Case 9

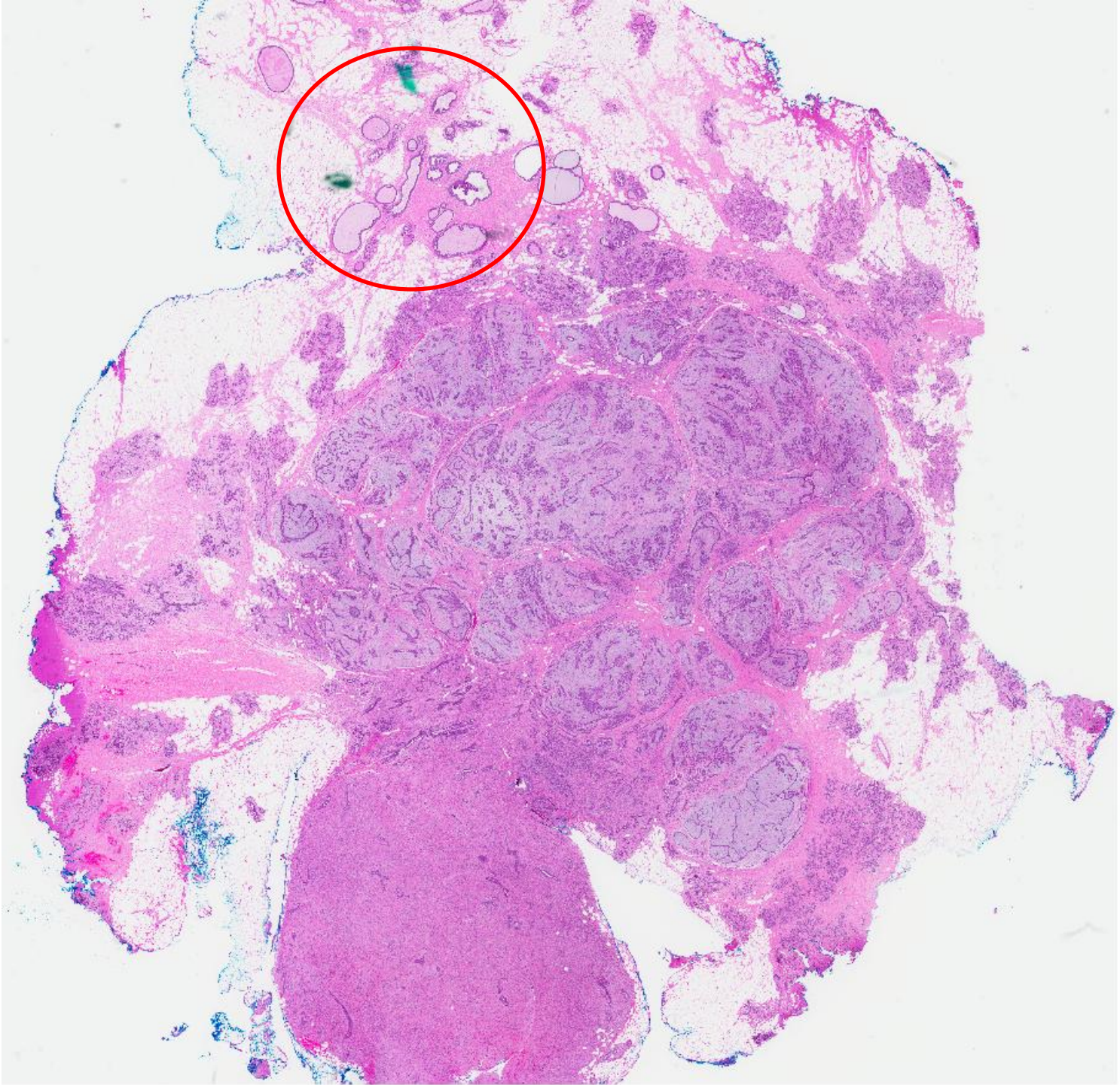
21 year old Malay lady with a family history of breast cancer, presented with 2 lumps in the right breast in 2010.

