Endometrial carcinoma: practical part

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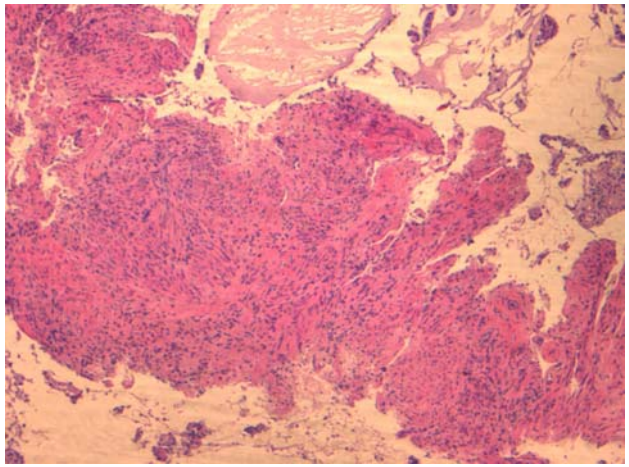
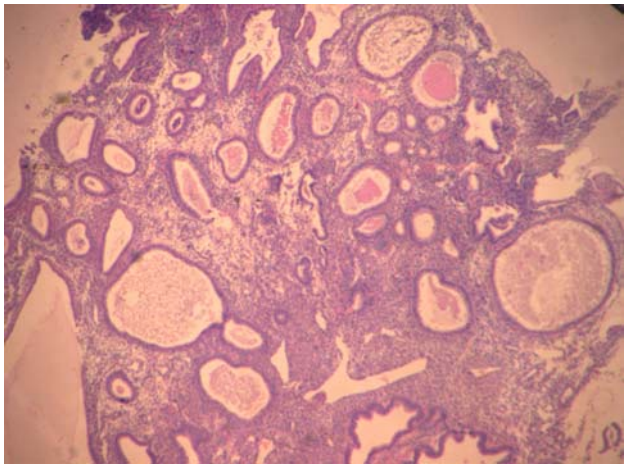
Case 1: presentation

- Age: 68 y
- Symptoms: postmenopausal bleeding
- US: Endometrial thickness 20mm
- Novak-biopsy: inconclusive

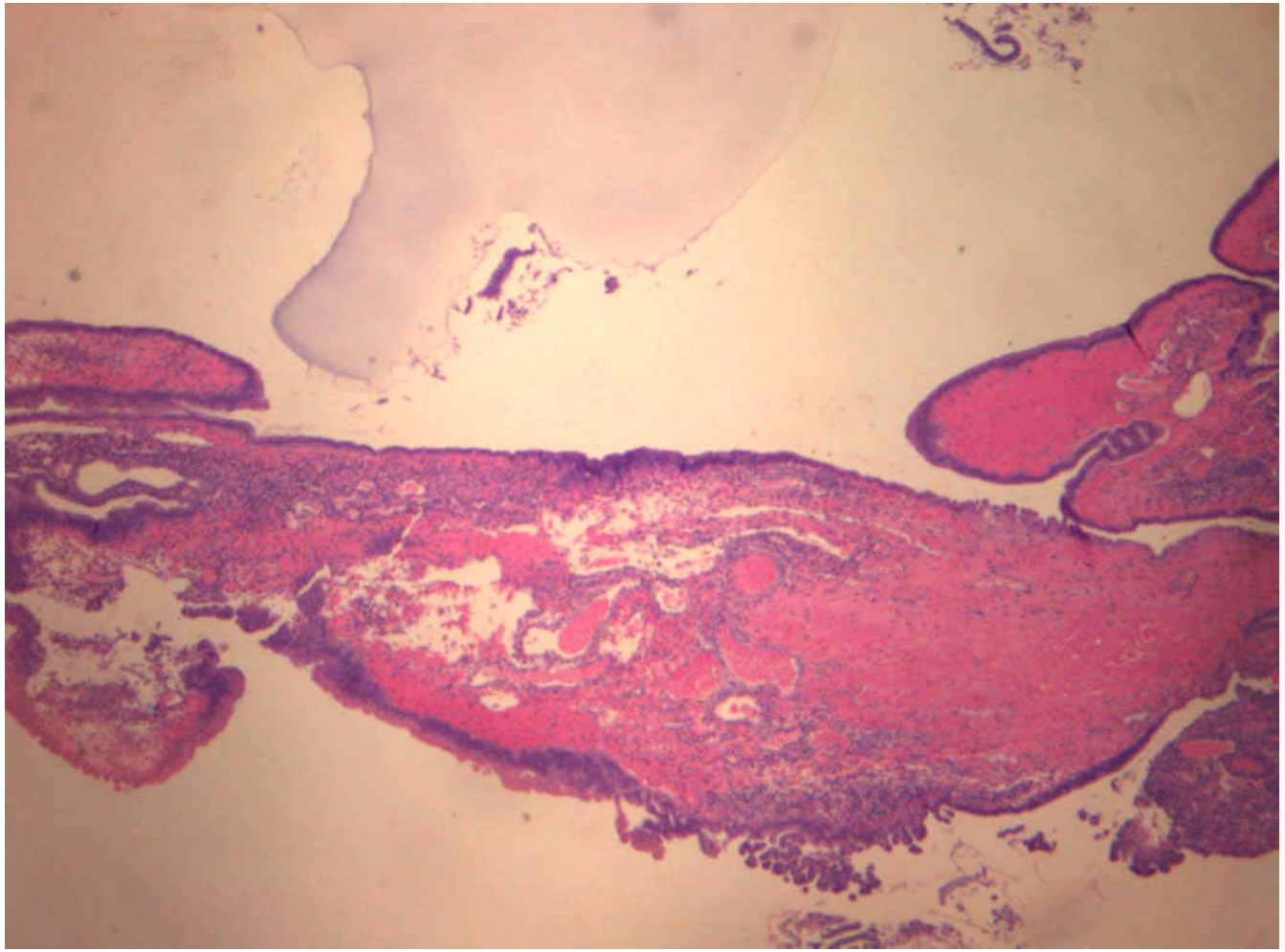
- D&C

Case 1: histology

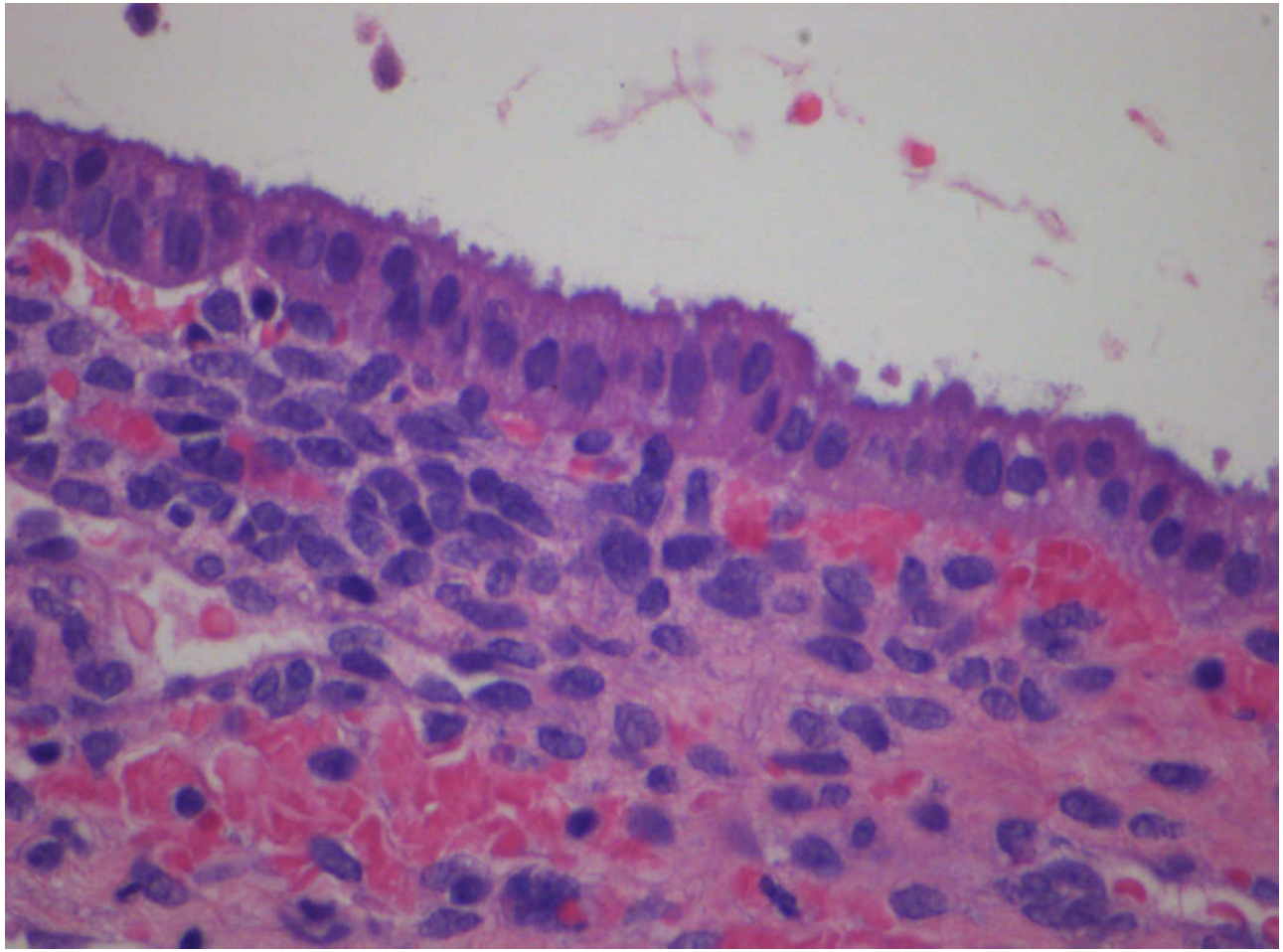


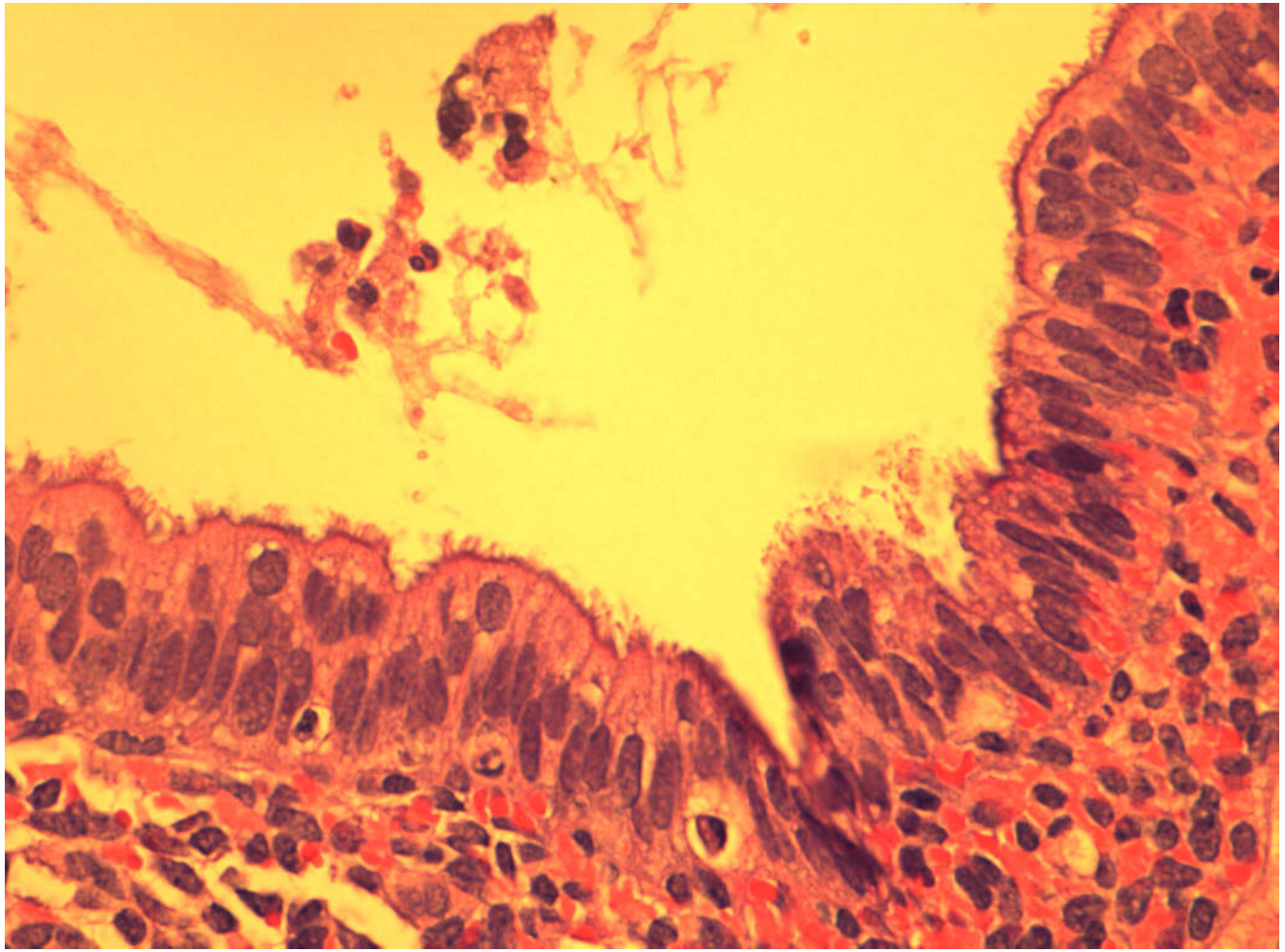


- Fragment of benign myoma
- Endometrial polyp

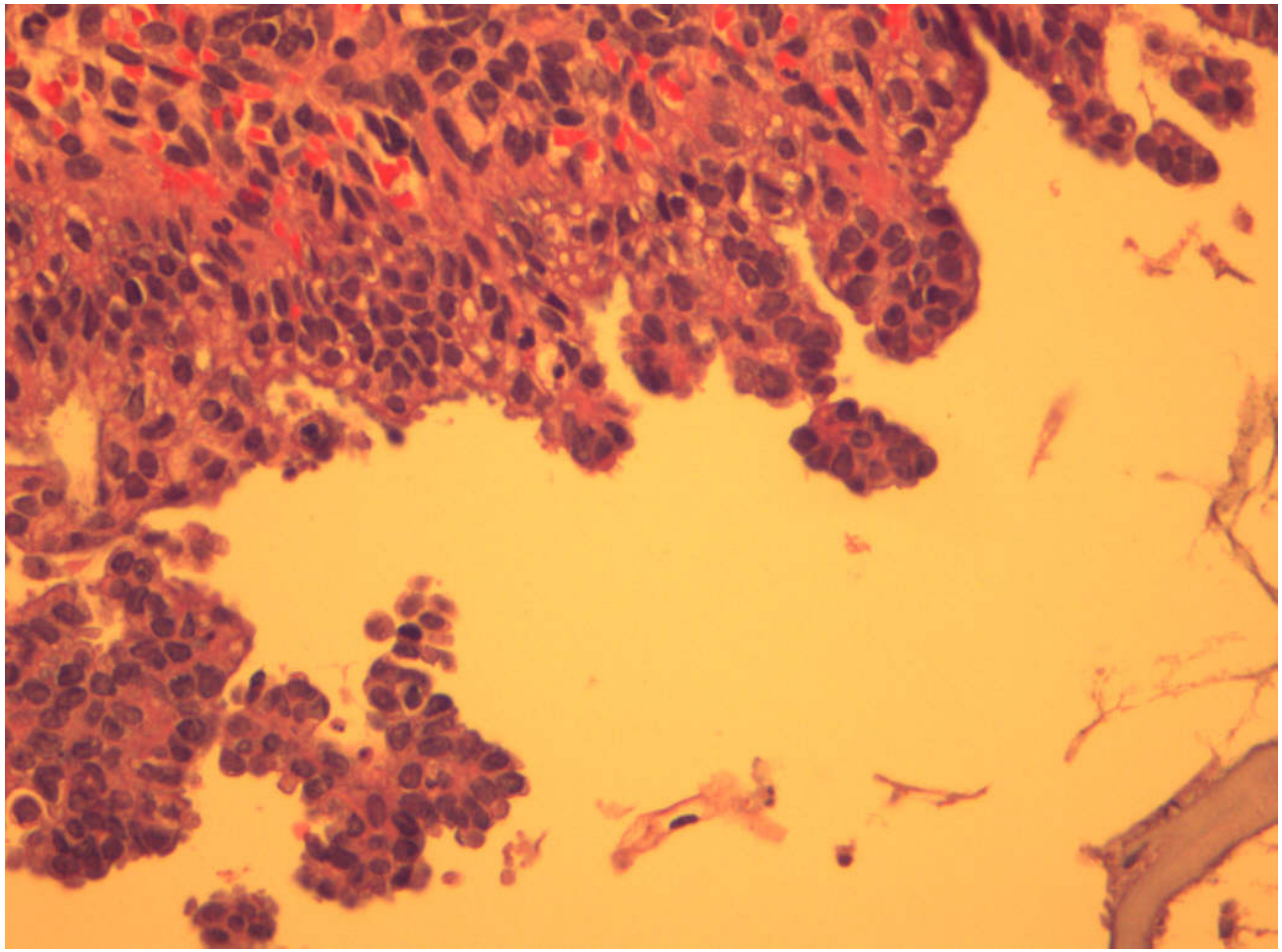


Tubal epithelium

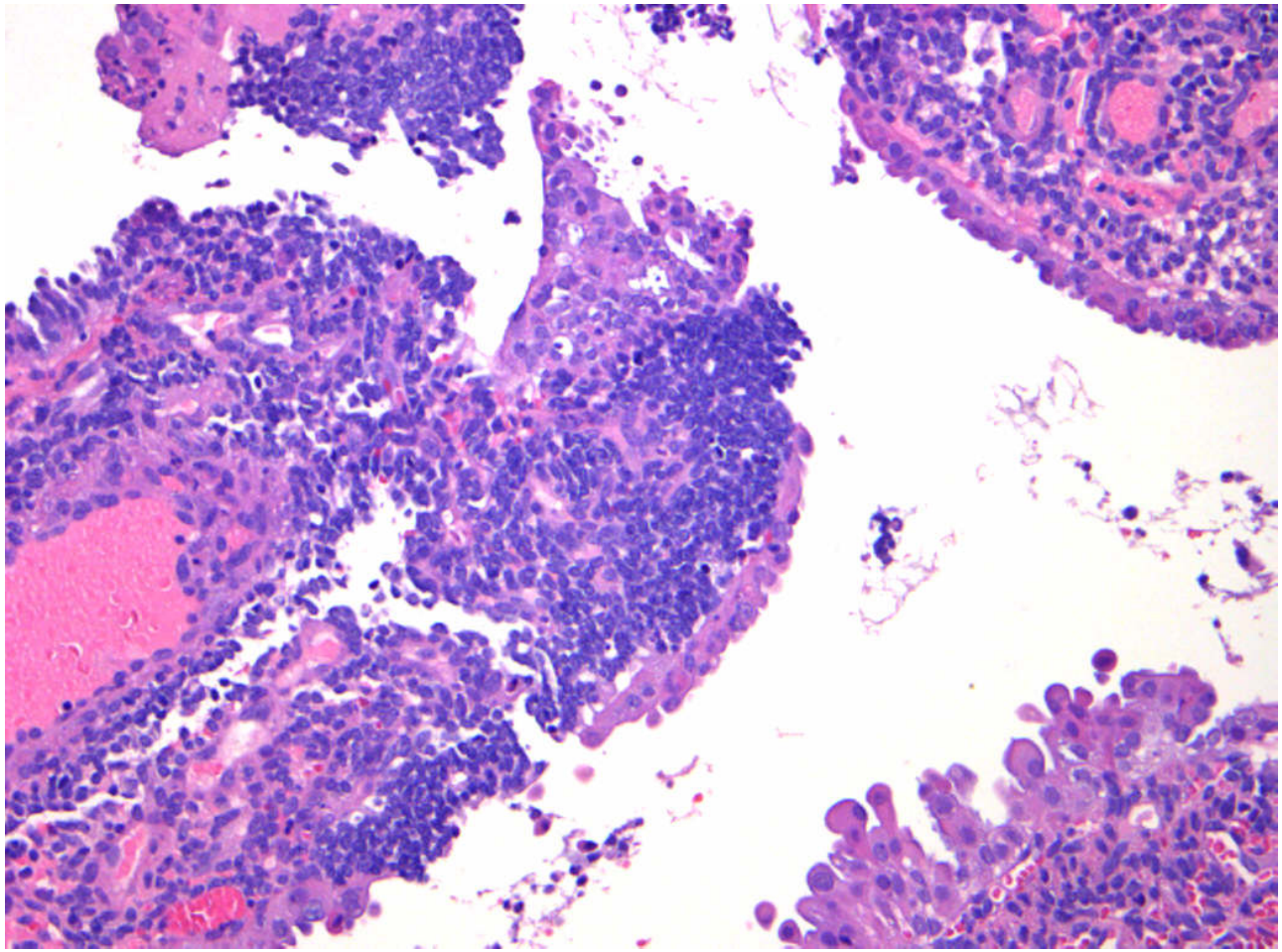




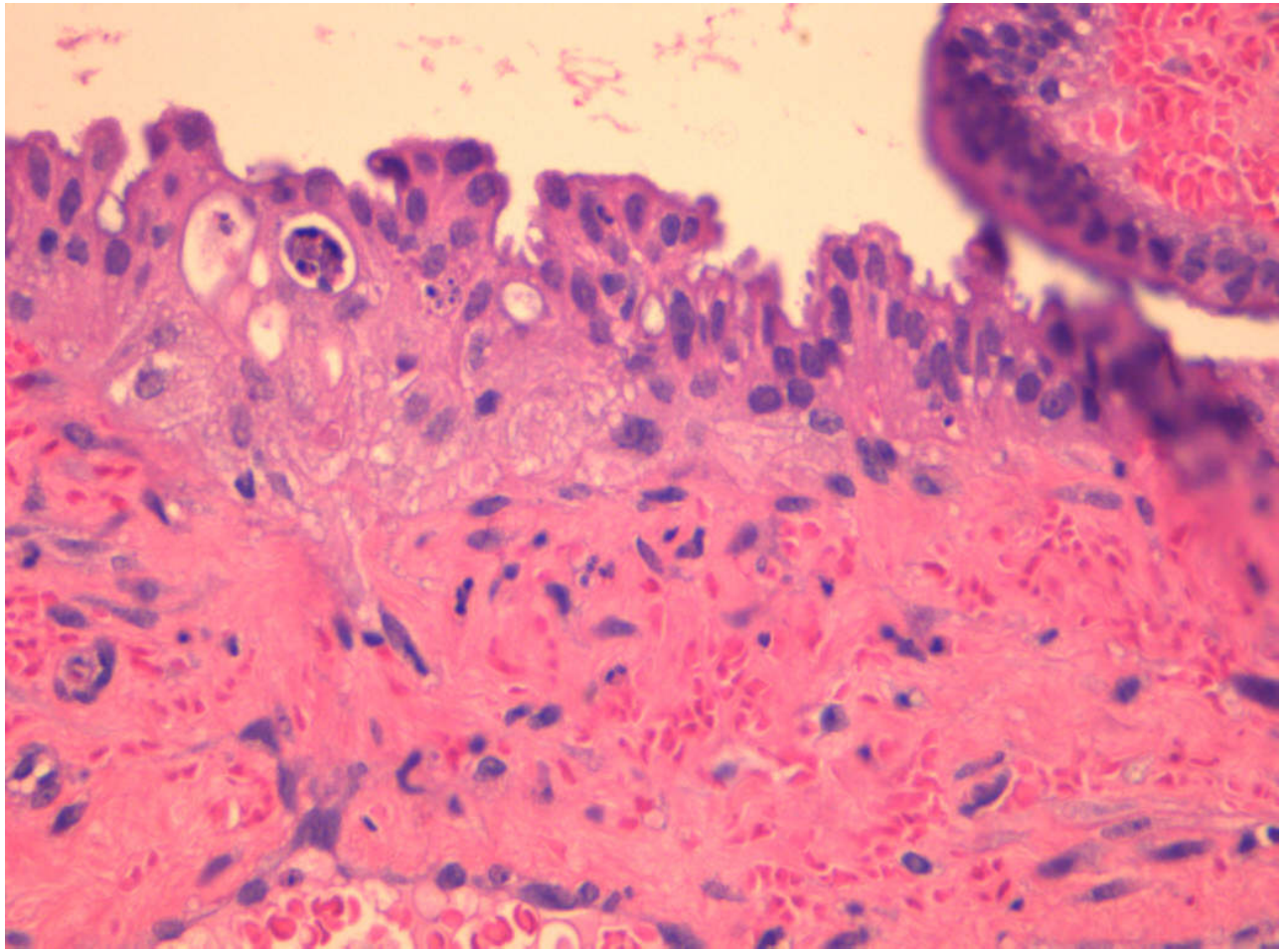
Micropapillary structures



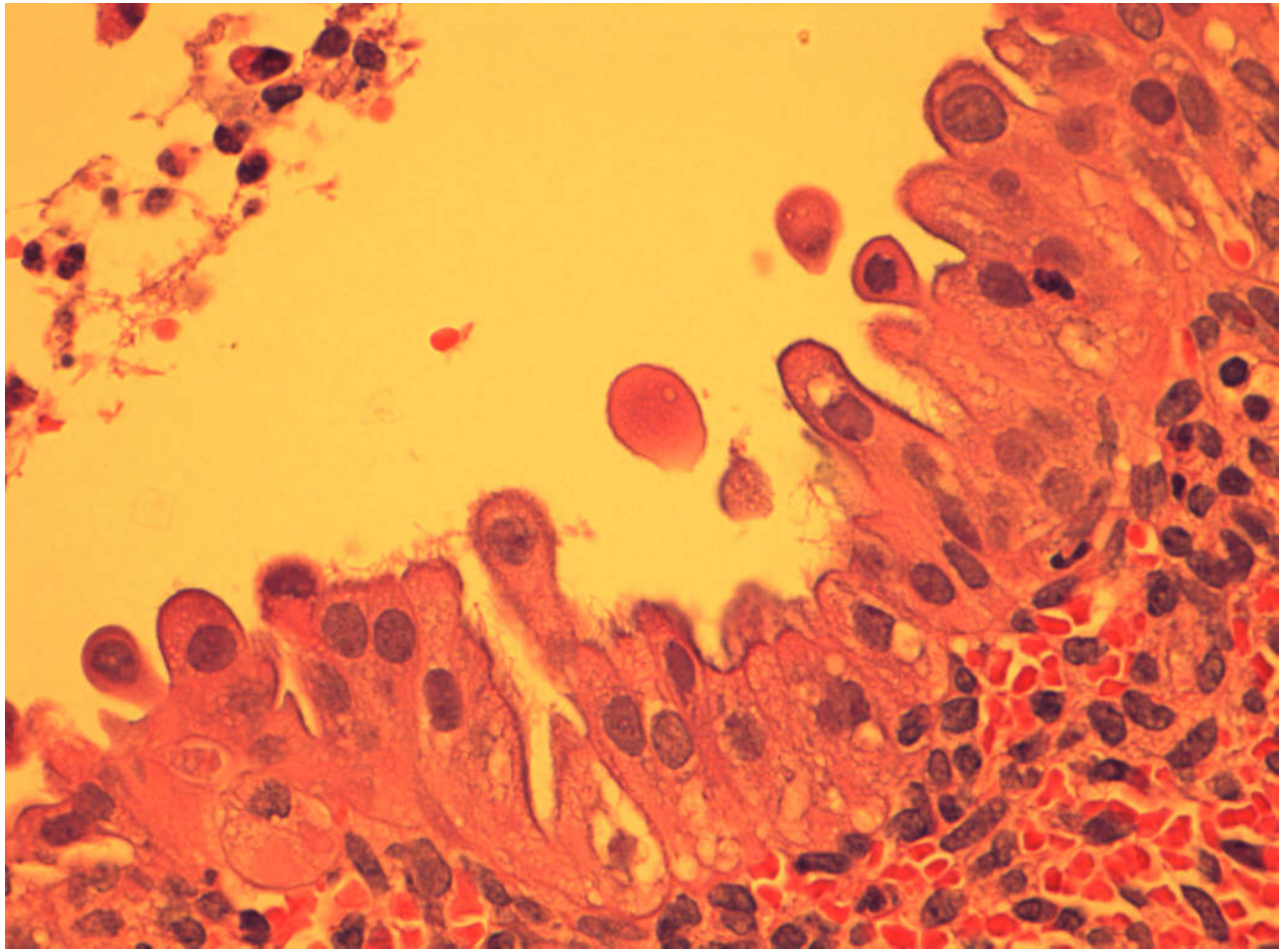
Syncytial structures on surface



Intra-epithelial neutrophils



Hobnailcells



Hobnail cells = neoplastic?

