

Japan-Korea-Taiwan GYN Conference
Mini Lecture

Seromucinous Tumor

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Do you like it ?

WHO2003

Mucinous tumors	
Intestinal	Benign
	Borderline
	Malignant
Endocervical-like	Borderline

WHO2014

Mucinous tumors	
	Benign
	Borderline
	Malignant

Seromucinous tumors	
	Benign
	Borderline
	Malignant

Overview

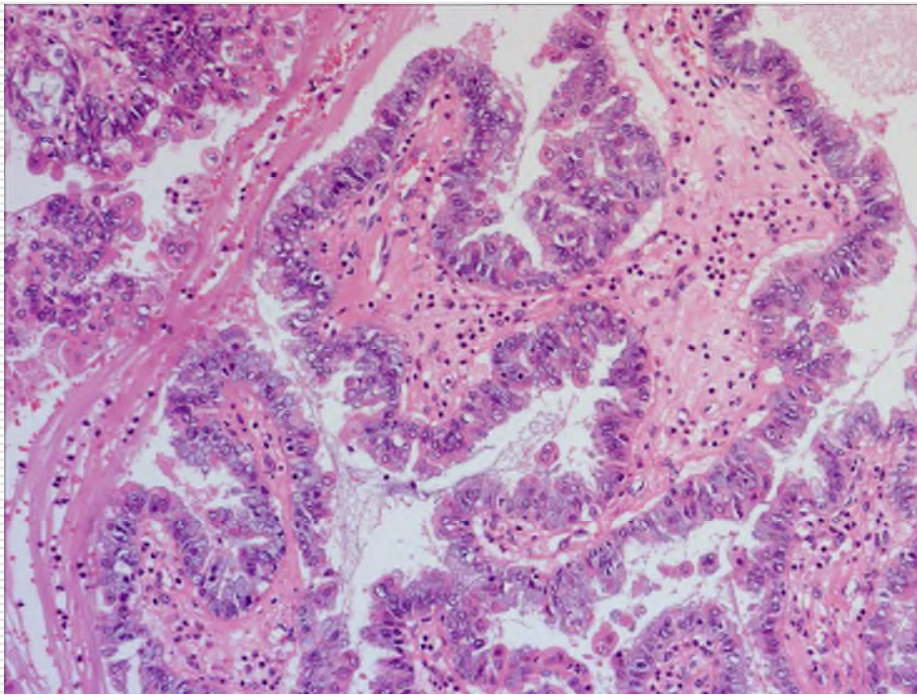
- **General understanding**
- Controversies
 - Discussion

Seromucinous borderline tumor

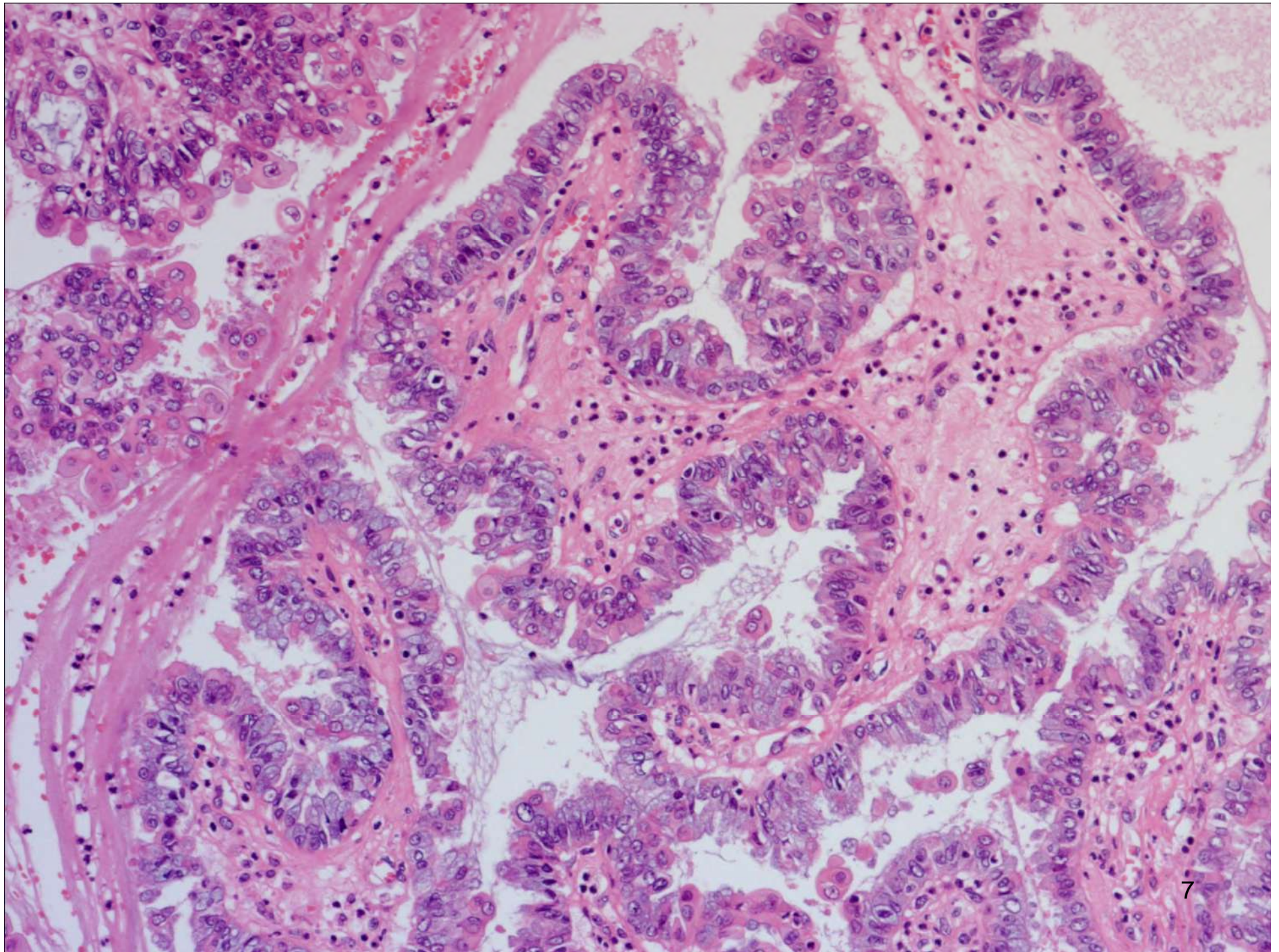


- Unilocular or oligolocular
- Granular or papillary excrescences
- Viscid and/or purulent material
- Frequently bilateral (40%) and a/w endometriosis (50%)

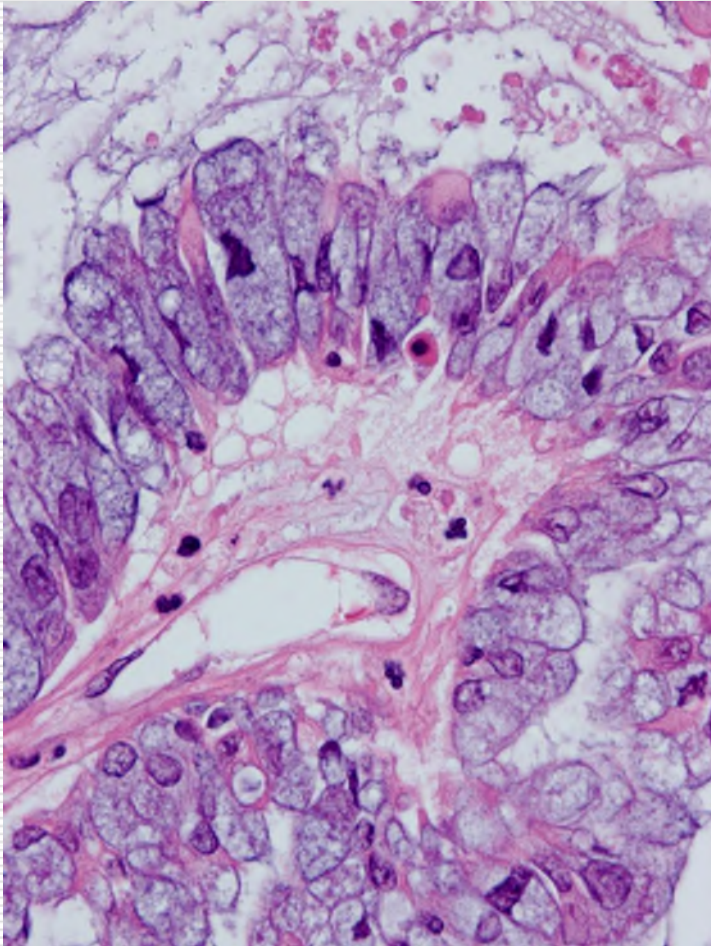
Seromucinous borderline tumor



- Microscopic features
 - ✓ Architecturally resembling SBT
 - ✓ Wide papillae showing hierarchical branching

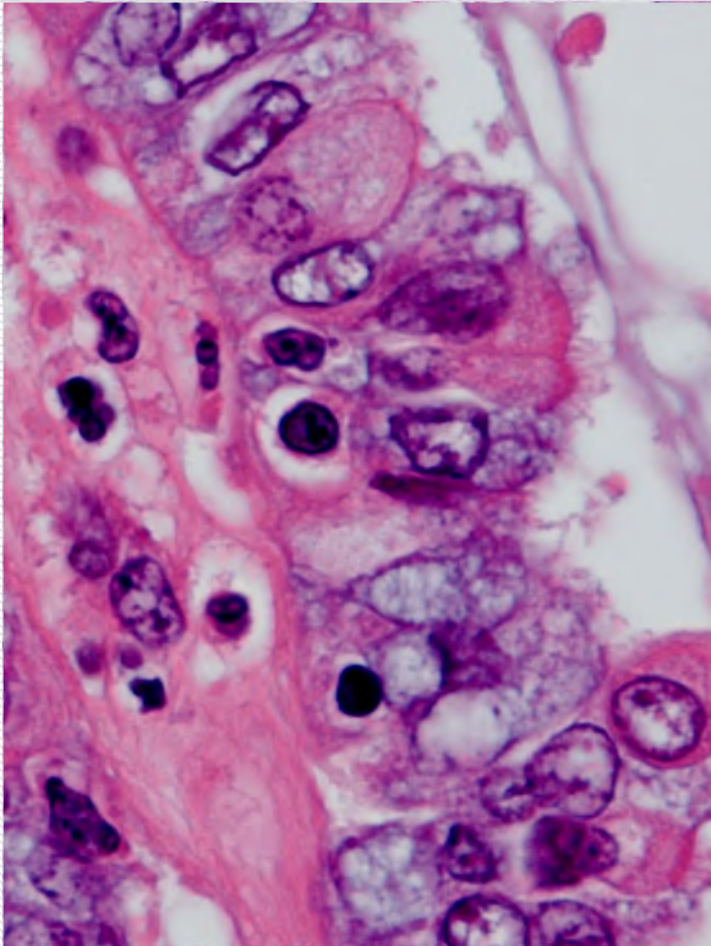


Seromucinous borderline tumor



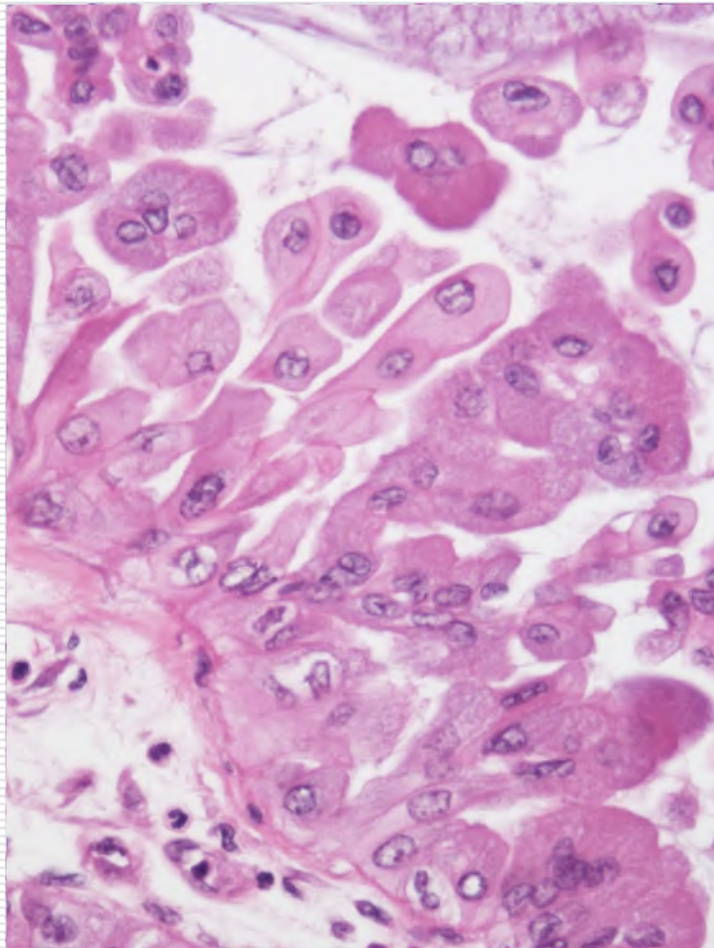
- Microscopic features
 - ✓ Cytology
 - Mucinous cells
 - Ciliated cells