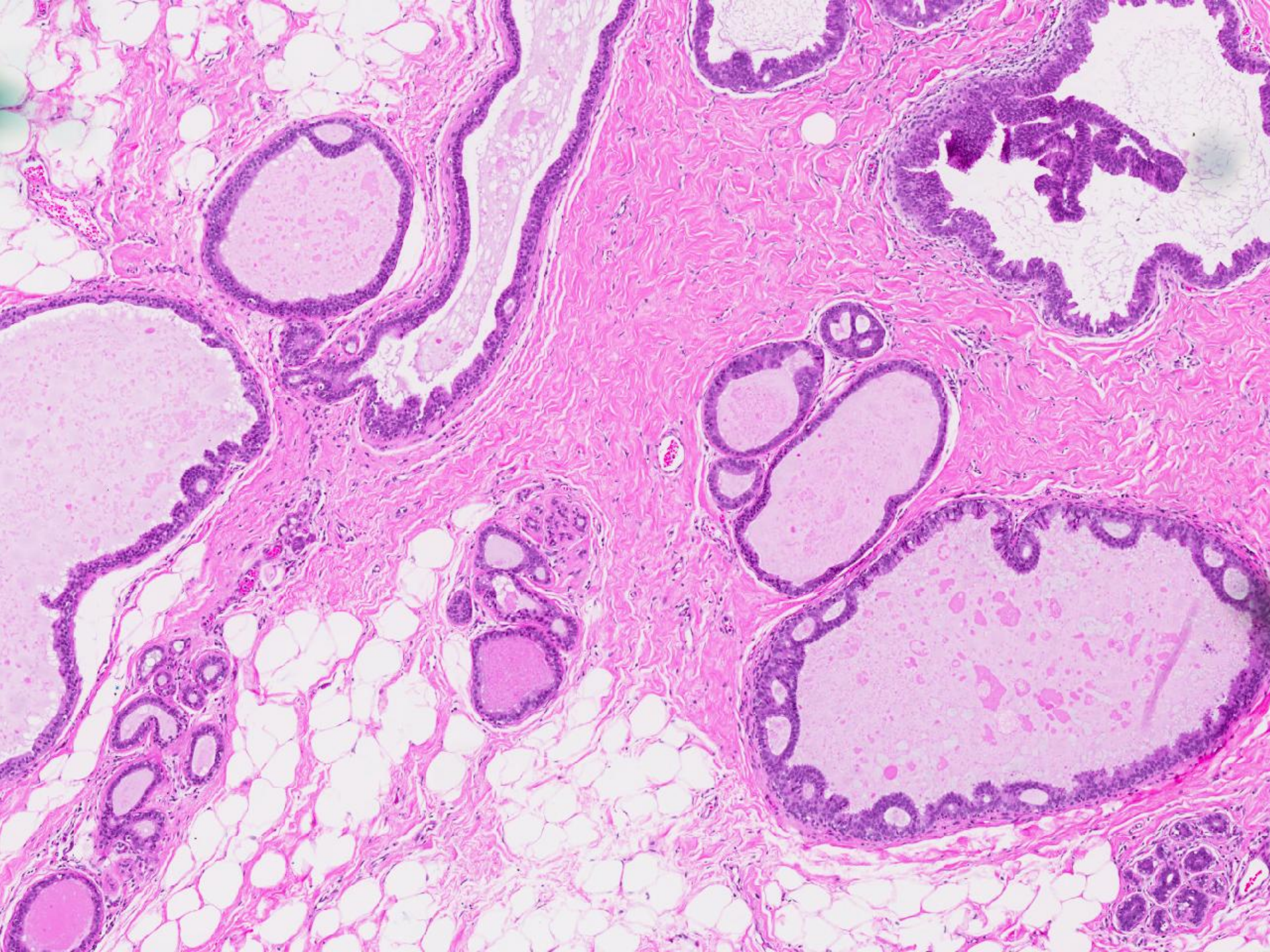
Core biopsies showed fibroadenomas with atypical ductal hyperplasia in one lump.