- Chromatin: coarse/open/smudged
- Mitoses?
- Neutrophils?
- Associated lesions?

Case 1: histology (2)

- Hobnailcells on surface
  - Nuclei not atypical
  - Intraepithelial neutrophils
- Ciliated cells
- Micropapillairy structures

Case 1: diagnosis

- Regenerative changes
- Endometrial epithelial metaplasia

Endometrial metaplasia

- Can affect epithelium and (rarely) stroma
- Can be seen in benign, premalignant and malignant situations
- Should alert to look for “something else”

Endometrial metaplasia: origin

- Most are rather “altered differentiation” towards type of epithelium in other part of Müllerian tractus
  - Mucinous: endocervix
  - Squamous: exocervix
  - Ciliated: salpinx

Major classes of metaplasia

- Degenerative
- Hormonal
- Neoplastic

Topography?

Degenerative type of metaplasia

- Cause: surface repair, stromal breakdown
- Topography: focal/multifocal/surface
- Associated lesions: polyp, infarction, neutrophils

- Example: papillary syncytial metaplasia

Hormonal type of metaplasia

- Cause: hormonal stimulation (estrogens)
- Topography: regularly irregular (cfr disordered proliferation)

- Example: tubal metaplasia

Neoplastic type of metaplasia

- Cause: local proliferation of cells with clonal changes
- Topography: local, expansive

- Example: secretory changes in EIN

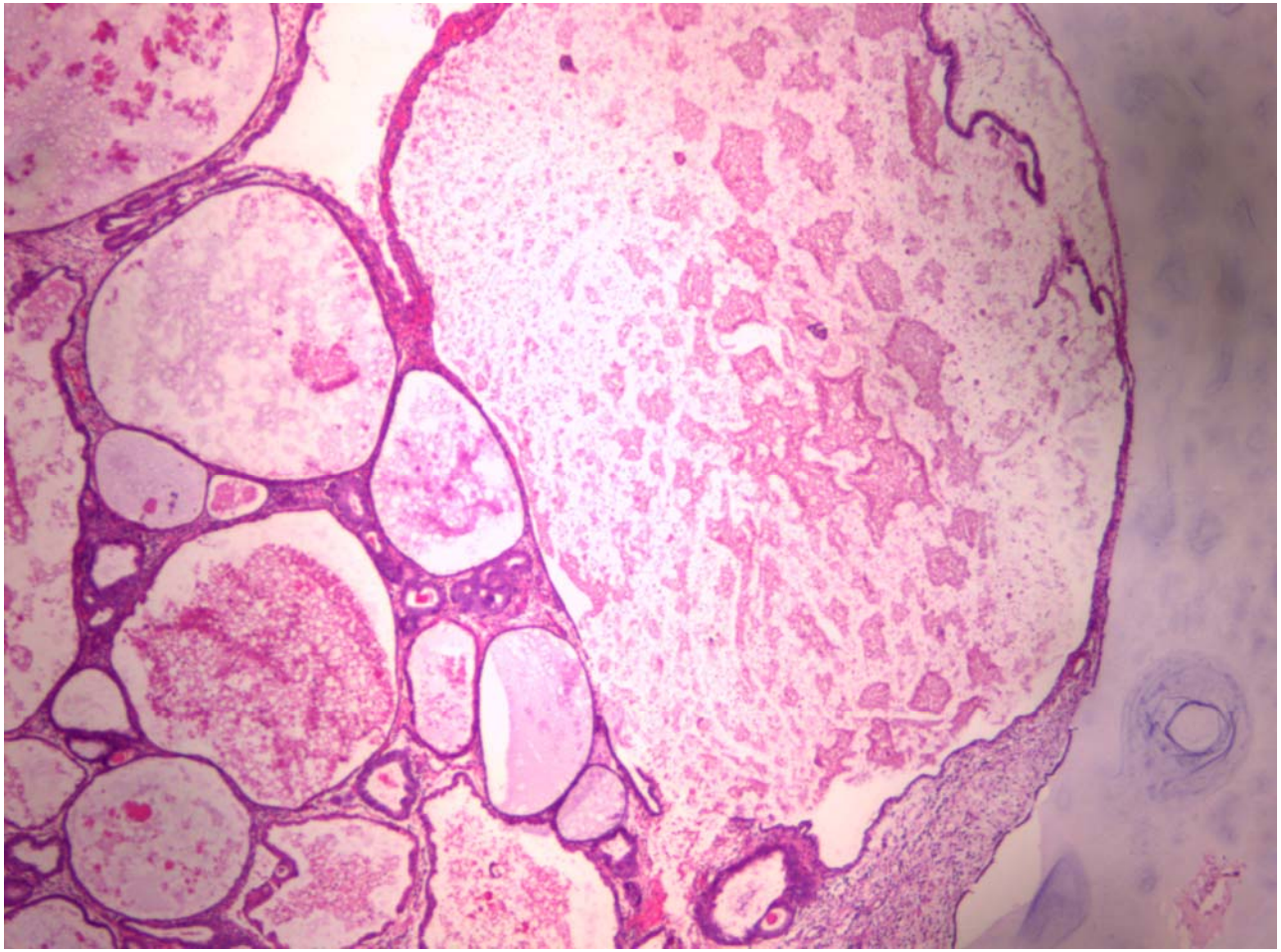
Importance of metaplasia

- Recognise it
- Look for cause
- Don’t overdiagnose (pre)malignancy

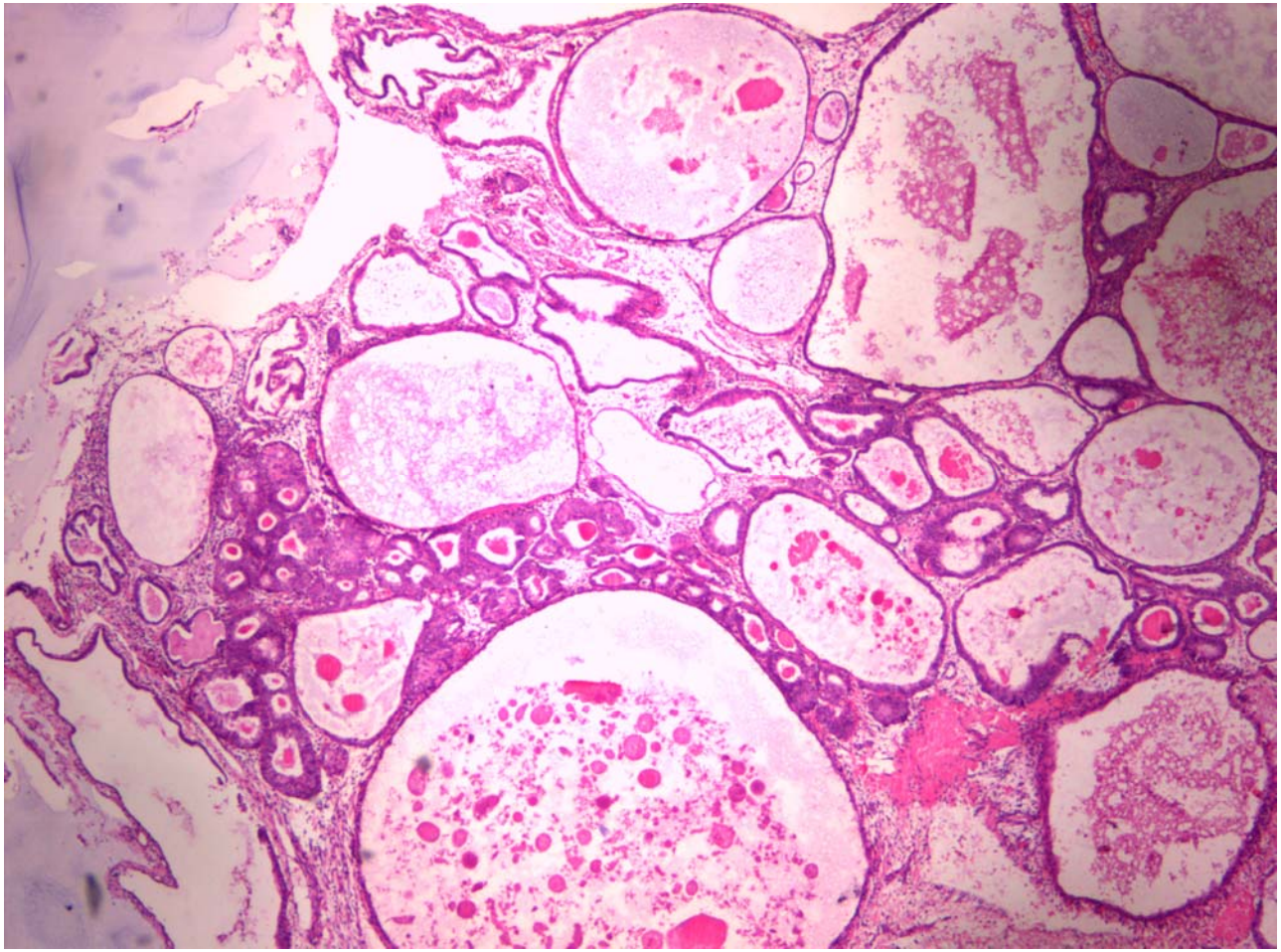
Case 2: presentation

- Age: 62 y
- Symptoms: postmenopausal bleeding
- Hysteroscopy: polyp

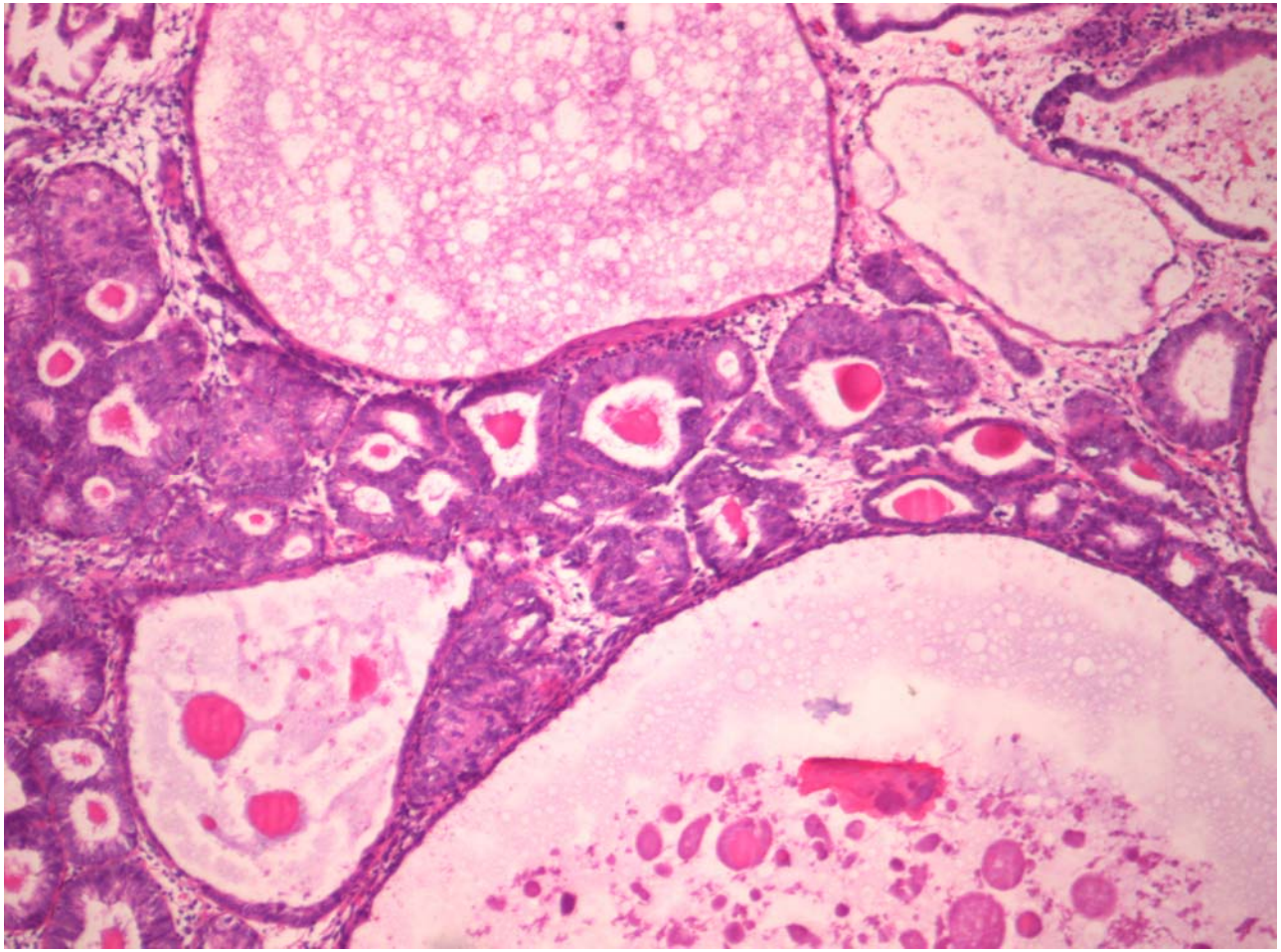
Case 2: Large fragment from polyp



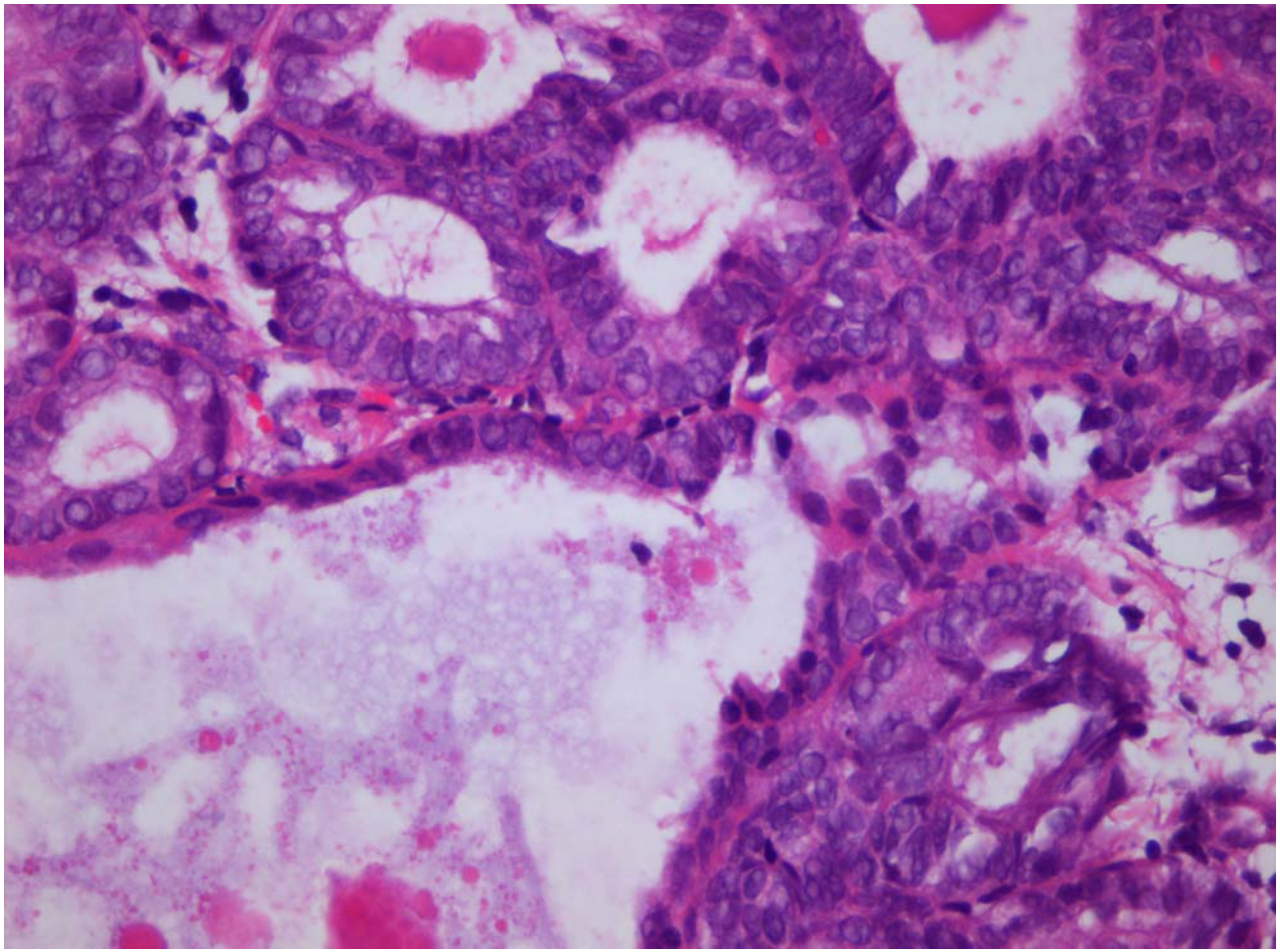
Case 2: area with crowded smaller glands