Seromucinous borderline tumor

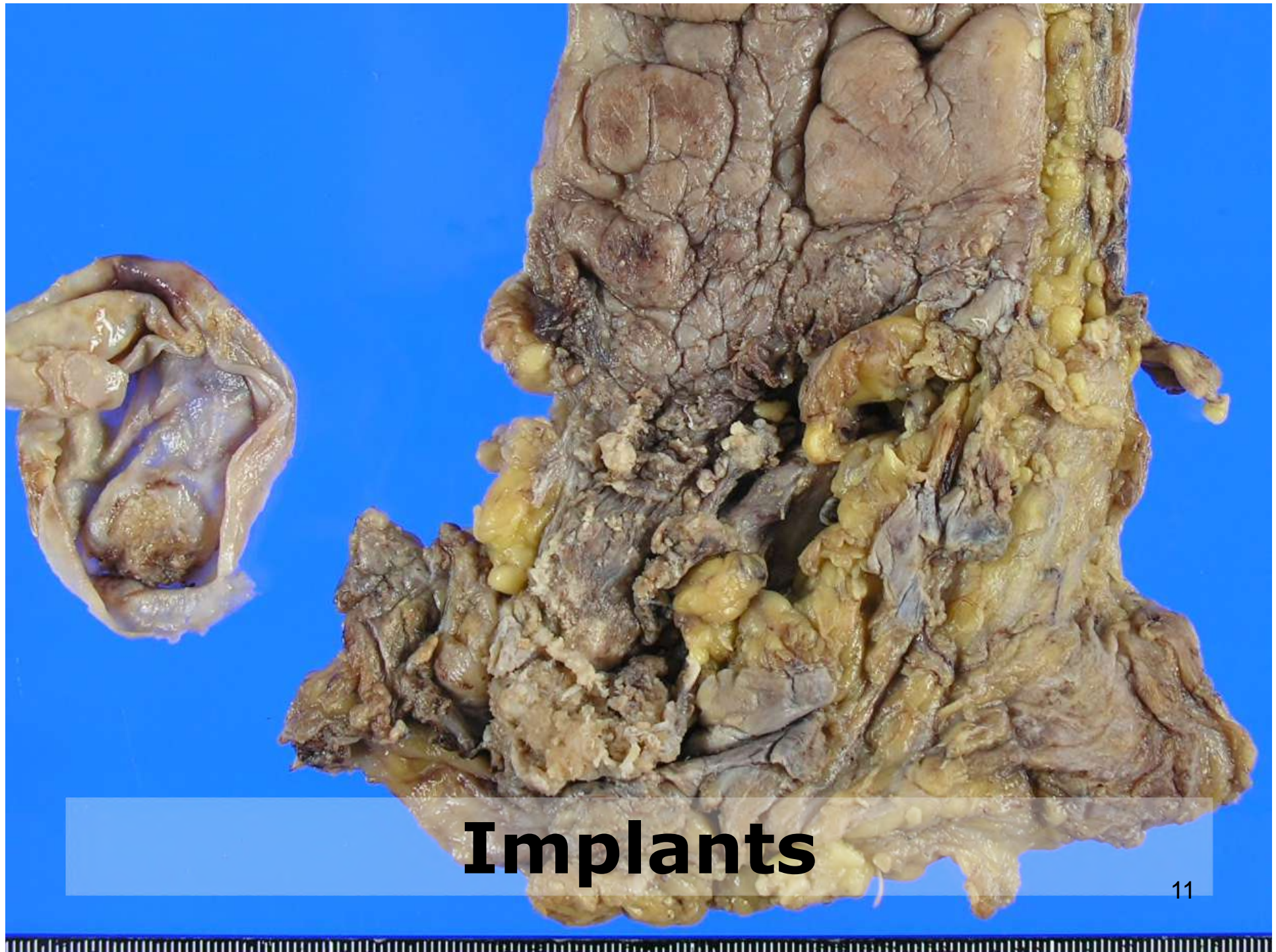


- Microscopic features
 - ✓ Cytology
 - Mucinous cells
 - Ciliated cells

Seromucinous borderline tumor



- Microscopic features
 - ✓ Cytology
 - Mucinous cells
 - Ciliated cells
 - Indifferent cells



Implants



Implants



Implants

A histological section stained with hematoxylin and eosin (H&E). The image shows a large, dense, pink-stained mass, likely a desmoplastic implant, which is irregular in shape and occupies the upper and central portions of the field. Below this mass, there is a layer of more organized tissue, possibly muscle or connective tissue, with some darker, purple-stained areas. At the bottom of the image, there are clusters of small, white, circular structures, which could be adipose tissue or small cysts. The overall texture is granular and dense.

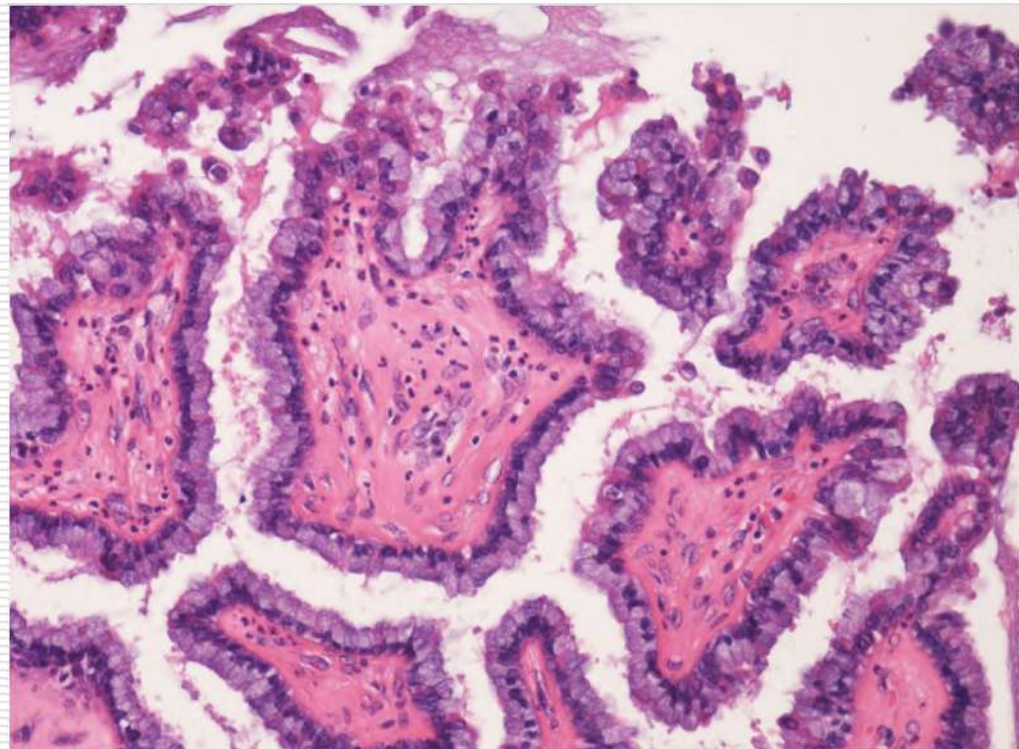
Implants (desmoplastic)

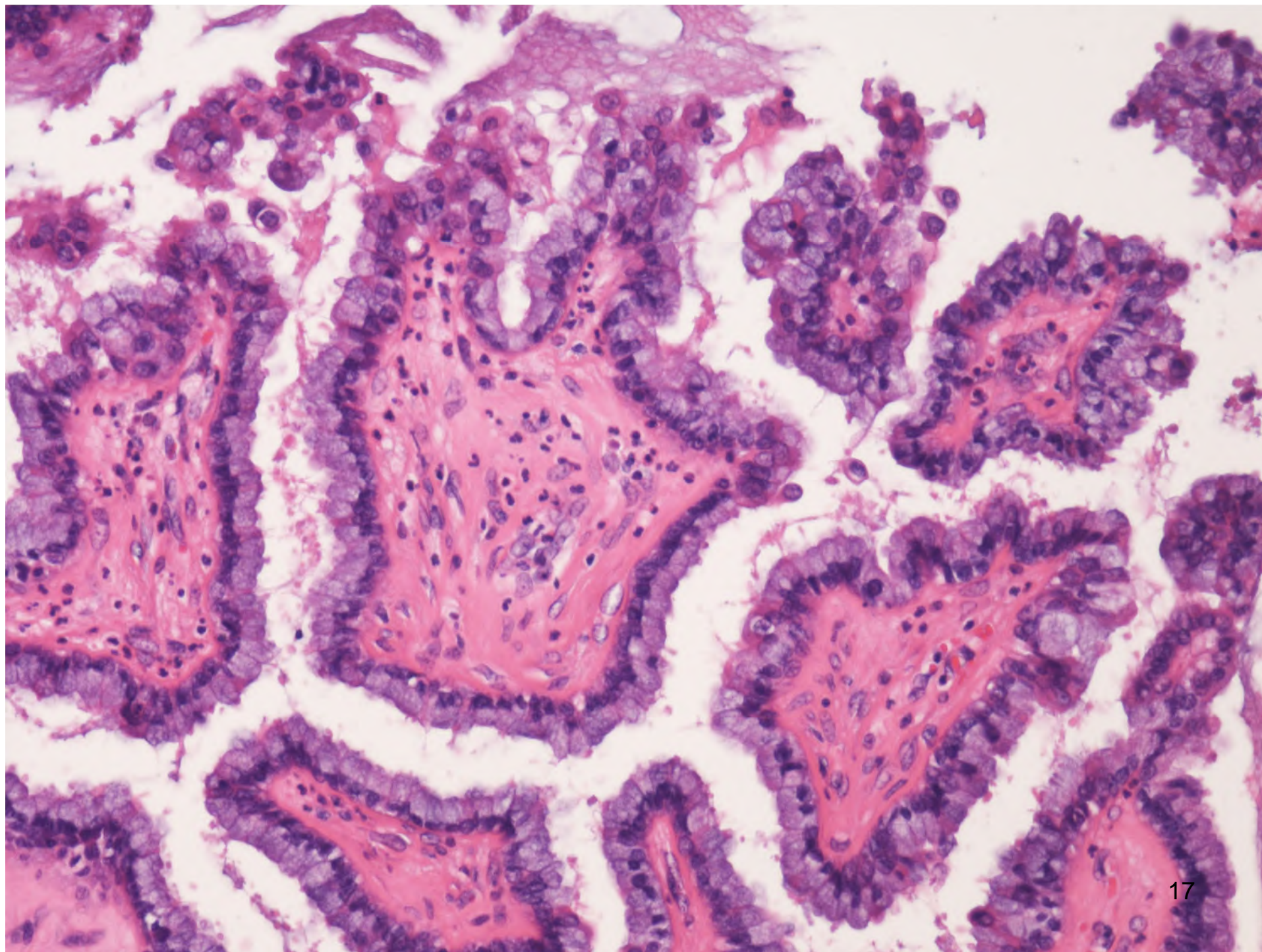


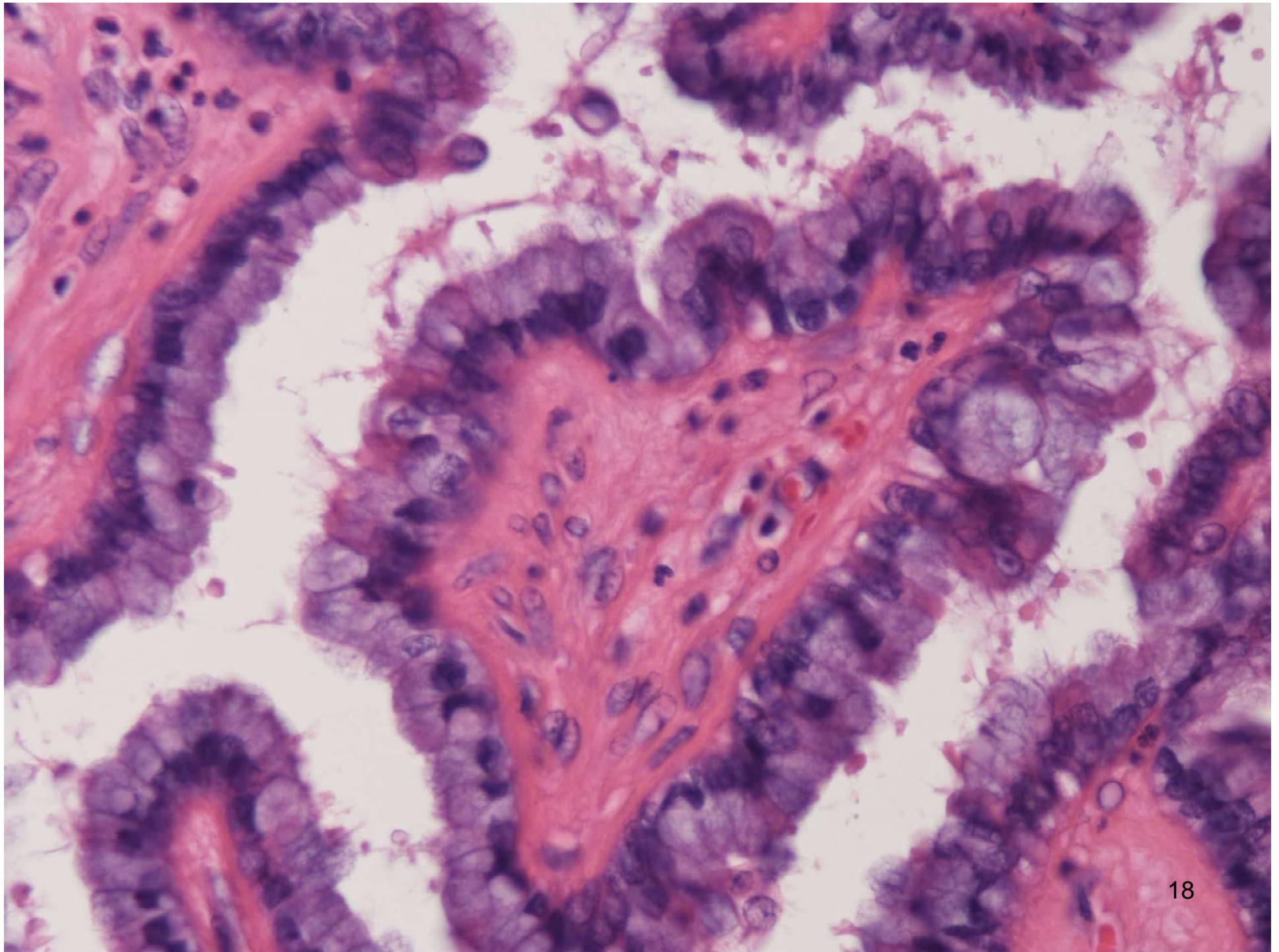
This histological image shows a tissue section stained with hematoxylin and eosin (H&E). The background is a dense, pink-stained fibrous stroma (desmoplasia) containing numerous small, dark-stained nuclei of inflammatory cells. Several larger, irregular, pale-stained structures are visible, which are the implants. These implants have a complex, multi-layered appearance with some internal structure, possibly representing foreign material or a specific type of implant used in the study.