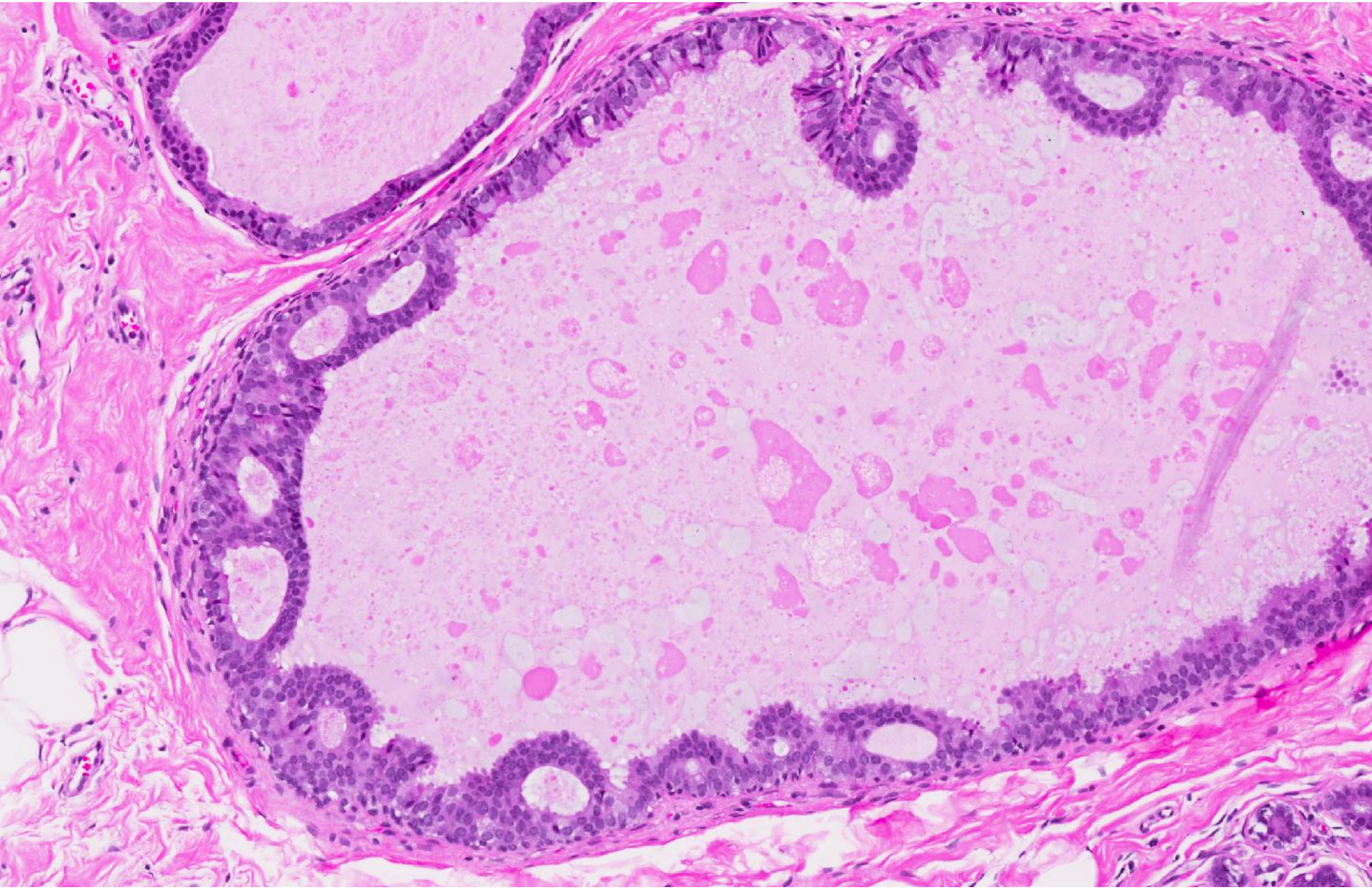
Subsequent excision disclosed benign changes without residual atypical hyperplasia.