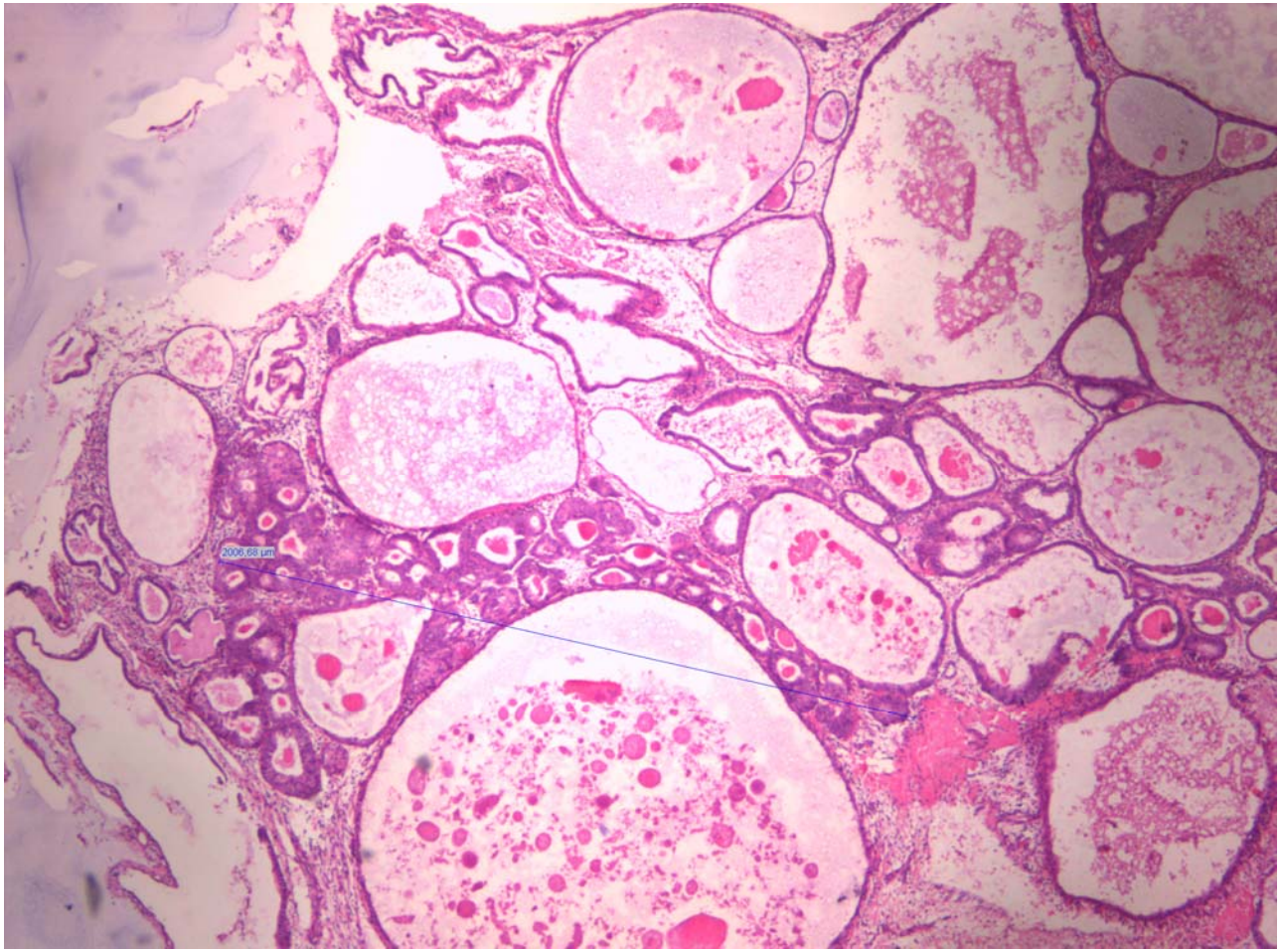
Case 2: VPS < 50%



Case 2: cytology different from dilated glands



Case 2: 2 mm



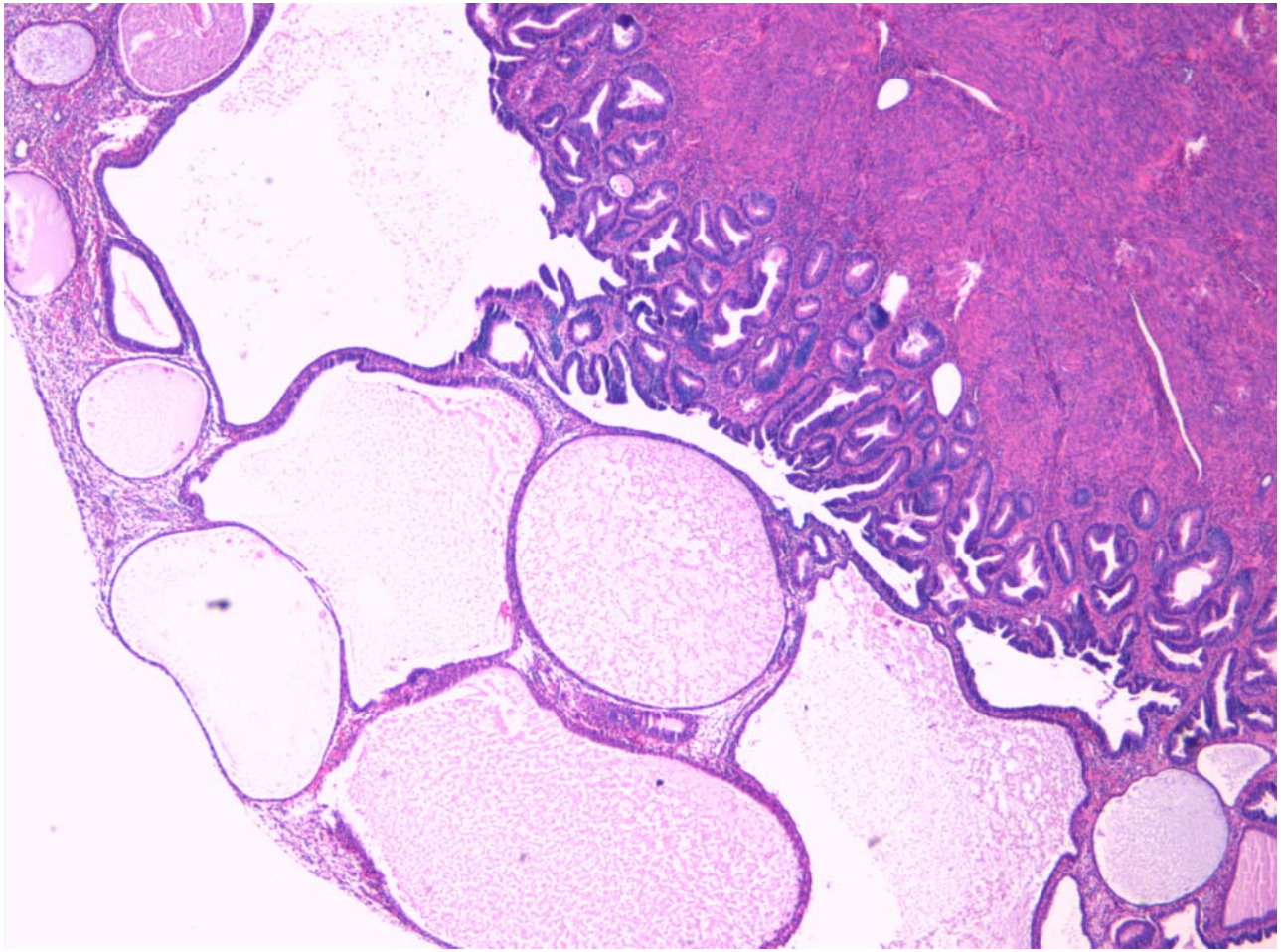
Case 2: diagnosis

- EIN
  - Crowded
  - Different (clonal) from rest of polyp
  - Size > 1mm

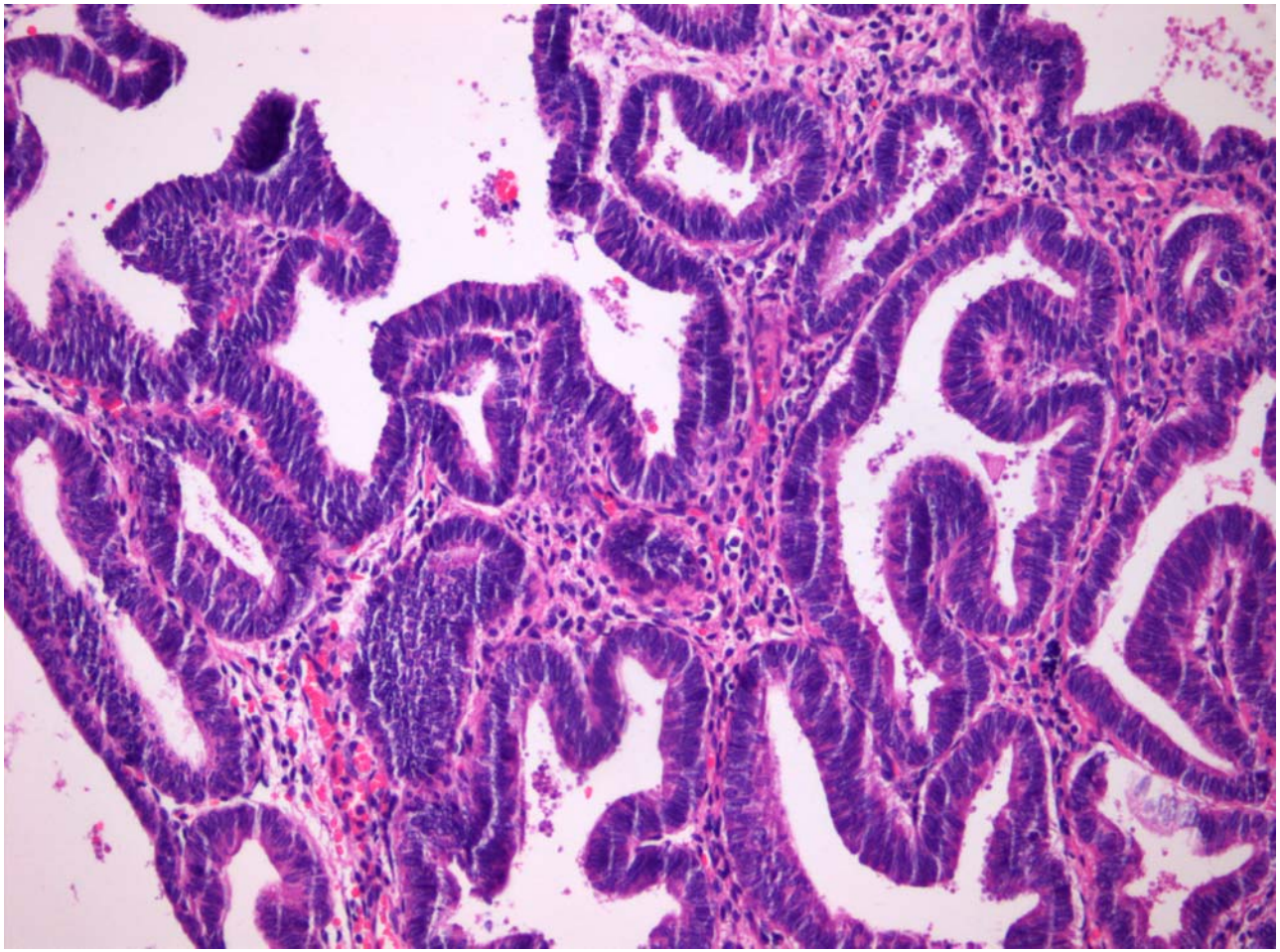
Case 3: presentation

- Age: 68 y
- Hysterectomy after diagnosis of EIN on D&C

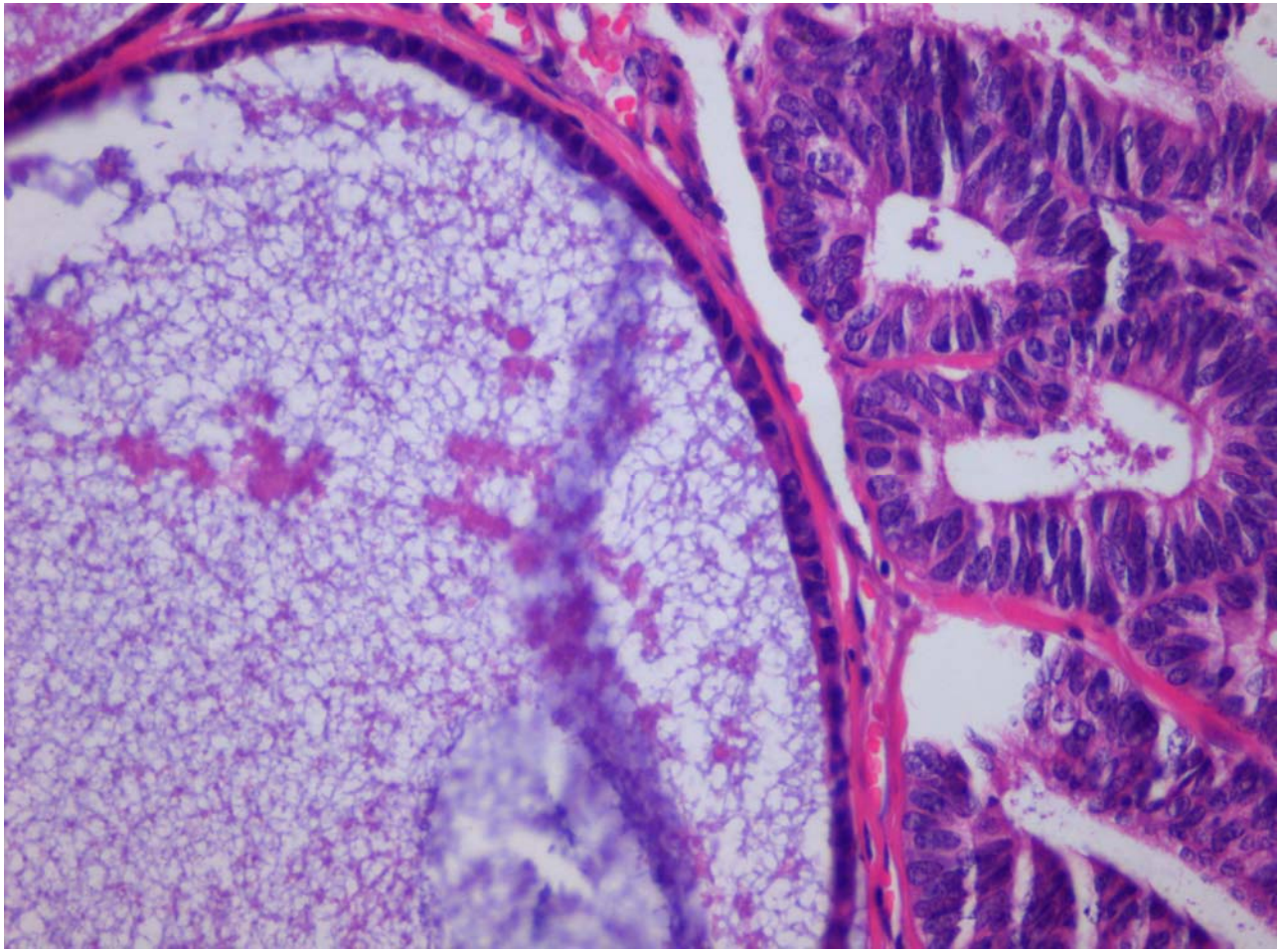
Endometrium: 2 types of glands



VPS < 50%



2 types of epithelium



EIN?

- Crowding
- Different
- > 1mm

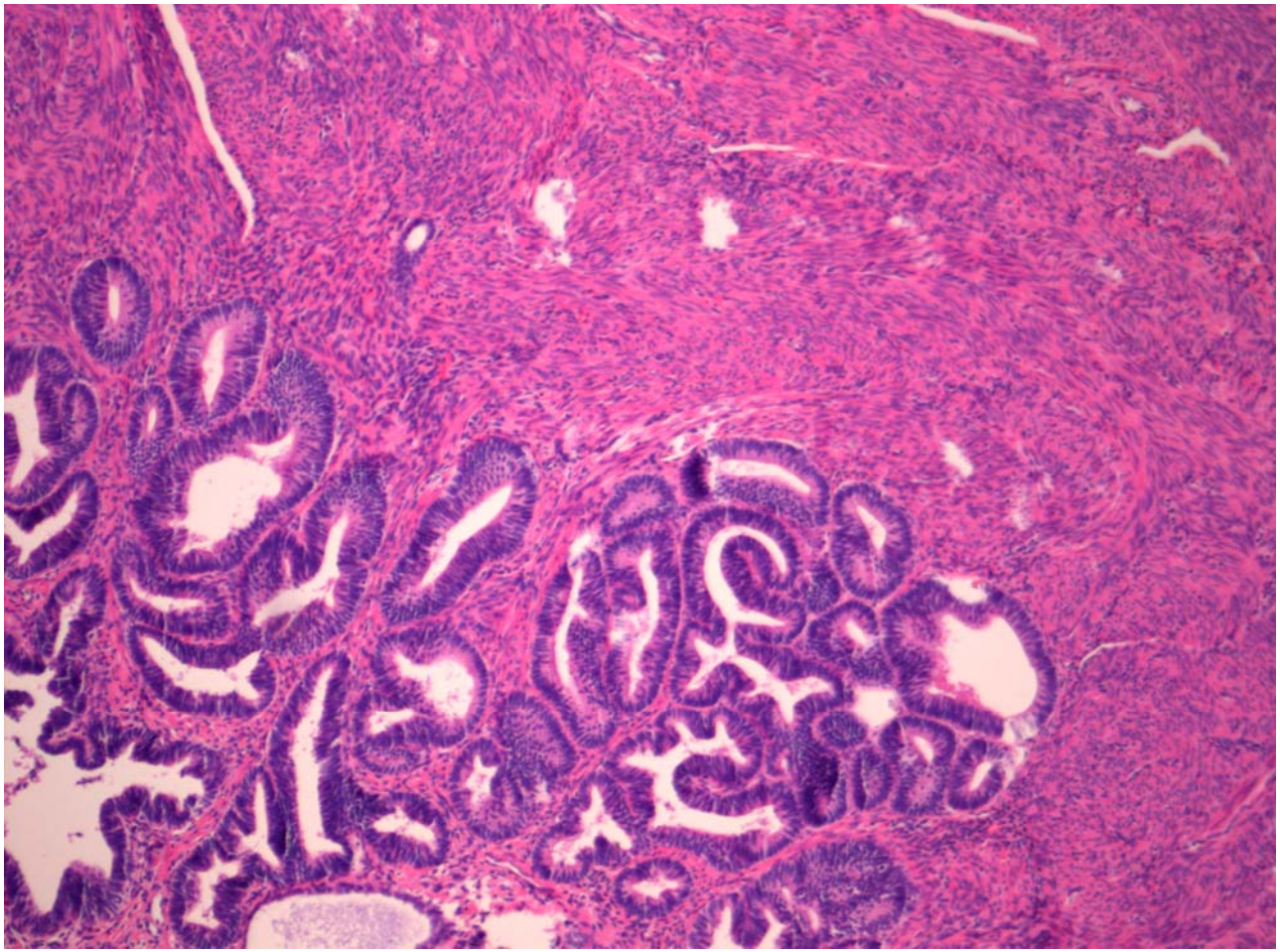
- Exclude benign mimcs
- Exclude invasive carcinoma

Invasive carcinoma if…

- Labyrinth growth: no
- Solid growth: no
- Cribriform: no

- Desmoplasia: no
- Villoglandular growth: no

What about myoinvasion?



In dubio abstine !!!!

- TNM general rule N° 4:

If there is doubt concerning the correct T,N, or M category to which a particular case should be allotted, then the lower (i.e., less advanced) category should be chosen.

Staging of endometrial tumours

- TNM 2009

  should be used in 2010

- Different staging for carcinoma and sarcoma !!!!!
- Carcinosarcoma is staged as carcinoma

Changes in endometrial Ca pT1

- pT1a and pT1b are grouped together as pT1a
- pT1c is now pT1b
- New TNM:
- pT1a: invasion in endometrium or inner half myometrium
- pT1b: invasion in outer half myometrium

Changes in endometrial Ca pT2

- pT2a is not separate stage
- pT2b has become pT2

- New pT2:
  Invasion in cervical stroma

Changes in endometrial Ca pT3

- Positive cytology is not longer pT3a

- New TNM pT3:
- pT3a: extension through serosa or adnexal involvement
- pT3b: involvement of vagina or parametria

Changes in endometrial Ca pN

- Which lymph nodes are involved?

- pN1a: pelvic
- pN1b: para-aortic

Staging pT1 is difficult

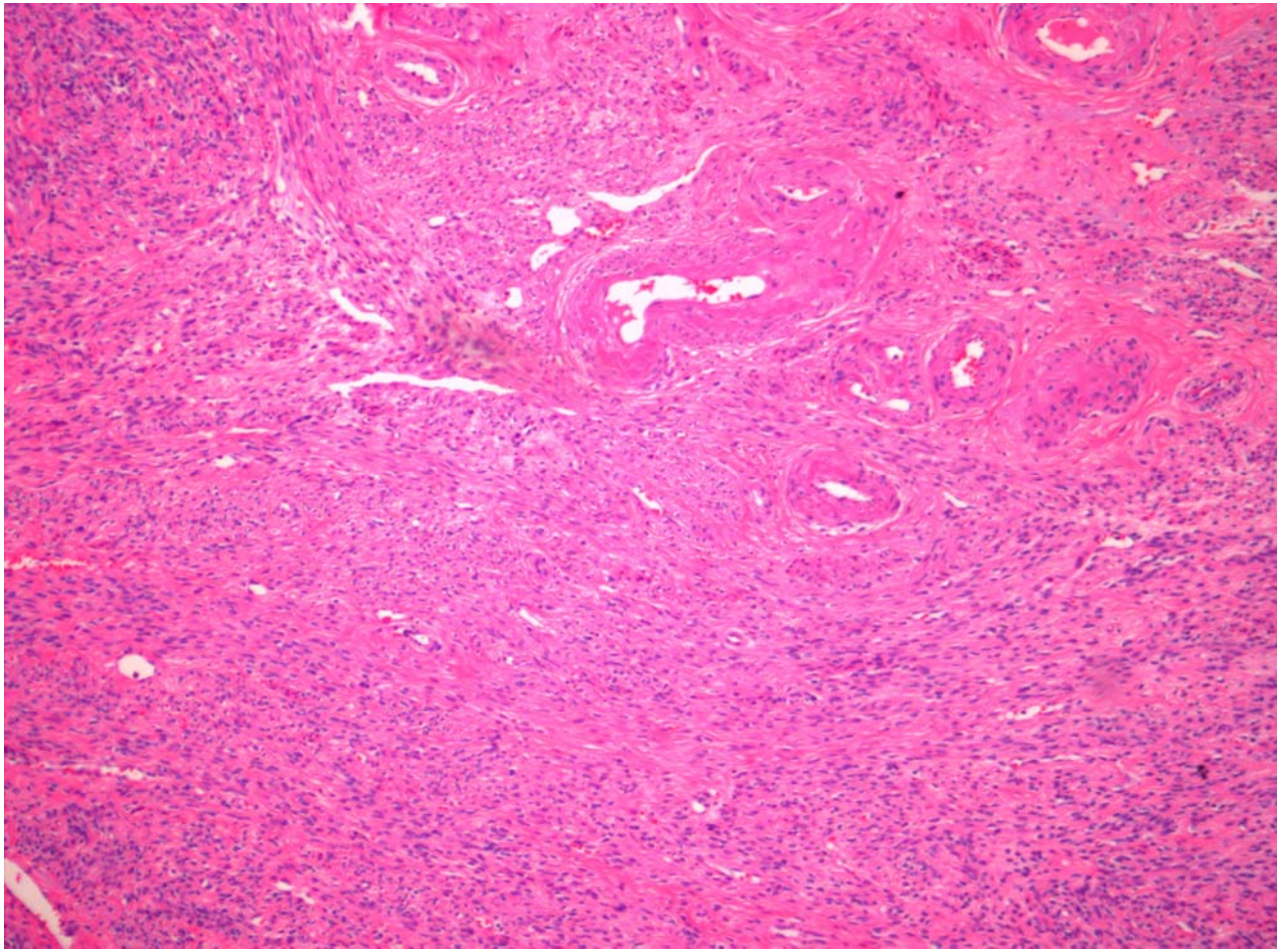
- Border between endometrium is not straight but undulating
  - where is half the myometrium?
- Myometrial thickness is variable and varies with age
  - distance to serosal surface cannot be used

How to deal with this problem?

- Anterior and posterior wall have same thickness
  - If only 1 wall is affected: measure thickness of myometrium and see if half of it is infiltrated
- Arcuate vascular plexus: inner limit at about 47,3% of myometrial thickness
  - Ca well into or through AVP = pT1b
  - Ca barely into AVP = pT1a