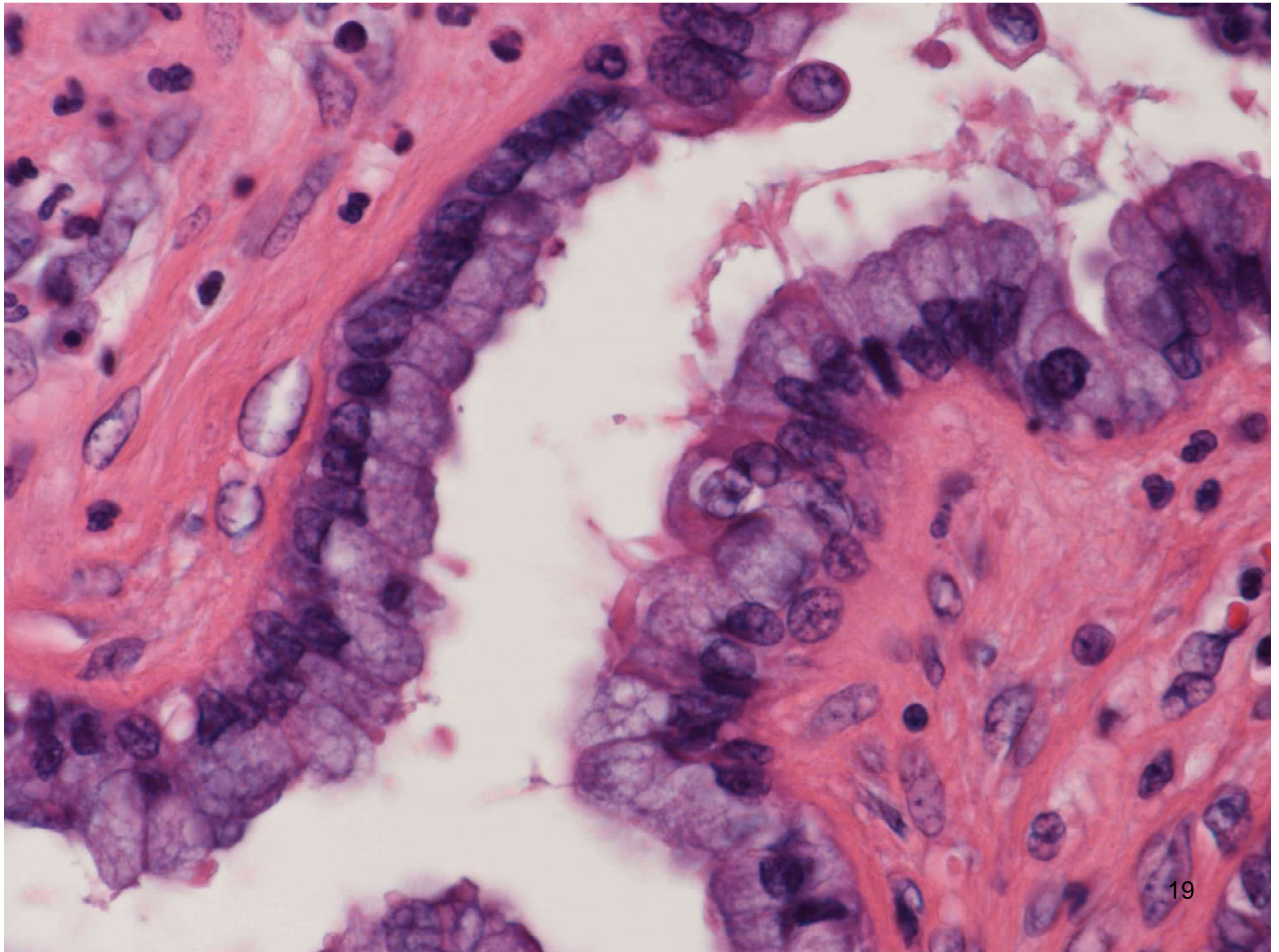
Implants (desmoplastic)

