

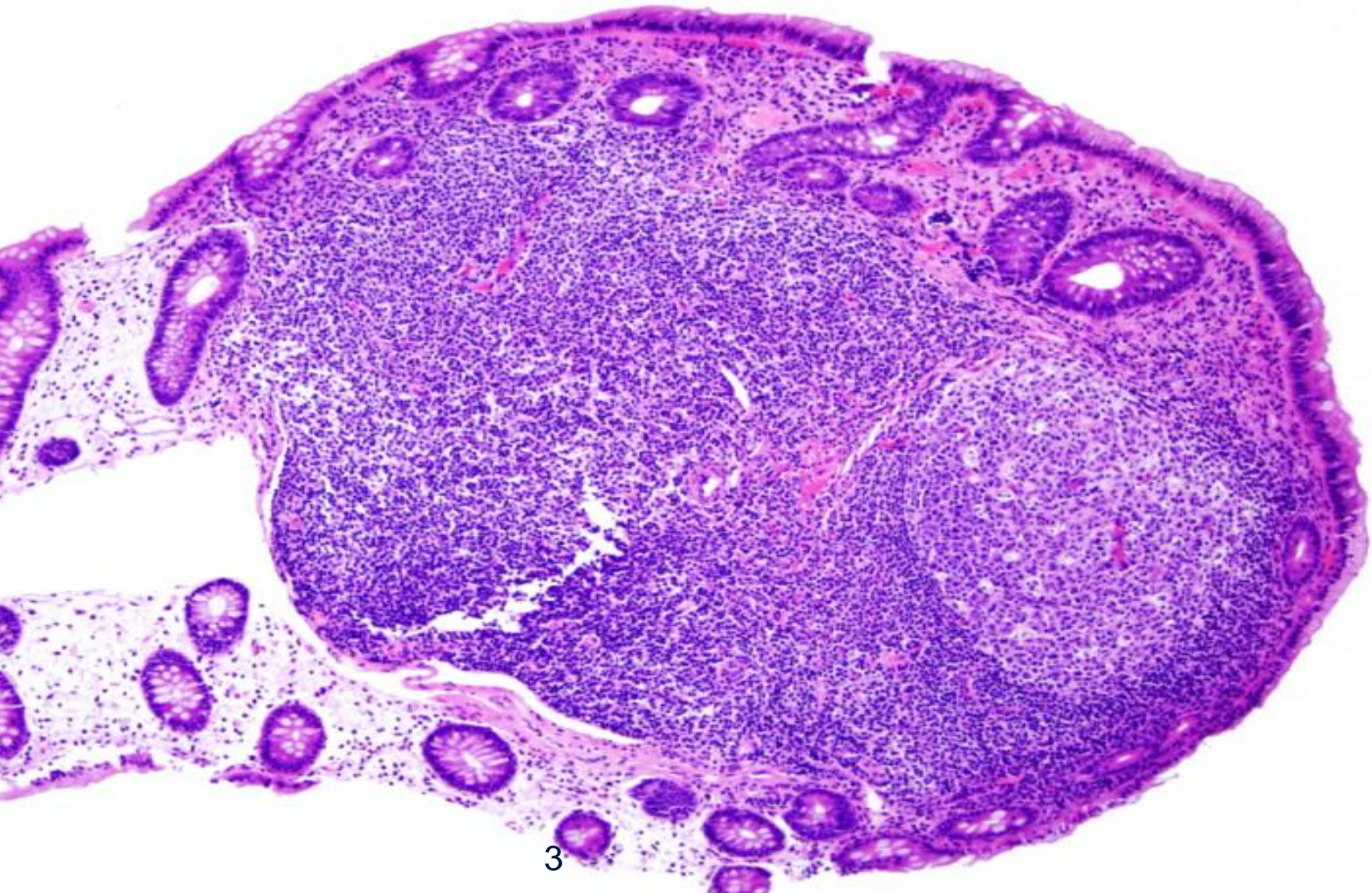
A Plethora of Colon Polyps

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