Williams: Int J Gynecol Pathol 25 (2006) 59-64

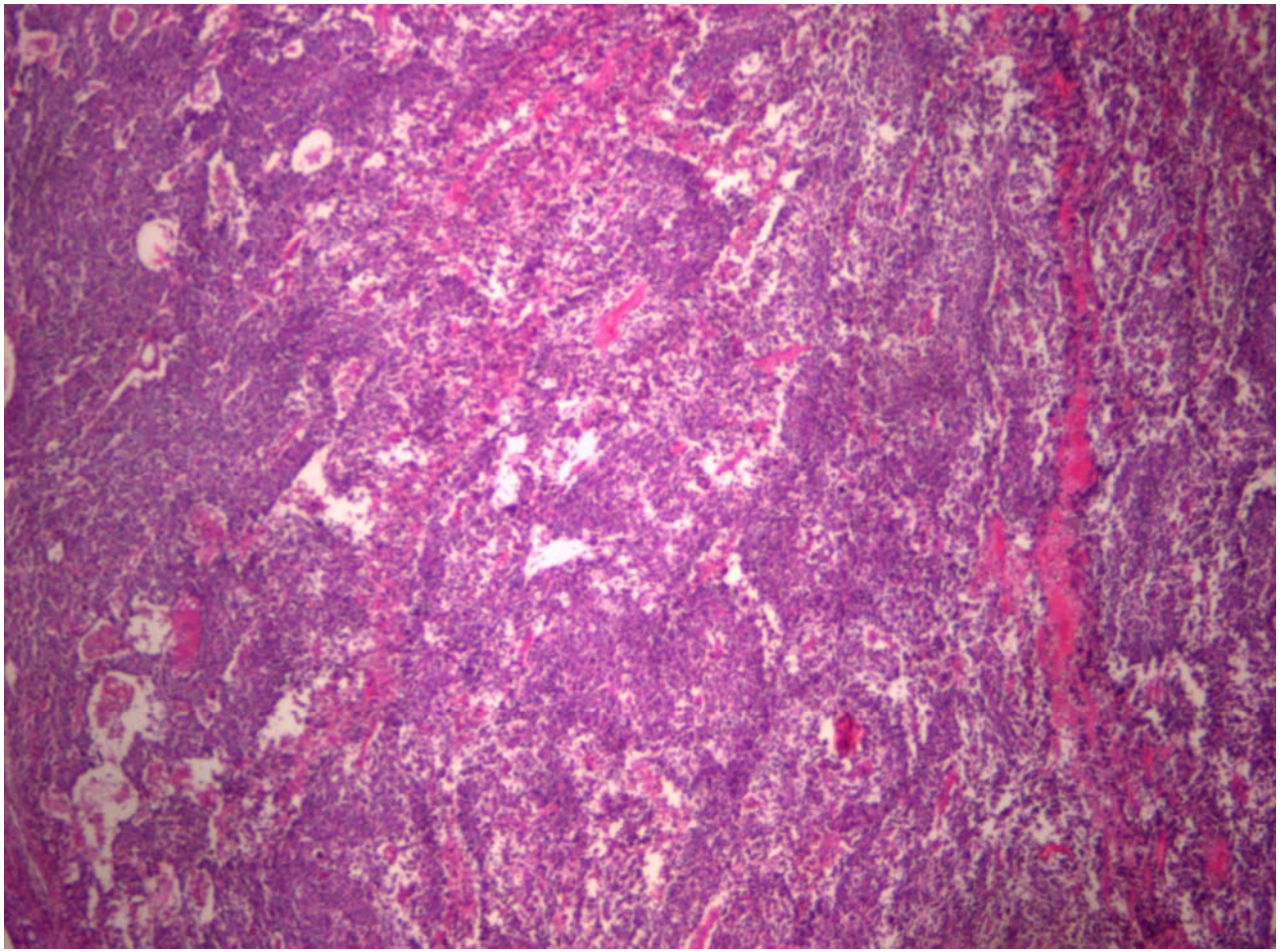
Arcuate vascular plexus



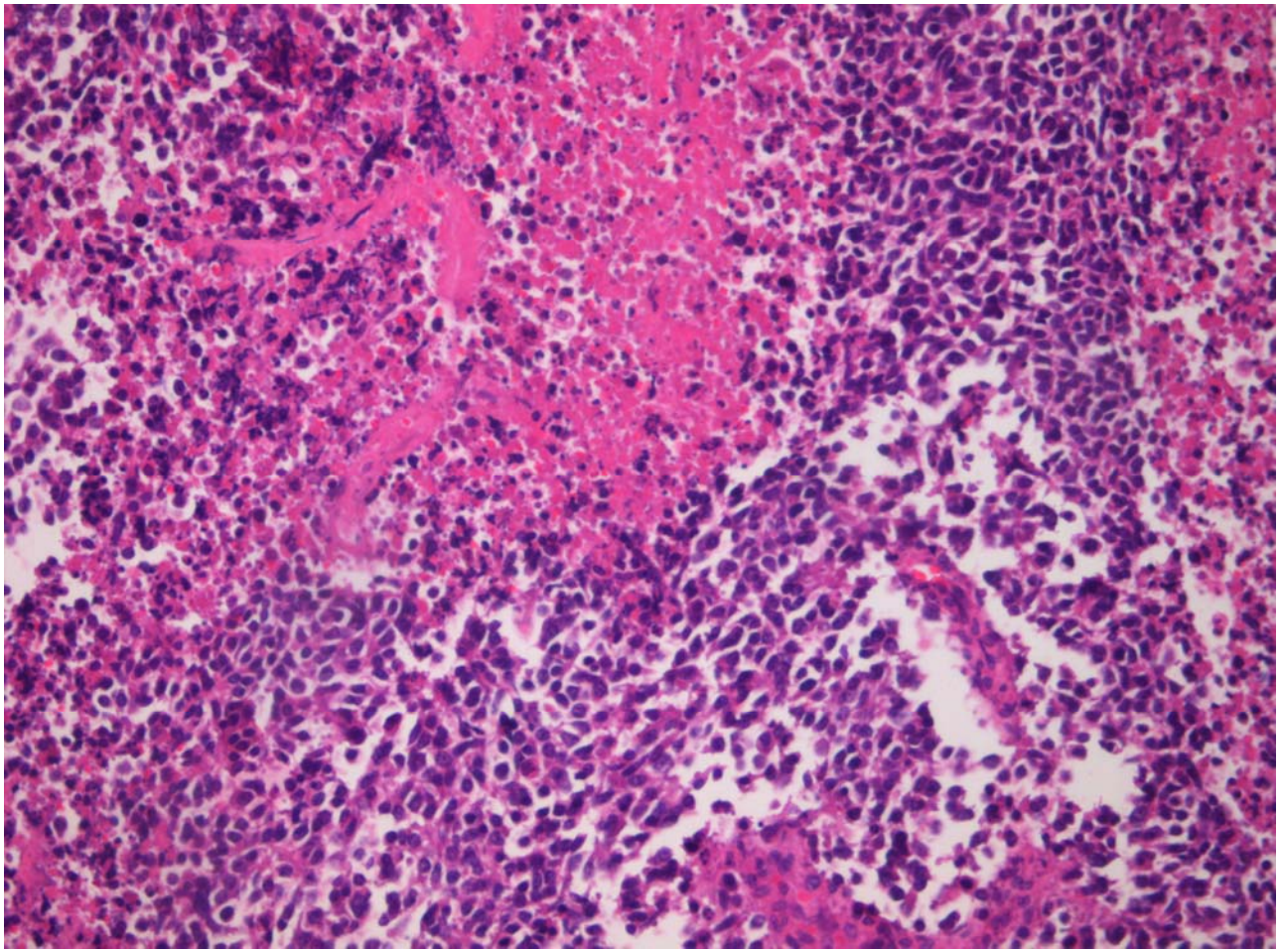
Case 4: presentation

- Age: 69 y
- Symptoms: postmenopausal bleeding

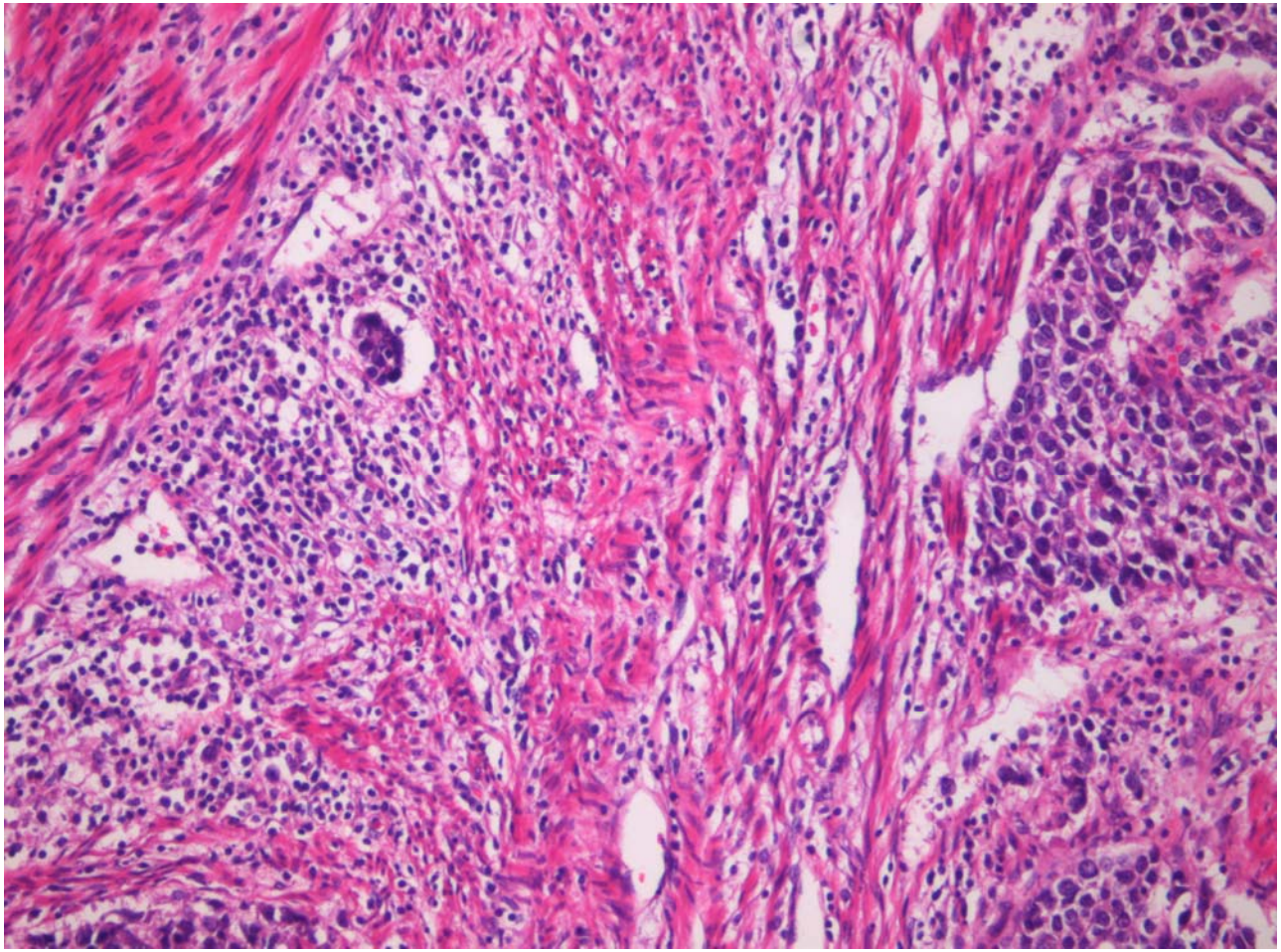
Case 4: highly cellular tumour



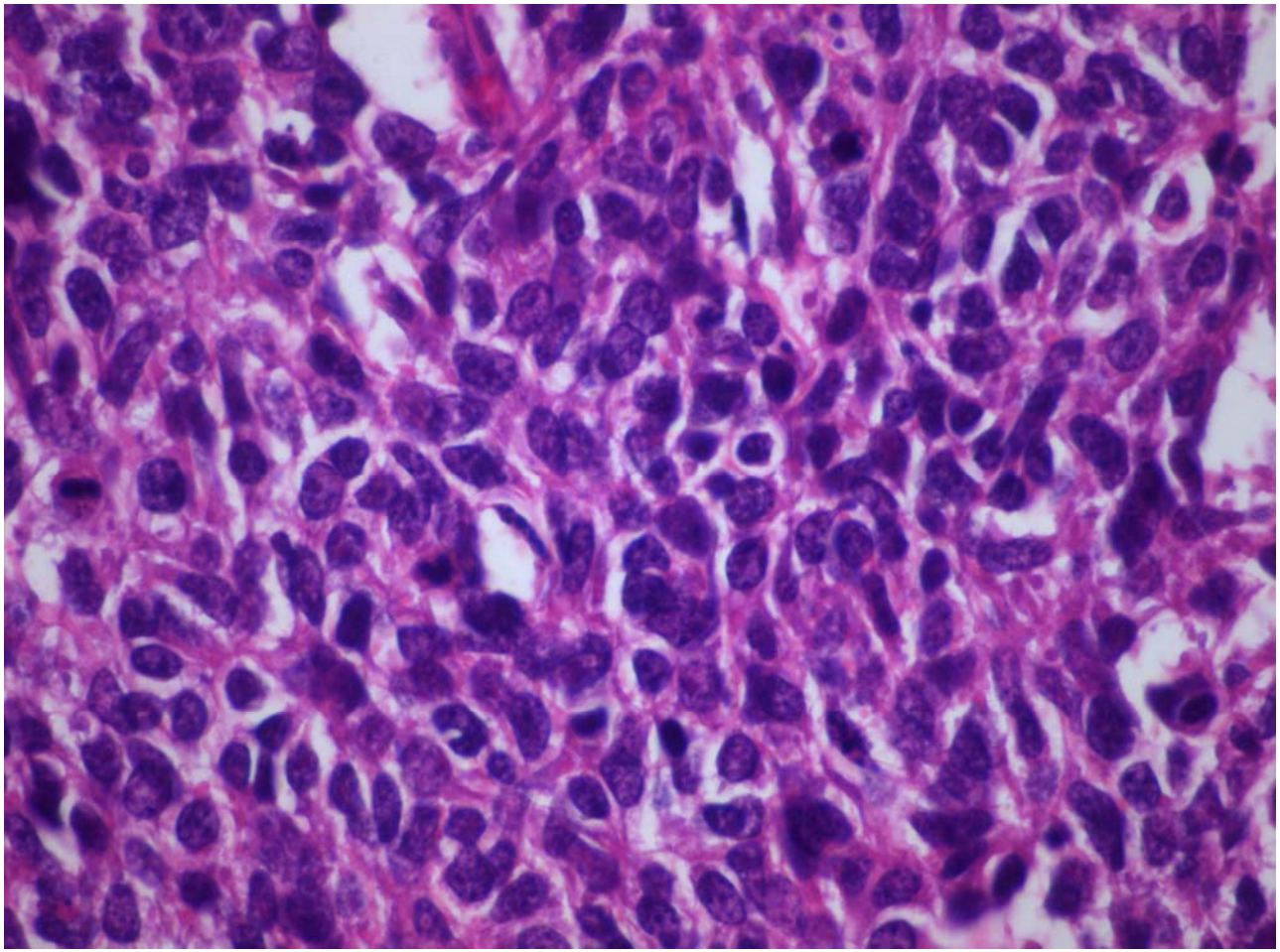
Case 4: necrosis



Case 4: Myometrial invasion and LVI



Case 4: highly atypical and pleomorphic



Case 4

Diagnosis ?????

Undifferentiated carcinoma

- Definition: lacks any differentiation

  (<1% glandular formation)

- Extreme form of grade 3 endometrioid Ca?

  Grade 3: < 50% formation glands

Undifferentiated carcinoma

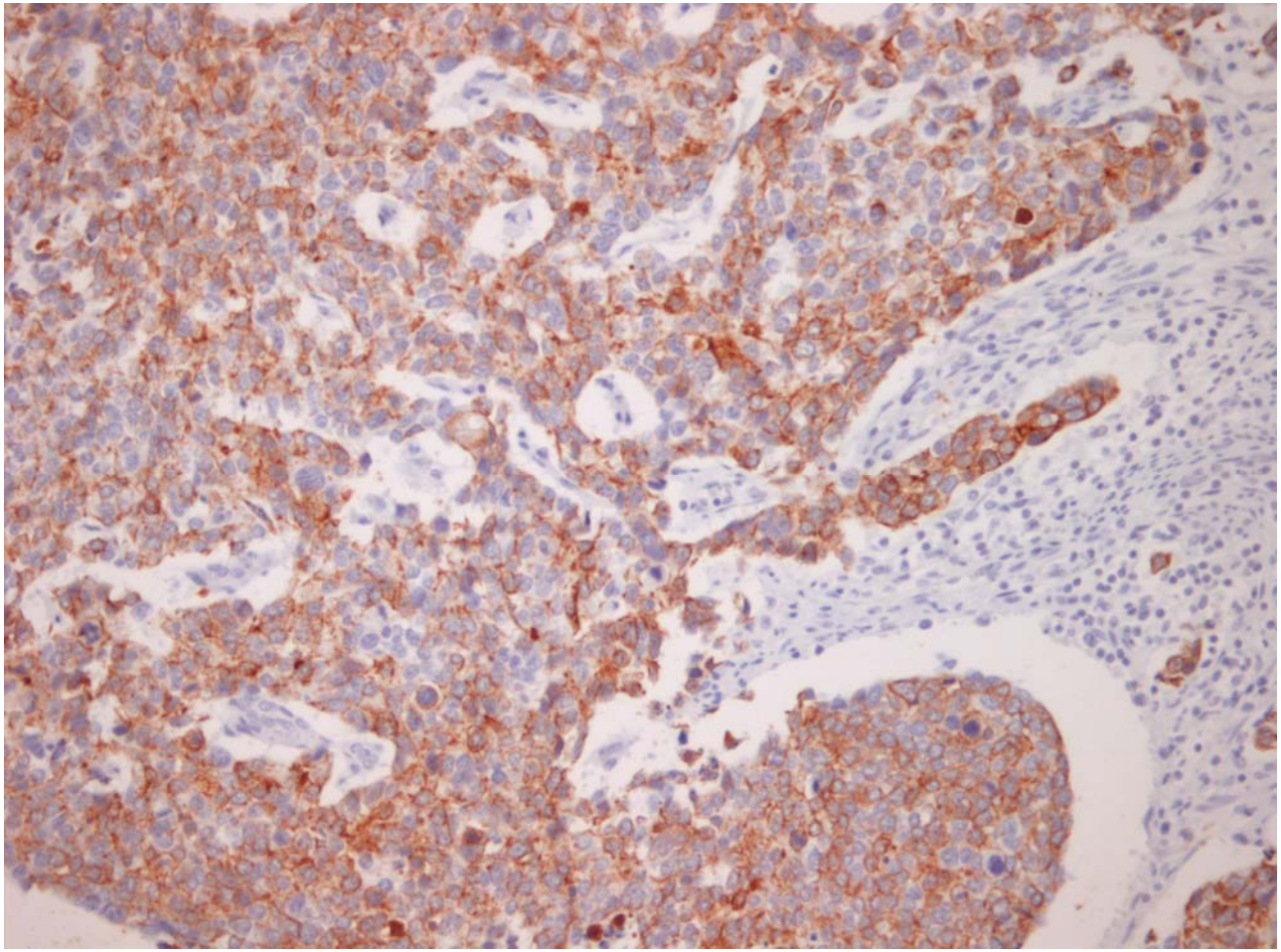
- Medium-sized, monotonous epithelial cells
- Solid sheets
- No specific pattern

Altrabulsi, Am J Surg Pathol 29 (2005) 1316-1325

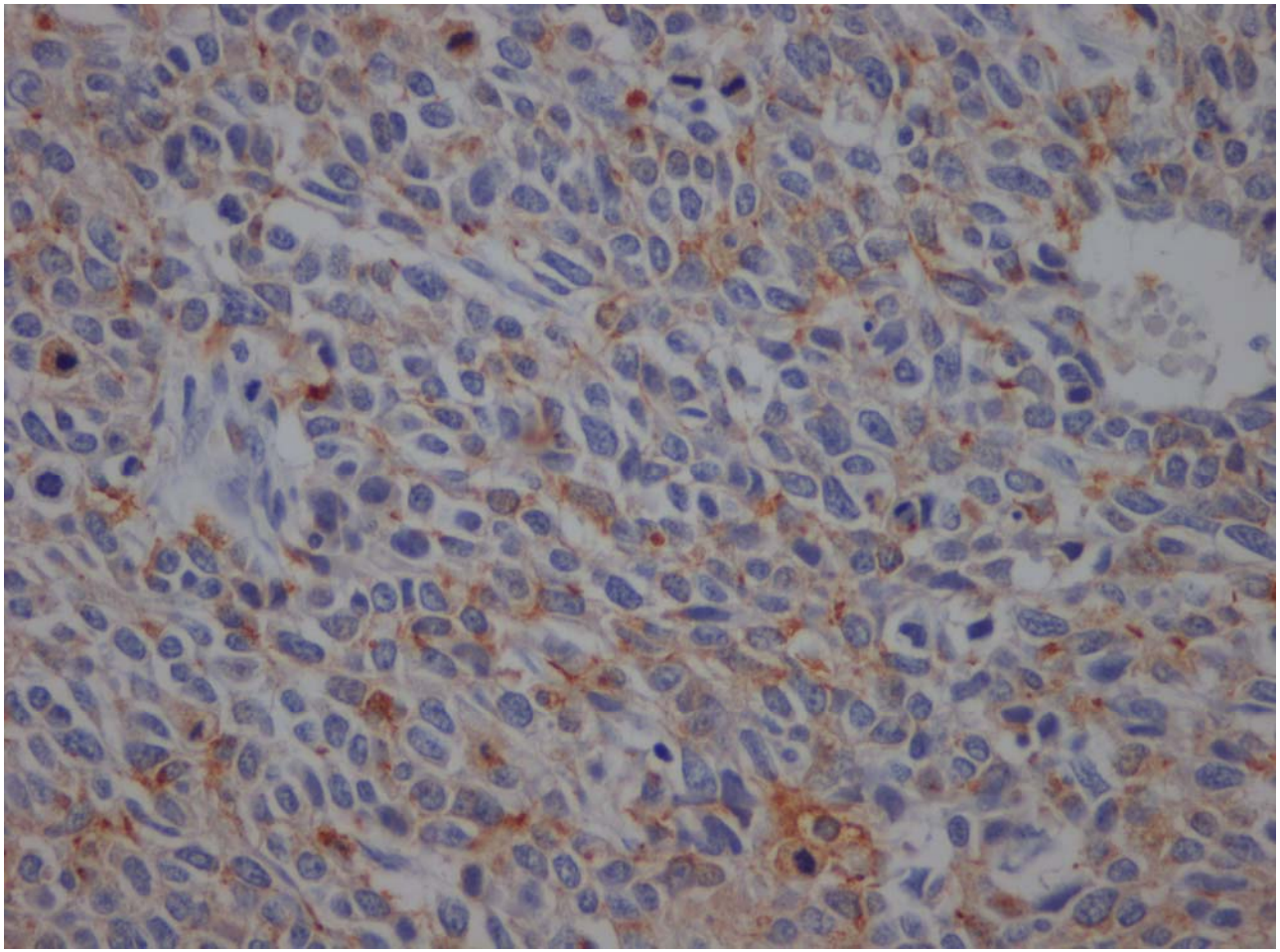
Undifferentiated carcinoma: IHC

- Keratin: focally positive (rarely diffuse)
  - If CK - : don’t conclude “sarcoma”
  - repeat on other block !!!!!
- NE-markers: negative

Case 4: Keratin diffuse positive



Case 4: chromogranin A



Case 4: Diagnosis

- Case 4 doesn't fit with the defintion by MD-Anderson group
  - Small cells
  - Pleomorphic rather than monotous
  - CK diffuse +
  - NE +

Case 4: Diagnosis

- Small cell neuroendocrine carcinoma of the endometrium

- Exclude metastase !!!!!

SCNE Carcinoma

- Rare : < 1% of EmCa

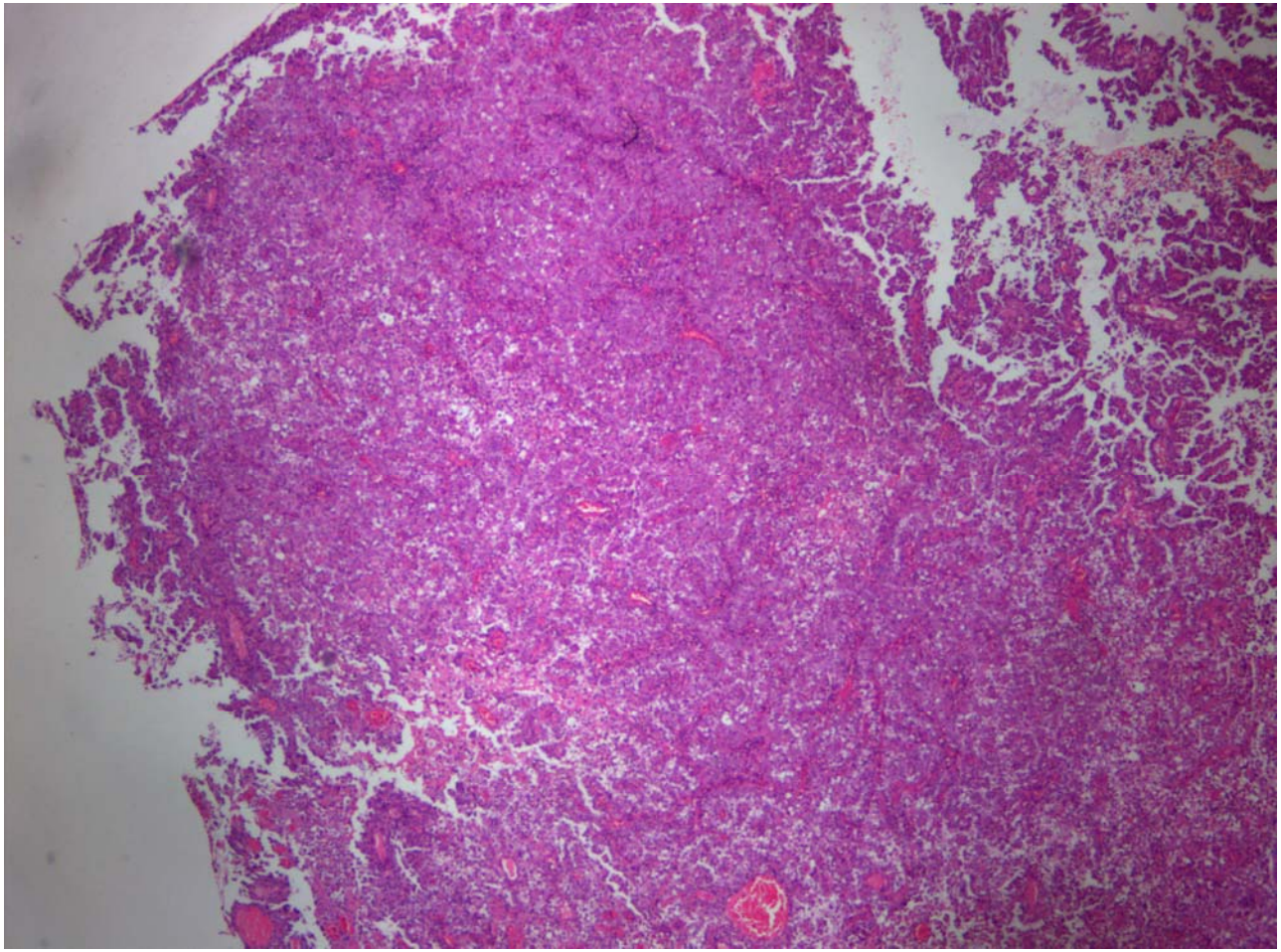
- Pagetoid spread to cervix is possible

  Posligua, Arch Pathol Lab Med 132 (2008) 1821-1824

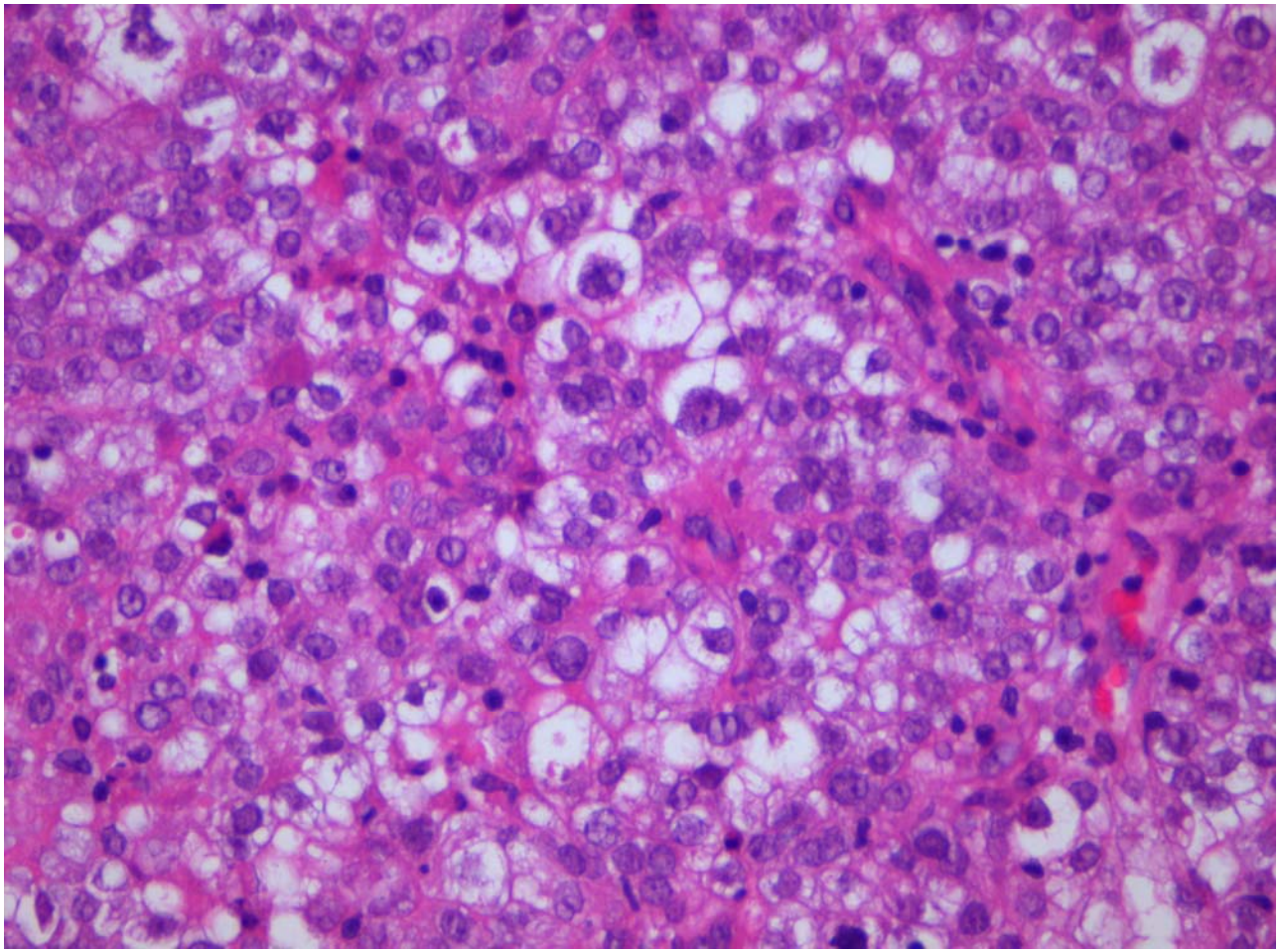
Case 5: Presentation

- Age: 78 y
- Biopsy from cervical mass lesion: “squamous cell carcinoma or adenocarcinoma cervix?”