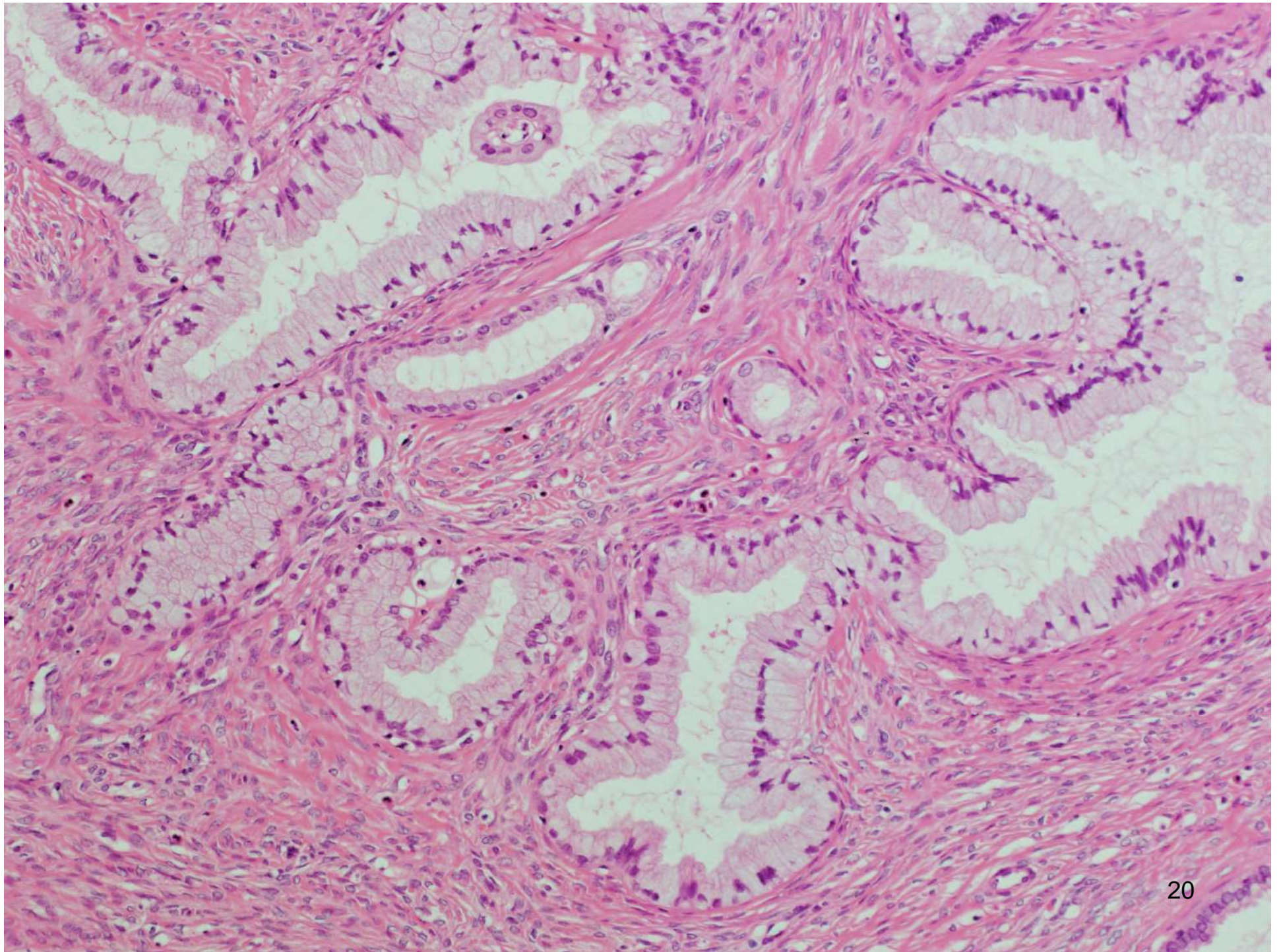
Seromucinous cystadenoma / adenofibroma

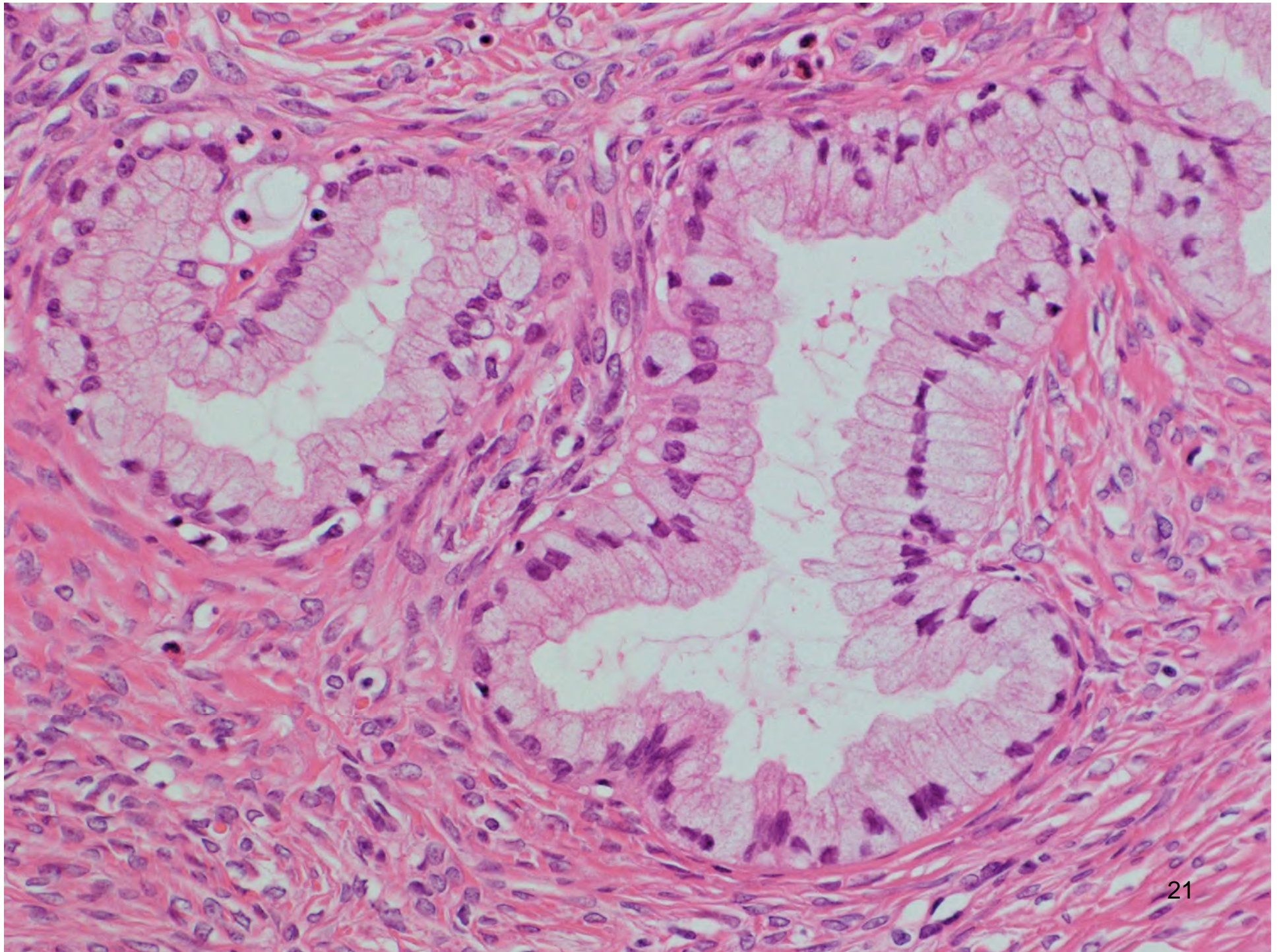




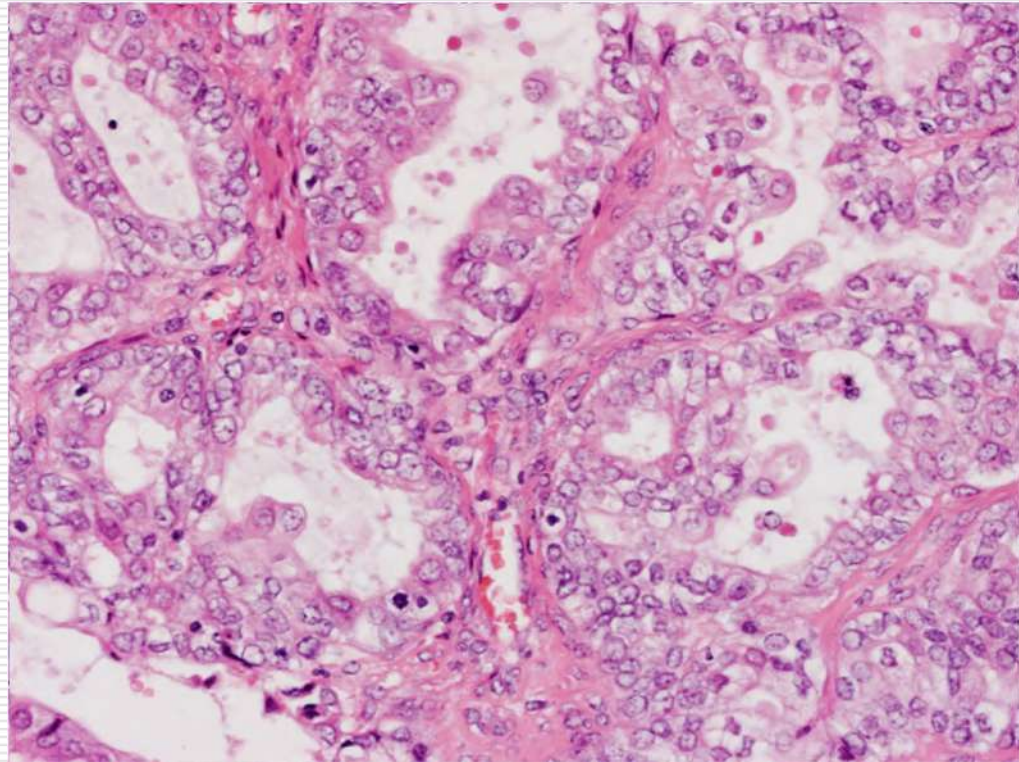


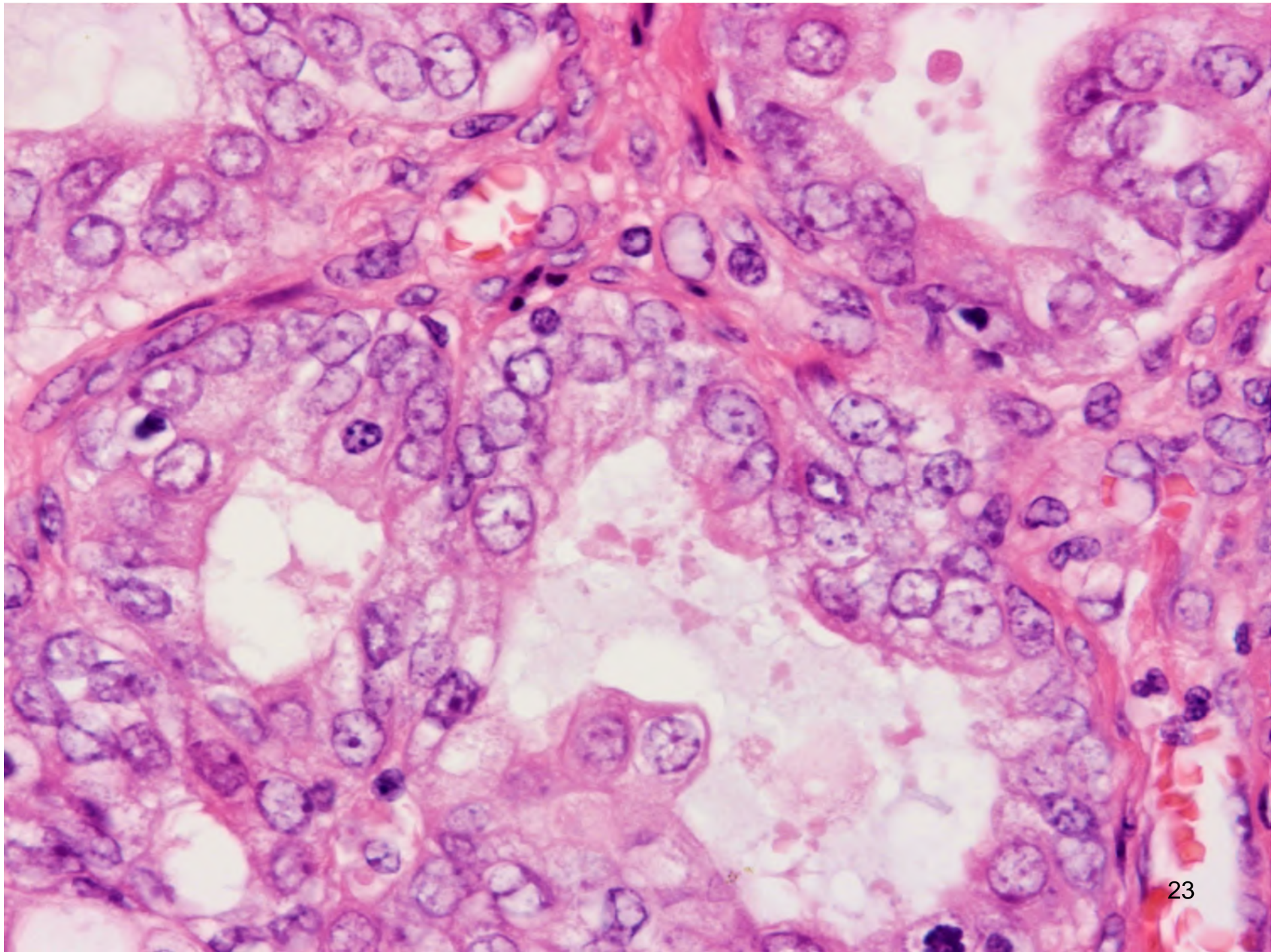




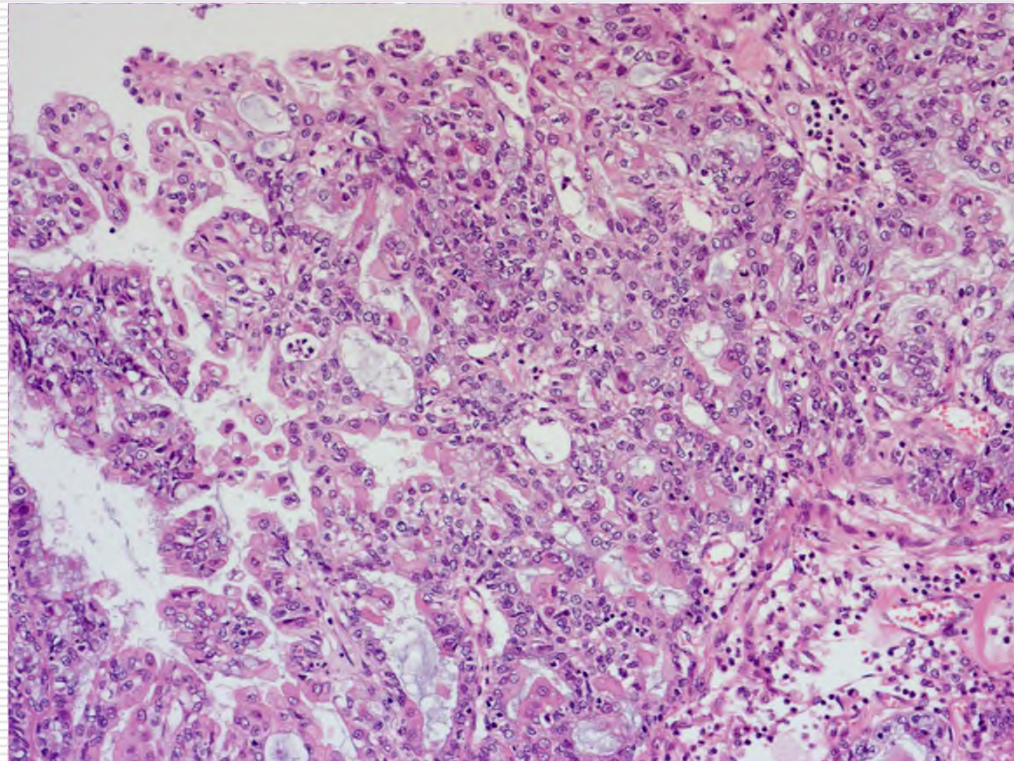


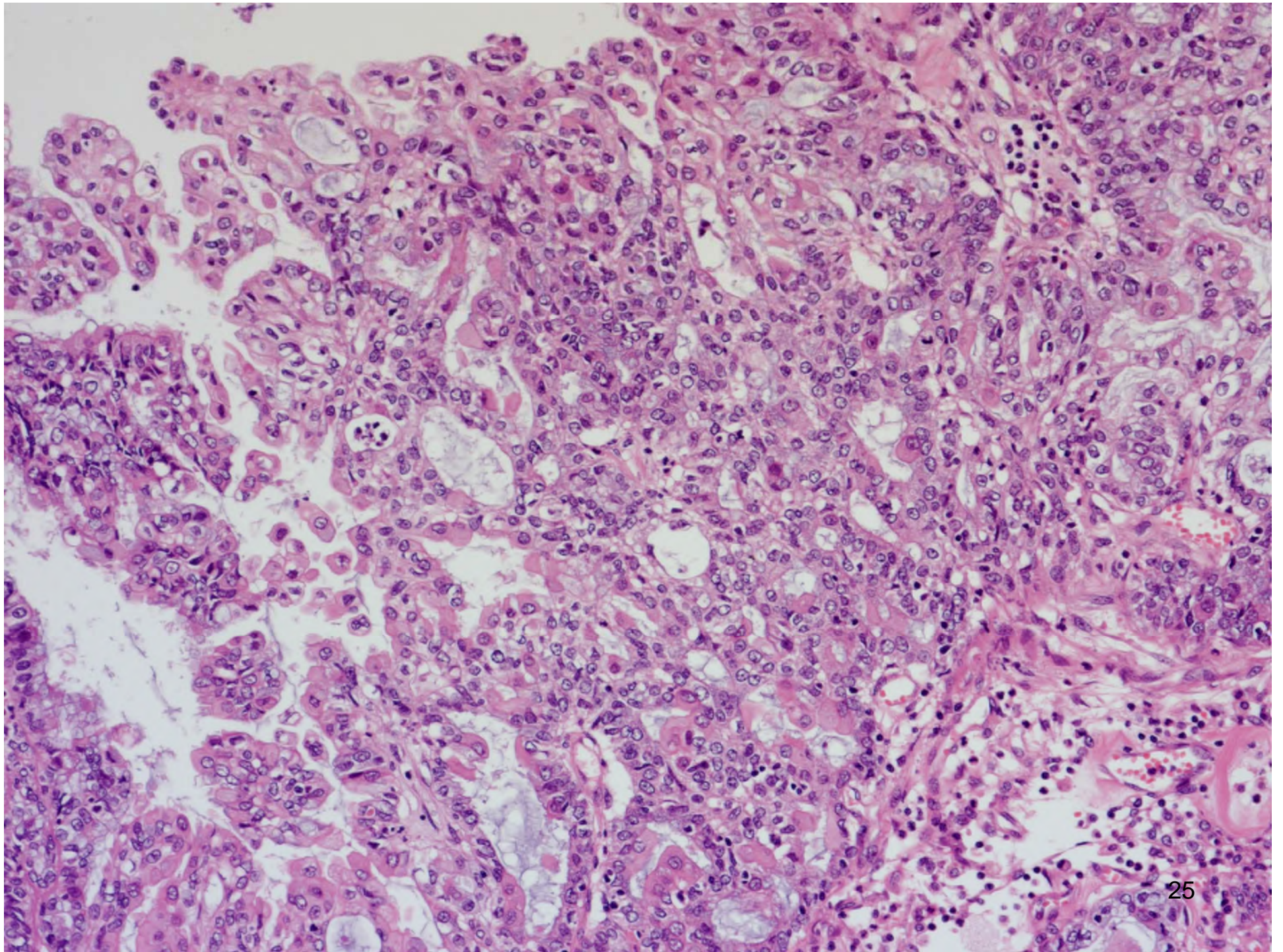
Seromucinous borderline tumor with intraepithelial carcinoma