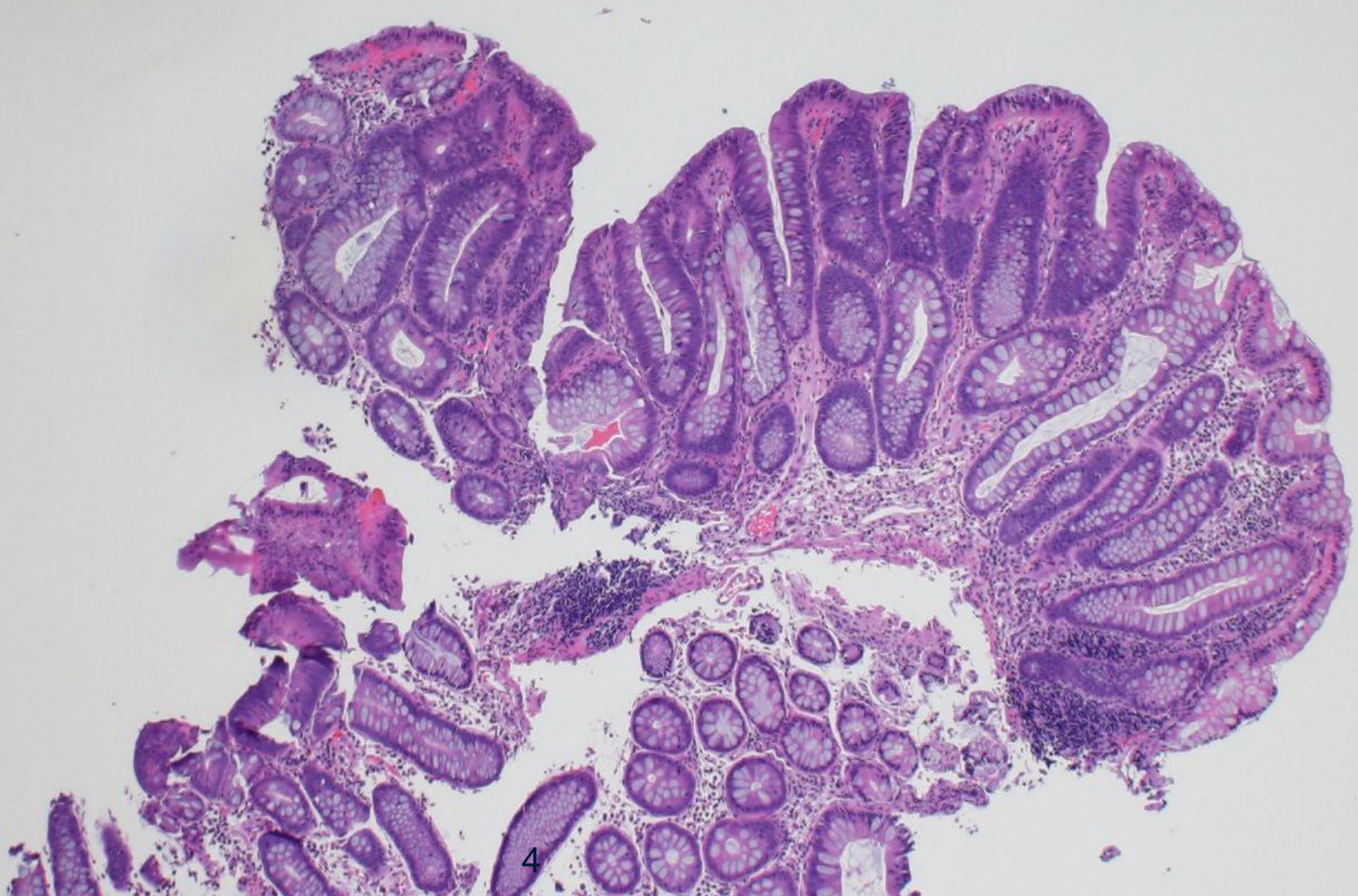
Background

- Clinical history:
