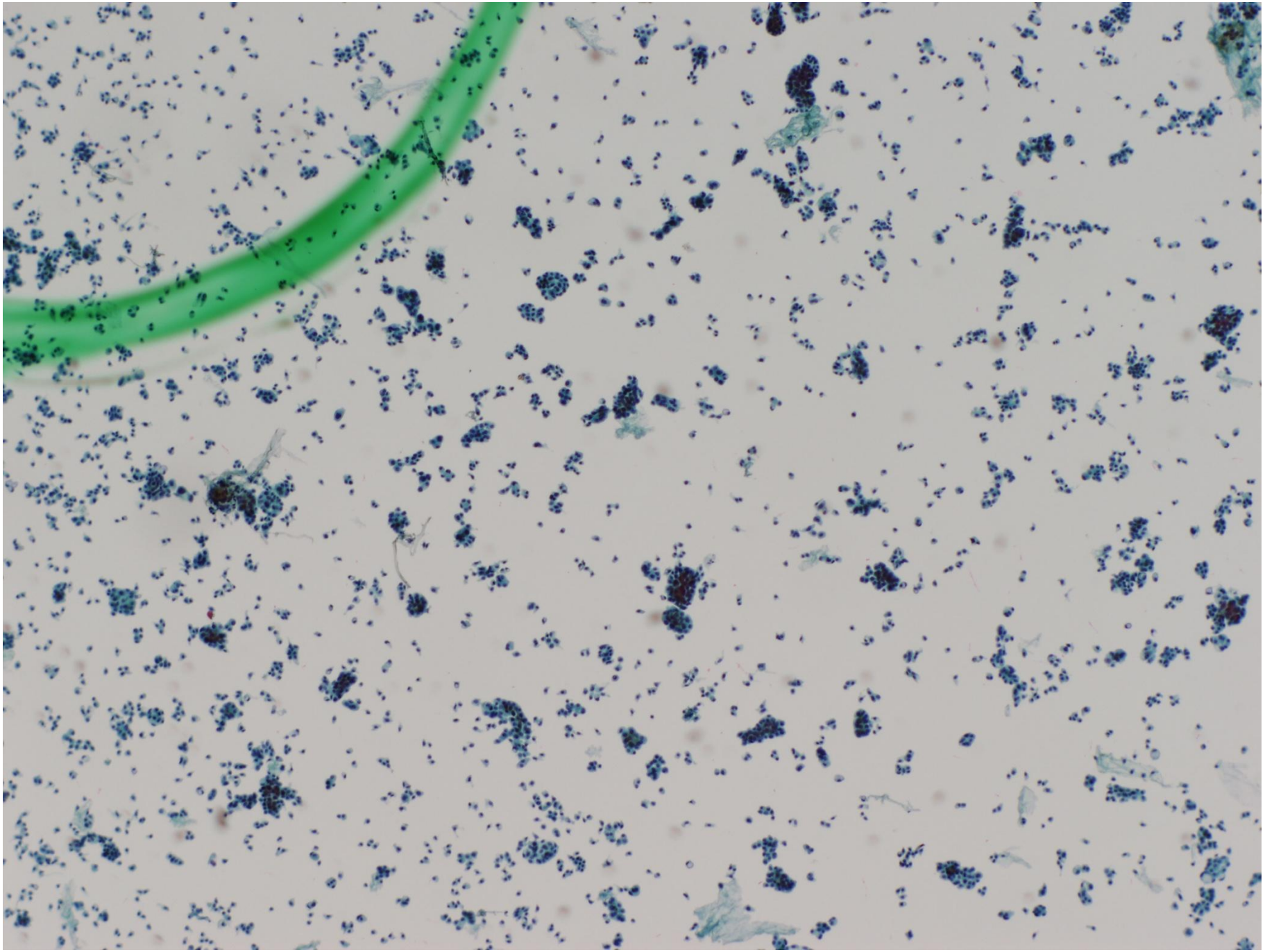
# Ancillary studies

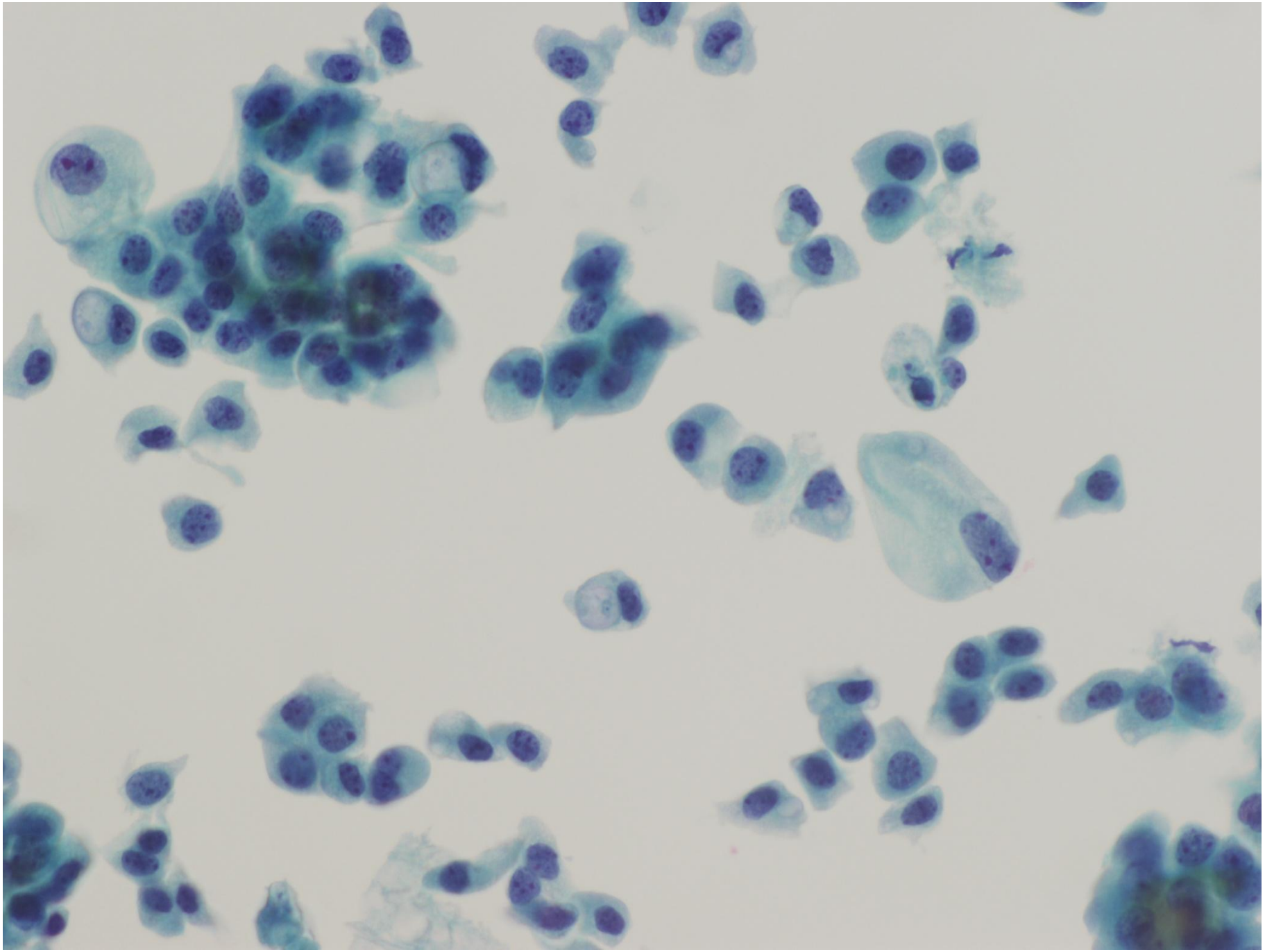
- ER/PR: requires validation for cytopathology protocols

  - studies show good concordance with LBC methods, air-dried smears, cell blocks
- HER2: ASCO/CAP guidelines suggest HER2 ISH on cell blocks