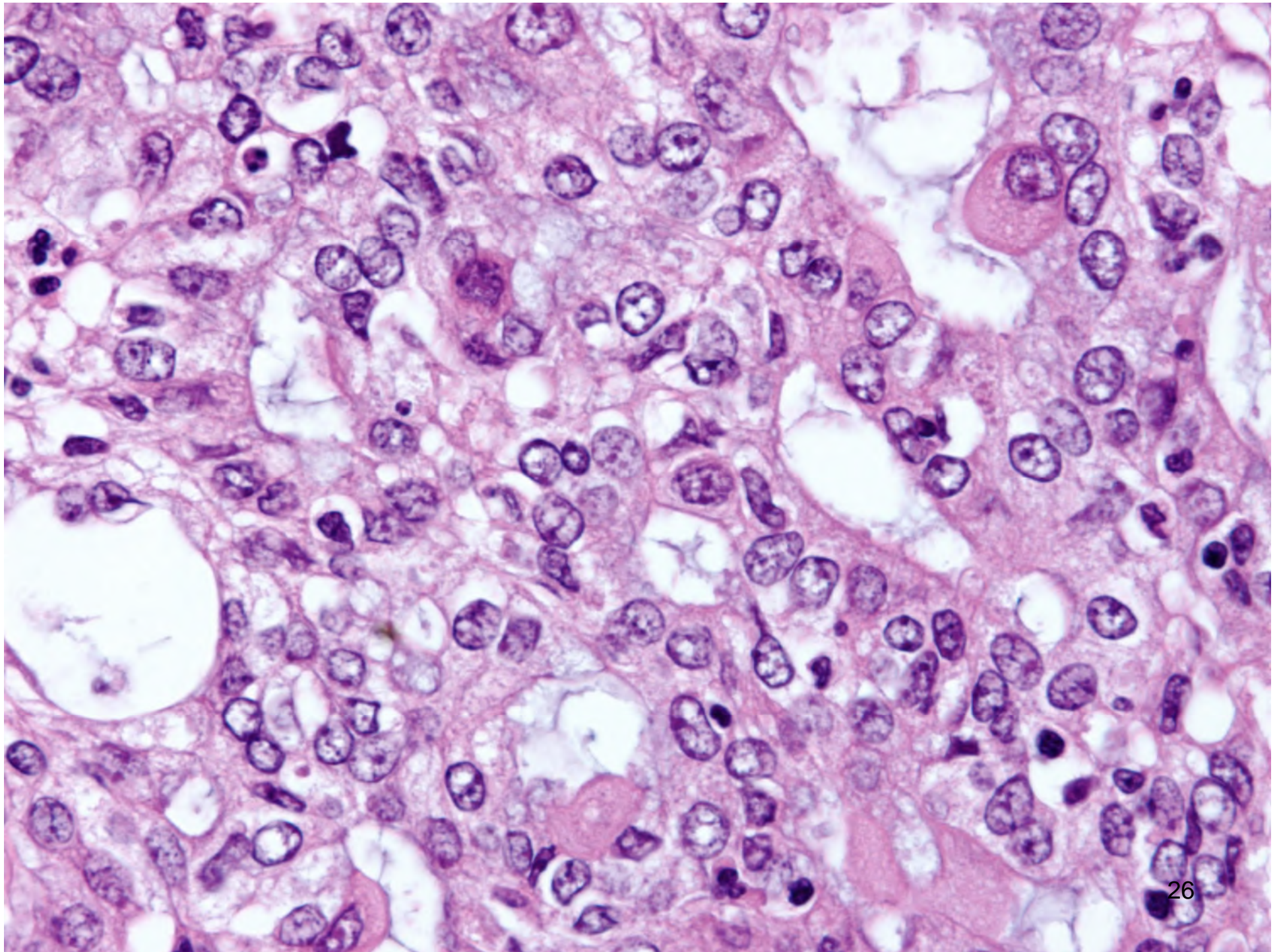


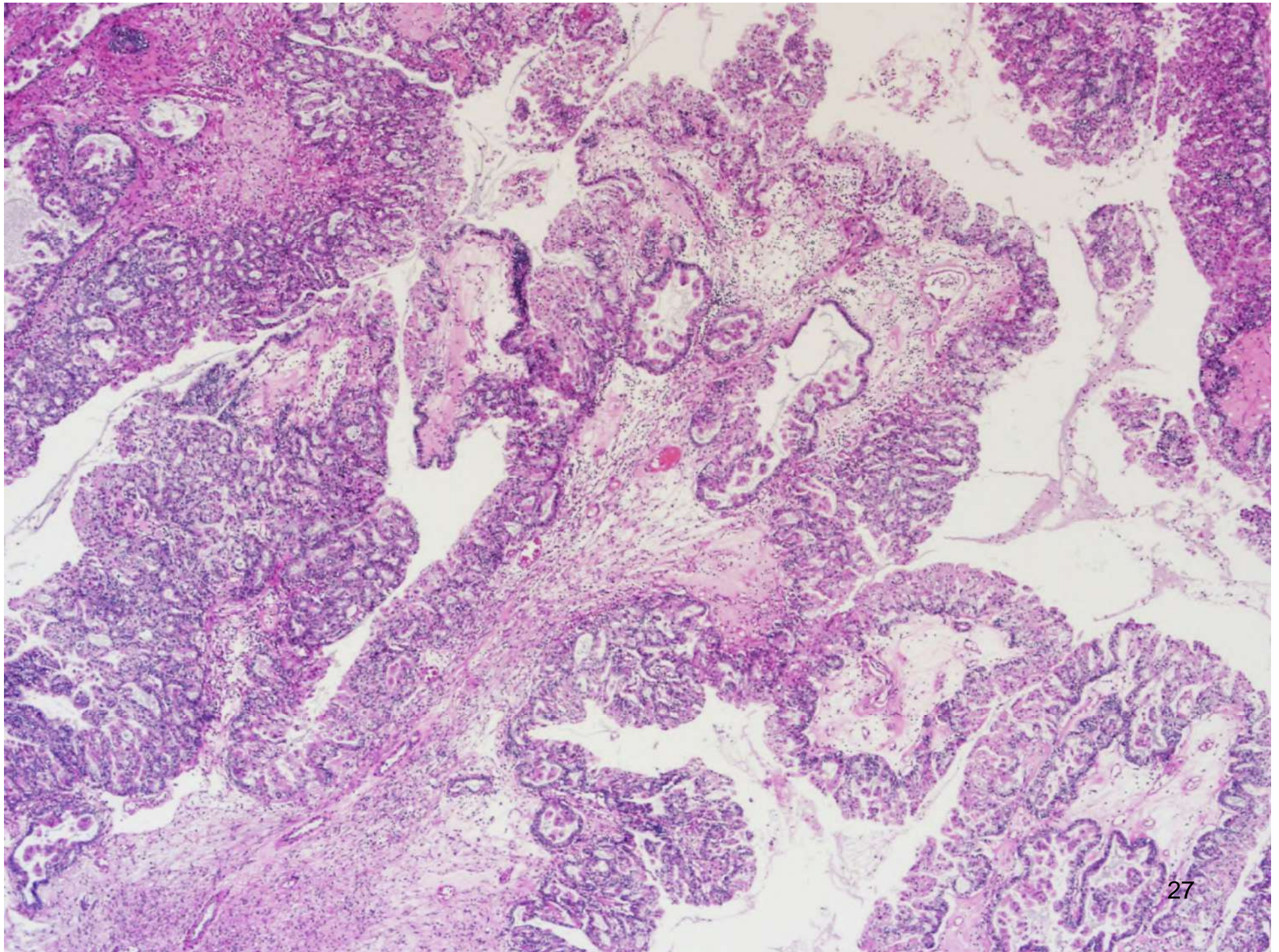


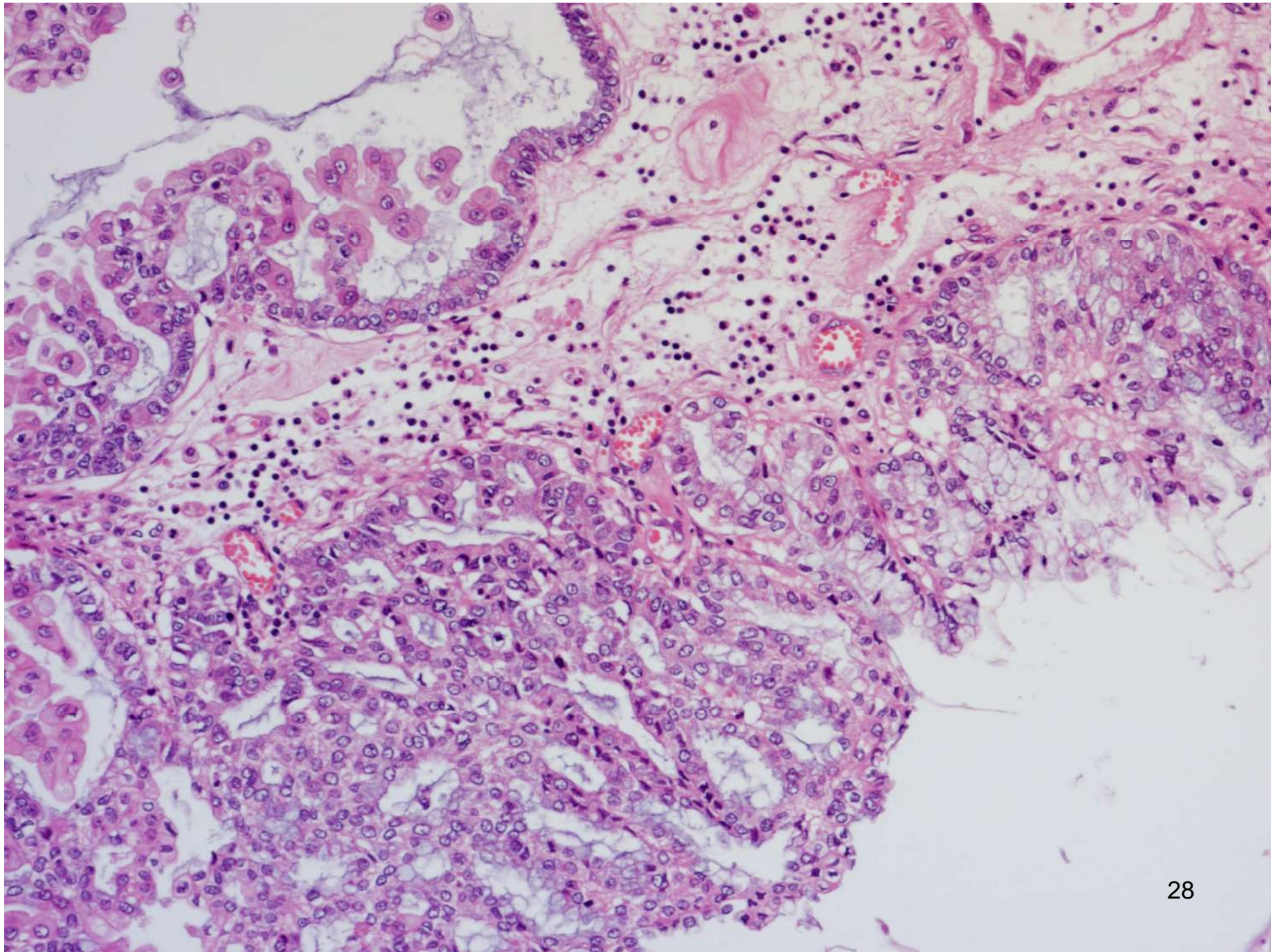
Seromucinous carcinoma





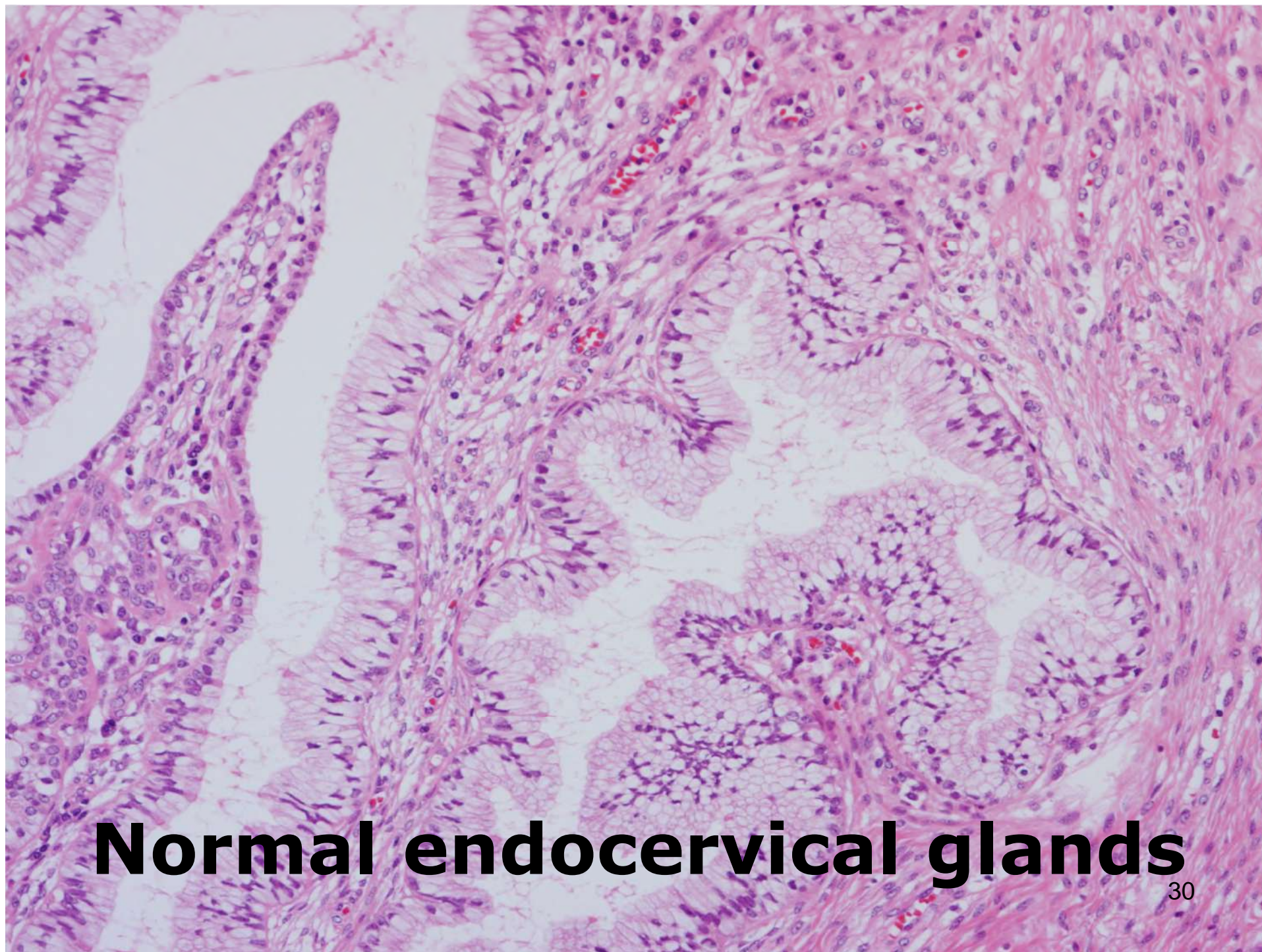






Overview

- General understanding
- **Controversies**
 - **Discussion**

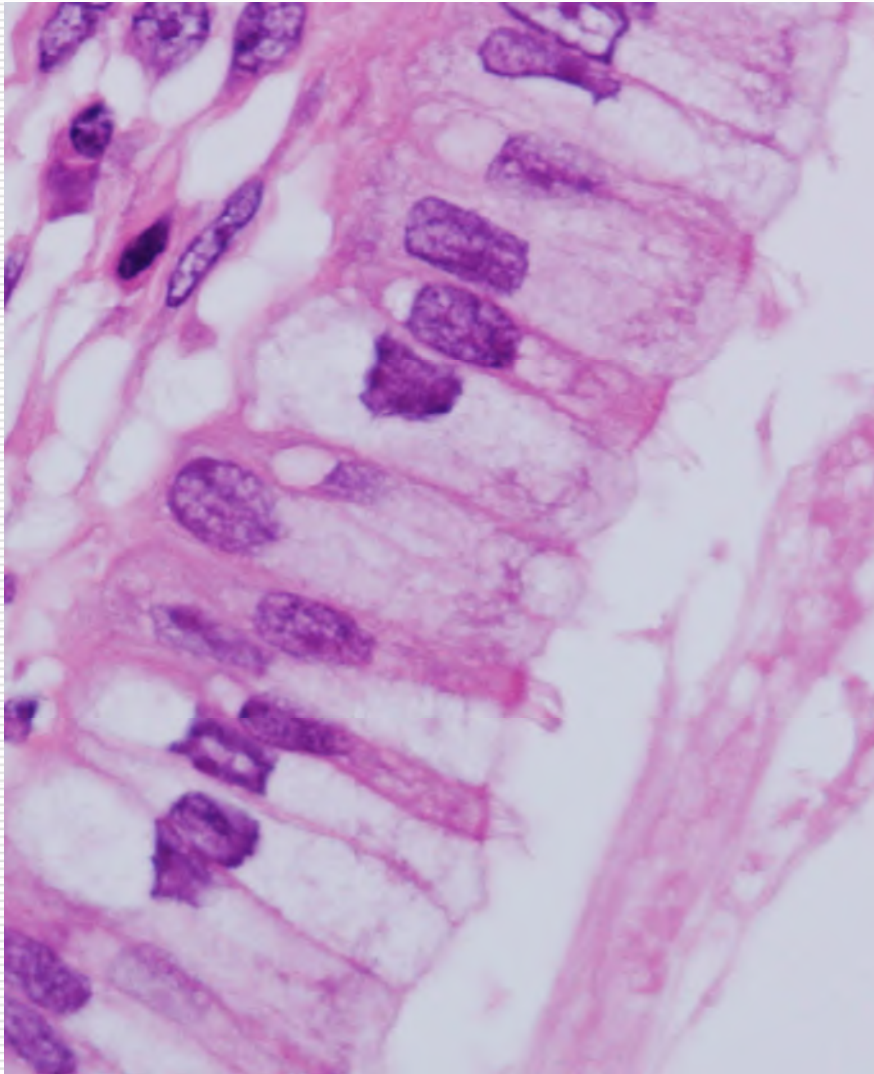


Normal endocervical glands

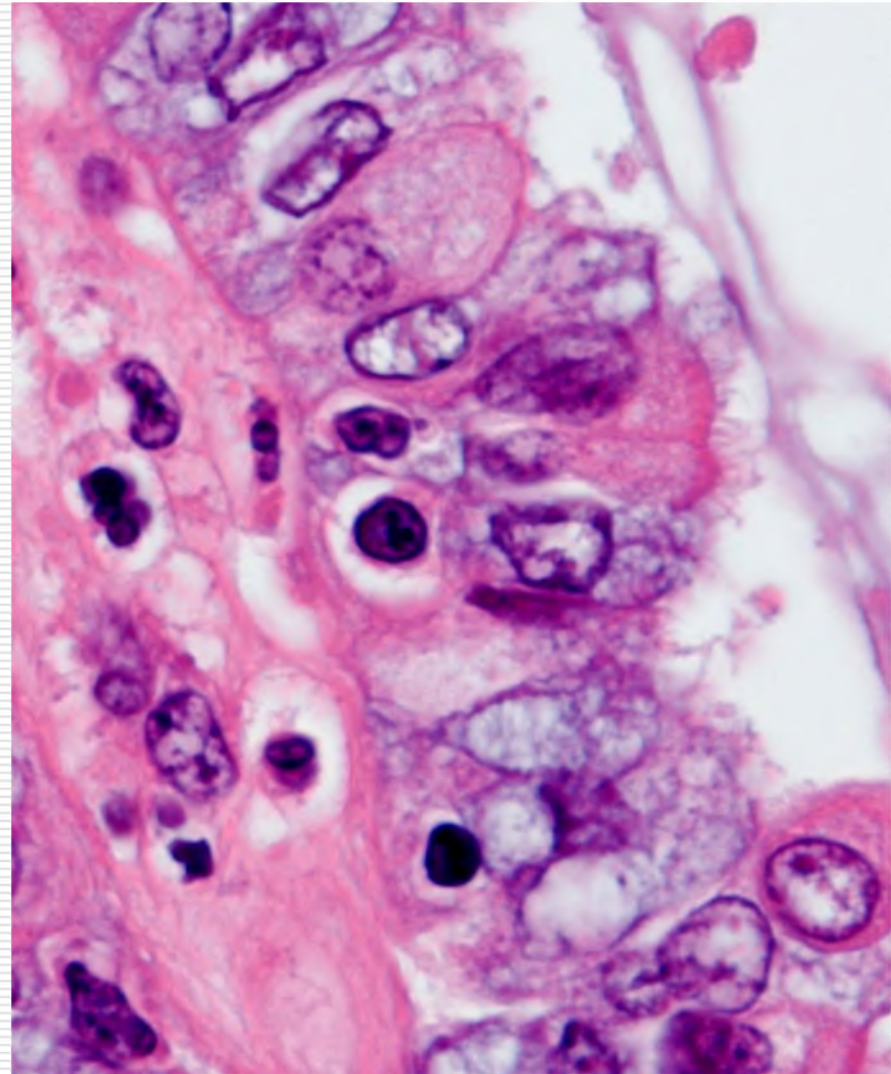


A histological section of the endocervix stained with hematoxylin and eosin (H&E). The image shows several endocervical glands, which are lined by a simple columnar epithelium. The glands are filled with a pink, eosinophilic secretory material. The nuclei of the epithelial cells are stained dark purple (hematoxylin) and are located at the base of the columnar cells. The overall architecture is organized and regular, characteristic of normal endocervical tissue.