 - 45 year old female with complaint of blood in stool
 - Underwent colonoscopy
 - Five 3-9 mm polyps throughout colon and internal hemorrhoids
 - Polyps completely removed and sent for pathology

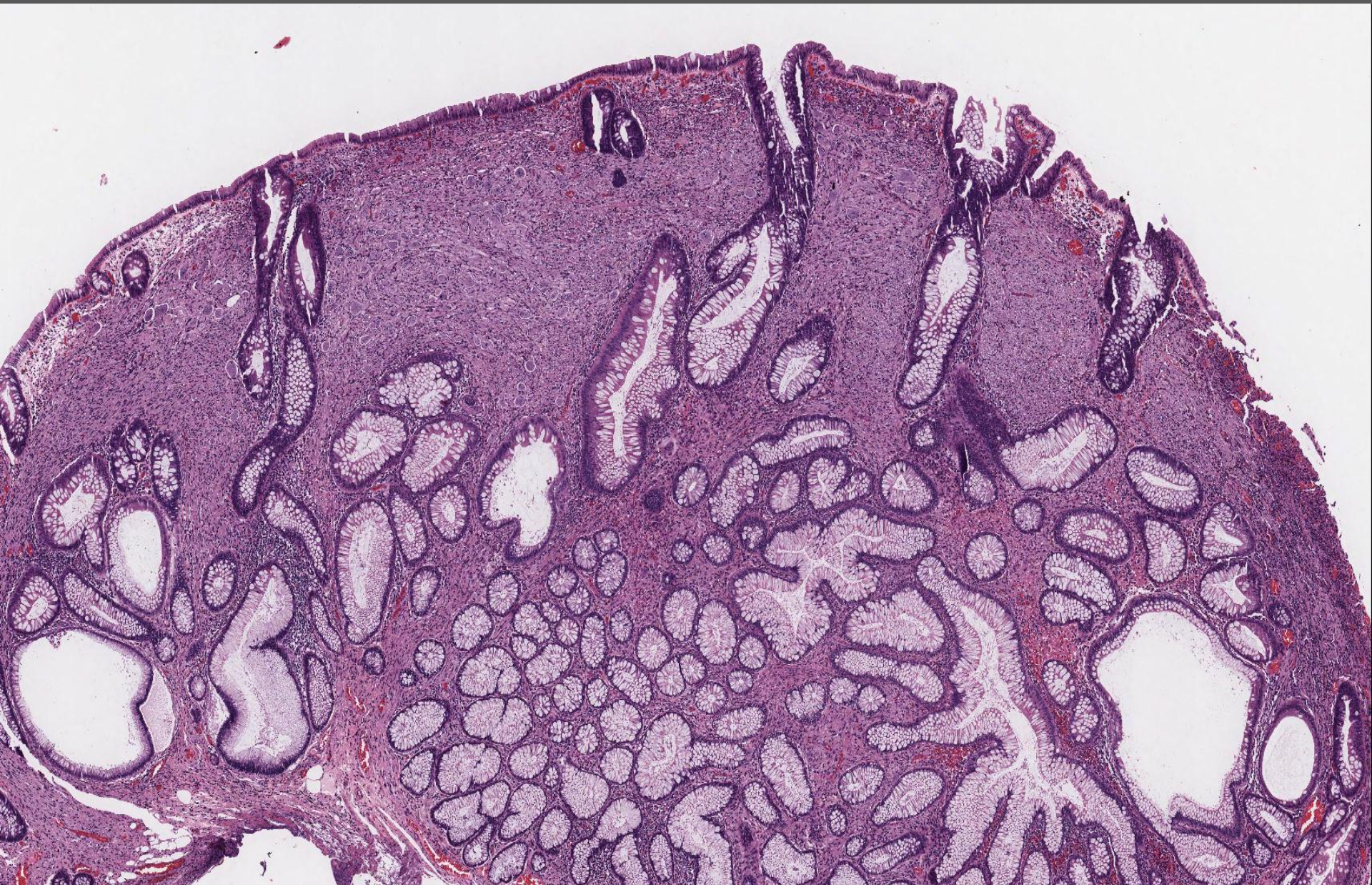