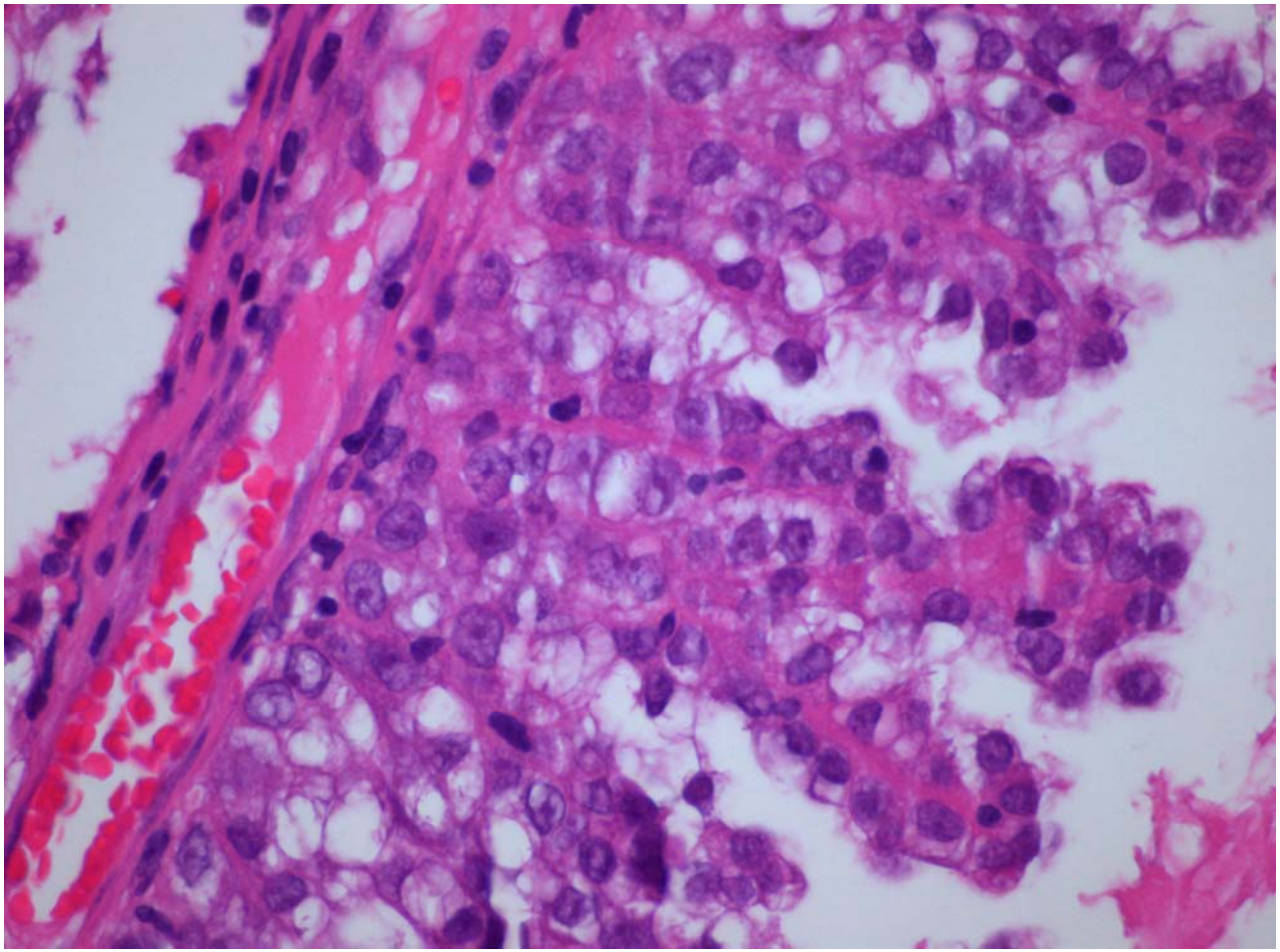
Case 5: mix of architectural patterns



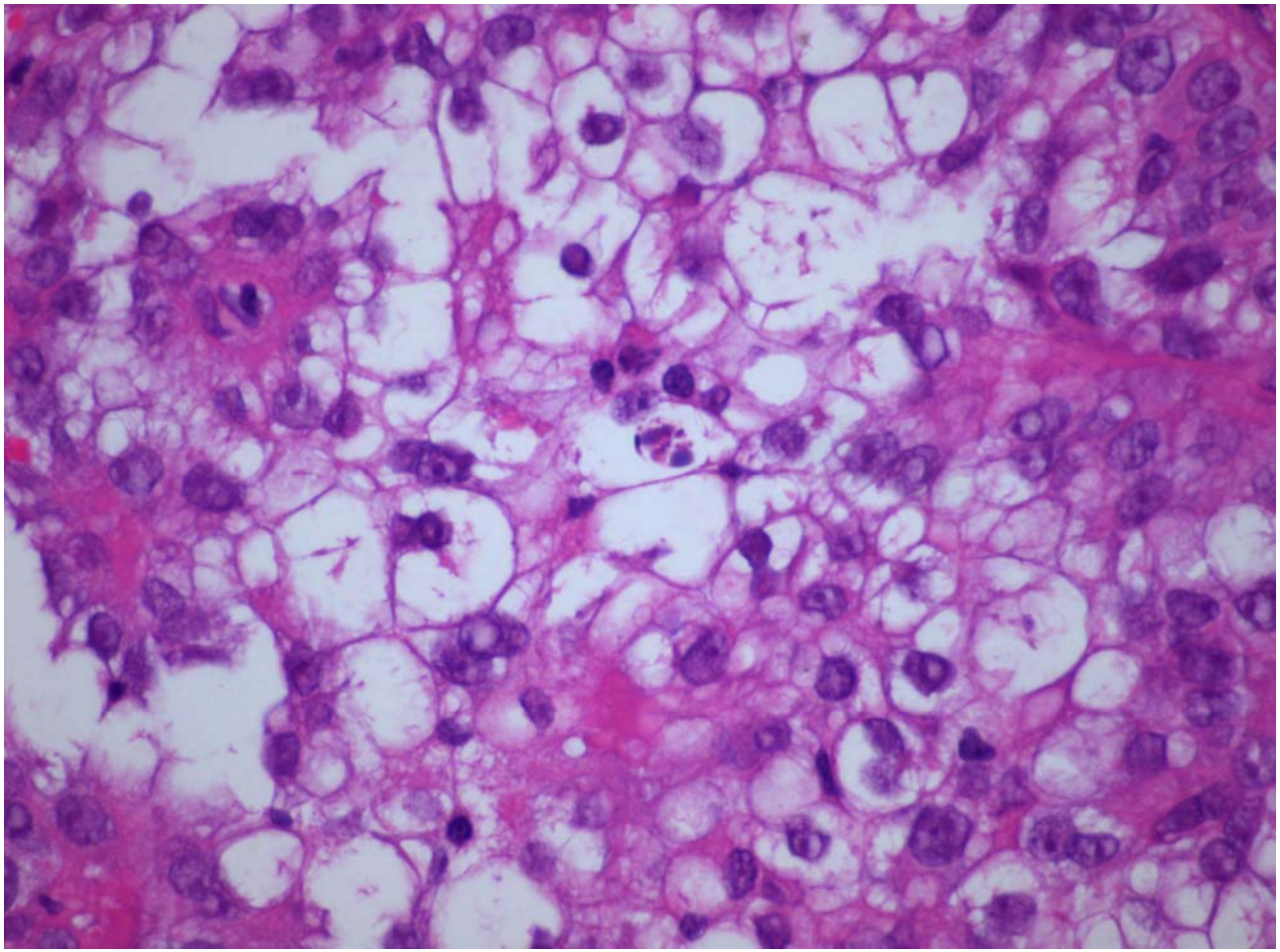
Case 5: polygonal cells



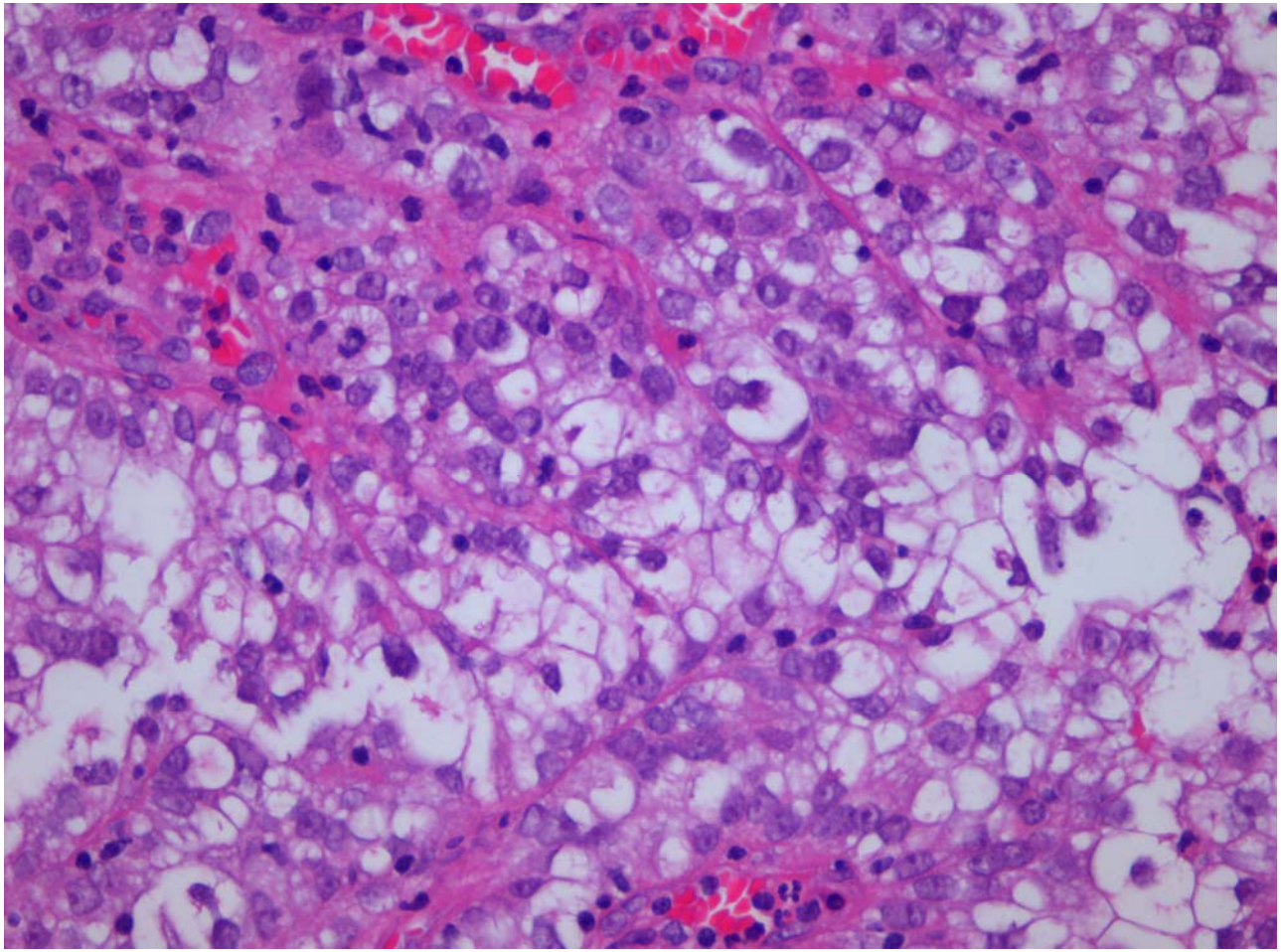
Case 5: hobnail cells



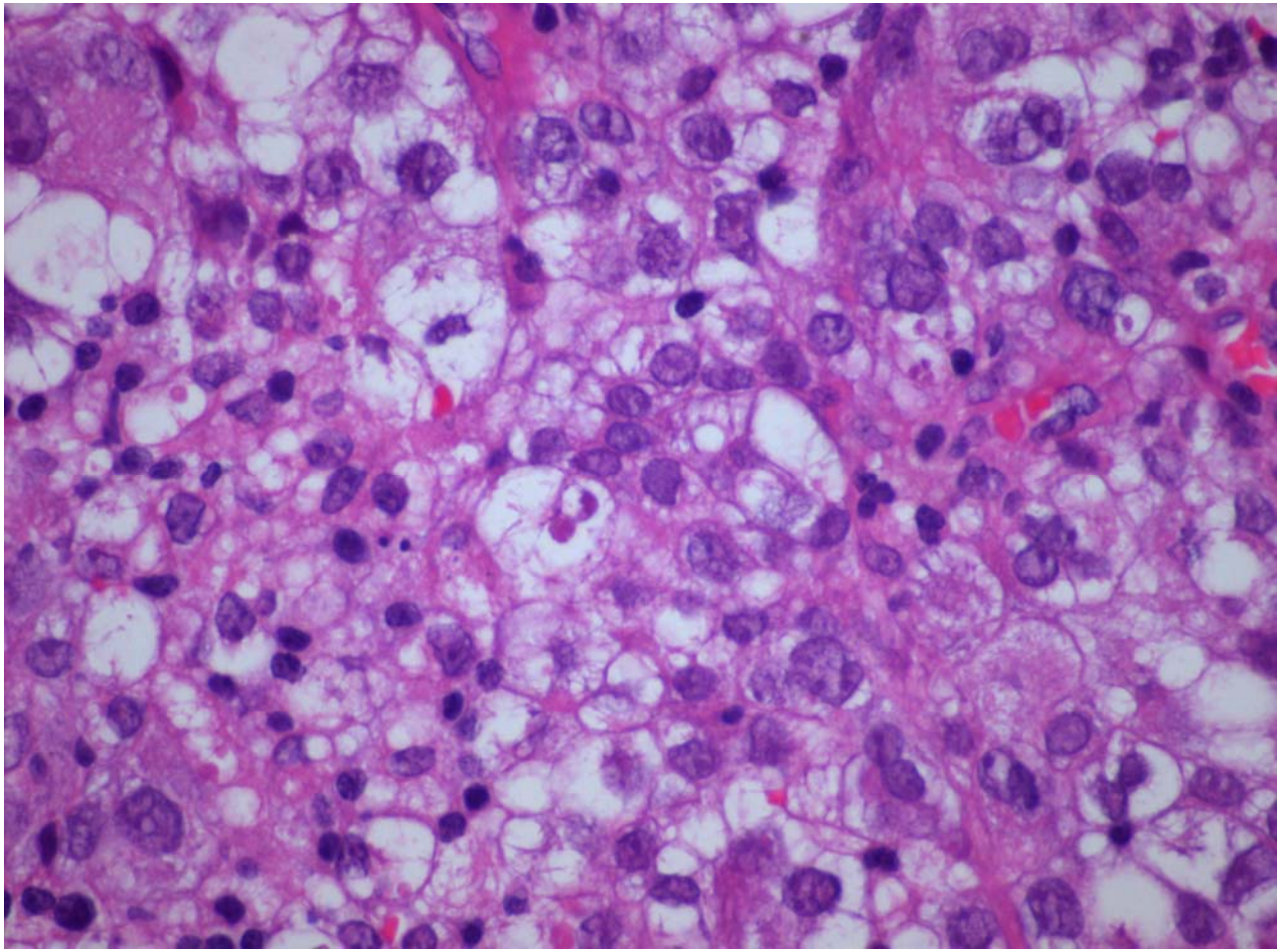
Case 5: atypical nuclei



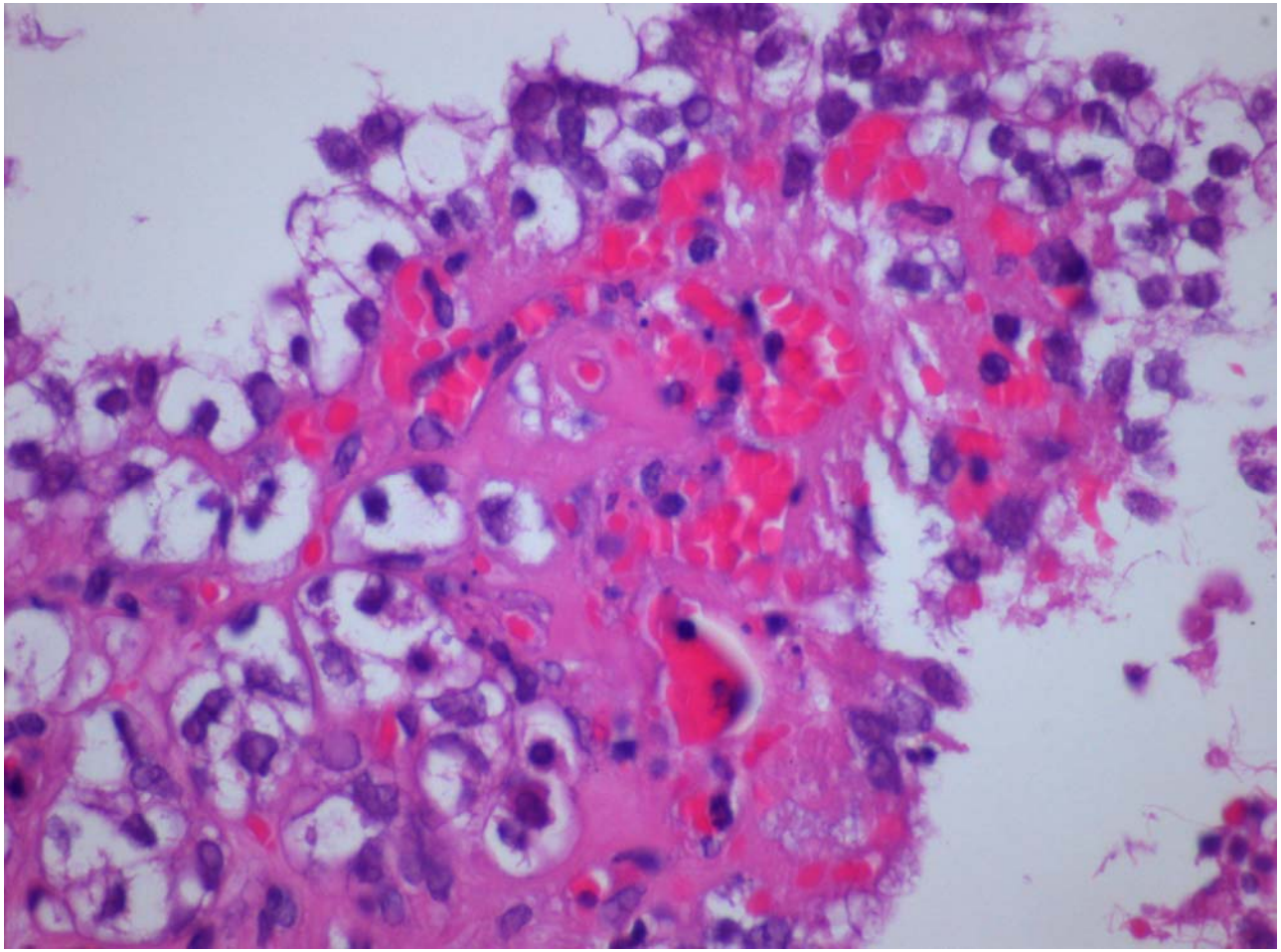
Case 5: Clear cytoplasm with distinct cell borders



Case 5: eosinophilic globules



Case 5: stromal hyalinisation



Case 5: Diagnosis

Clear cell carcinoma

Types of EmCa

- Endometrioid
  - Villoglandular
  - Secretory
  - Squamous differentiation
  - Ciliated
- Mucinous

- Serous: 10 %
- Clear cell: 2-3 %

- Carcinosarcoma

Clear cell Ca: patterns

- Typical admixture of patterns:
  - Solid
  - Papillary
  - Tubular

Clear cell Ca: cytology

- Clear cytoplasm (sometimes eosinophilic)
- Marked atypia but not much mitoses
- Less exfoliation than serous Ca

Look for:

- Hyalinised stroma
- Eosinophilic globules

IHC

- P53 +
- Ki67 +
- ER –
- HNF1β +

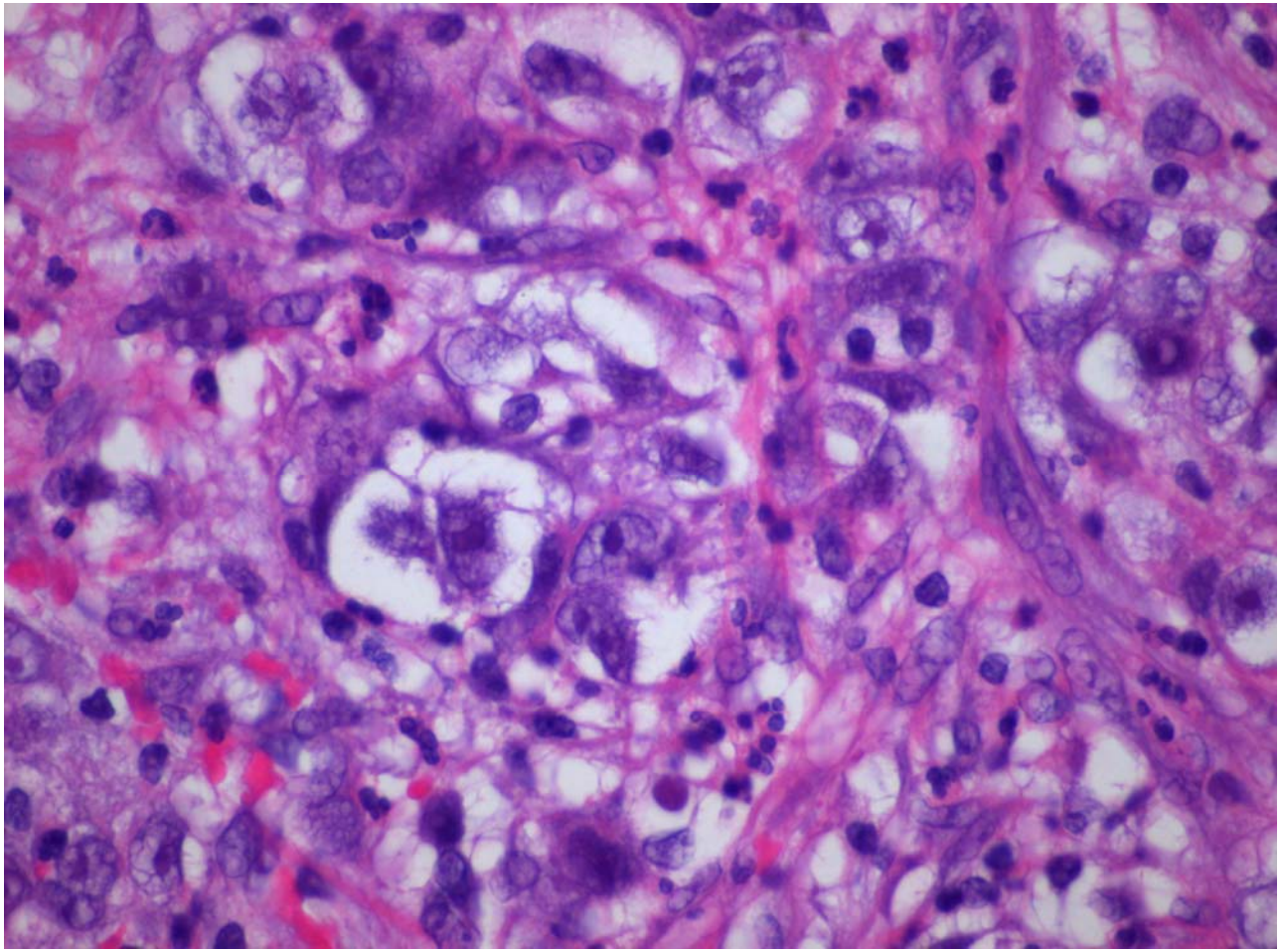
Clear cell carcinoma: DD

- CCCa-component in other type Ca
- Clear cells in other type
- Clear cell change after chemotherapy
- Clear cell change after Mirena

Clear cell change after neoadjuvant chemotherapy

- NAC for Ovarian Ca
- NAC for EmCa

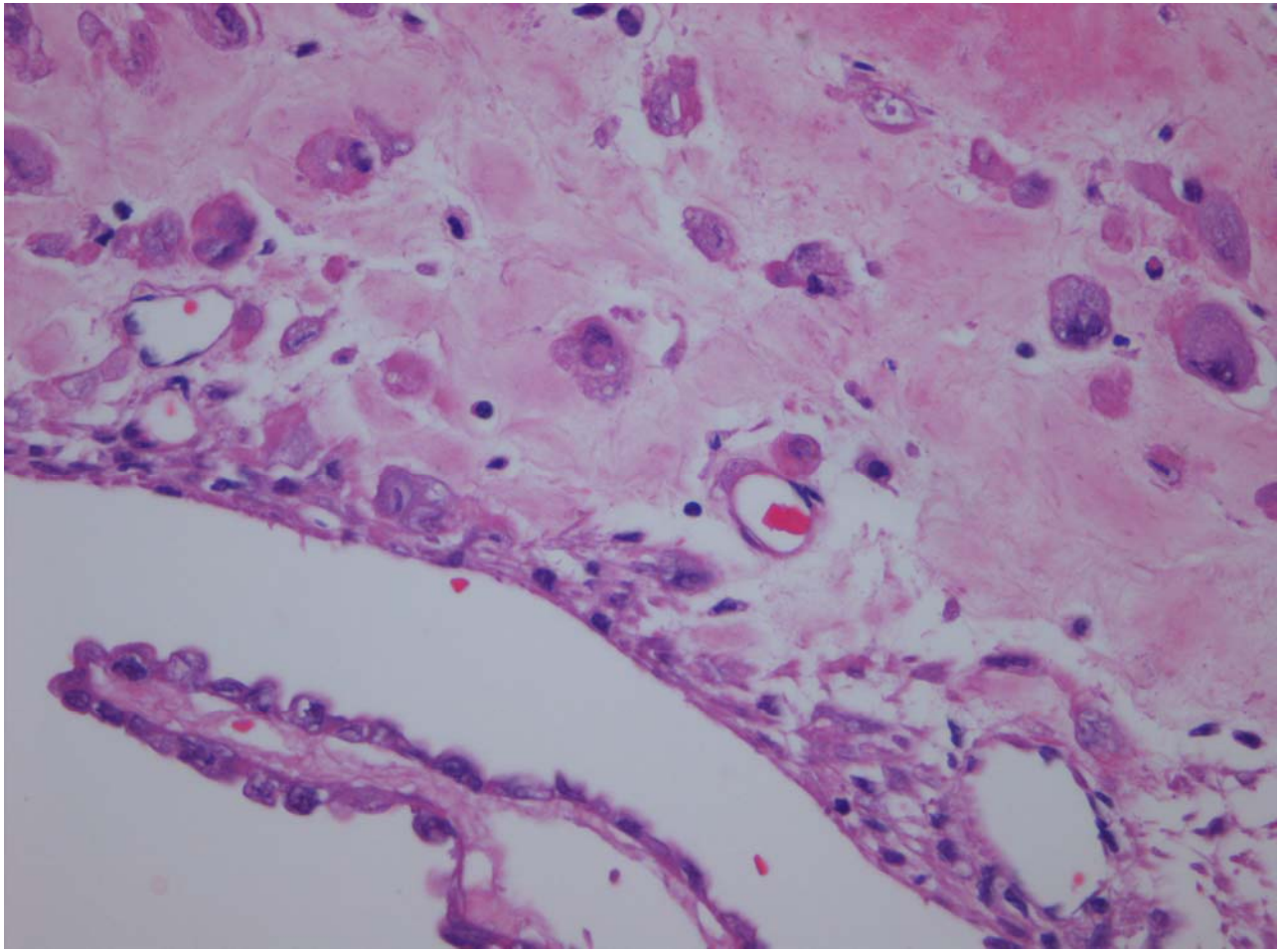
Serous Ca after NAC



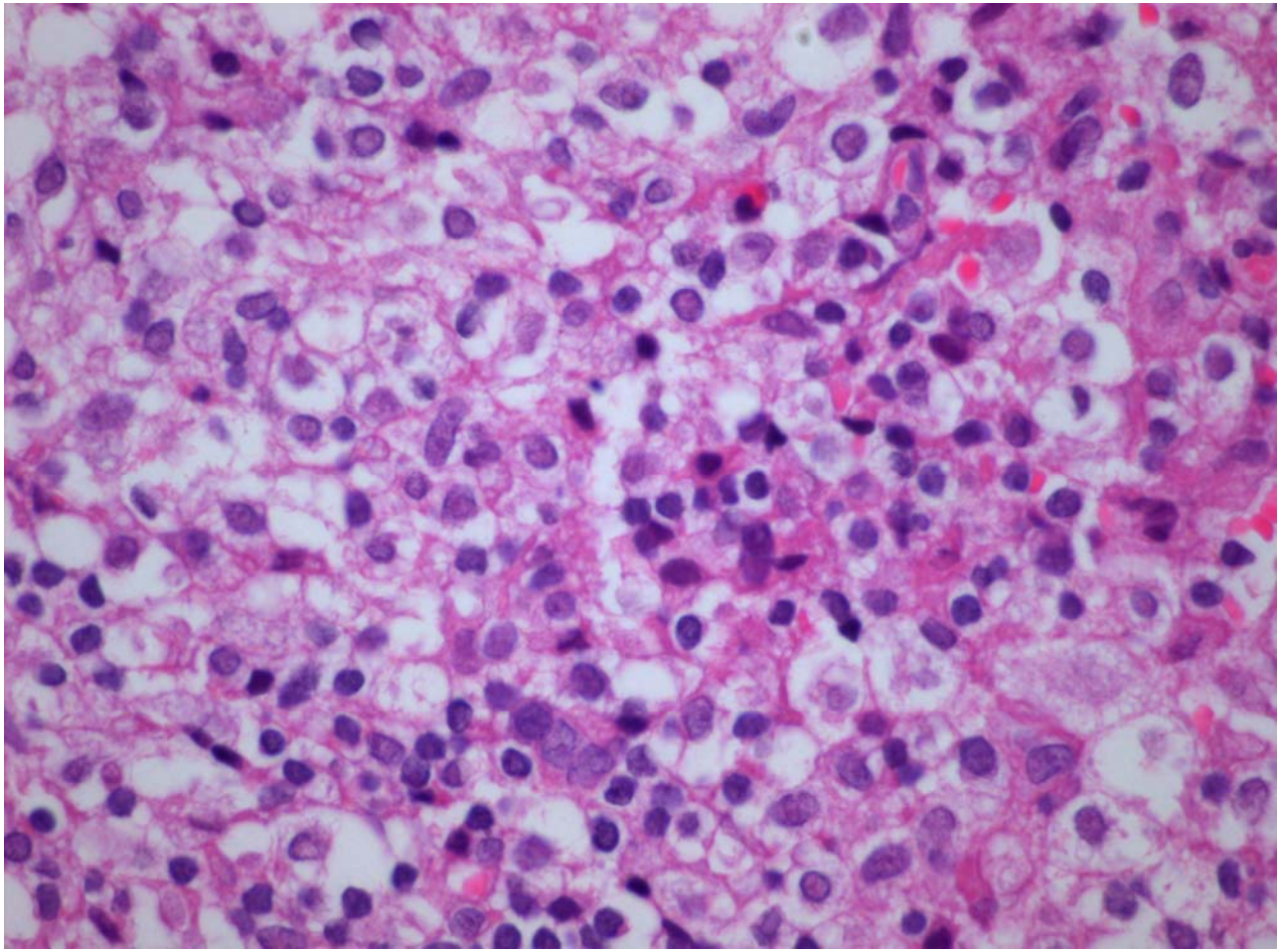
Clear cell change after Mirena

- Clear cells between “more normal” cells
- No abrupt transition
- Ki67 -

Mirena: hobnail cells



Not all clear cells are clear cell Ca !