Normal endocervical glands



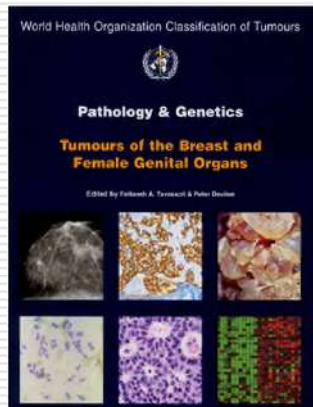
**Normal
Endocervical gland**



Seromucinous
32

Endocervical-like mucinous borderline tumor

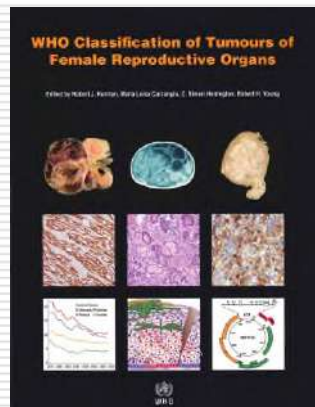
- Ovarian tumors of low malignant potential exhibiting an epithelial proliferation of mucinous type cells greater than seen in their benign counterparts but without destructive stromal invasion
- The mucinous epithelial cells resemble endocervical epithelium



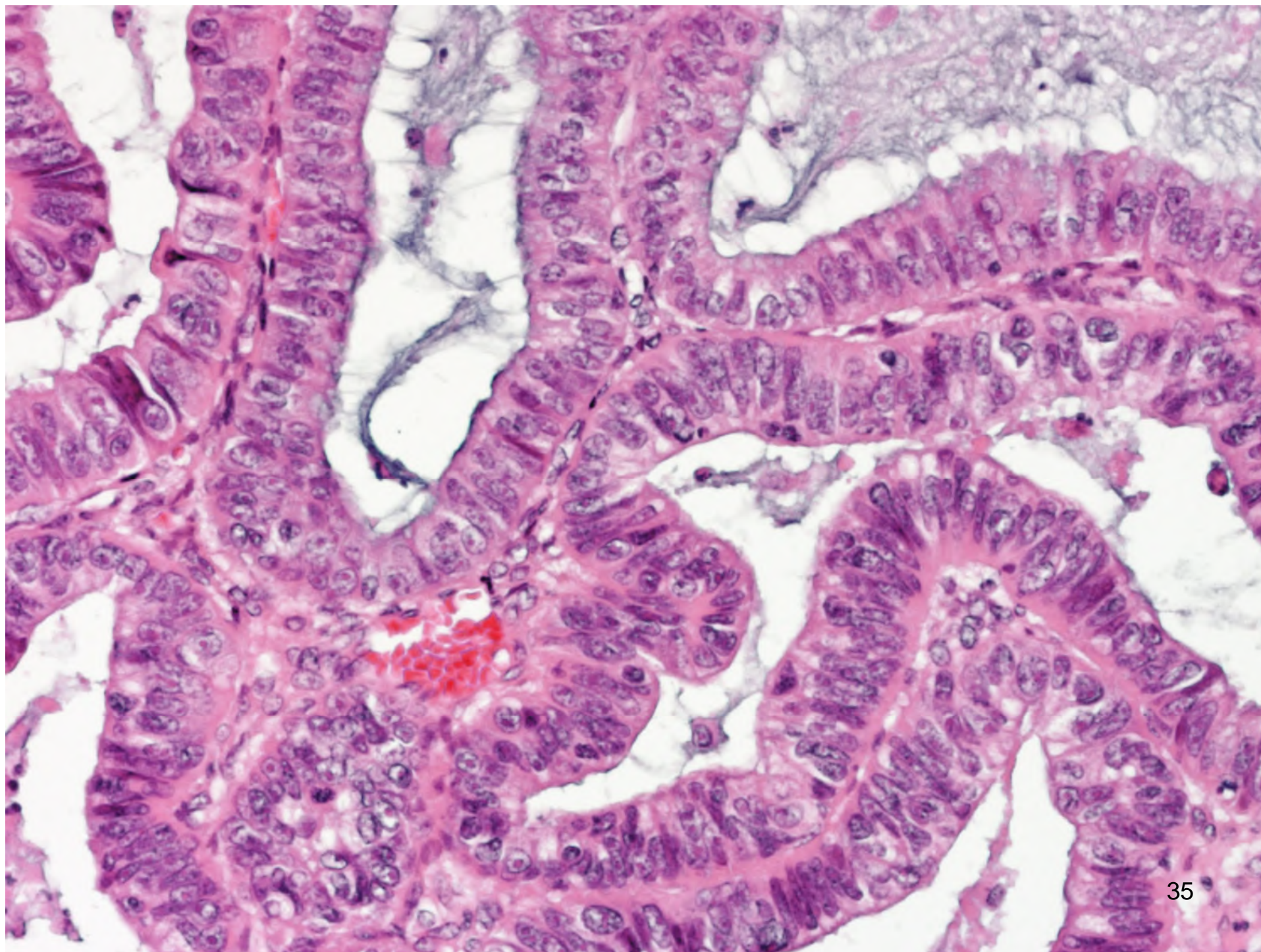
WHO2003

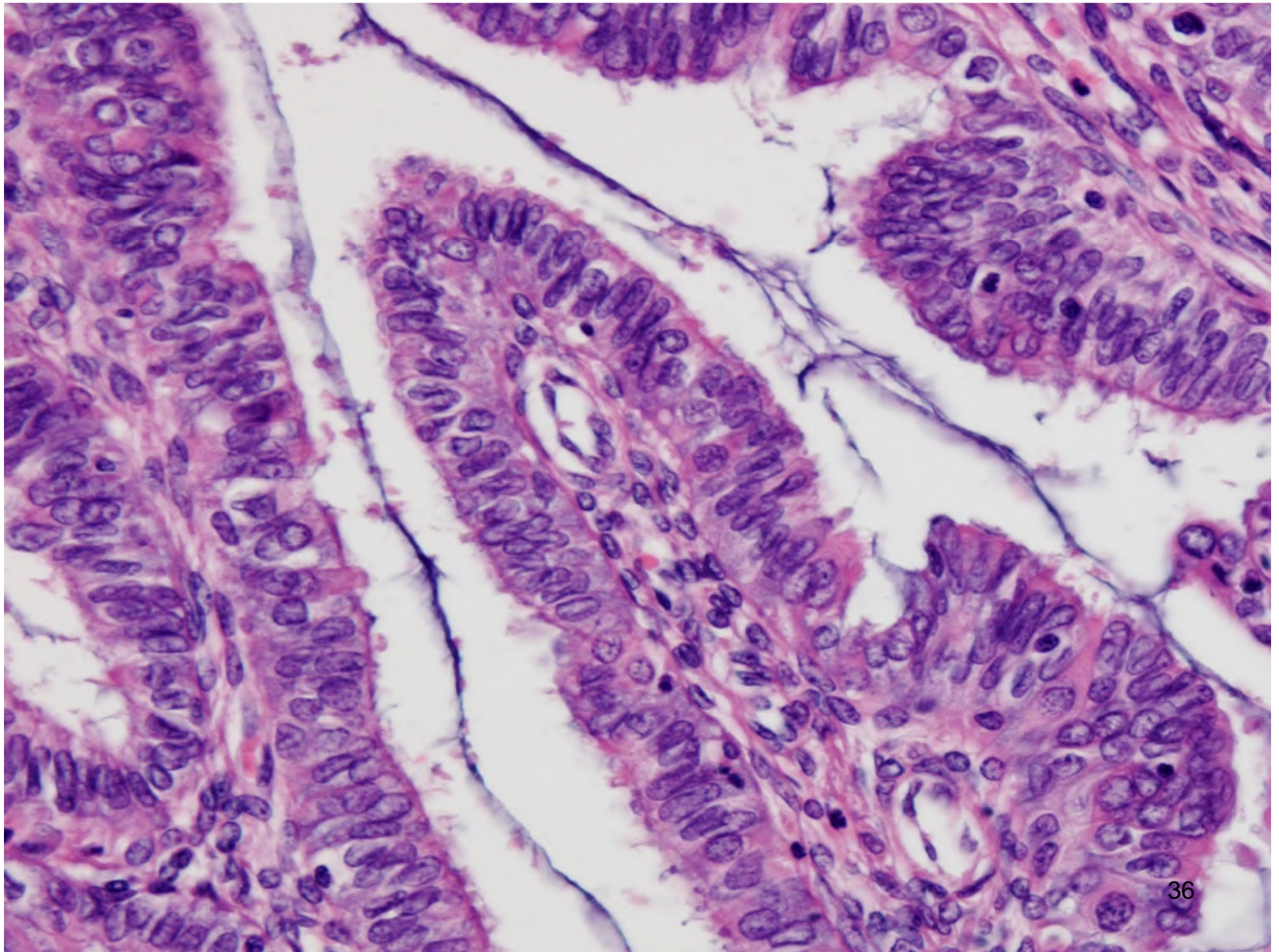
Seromucinous borderline tumor

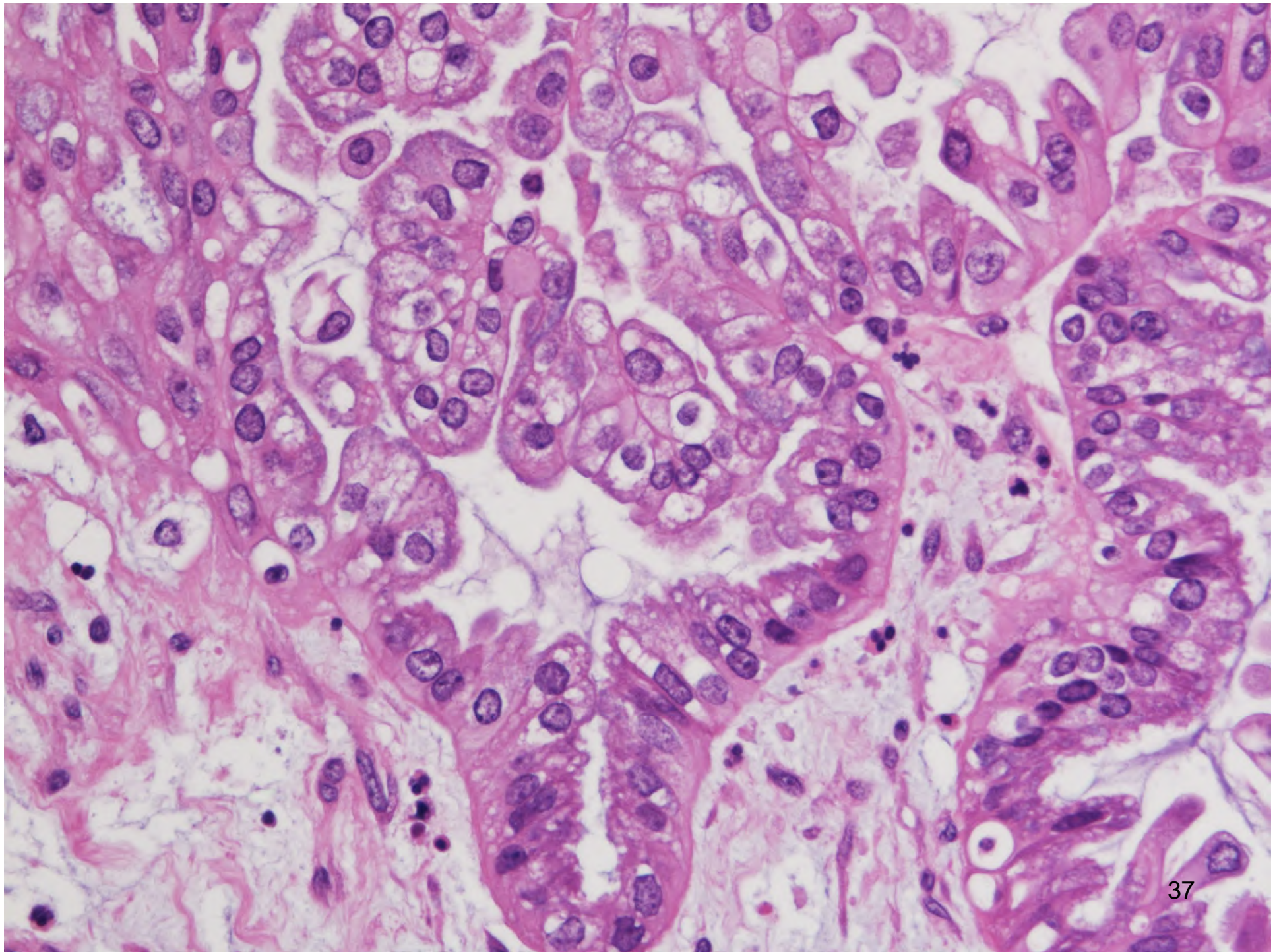
- Non-invasive proliferative tumor composed of more than one types of epithelial cells
- Predominantly serous and endocervical types
- Occasionally admixed with endometrioid, clear cell, and squamous epithelium