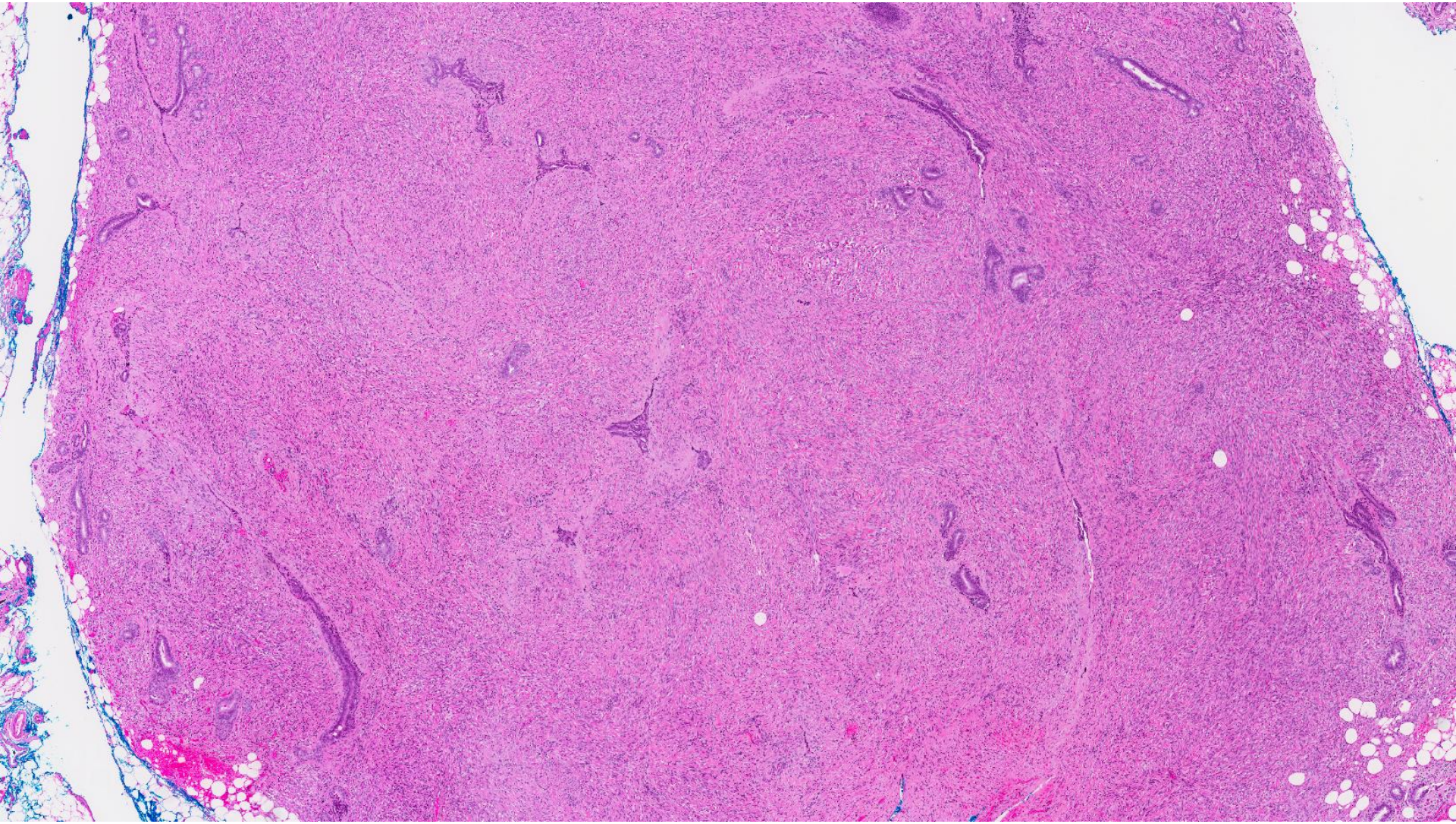
Recently (2012) presented with another lump in the right breast, which