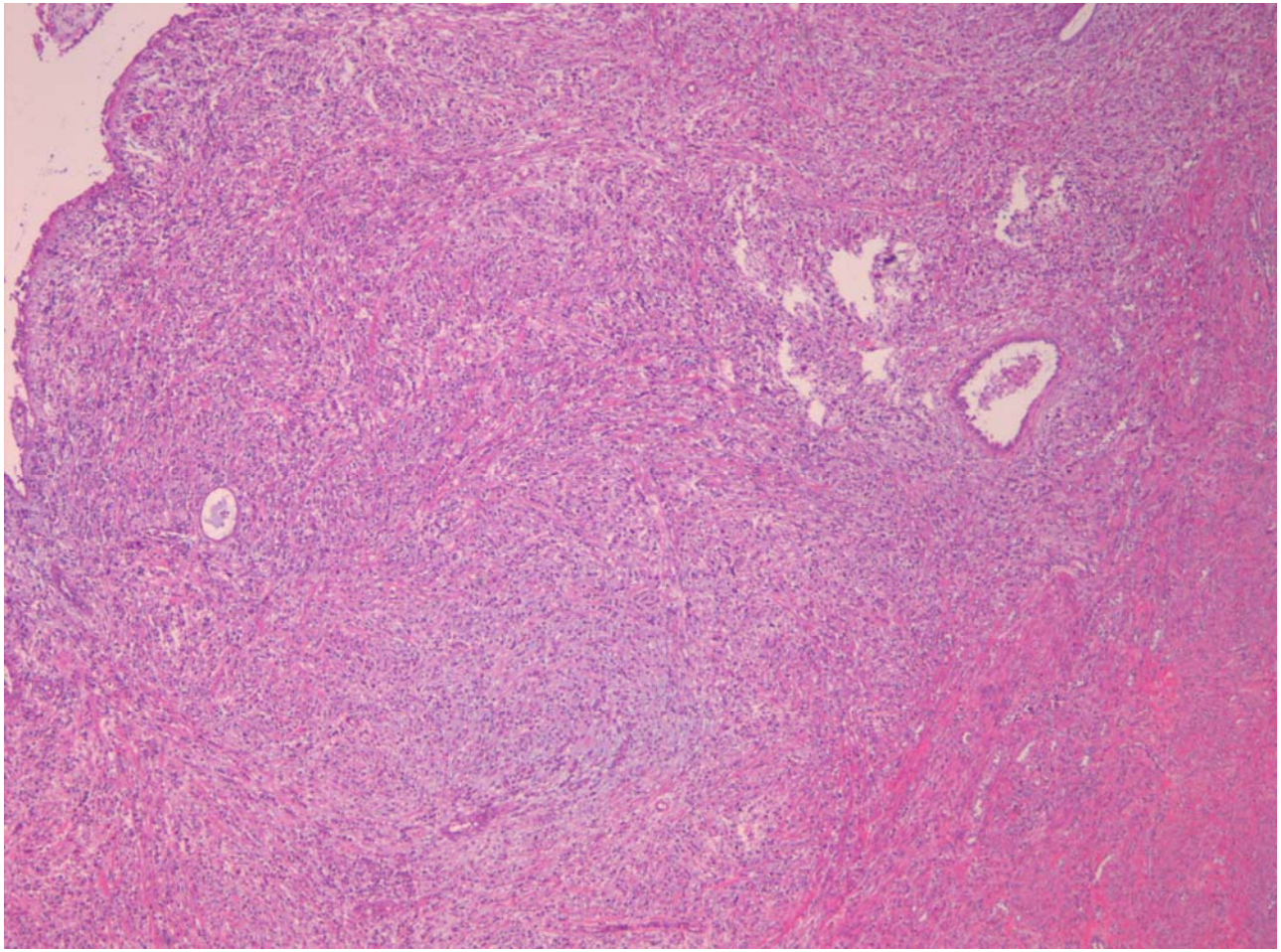


Case 6: Presentation

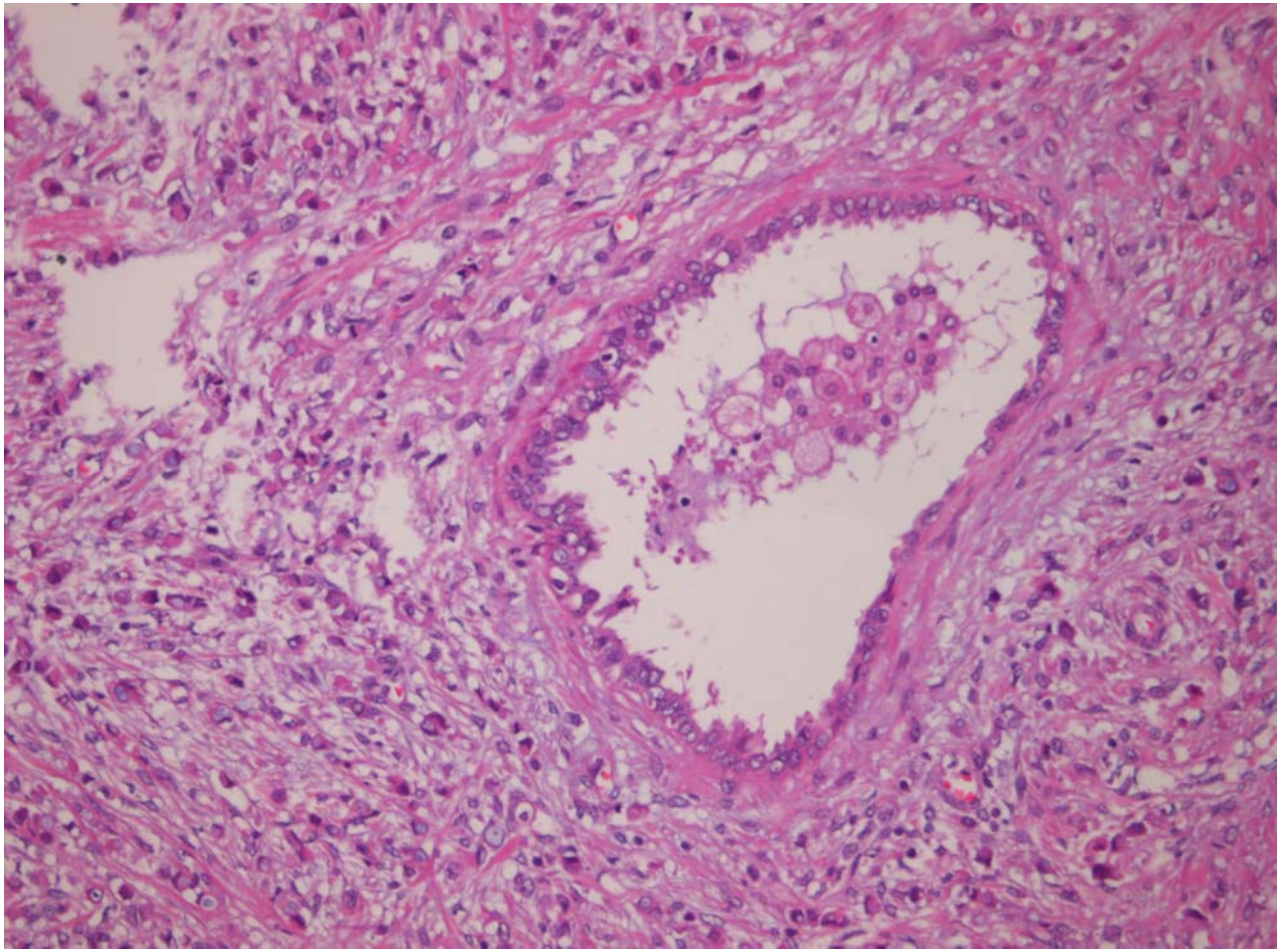
- Age: 56 y

- US: Thick endometrium
- Hysteroscopy: Nodule in dorsal part of cavum

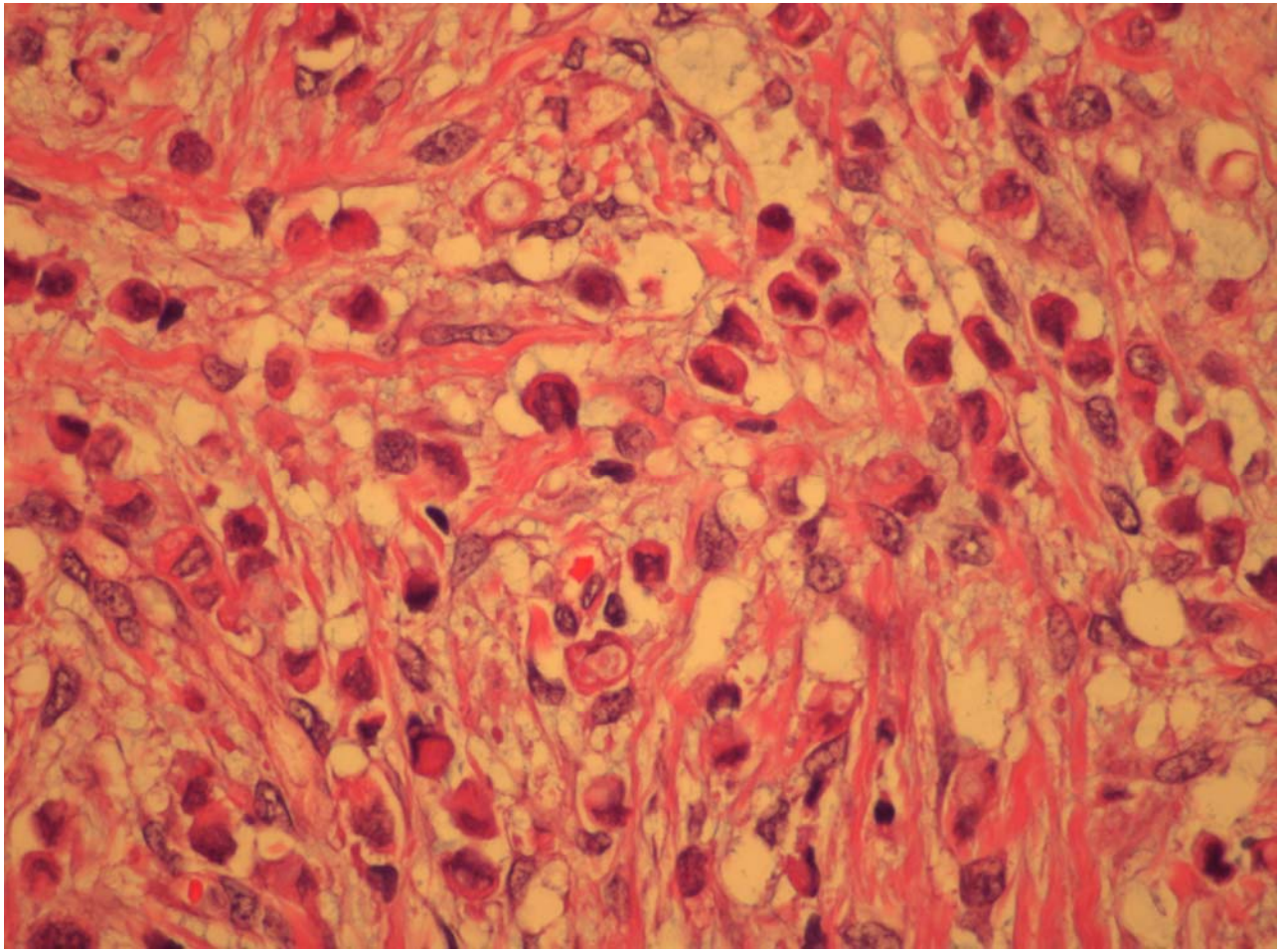
Case 6: thick endometrium



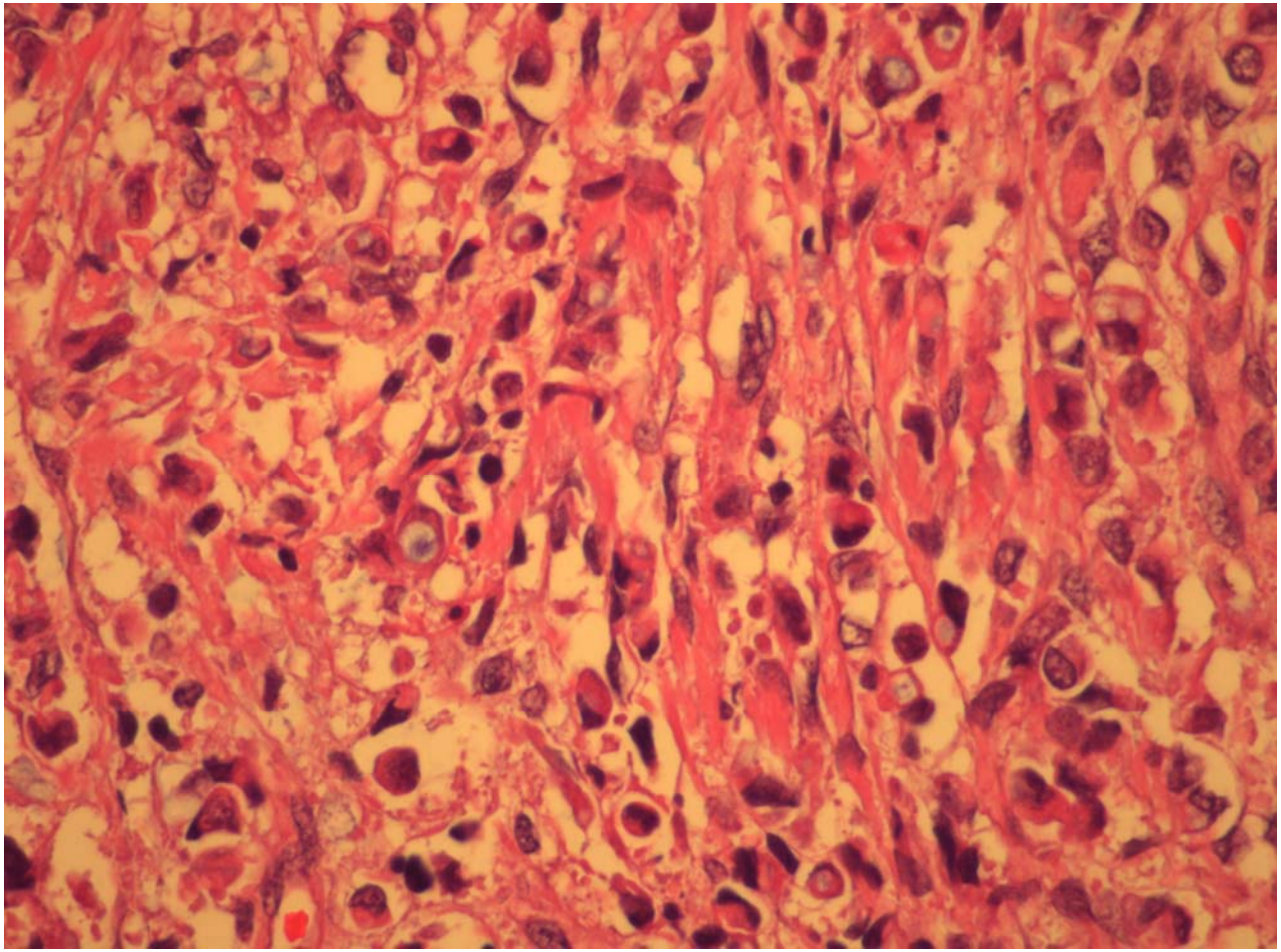
Case 6: infiltration spares glands



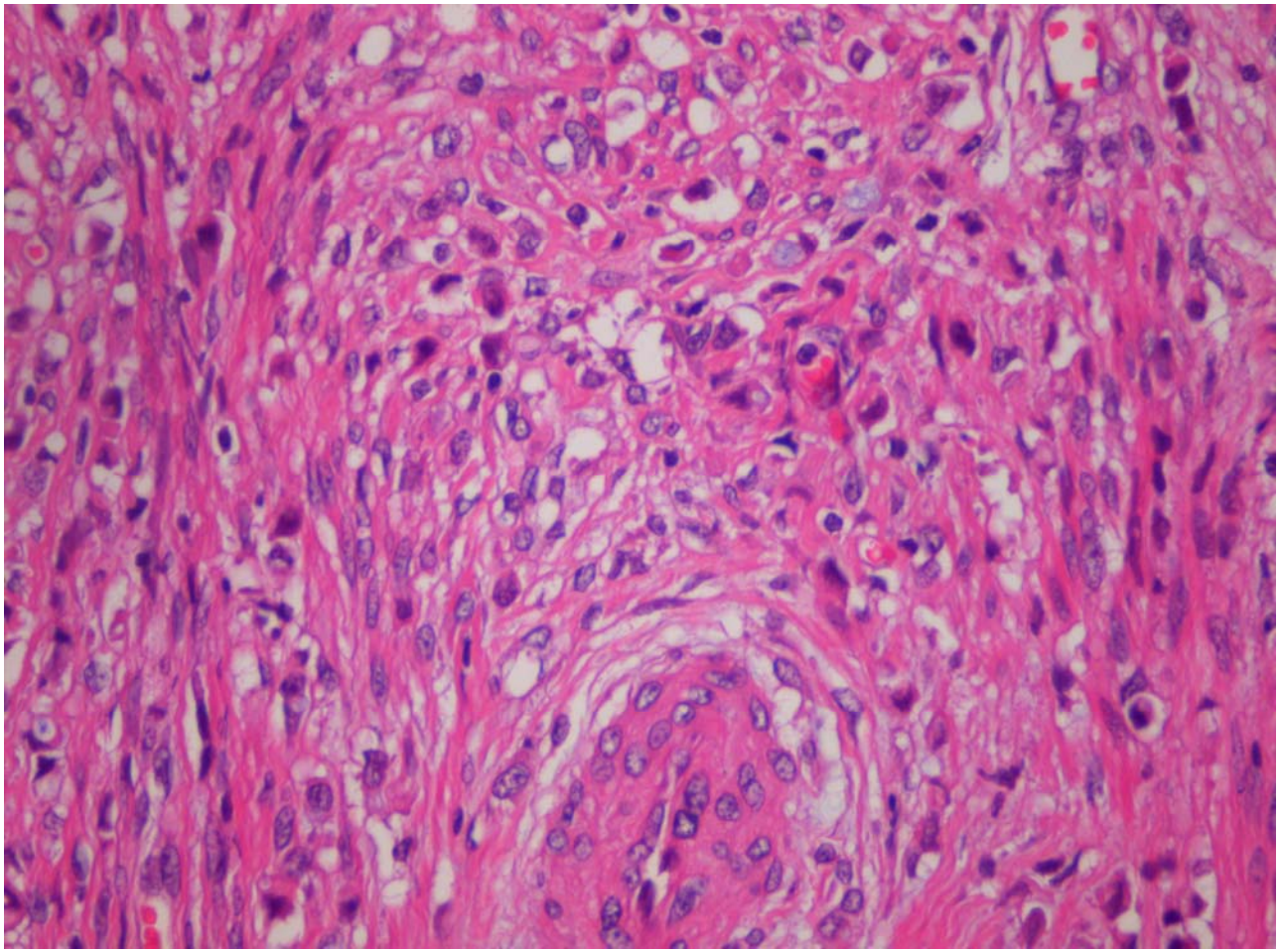
Case 6: individual cells



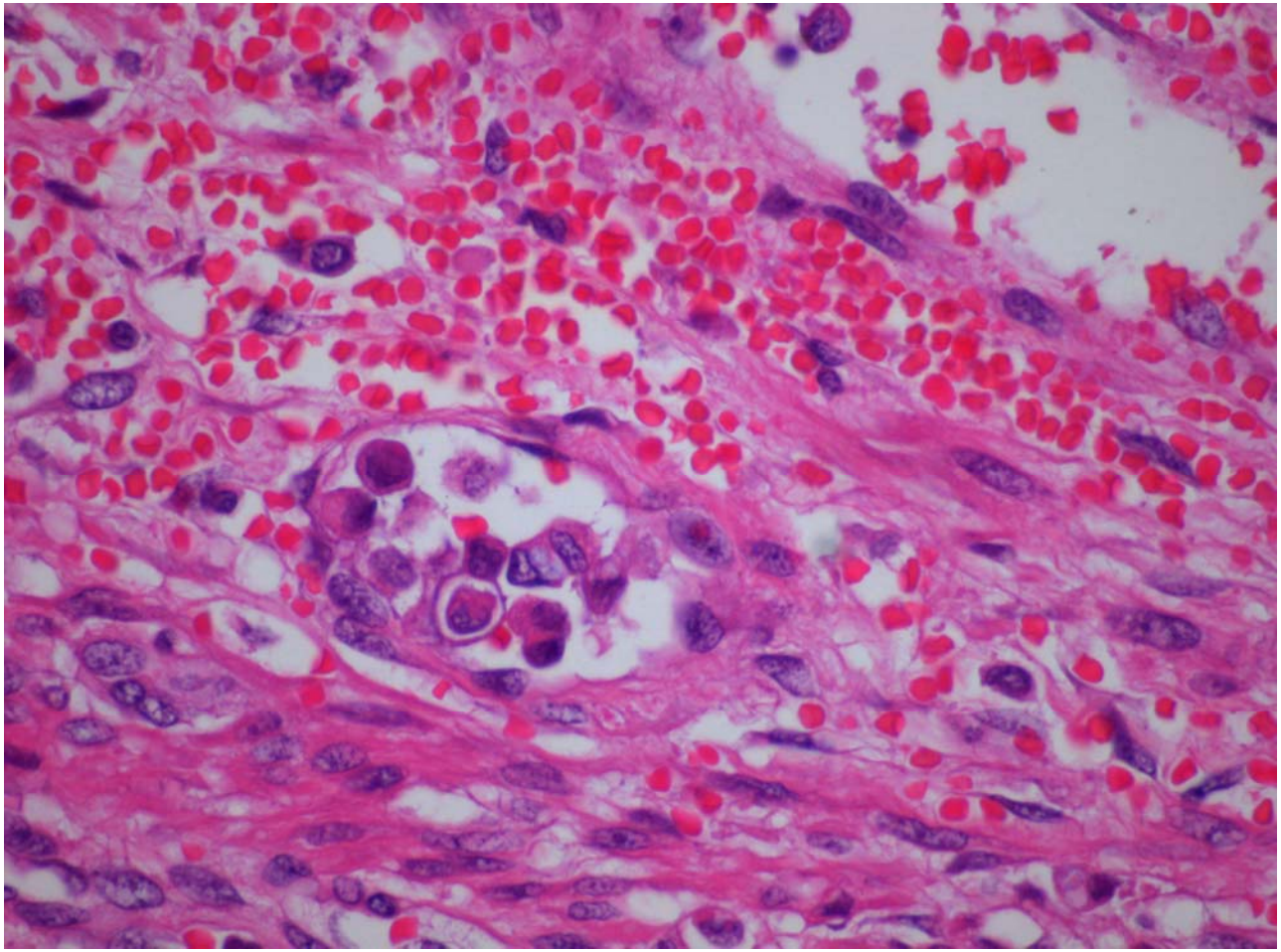
Case 6: mucin in cytoplasm



Case 6: tumour invades deeply in myometrium



Case 6: vascular invasion



Case 6: what's special?

- Signet ring cells
- Deep myometrial involvement
- LVI

Case 6: diagnosis

- Metastatic lobular carcinoma of the breast
- 2 years prior: mastectomy

Metastases to endometrium

- Rare
- Myometrium more often affected

- Think of it !!!

What should alert you?

- Clinical history
- Morphology:
  - Signet ring cell carcinoma of endometrium ??
  - Infiltration stroma with preservation of glands
- LVI

Are signet ring cells impossible?

Int J Gynecol Pathol. 2010 Sep 28. [Epub ahead of print]

Endometrial Adenocarcinoma With Signet Ring Cells: Report of Two Cases of an Extremely Rare Phenomenon.

Boyd C, Cameron I, McCluggage.Department of Pathology (C.B., W.G.M.), Belfast Health and Social Care Trust, Belfast Department of Pathology (I.C.), Altnagelvin Area Hospital, Londonderry, Northern Ireland.

AbstractThe presence of signet ring cells in a carcinoma within the uterine corpus strongly raises the possibility of a metastasis from a primary tumor in the breast, gastrointestinal tract, or elsewhere. Signet ring cells are extremely rare in primary endometrial adenocarcinomas with only a single prior case report. We report 2 cases of primary endometrial adenocarcinoma, one of mucinous and the other of endometrioid type, with a significant component of signet ring cells. One of the neoplasms arose within adenomyosis. In reporting these cases, we illustrate that the presence of signet ring cells does not preclude a primary endometrial adenocarcinoma. We discuss signet ring cells in the endometrium.

Which primary?

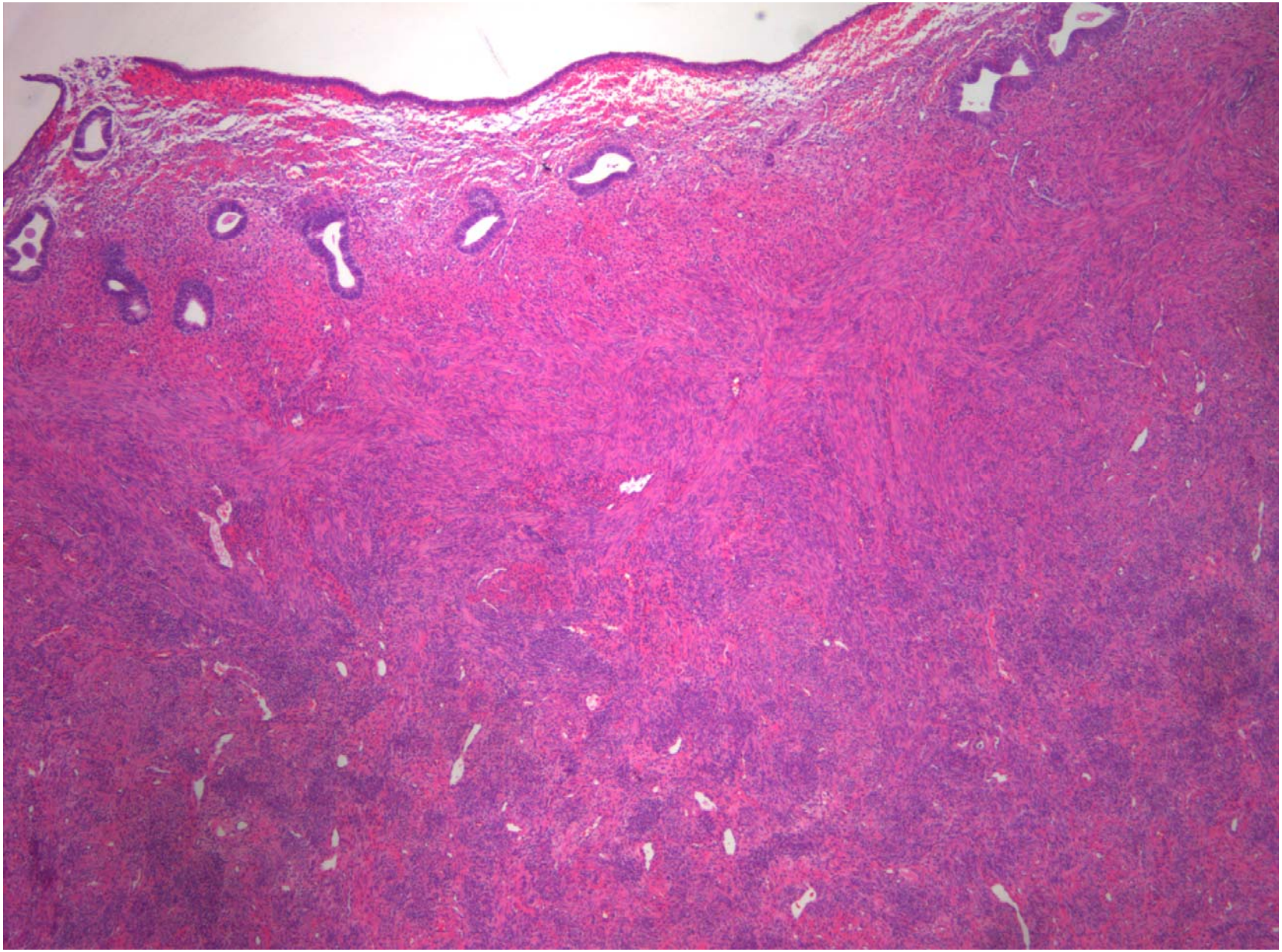
- Cervix
- Ovary / Fallopian tube

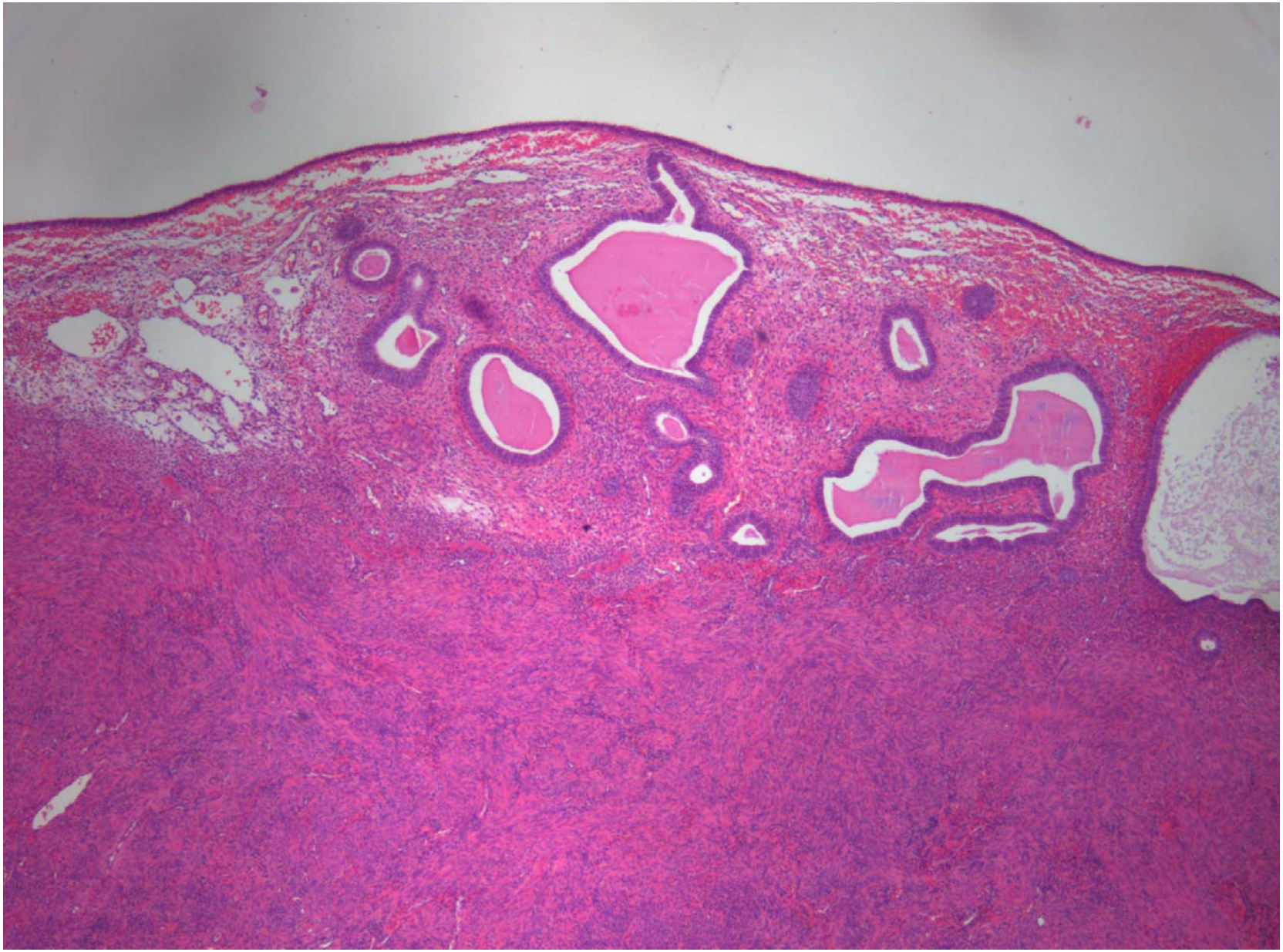
- Gastro-intestinal
  - Stomach
  - Colon