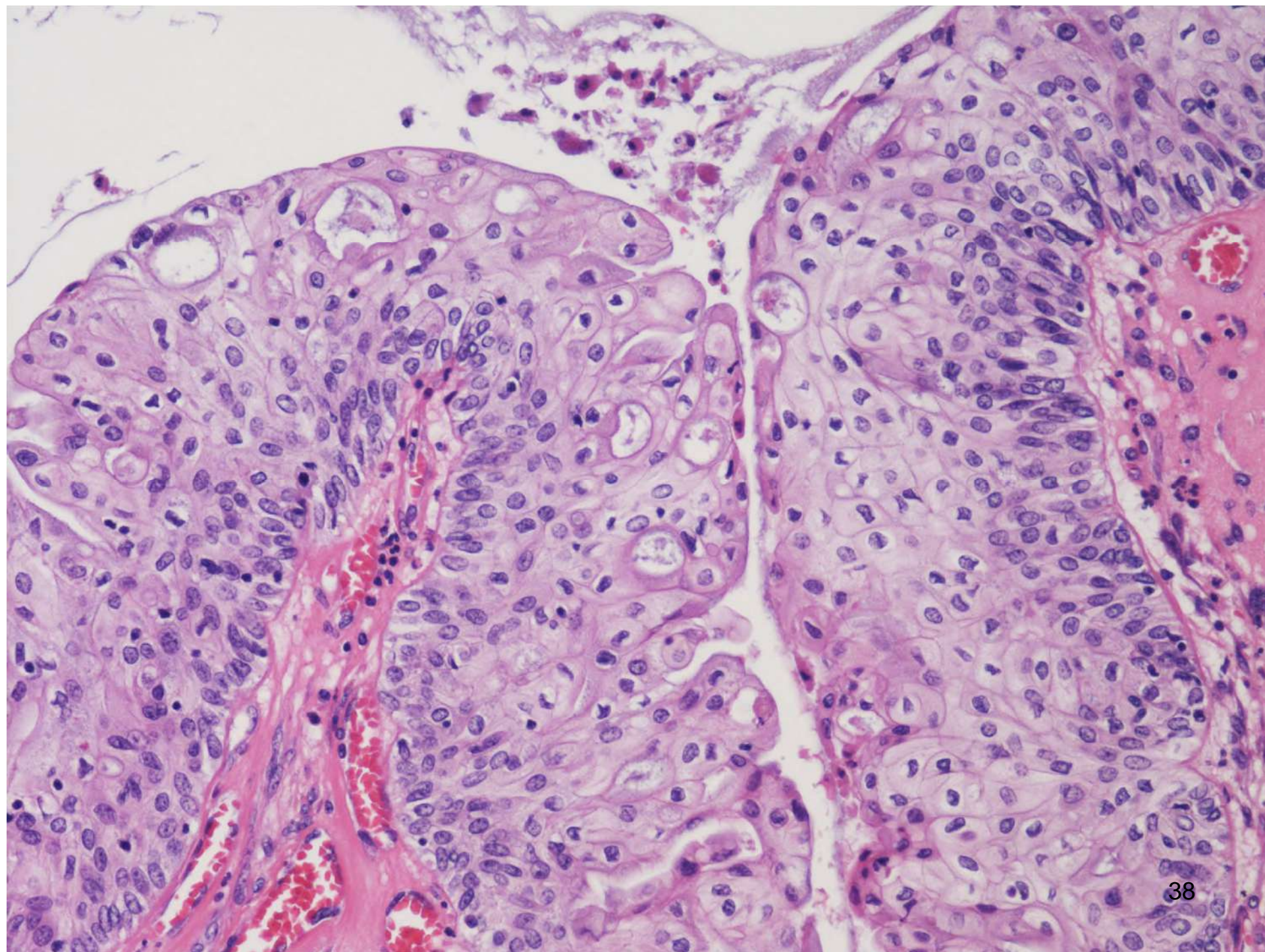


WHO2014





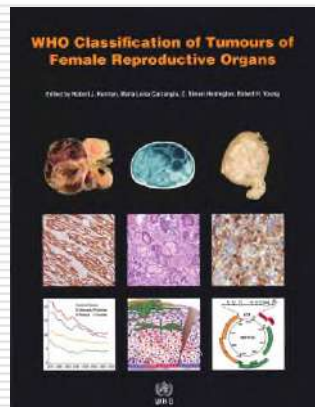




Seromucinous borderline tumor

Synonyms

- Endocervical-like MBT
- Müllerian MBT
- Borderline müllerian tumor

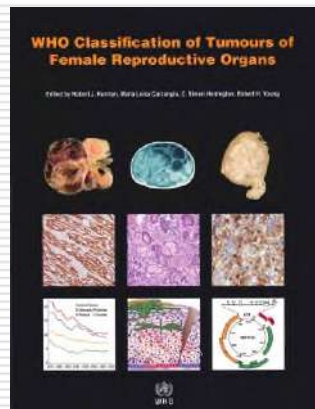


WHO2014

Seromucinous borderline tumor

Name	Morphology	Definition
"Seromucinous"	Endocervical	Mixed müllerian

Discrepancy



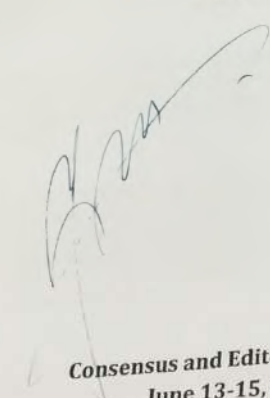
WHO2014



**WHO Classification of
Tumours of Female Reproductive Organs**

Text and references

DRAFT


**Consensus and Editorial Meeting
June 13-15, 2013
International Agency for Research on Cancer, Lyon**

**WHO Classification of
Tumours of Female Reproductive Organs**

Classification

DRAFT

**Consensus and Editorial Meeting
June 13-15, 2013
International Agency for Research on Cancer, Lyon**

1-6B. Müllerian tumours of mixed cell type, borderline

1-6B-i. Borderline müllerian tumours of mixed cell type

Definition

A noninvasive proliferative epithelial tumour composed of more than one epithelial cell type most often serous and endocervical-type mucinous, sometimes endometrioid, and less often clear cell, transitional or squamous.

ICD-O code

8323/1

Synonyms

Endocervical-type mucinous borderline tumour, seromucinous borderline tumour, müllerian mucinous borderline tumour, mixed müllerian tumour, atypical proliferative (borderline) müllerian tumour

Epidemiology

This is an uncommon tumor and accounts for approximately 1% of ovarian atypical proliferative tumours. In the past they have been considered a subset of mucinous tumors (endocervical type), and therefore of all mucinous atypical proliferative (borderline) tumors, they account for 4-15% of cases {3334969}.

Seromucinous borderline tumor

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Endocervical type

Serous type
Endometrioid type
Clear cell type
Squamous type
(Transitional type)

! No strict quantitative criteria

Seromucinous borderline tumor

Definition

A noninvasive proliferative epithelial tumour composed of more than one epithelial cell type most often serous and endocervical-type mucinous, sometimes endometrioid, and less often clear cell, transitional or squamous.

Seromucinous ?????

**Serous type
Endometrioid type
Clear cell type
Squamous type
(Transitional type)**

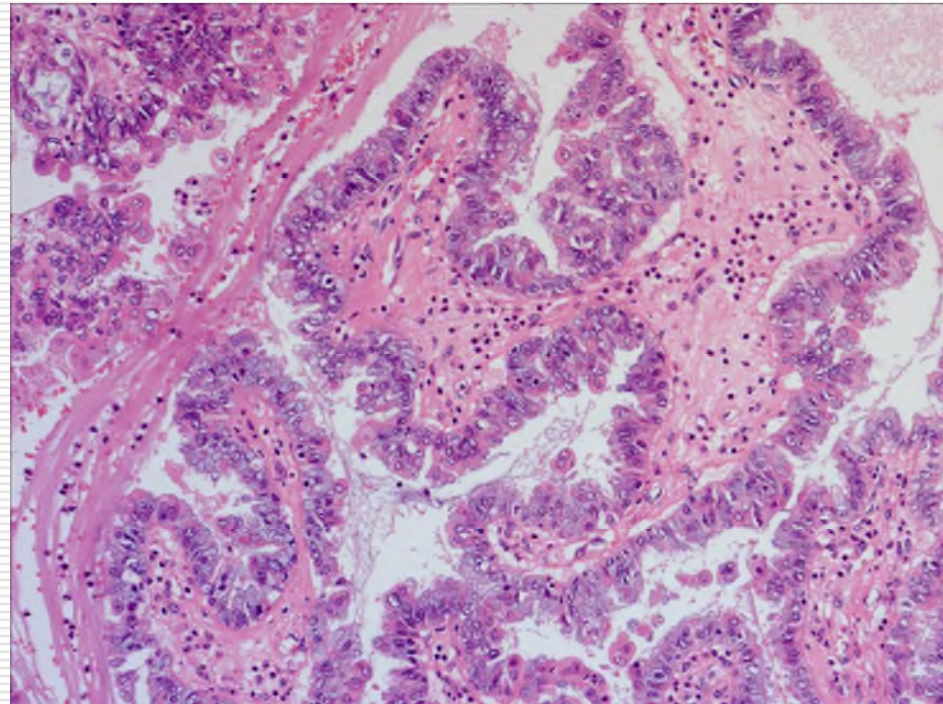
Endocervical type

! No strict quantitative criteria

Seromucinous borderline tumor

KRAS mutation
(Kim KR et al,
2010)

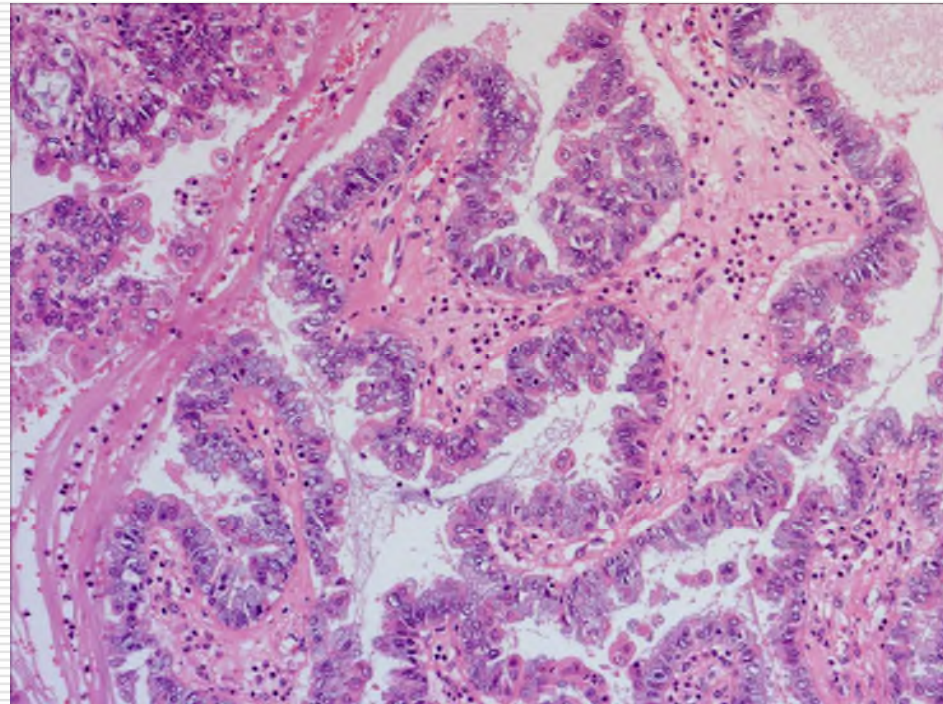
Similar to
endometrioid
tumors



Seromucinous borderline tumor

ER/PR +
WT1 –
CK20 –、CDX2 –
ARID1A mutation
(Kurman et al. 2016)

Similar to
endometrioid or
clear cell tumors



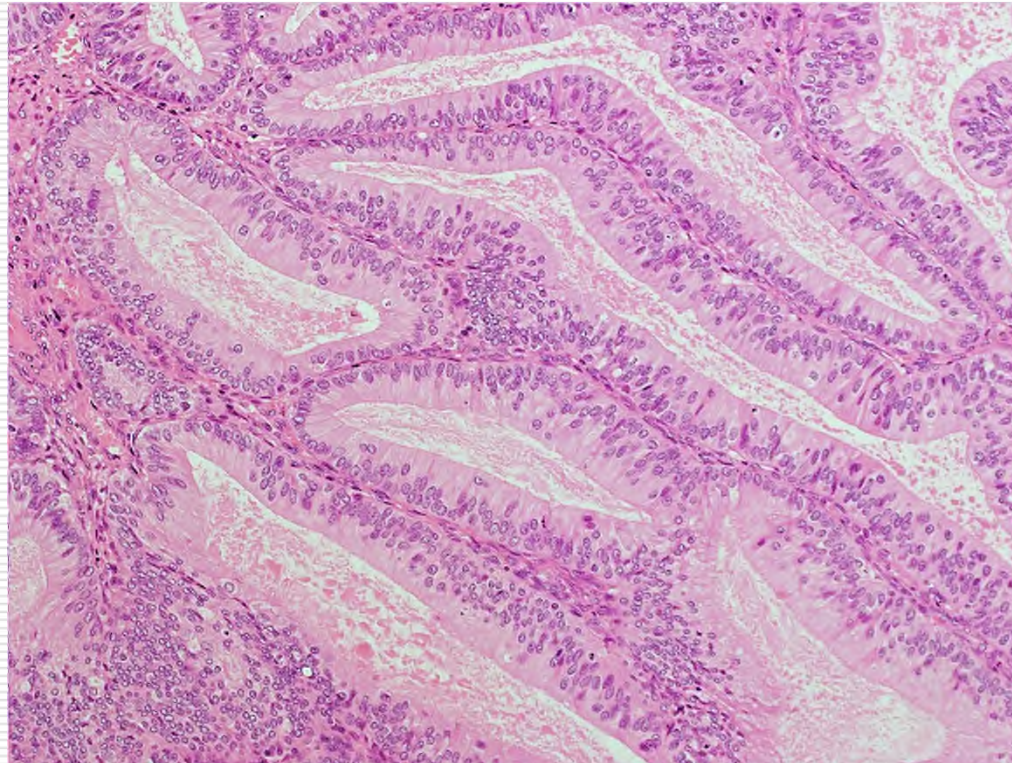
Seromucinous Tumors of the Ovary

What's in a Name ?