was excised.

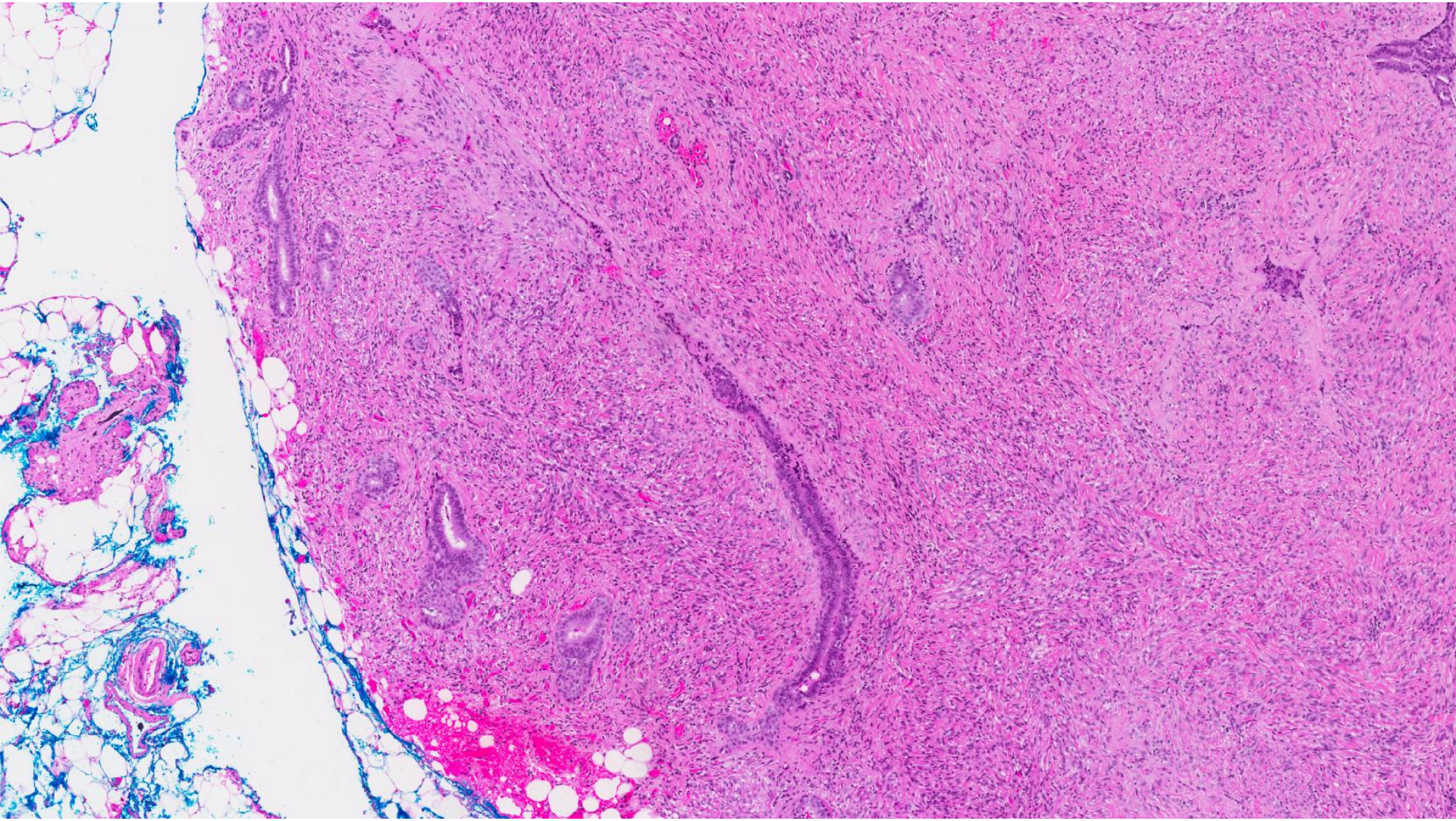
Current section is from the 2012 excision.