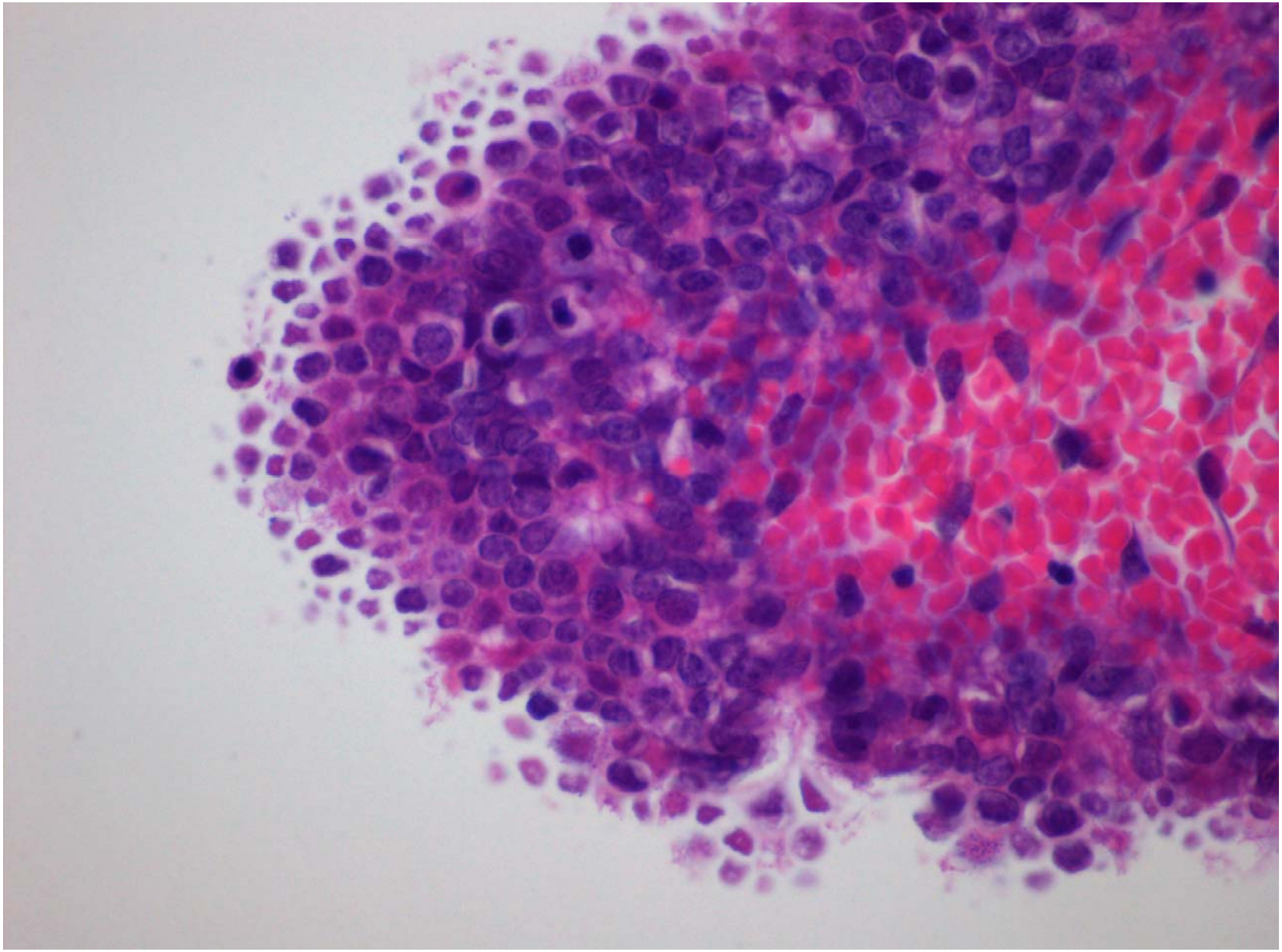
- Breast: 2-15 % of all breast Ca gives metastases to uterus

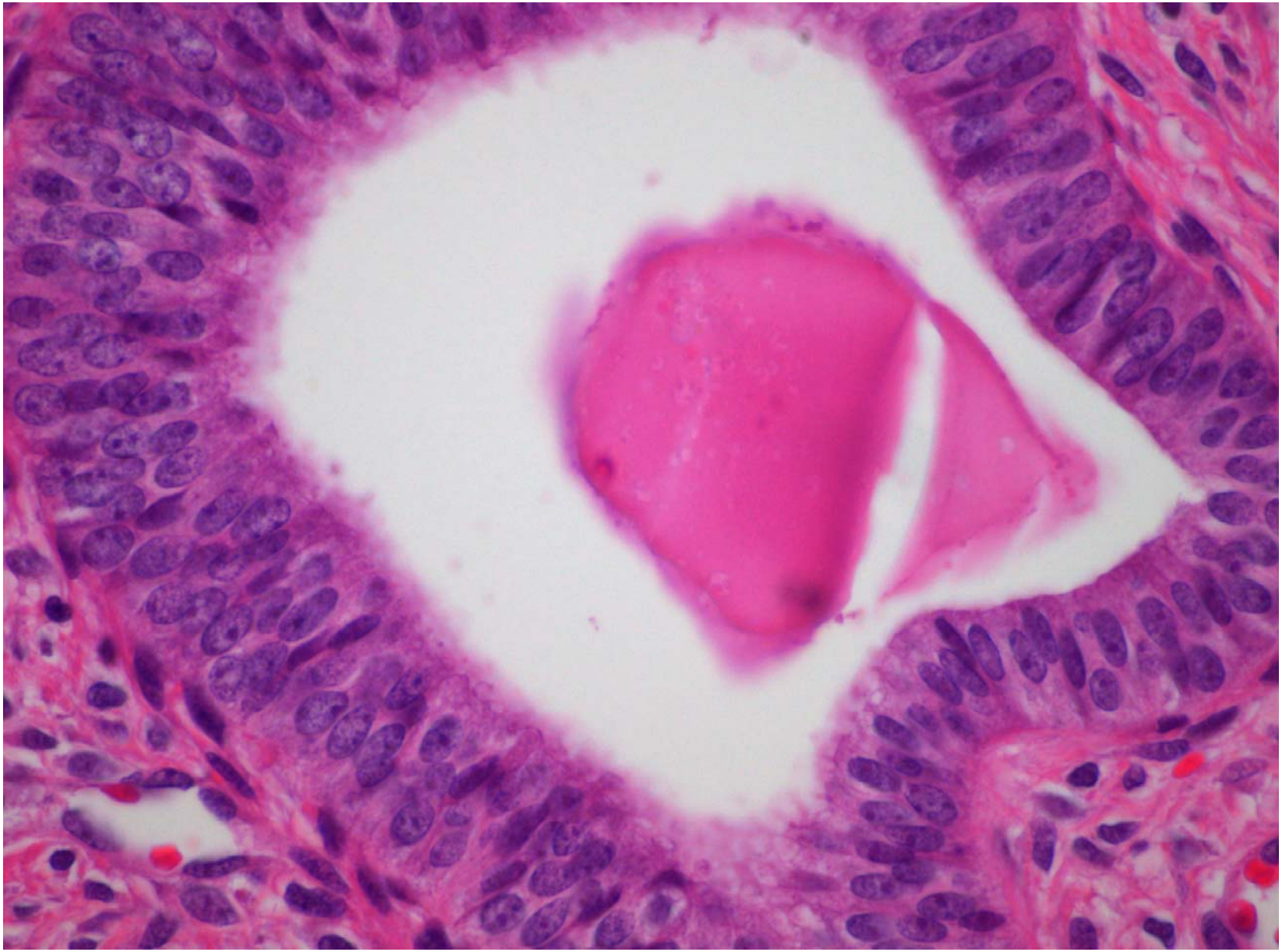
Case 7: presentation

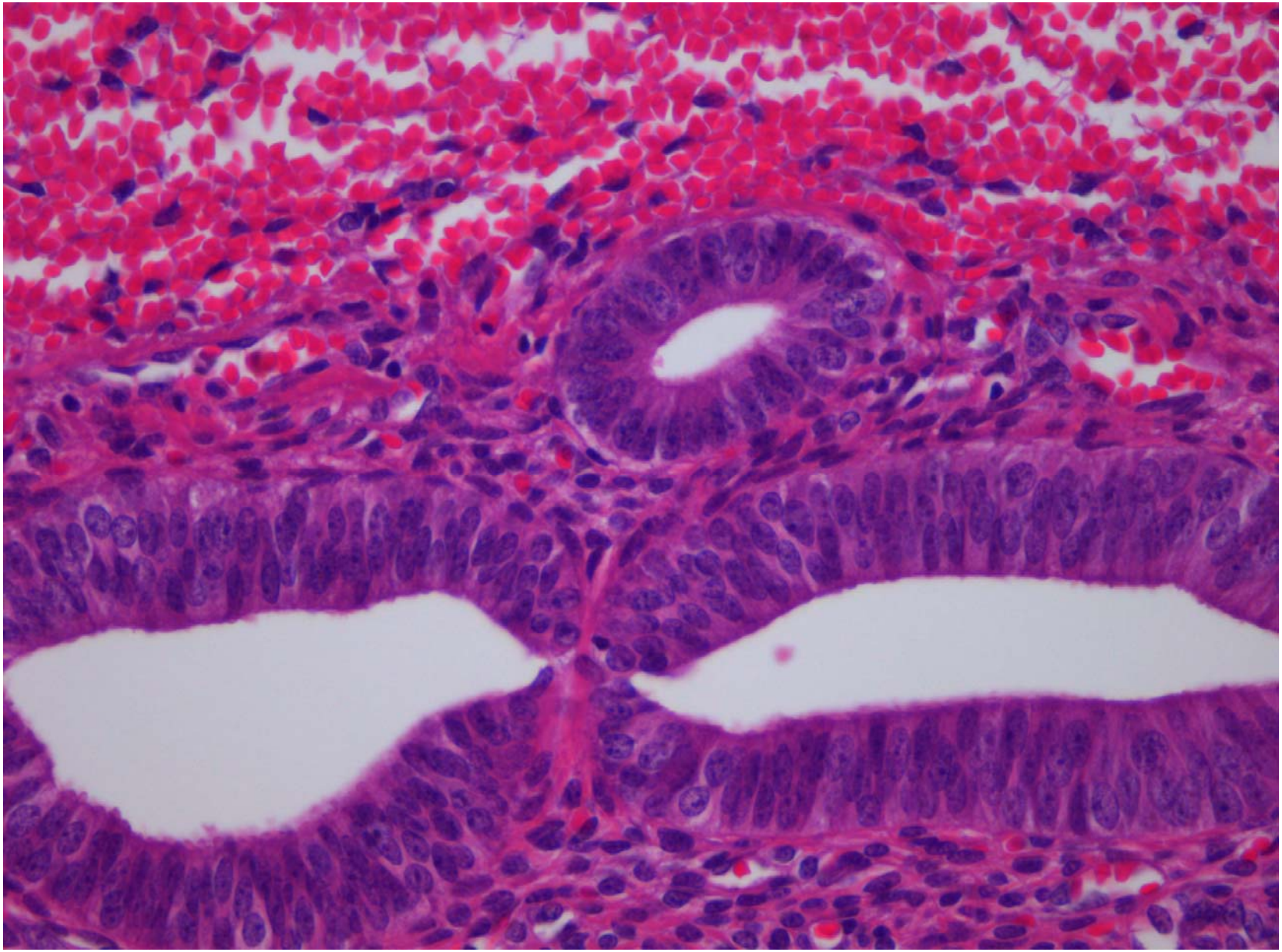
- Age: 77 y
- Hysterectomy because of prolaps
- No bleeding
- No treatment
- No prior biopsy/procedure