4 mm cecal polyp

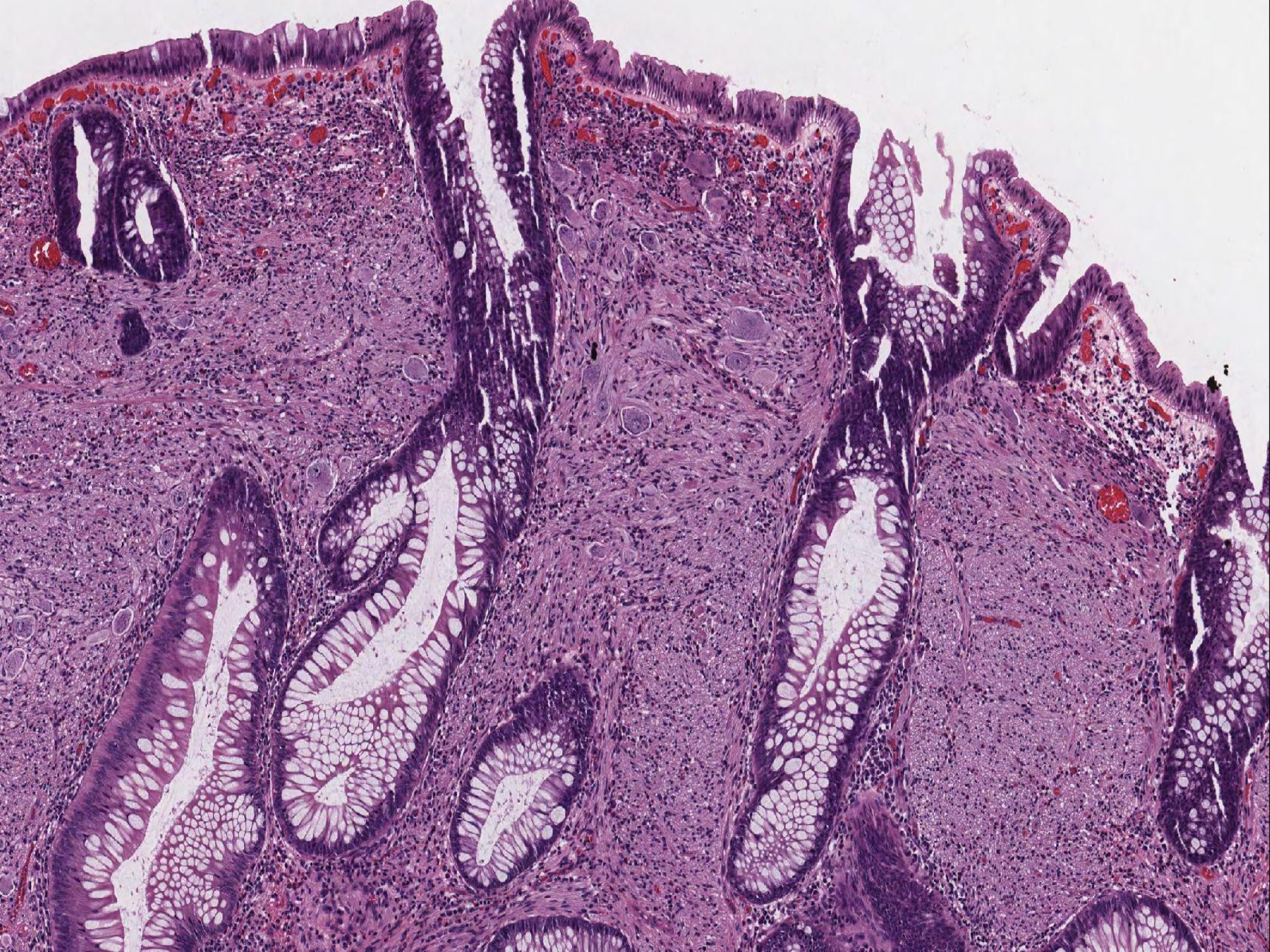


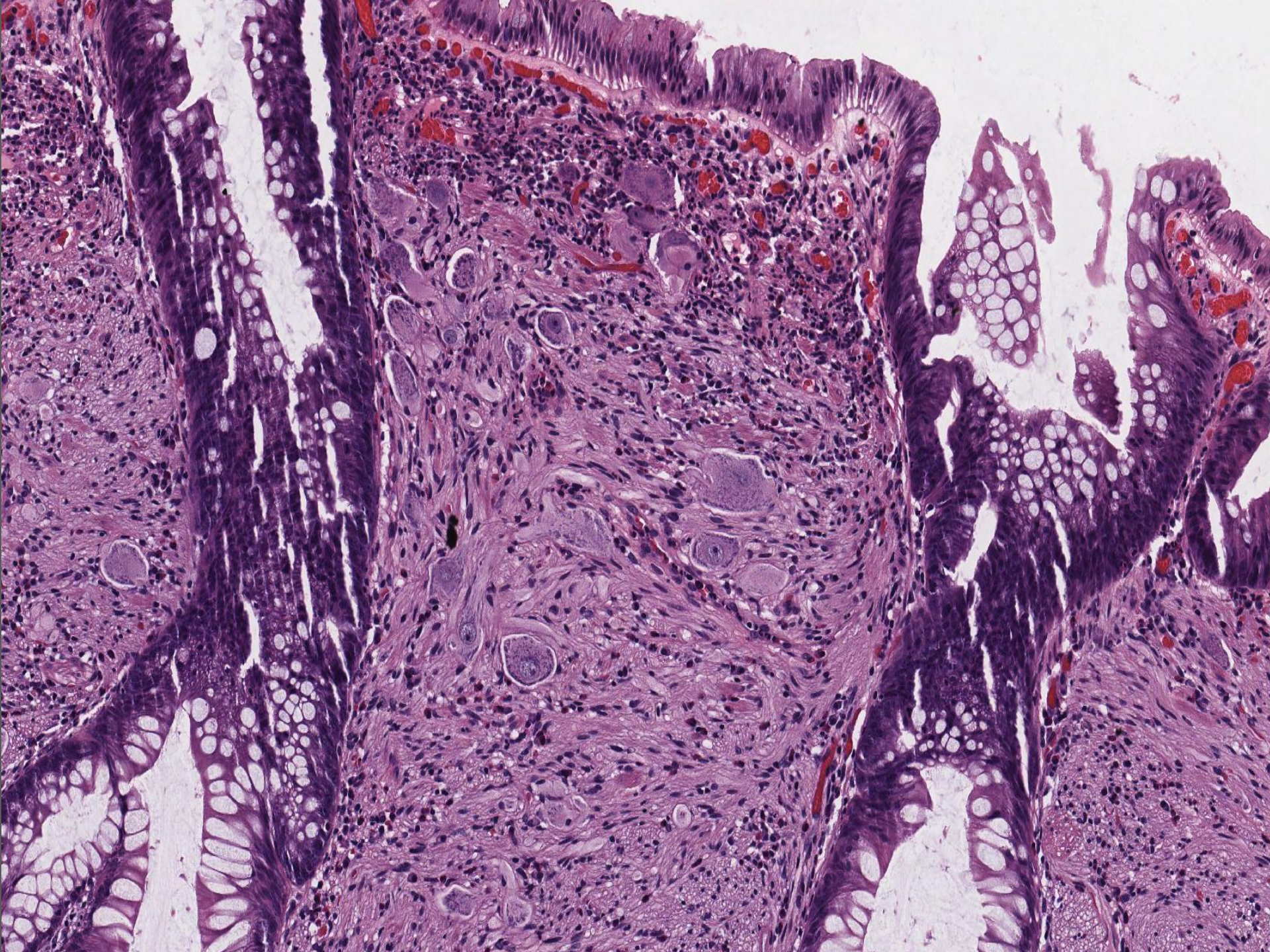