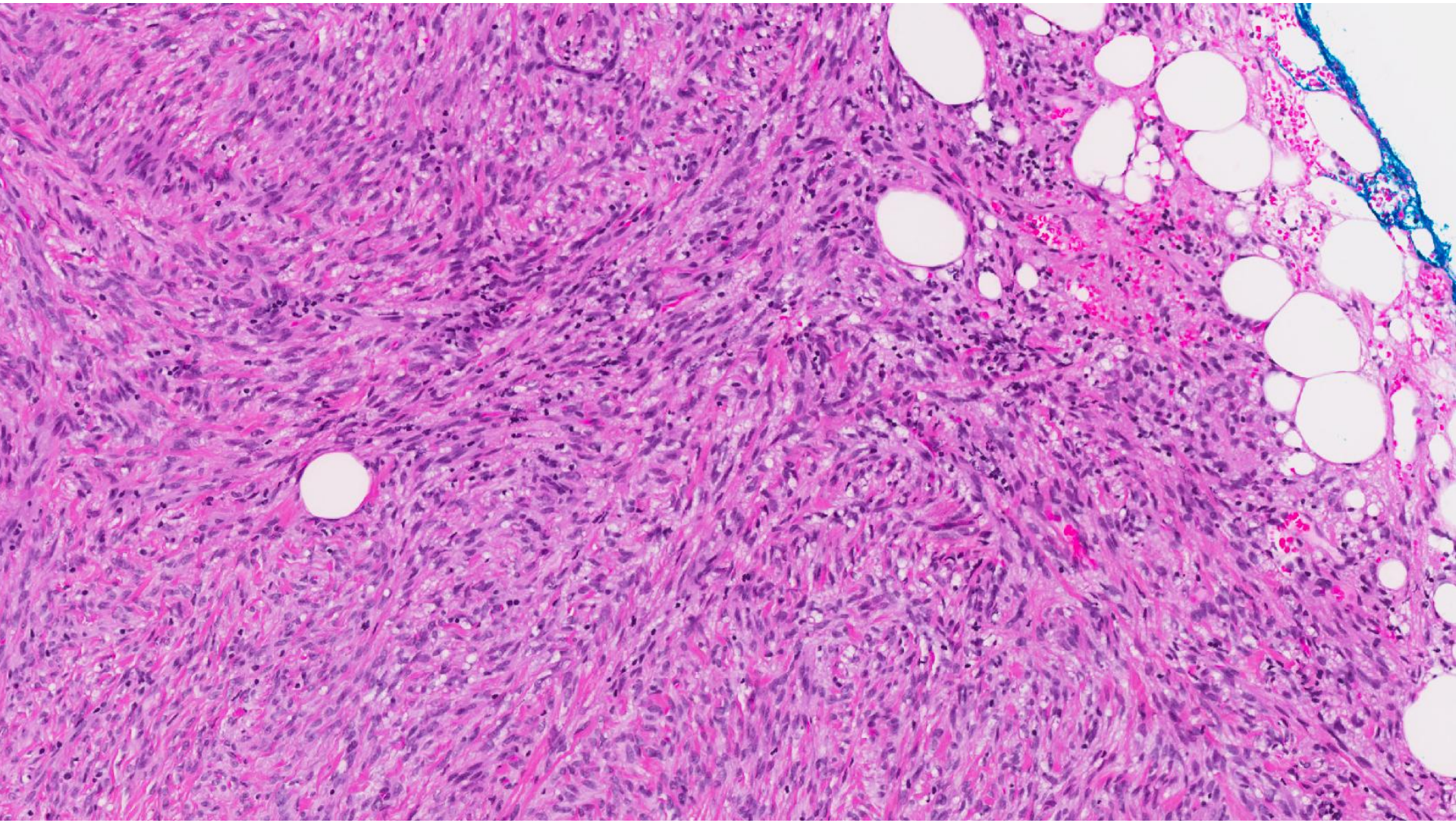


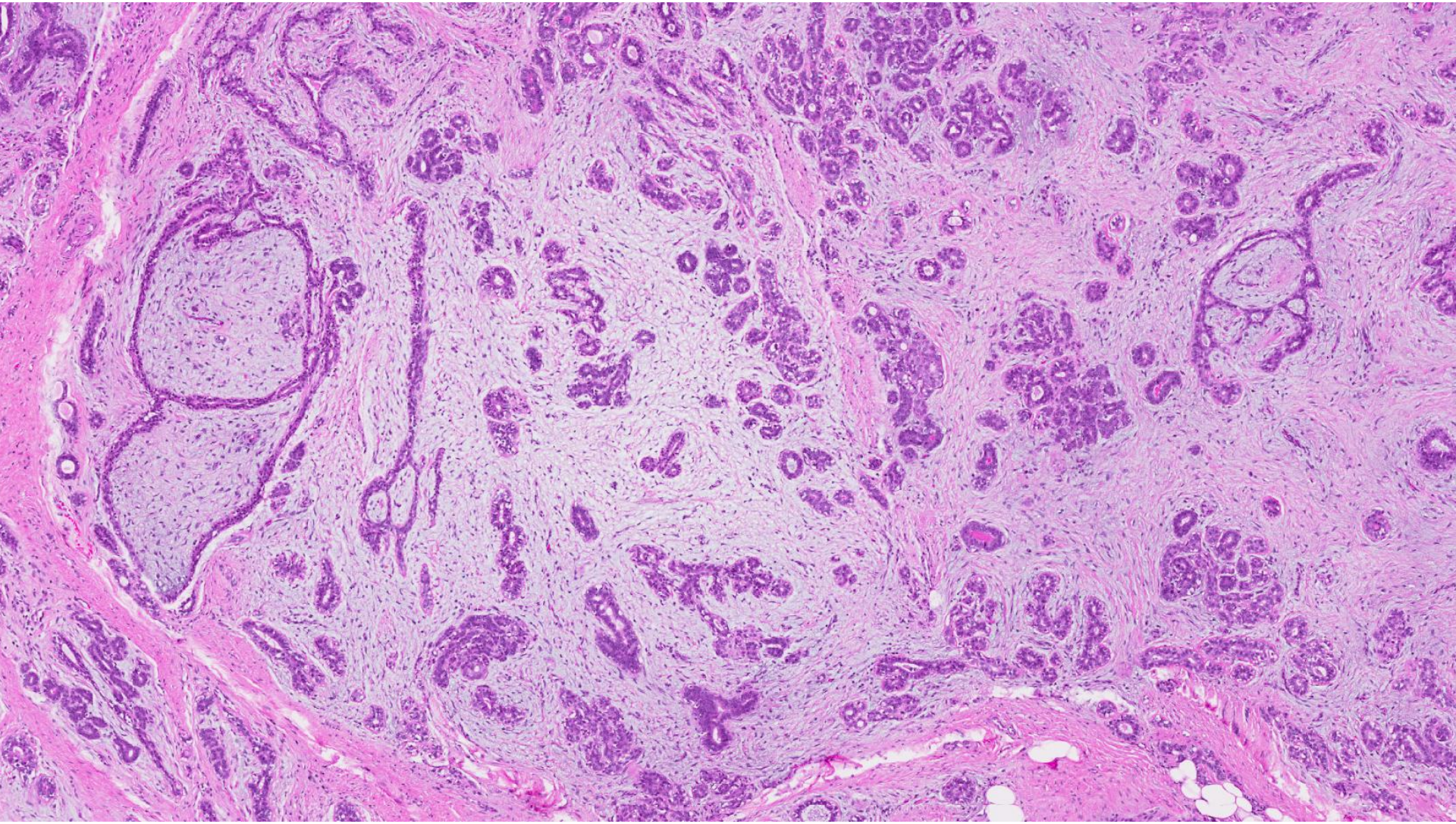












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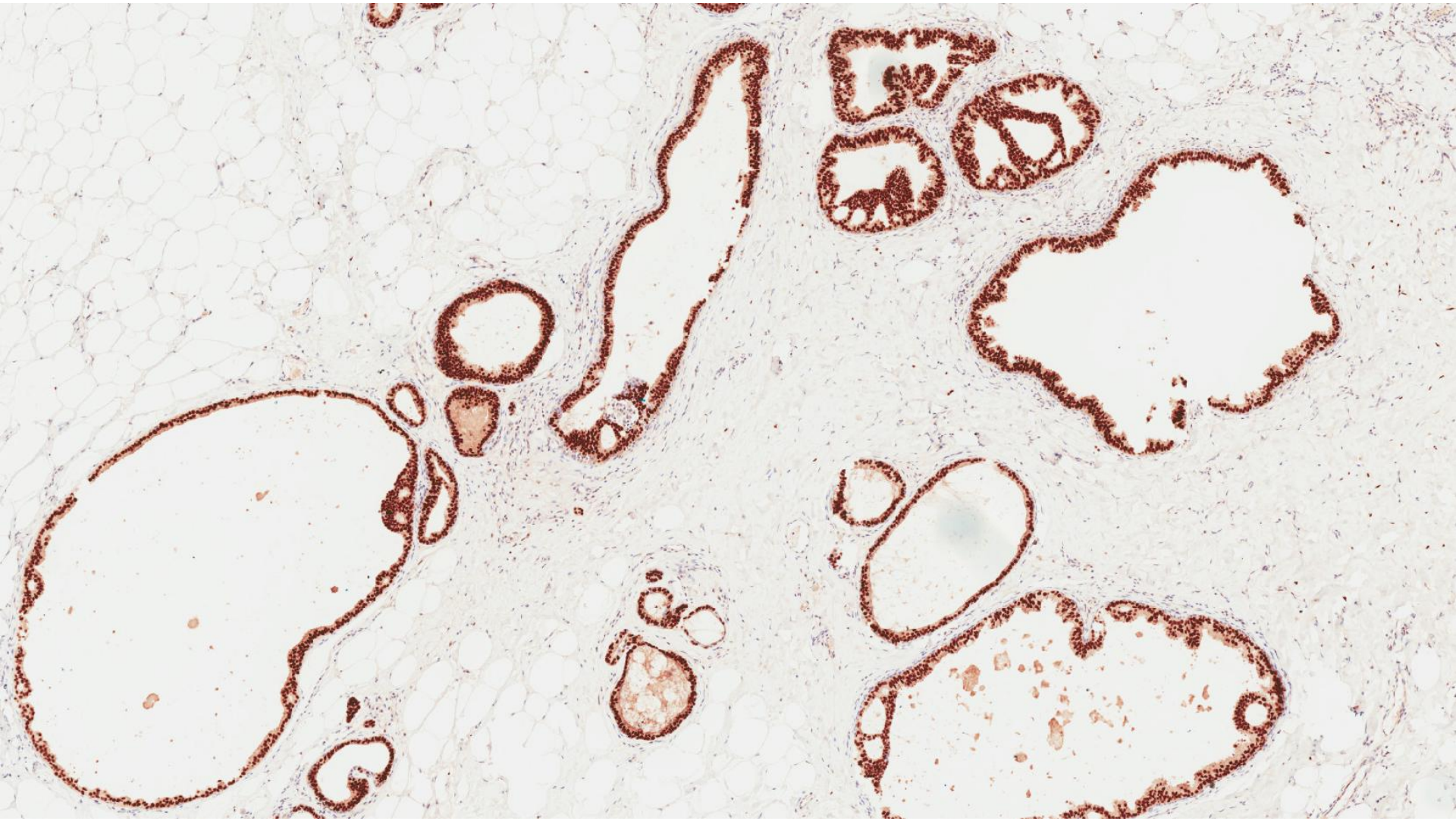

Diagnosis

Cellular fibroadenoma with adjacent low nuclear grade ductal carcinoma in situ

Cellular fibroadenoma

- Fibroadenoma with focal or diffuse stromal hypercellularity.
- Difficult to distinguish from phyllodes tumour, especially for the cellular fibroadenoma with an intracanalicular pattern.
- Overlaps with juvenile fibroadenoma.