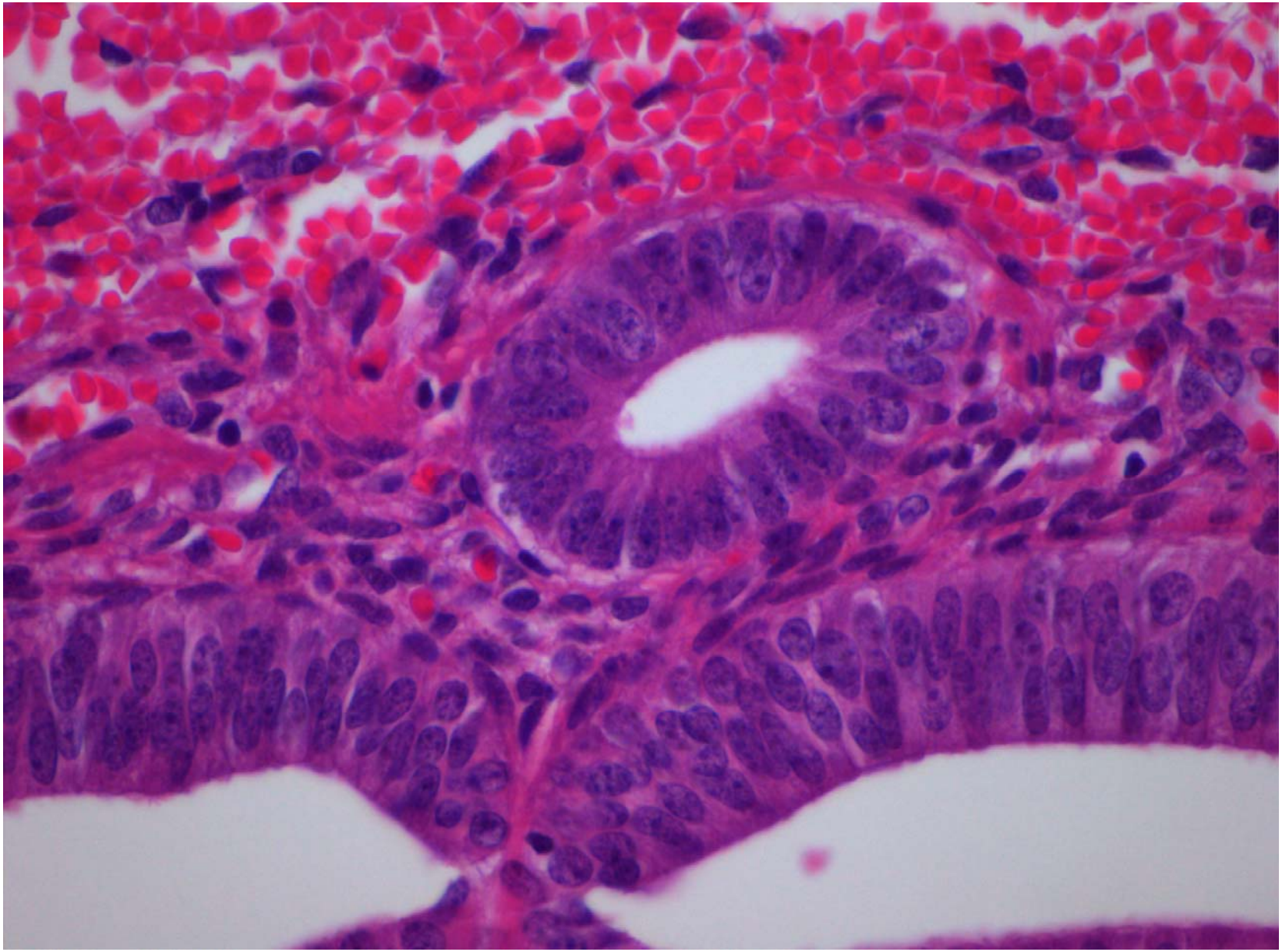


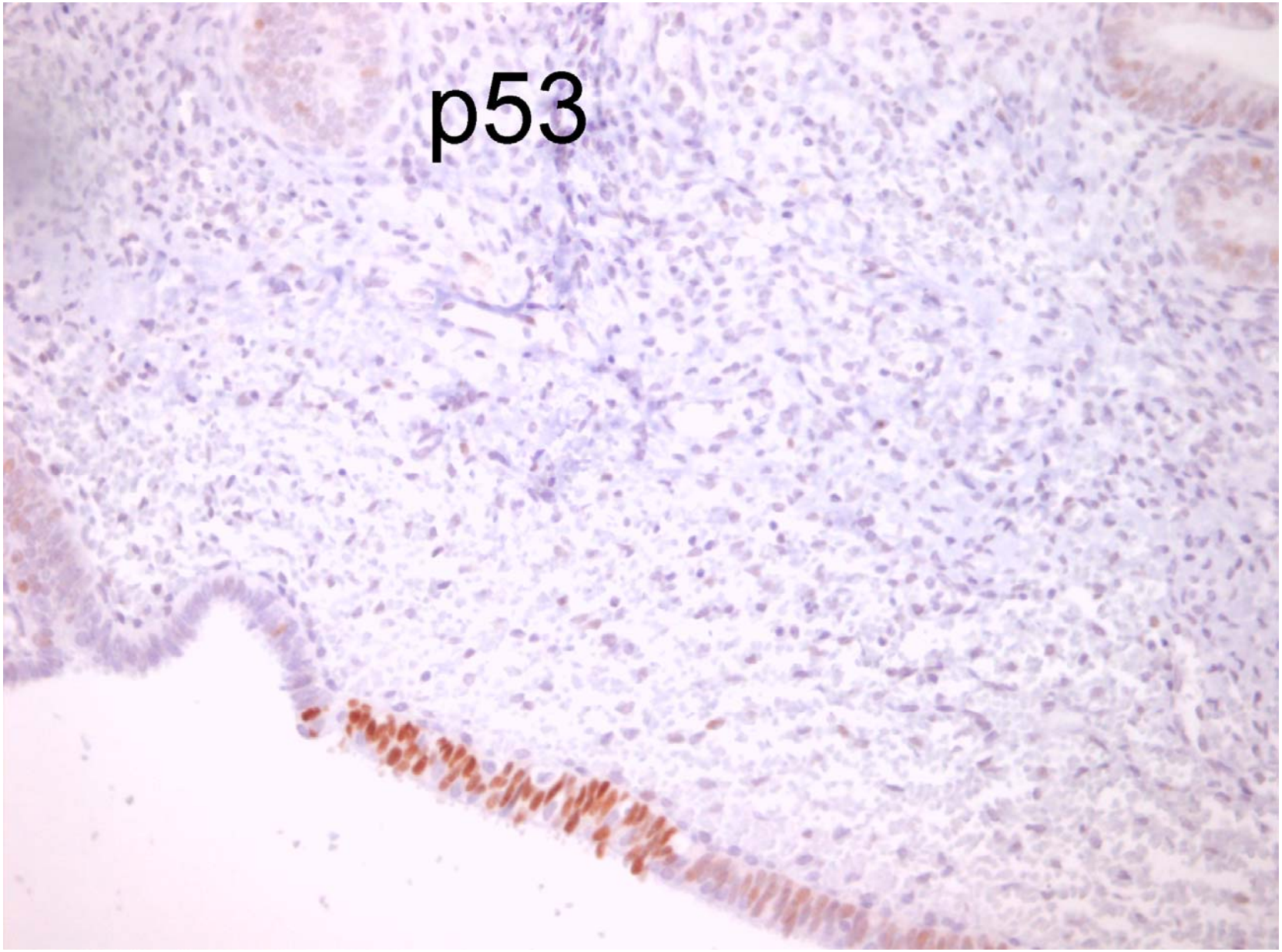


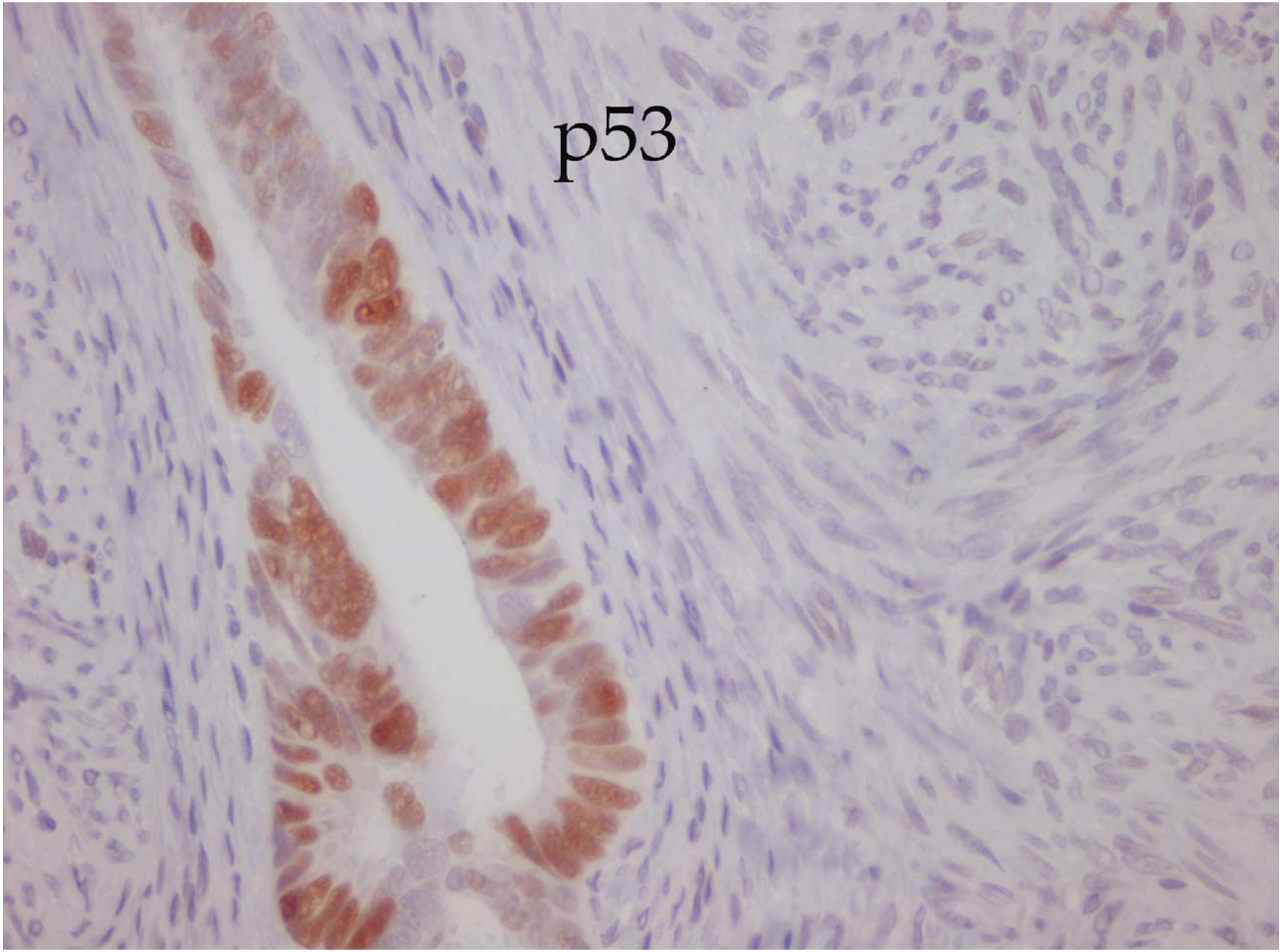









p53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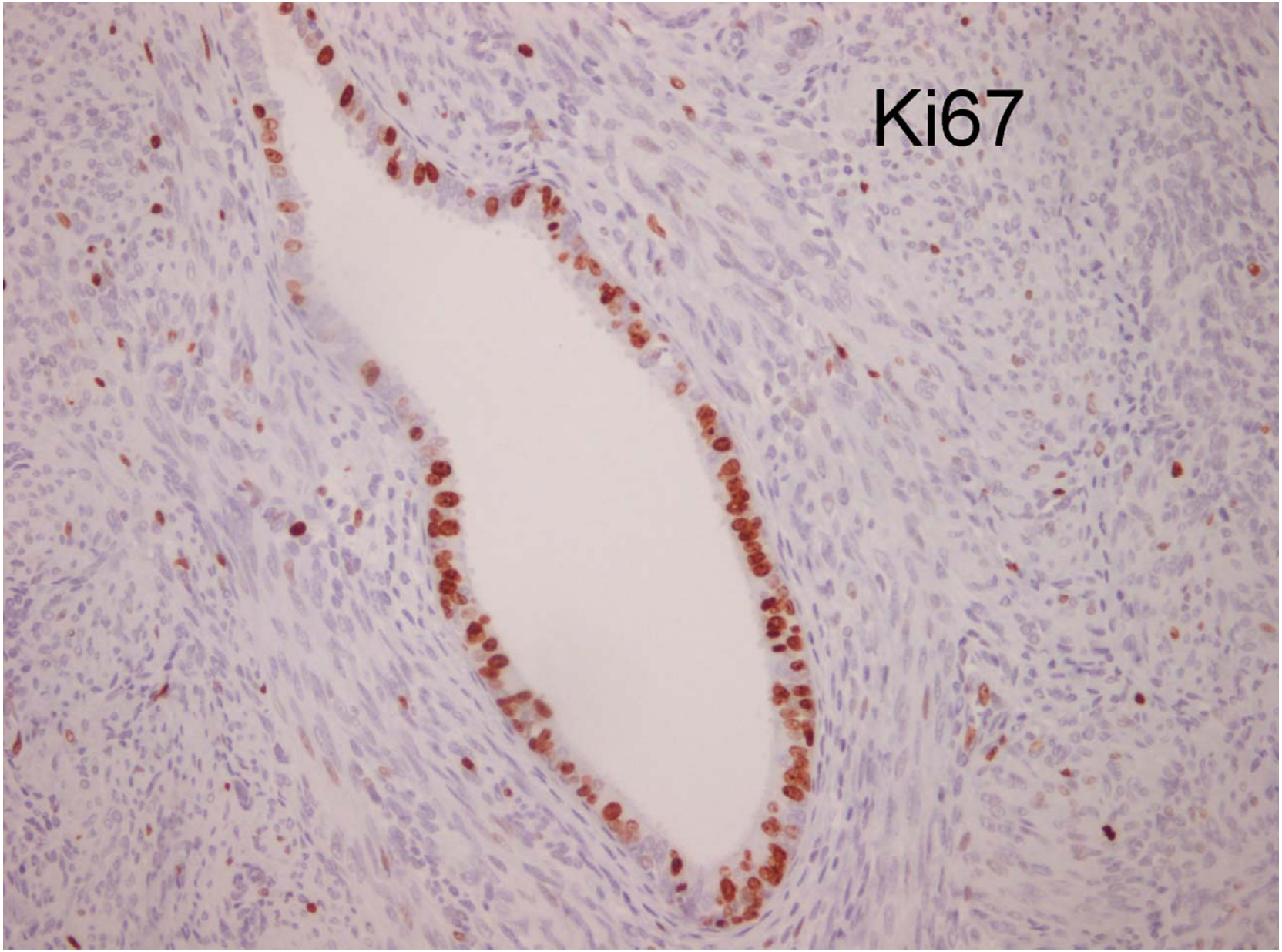
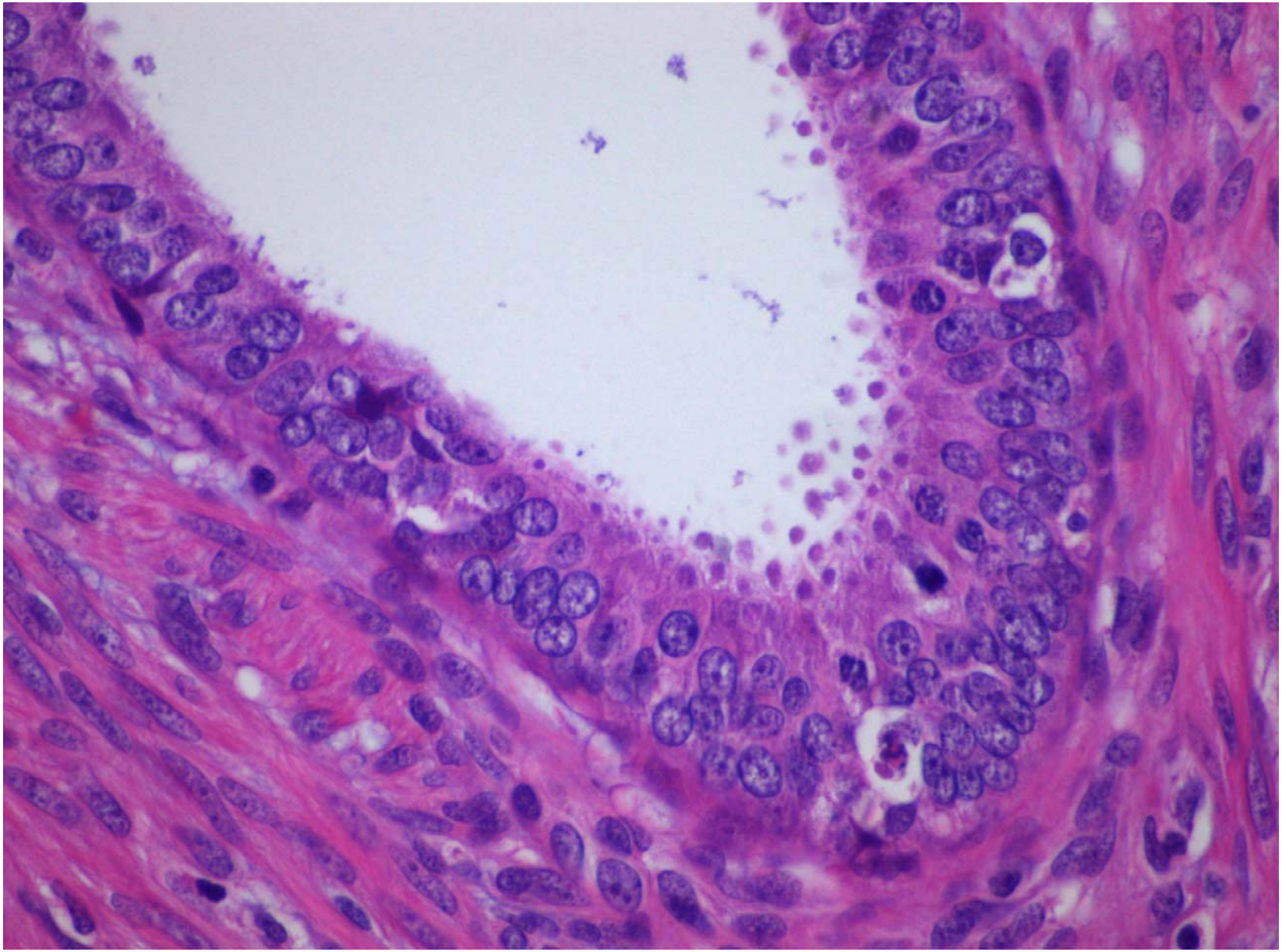

Ki67



Case 7: histology

- Few glands (atrophic type of architecture)
  - NOT hyperplastic/EIN
- Cells are not resting
- Nucleoli prominent
- Atypia not severe enough for EIC
- P53 en Ki67 pos but localised

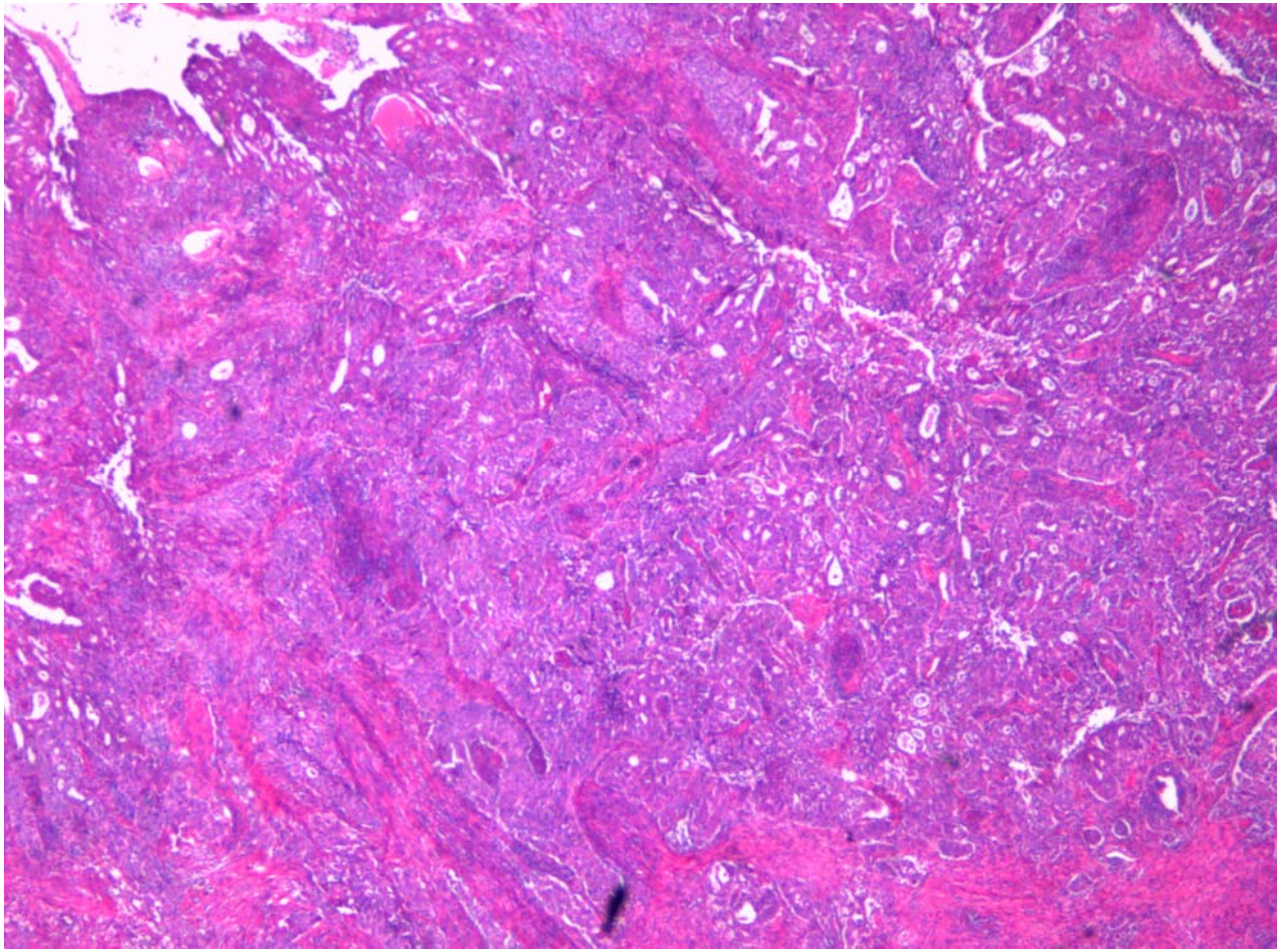
Case 7: diagnosis

- Endometrial glandular dysplasia?
- If , add comment !!

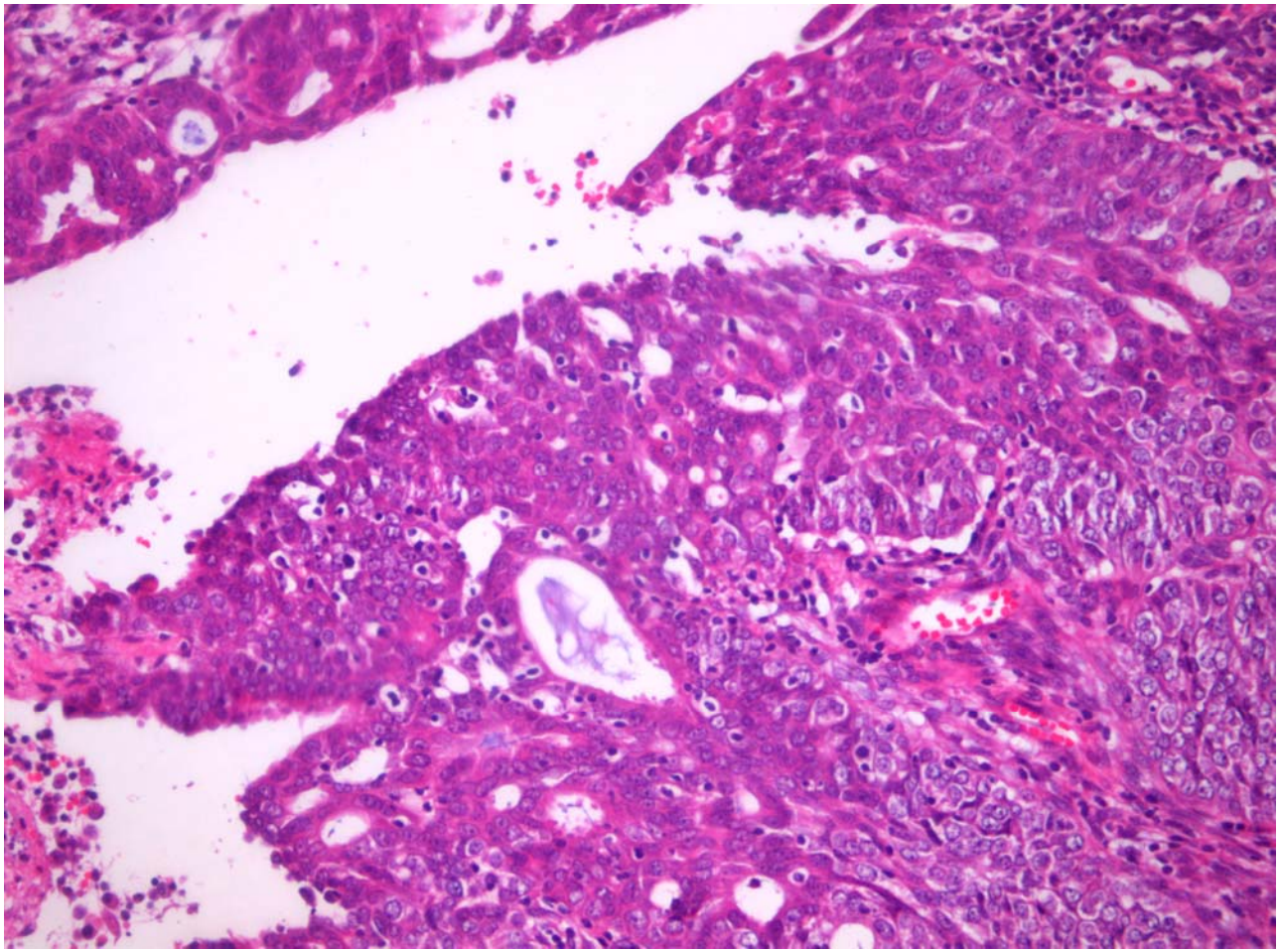
Case 8: presentation

- Age: 46 y
- Bleeding

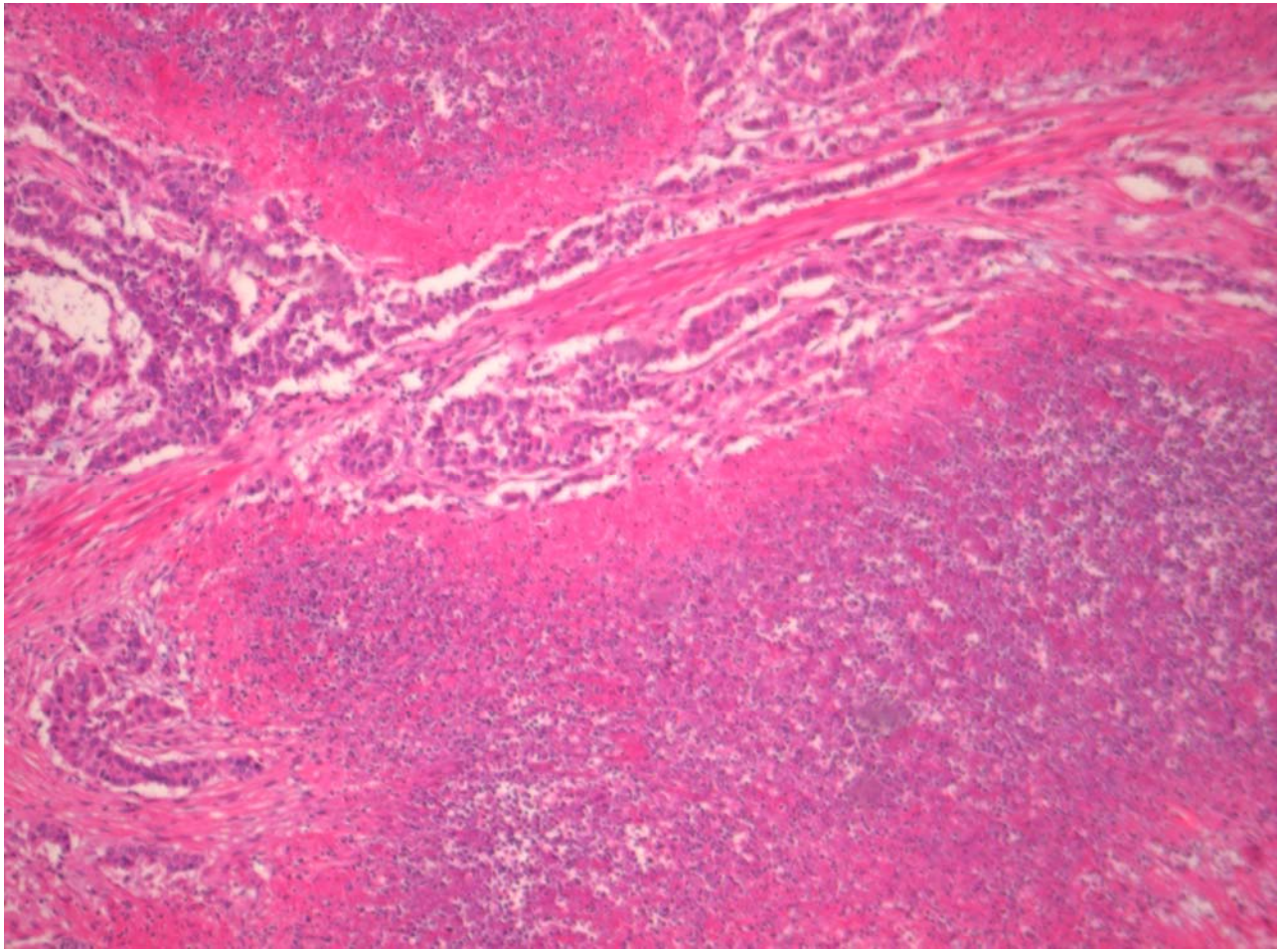
Case 8: Deeply invasive tumour



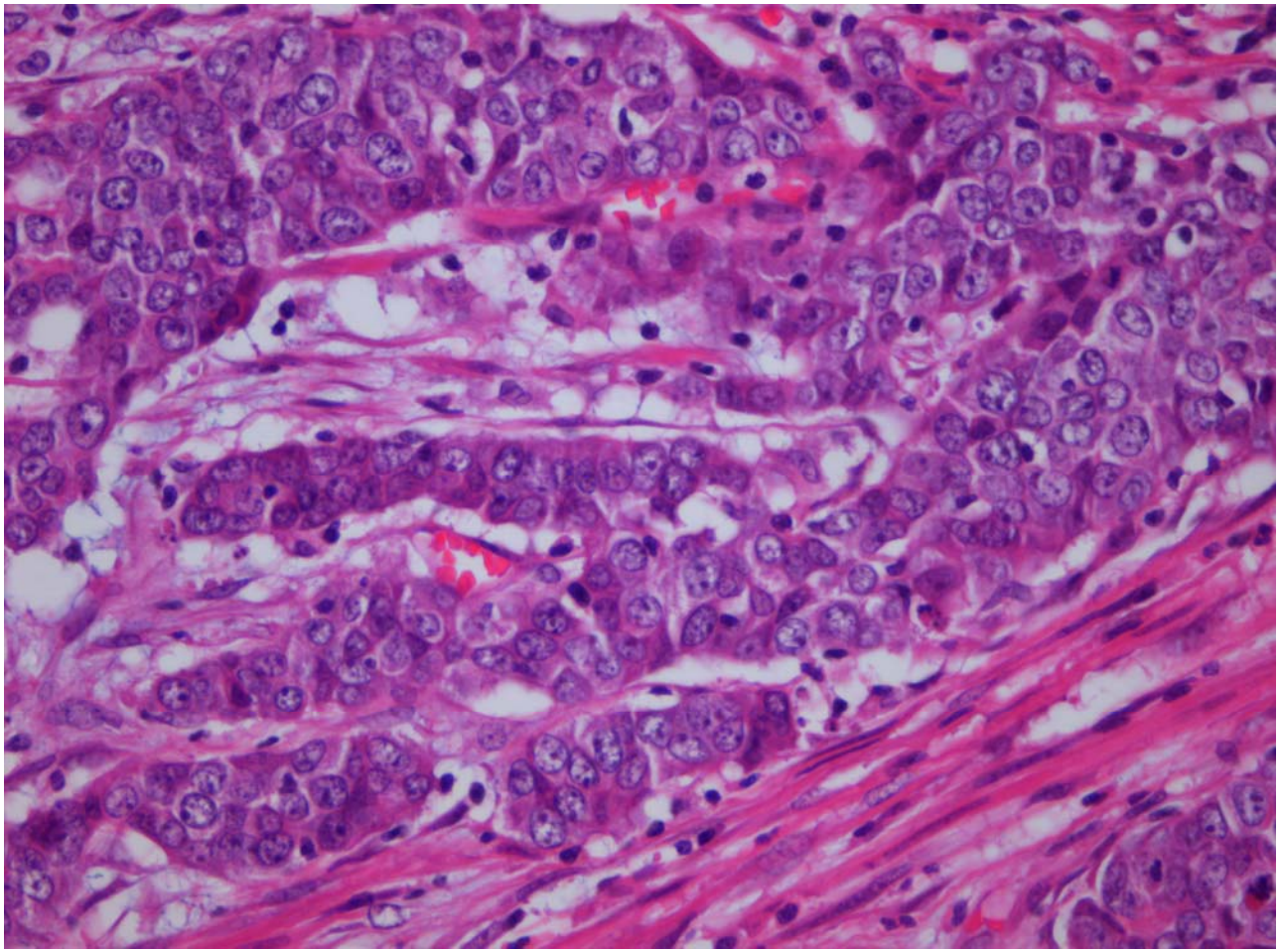
Case 8: endometrioid adenoCa



Case 8: necrosis



Case 8: lymfocytes



Case 8: what's special?

- Clinical: Very young for EmCa
- Histology: endometrioid but not low grade
- High number of tumour infiltrating lymphocyts

Case 8: diagnosis

- Endometrial carcinoma with morphology as can be expected in Lynch syndrome

Lynch syndrome (HNPCC)

Women with Lynch have greater risk of developing EmCa (27-71%) than colorectal Ca

- 30% has family history
- 2-5 % of all EmCa because of Lynch !!!

- Often young patients with low BMI
  - EmCa<40y: 10% is Lynch

EmCa in Lynch syndrome

- MSI-High in > 70%

- hMSH6 > hMSH2 > hMLH1 (EmCa)
- hMLH1 = hMSH2 > hMSH6 (CRC)

Think of Lynch when: too young for this type of Ca!

- Endometrioid type < 50 y

- Serous, Clear cell, Carcinosarcoma, Undifferentiated type < 60 y

Think of Lynch when: topography

- 30% of EmCa located in isthus is Lynch !!

- Multiple endometrial tumours (collision)

Think of Lynch when:
synchronous tumours of special type!

- Clear cell carcinoma ovary
- Endometriosis associated tumours
- Endometrioid carcinoma with grade > 1

Think of Lynch when:

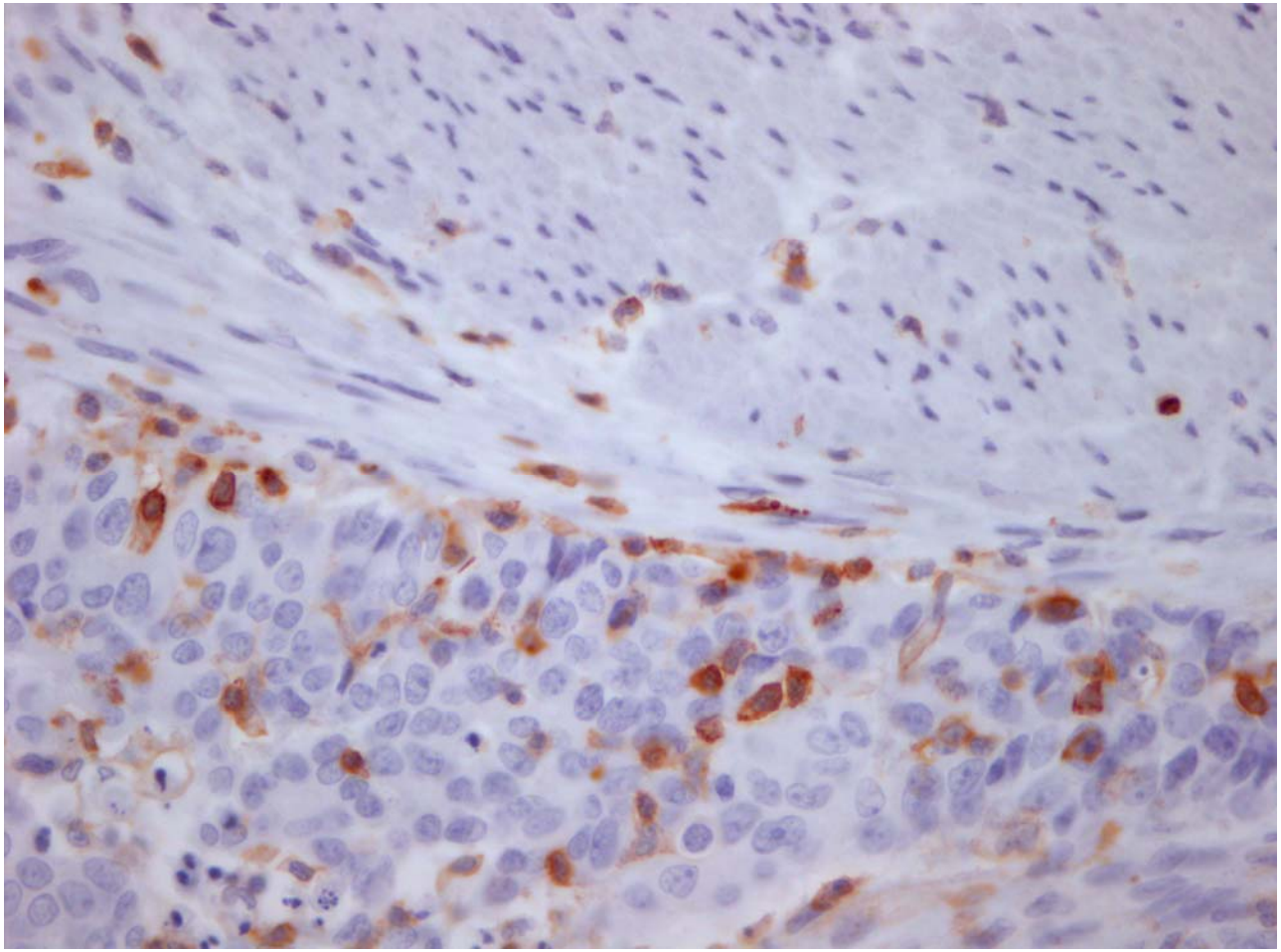
endometrioid type with special features!

- Peritumoral lymphocytes
- Tumour infiltrating lymphocytes
- Deeply invasive
- pL1
- Grade 3
- Mix of architectural patterns and/or cytological features
- Dedifferentiated carcinoma

Tumour infiltrating lymphocytes

- TIL >42/10 HPF
- 85% sensitive for MSI-H
- 46% specific for MSI-H

Tumour Infiltrating Lymfocyts



What if you see it ???

- Ignore and just report what they want to know: type, grade, stage
- Report what you see and don’t bother
- Report and mention the association
- Test for Lynch
  - IHC followed by single gene sequencing

Problem

There are to date no national guidelines for this kind of issues !!!!!!!!

Can we test for genetic syndrome without informed consent ???????