# Case 4

- 79 year old female
- Left breast mass





# Cytological interpretation

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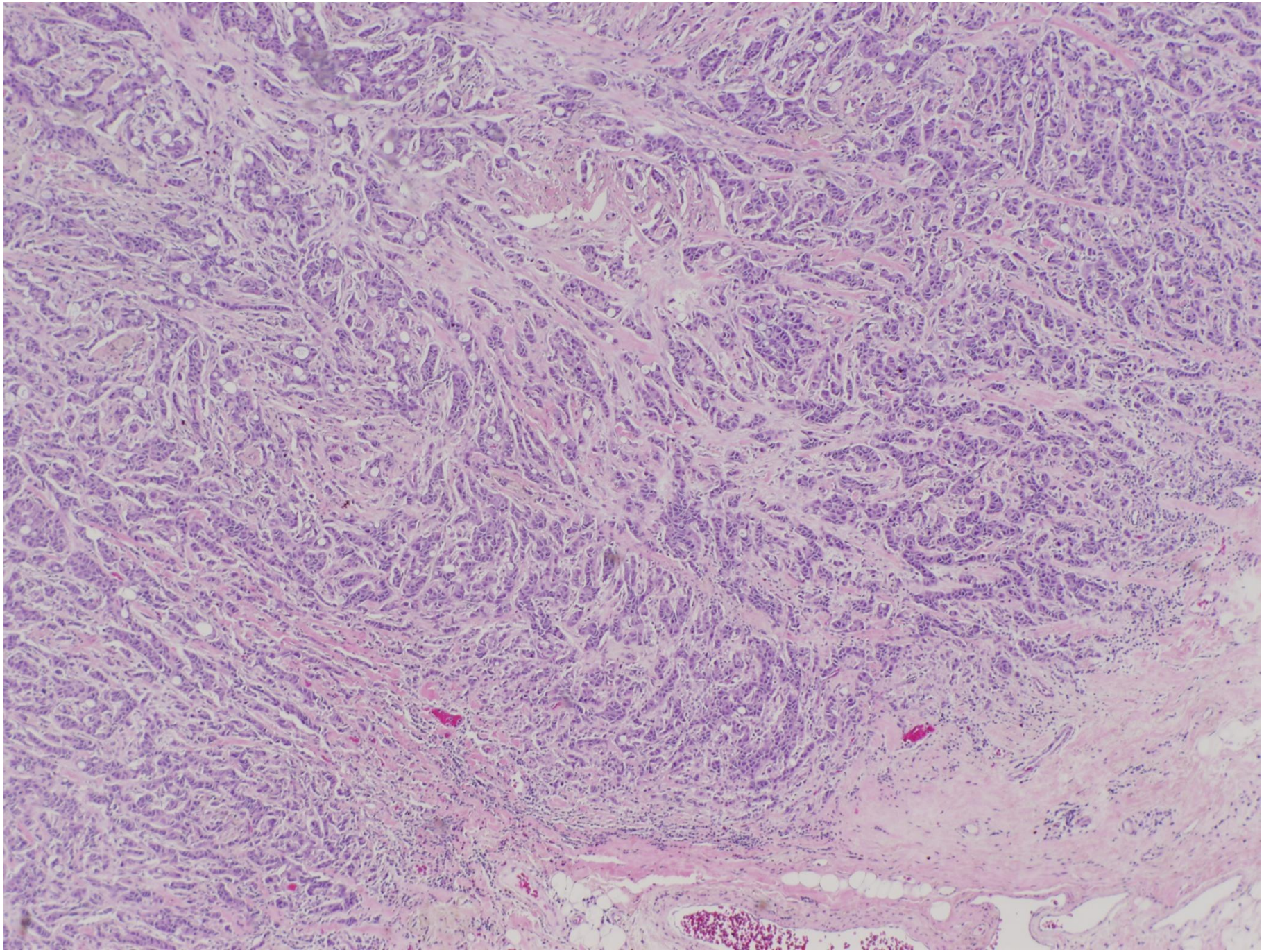
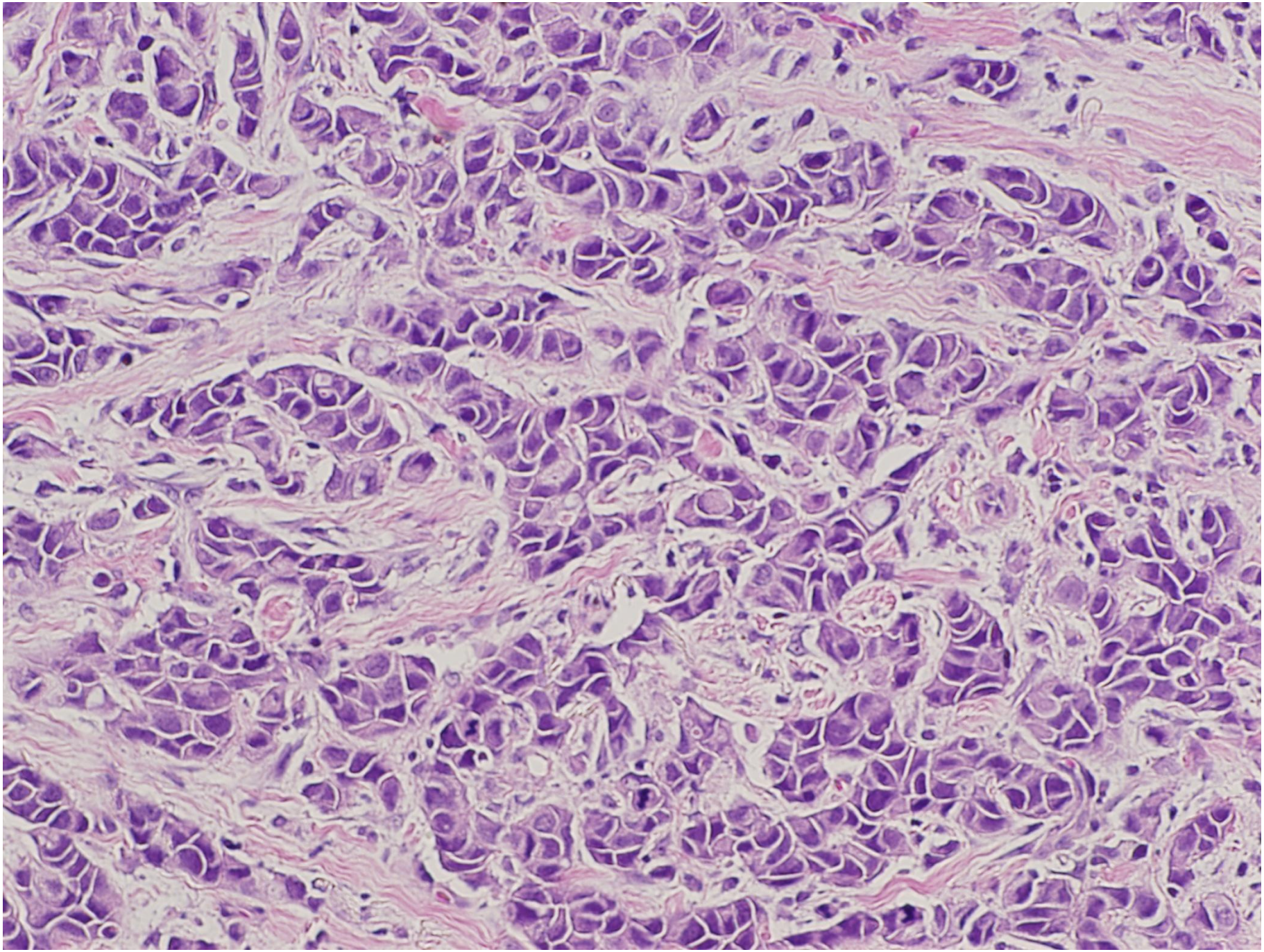