Ductal carcinoma in situ

- 2–3% of palpable breast cancers in pre-mammographic era.
- 20–25% of newly diagnosed breast cancers in the USA currently.
- 26% of all screen detected cancers in BreastScreen Singapore.

Ductal carcinoma in situ: *risk factors*

- Family history.
- Nulliparity.
- Late age at first birth.
- Late menopause.
- Elevated body mass index (BMI) after menopause.
- High mammographic breast density.

Ductal carcinoma in situ: *breast cancer-specific mortality*

- Extremely low, with 1.0–2.6% dying from invasive breast cancer 8–10 years after a diagnosis of DCIS.
- Breast-cancer deaths after DCIS due to:
  - Undetected invasive carcinoma at initial diagnosis.
  - Invasive recurrence after treatment.
- DCIS itself does not result in mortality.

Ductal carcinoma in situ: *radiological presentation*

- 80% to 85% of cases of DCIS.
- Calcifications:
  - High grade DCIS:
    - Pleomorphic, amorphous, linear and segmental.
  - Low to intermediate grade DCIS:
    - Granular, segmental.
- MRI:
  - Non-mass-like enhancement with delayed peak enhancement profiles.

Ductal carcinoma in situ: *nuclear grading scheme*

- 3 tiers: low, intermediate, high.
- Heterogeneity may be seen.
- Low and high grade usually not observed together.
- Low and high grade DCIS are likely distinct diseases.

Low nuclear grade DCIS

- Small, monomorphic cells with uniform nuclei, regular chromatin, inconspicuous nucleoli.
- Rare mitoses.
- Arcades, micropapillae, cribriform or solid patterns.
- Solid pattern may show microacini in which cells are polarized around small extra-cellular lumina in a rosette-type arrangement.
- Microcalcifications are often of the psammomatous type.
- Necrosis is uncommon.
- Micropapillary pattern may be associated with more extensive disease with multiquadrant involvement.

Ductal carcinoma in situ: *clinical course and prognosis*

- Clinical, pathological, molecular data indicate that DCIS is a precursor, albeit not obligate, to invasive breast cancer.
- Radiographic-pathological correlation studies show that DCIS is in most cases confined to a single segment or ductal-lobular system.
- Involvement of the segment may be extensive and “skipped” areas may occur, especially in low nuclear grade DCIS.

Ductal carcinoma in situ: *clinical course and prognosis*

- Interval between DCIS and development of invasive carcinoma is shorter for high-grade DCIS (average 5 years) than for low-grade DCIS (>15 years).
- Lesion size and adequacy of excision were not assessed in these studies.
- Local recurrences after breast-conserving therapy for DCIS:
  - 50% invasive carcinoma.
  - 50% DCIS.

Ductal carcinoma in situ: *clinical course and prognosis*

- Increased risk of local recurrence and/or progression to invasive cancer:
  - Young age.
  - Larger lesion size.
  - High nuclear grade.
  - Comedo necrosis.
  - Positive margin status.

Ductal carcinoma in situ: *differential diagnosis*

- UDH and ADH.
- Invasive carcinoma:
  - High nuclear grade DCIS in lobules ('cancerisation of lobules').
  - DCIS superimposed on sclerosing adenosis.
  - Cribriform DCIS mimicking invasive cribriform carcinoma.
- Lobular carcinoma in situ.

Table 5.01 Morphological characteristics useful in distinguishing ADH from UDH and from low **nuclear** -grade DCIS

Characteristic	UDH	ADH	DCIS (low grade)
Architecture	Cellular swirling and streaming; stretched or twisted epithelial bridges; peripheral, irregular, and slit-like fenestrations.	Rigid cellular bars; bulbous micropapillae; round, punched out spaces.	Rigid cellular bars; bulbous micropapillae; round, punched out spaces.
Cytology	Multiple cell types; uneven distribution and overlapping of cells and nuclei; indistinct cell borders.	Cellular uniformity; even cell placement; distinct cell borders; residual normally polarized cells.	Cellular uniformity; even cell placement; distinct cell borders; no residual normally polarized cells.
Extent	Variable, ranging from one to multiple TDLUs.	Partial involvement of multiple spaces; complete involvement of < 2 spaces or ≤ 2 mm in extent (see text).	Complete involvement of ≥ 2 spaces or > 2 mm in extent (see text).
Risk of developing breast cancer; laterality of risk	Slight risk; generalized bilateral risk.	Moderate risk; generalized bilateral risk.	High risk; regional ipsilateral risk.

ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma in situ; TDLU, terminal-duct lobular unit; UDH, usual ductal hyperplasia.

WHO Classification of Breast Tumours 2012