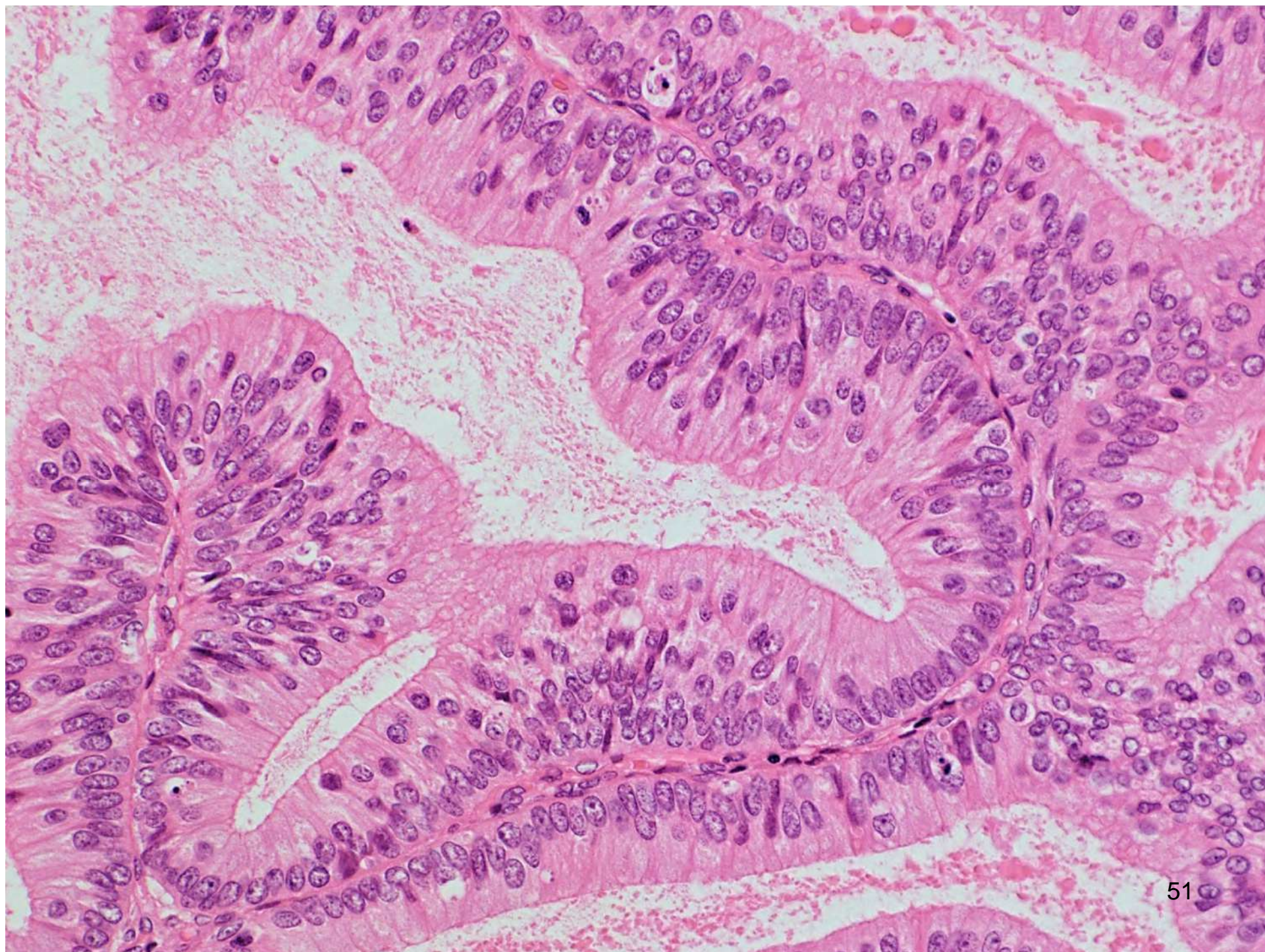
Kurman RJ and Shih I-M. Int J Gynecol Pathol 2016; 35: 78-81

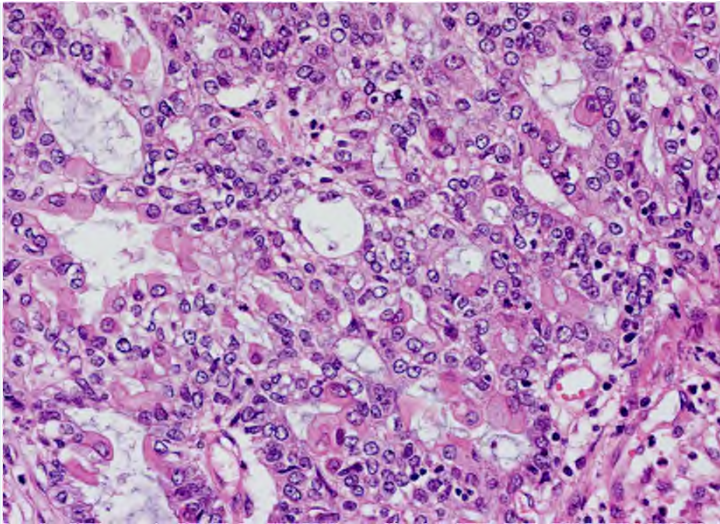
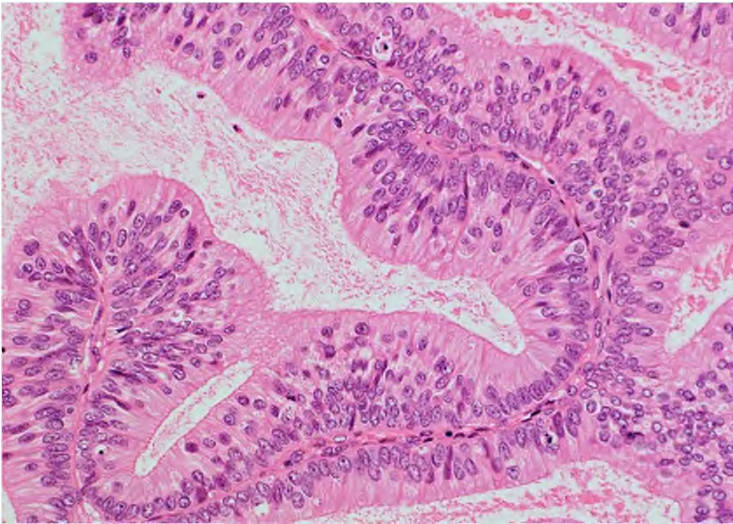
... Based on their clinicopathologic, immunohistochemical and molecular genetic features we believe a more appropriate designation for this group of tumors is "mixed müllerian tumors" which can be subcategorized as "mixed müllerian cystadenomas", "mixed müllerian atypical proliferative (borderline) tumors" and "mixed müllerian carcinomas".

Seromucinous carcinoma



Vs Endometrioid carcinoma with mucinous differentiation



	Seromucinous carcinoma	Endometrioid carcinoma with mucinous differentiation
		
Background	Seromucinous borderline tumor	Prototypical endometrioid carcinoma

Morphologic Reproducibility, Genotyping, and Immunohistochemical Profiling Do Not Support a Category of Seromucinous Carcinoma of the Ovary

Peter F. Rambau, MD,*† John B. McIntyre, PhD,‡ Jennifer Taylor, MD,§ Sandra Lee, MD,*
Travis Ogilvie, MD,* Anna Sienko, MD,* Don Morris, MD,‡|| Máire A. Duggan, MD,*
W. Glenn McCluggage, MD,§ and Martin Köbel, MD*

Abstract: The 2014 World Health Organization Classification of Tumors of Female Reproductive Organs endorsed the new category of seromucinous carcinoma, a neoplasm that exhibits morphologic and immunophenotypic overlap with other histotypes of ovarian carcinoma. The goal of this study was to determine whether seromucinous carcinoma was a distinct histotype by assessing its diagnostic reproducibility and comparing its molecular composition to the 5 major histotypes of ovarian carcinoma. Thirty-two tumors diagnosed as seromucinous carcinomas from 2 centers were studied. Eighteen cases were randomly selected for a review set comprising a total of 50 ovarian carcinomas of various histotypes. Morphologic histotype was independently assessed by 4 pathologists. For the 32 seromucinous carcinomas, a histotype-specific immunophenotype was assigned using a diagnostic immunohistochemical panel. Histotype-specific genotype was assigned using a combination of immunohistochemistry and targeted next-generation sequencing for somatic mutations, including genes recurrently mutated in ovarian carcinomas. There was low to modest agreement between pathologists with the reference diagnosis of seromucinous carcinoma, ranging from 39% to 56% for the 4 observers. The immunophenotype was not unique but overlapped predominantly with endometrioid and to a lesser extent with mucinous and low-grade serous carcinoma. Genomic and immunohistochemical alterations were

detected in a number of target genes, including *KRAS* (70%), *PIK3CA* (37%), *PTEN* (19%), and *ARID1A* (16%); no *CTNNB1* mutations were identified. Nine cases (30%) harbored concurrent *KRAS/PIK3CA* mutations. An endometrioid genotype was assigned to 19 cases, a low-grade serous genotype to 9, and a mucinous genotype to 1 and 3 cases were uninformative. Integrating morphology, immunophenotype, and genotyping resulted in reclassifying the seromucinous carcinomas to endometrioid 23/32 (72%), low-grade serous 8/32 (25%), and mucinous 1/32 (3%). The morphologic diagnosis of seromucinous carcinomas is not very reliable and it does not exhibit a distinct immunophenotype or genotype. The molecular features overlap mostly with endometrioid and low-grade serous carcinomas. Our data suggest the category of seromucinous carcinoma be discontinued as ancillary molecular tests can assign cases to one of the major histotypes.

Key Words: seromucinous, mixed Müllerian, mixed cell type, endocervical-type mucinous, endometrioid, low-grade serous
(*Am J Surg Pathol* 2017;41:685-695)

In the revised 2014 World Health Organization (WHO) Classification of Tumors of Female Reproductive Organs, seromucinous carcinoma was endorsed as a separate histologic type of ovarian carcinoma. Previously, the

- Seromucinous carcinoma may be reclassified to endometrioid, low-grade serous, and mucinous carcinomas by integrating morphology, immunophenotype, and genotype.
- the category of seromucinous carcinoma be discontinued as ancillary molecular tests can assign cases to one of the major histotypes

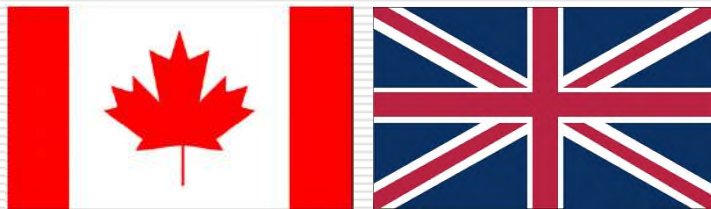


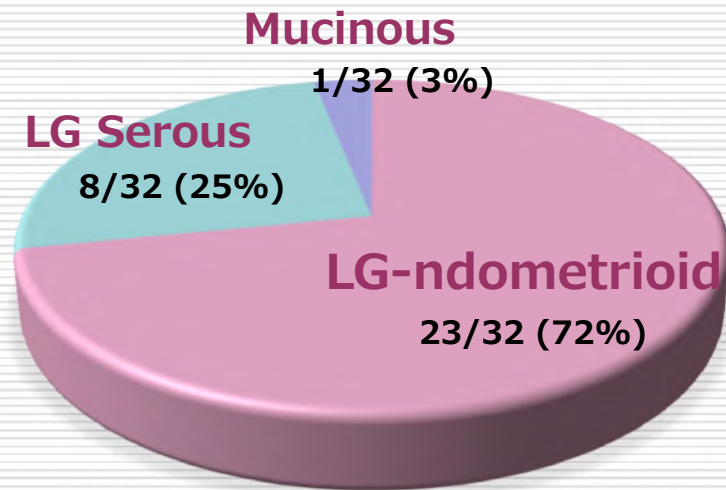
TABLE 1. Histotype-specific IHC Phenotype and Genotype Definitions

Histotype	Immunophenotype ¹¹	Genotype
Low-grade serous	WT1 present, p53 normal	<i>KRAS</i> , <i>BRAF</i> , <i>NRAS</i> , <i>ERBB2</i> , or <i>FGFR2</i> ^{18,19}
Endometrioid	WT1 absent, Napsin A absent, PR present	<i>CTNNB1</i> , <i>PTEN</i> , <i>PPP2R1A</i> , <i>PIK3R1</i> , <i>POLE</i> , <i>SPOP</i> , <i>FBXW7</i> , <i>RPL22</i> , or deficient mismatch repair ^{16,20,21} Co-occurrence of <i>KRAS</i> and <i>PIK3CA</i> mutation
Endometrioid/clear cell	WT1 absent, Napsin present	<i>PIK3CA</i> and <i>ARID1A</i> ^{22,23}
Mucinous	WT1 absent, Napsin A absent, PR absent	Co-occurrence of <i>KRAS</i> and <i>TP53</i> or <i>ERBB2</i> amplification ²⁴

IHC indicates immunohistochemistry.

- Seromucinous carcinoma may be reclassified to endometrioid, low-grade serous, and mucinous carcinomas by integrating morphology, immunophenotype, and genotype.
- the category of seromucinous carcinoma be discontinued as ancillary molecular tests can assign cases to one of the major histotypes





"SEROMUCINOUS
CARCINOMA"



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- the category of seromucinous carcinoma be discontinued as ancillary molecular tests can assign cases to one of the major histotypes

TAKE HOME

Do you like it ?



**Thank you for
your attention**

Yoshiki Mikami, M.D.

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