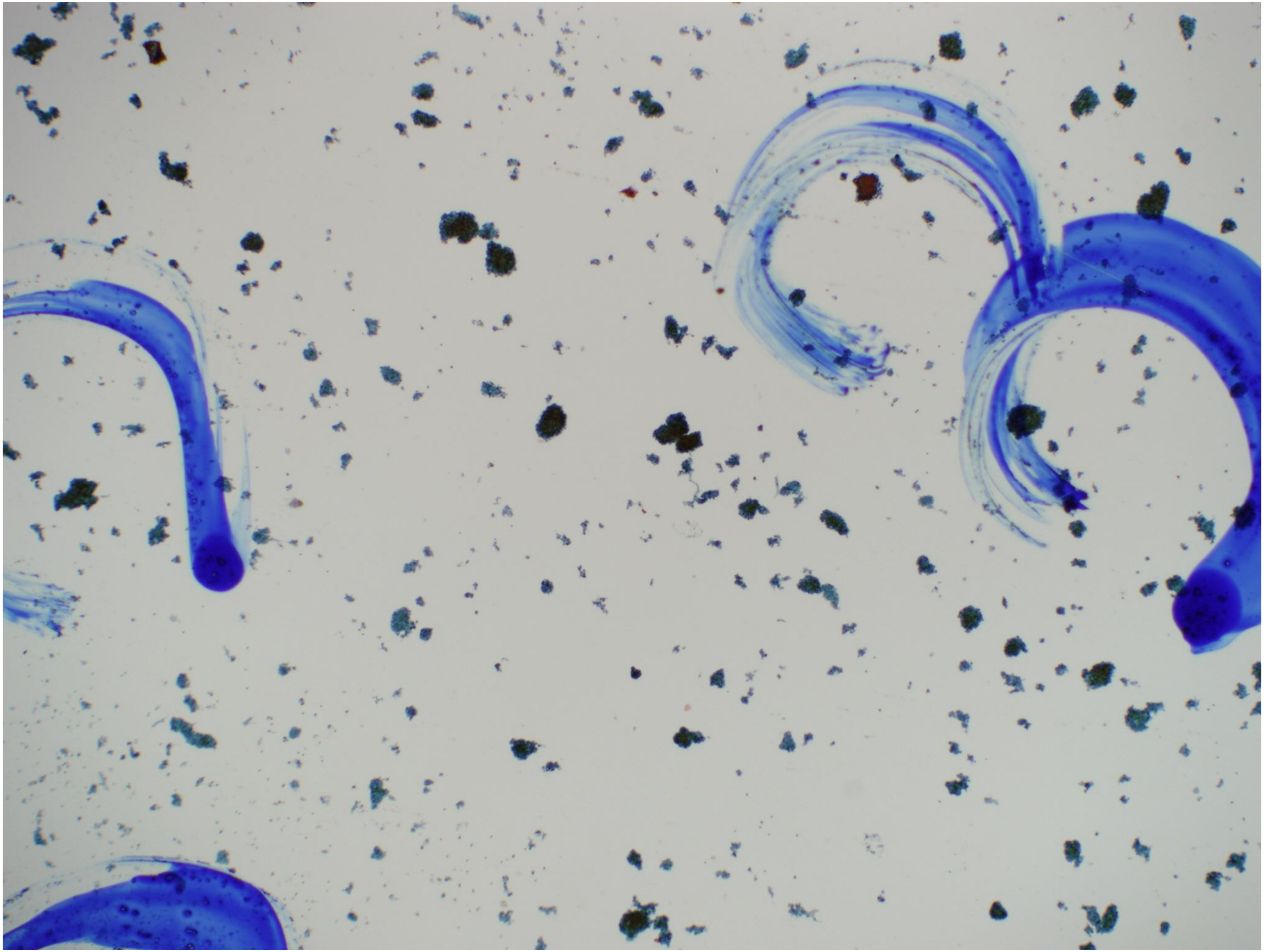


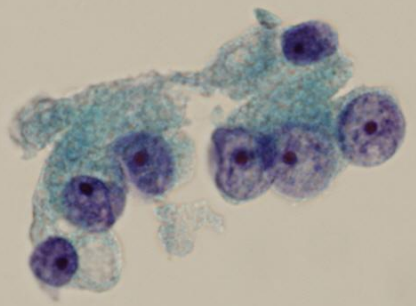
# Case 4

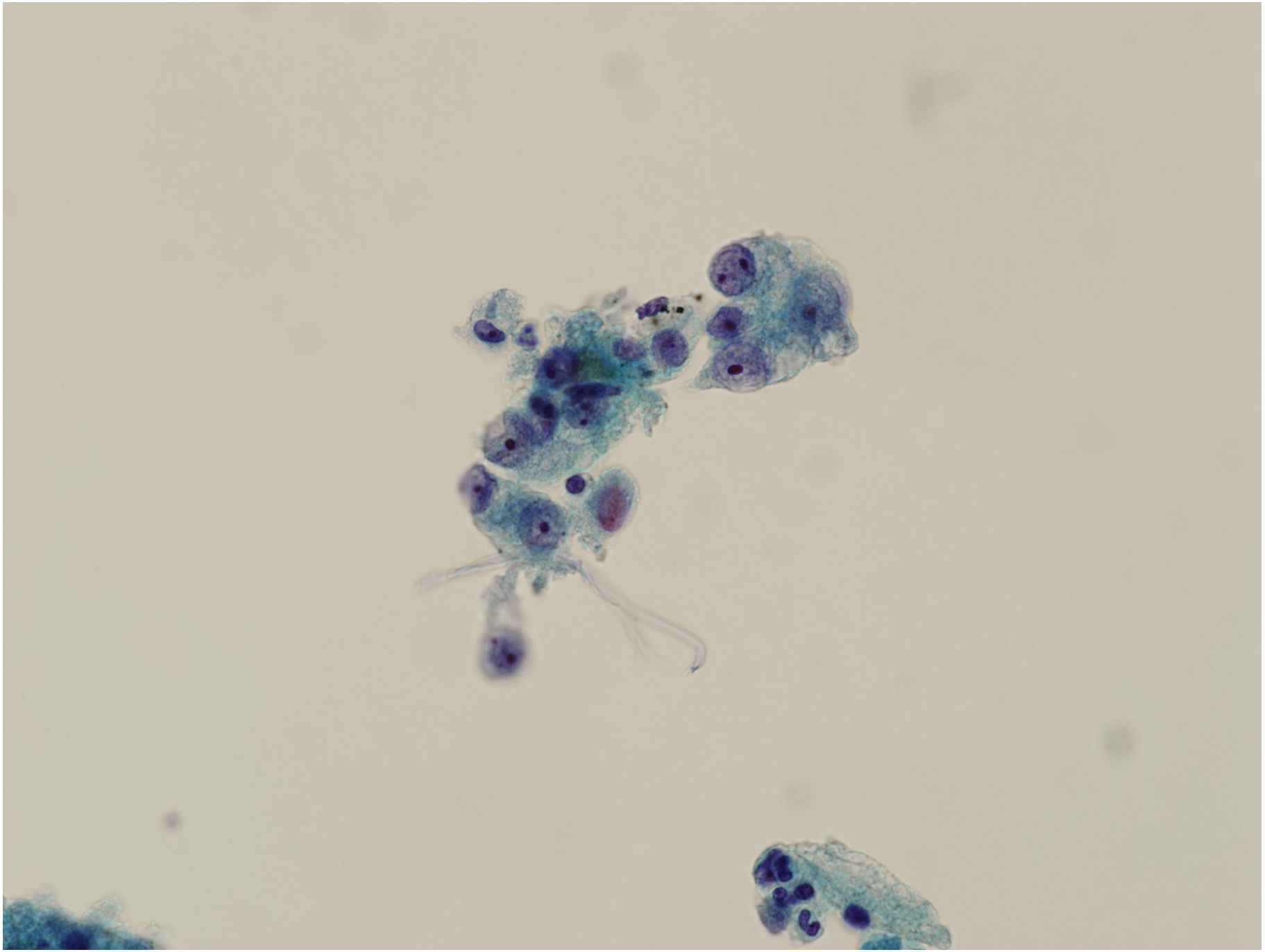
- Multifocal invasive ductal carcinoma, NST
- Nottingham grade 3
- ER positive, PR negative
- HER2 positive

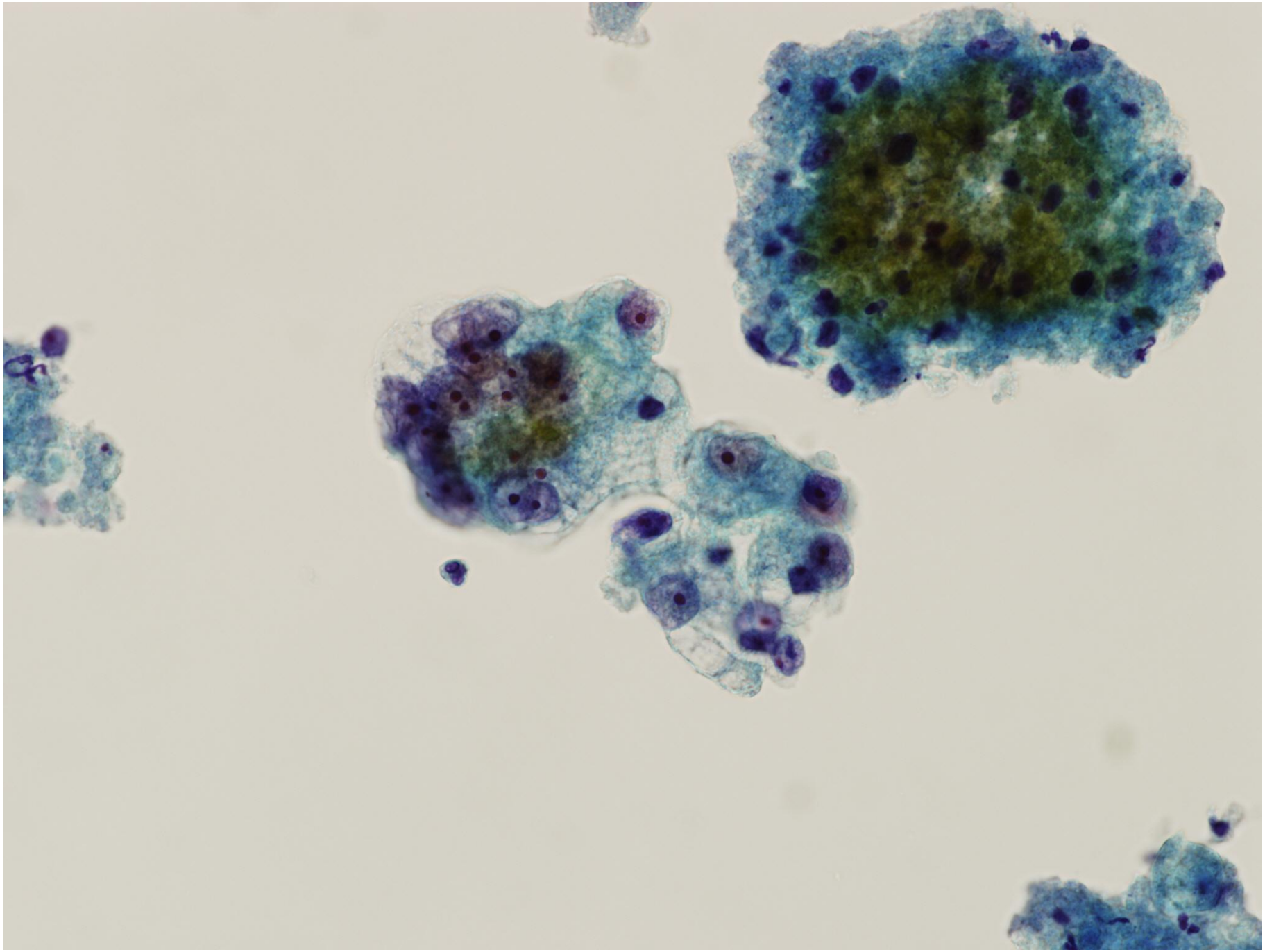
# Case 5

- 86 year old female
- FNA large breast mass









# Cytologic interpretation

- Positive for malignant cells
- Past history very helpful
- Consistent with metastatic renal cell carcinoma

# Metastatic neoplasms to breast

- Incidence 0.13-0.45% (excluding contralateral breast Ca, lymphoma)
- Main sites of origin: lung (small cell/non-small cell), ovary/uterus/cervix, melanoma, neuroendocrine tumours, prostate carcinoma
- Less common sites: medullary thyroid, renal cell, gastric carcinomas; sarcoma, hepatocellular carcinoma, urothelial carcinoma

# Metastatic neoplasms to breast

- Colorectal adenocarcinoma rarely metastasizes to breast (except neuroendocrine tumors)
- Consider secondary neoplasm if tumor displays unusual clinical, radiological, gross or microscopic features
- Metastases tend to be discrete, round without spiculations, calcification is uncommon, no DCIS, usually a single lesion (~85%), may involve ipsilateral axillary LN’s

# Secondary neoplasms to breast

- Correct interpretation dependent on

  1) clinical history (~25% present with breast mass and no past history of malignancy)

  2) recognition of cytology as not typical of breast primary

- With FNA it may not be possible to distinguish 1º from 2º neoplasms

# References


- Bedard YC, Hayes M, Ho C et al. Canadian Society of Cytology recommended guidelines for the practice of breast cytopathology. 2003
- National Cancer Institute. The uniform approach to breast fine-needle aspiration biopsy. *Diagn. Cytopathol.* 1997;16(4)295-311.
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