3 mm ascending colon polyp



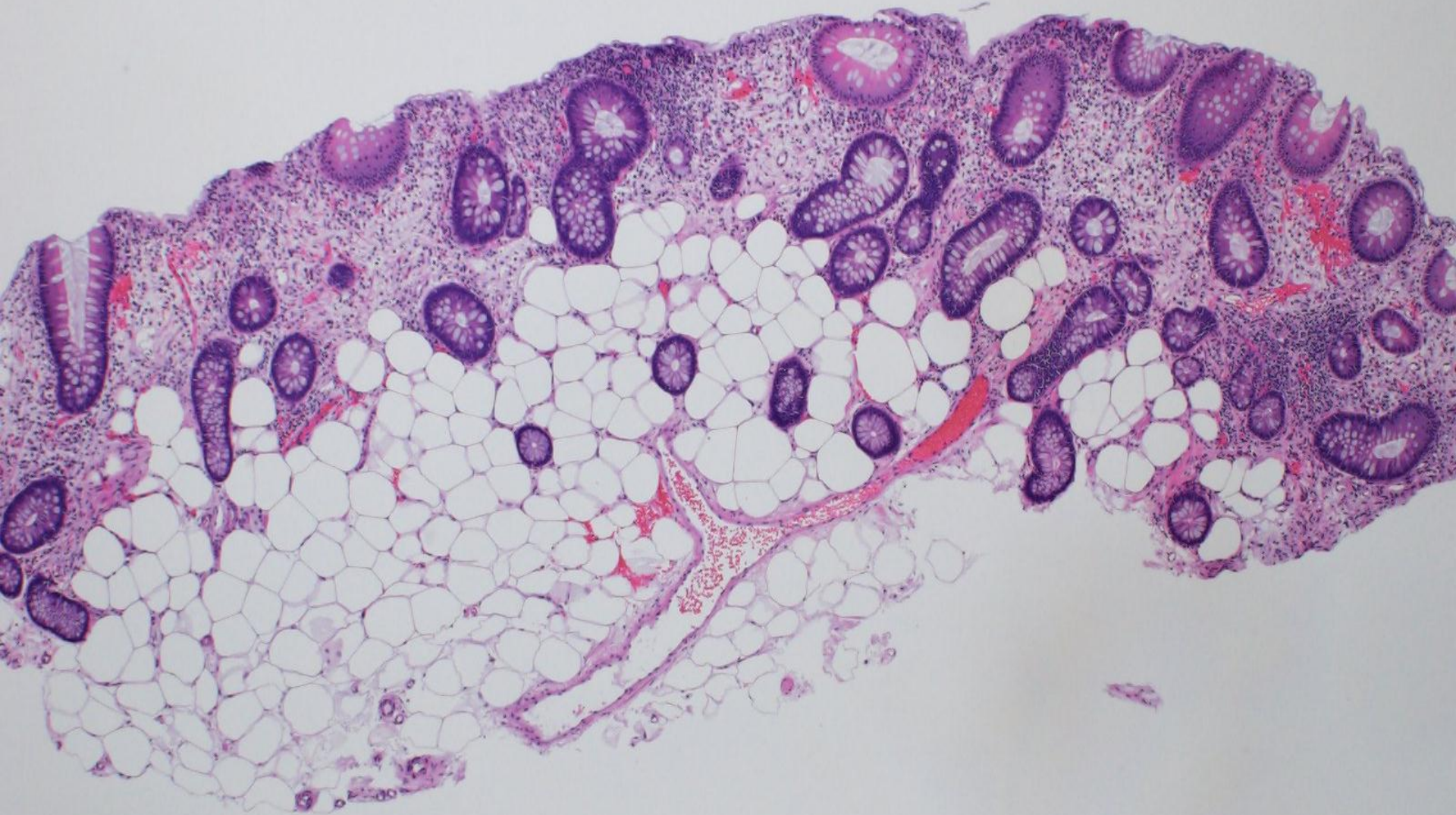
6 mm hepatic flexure polyp

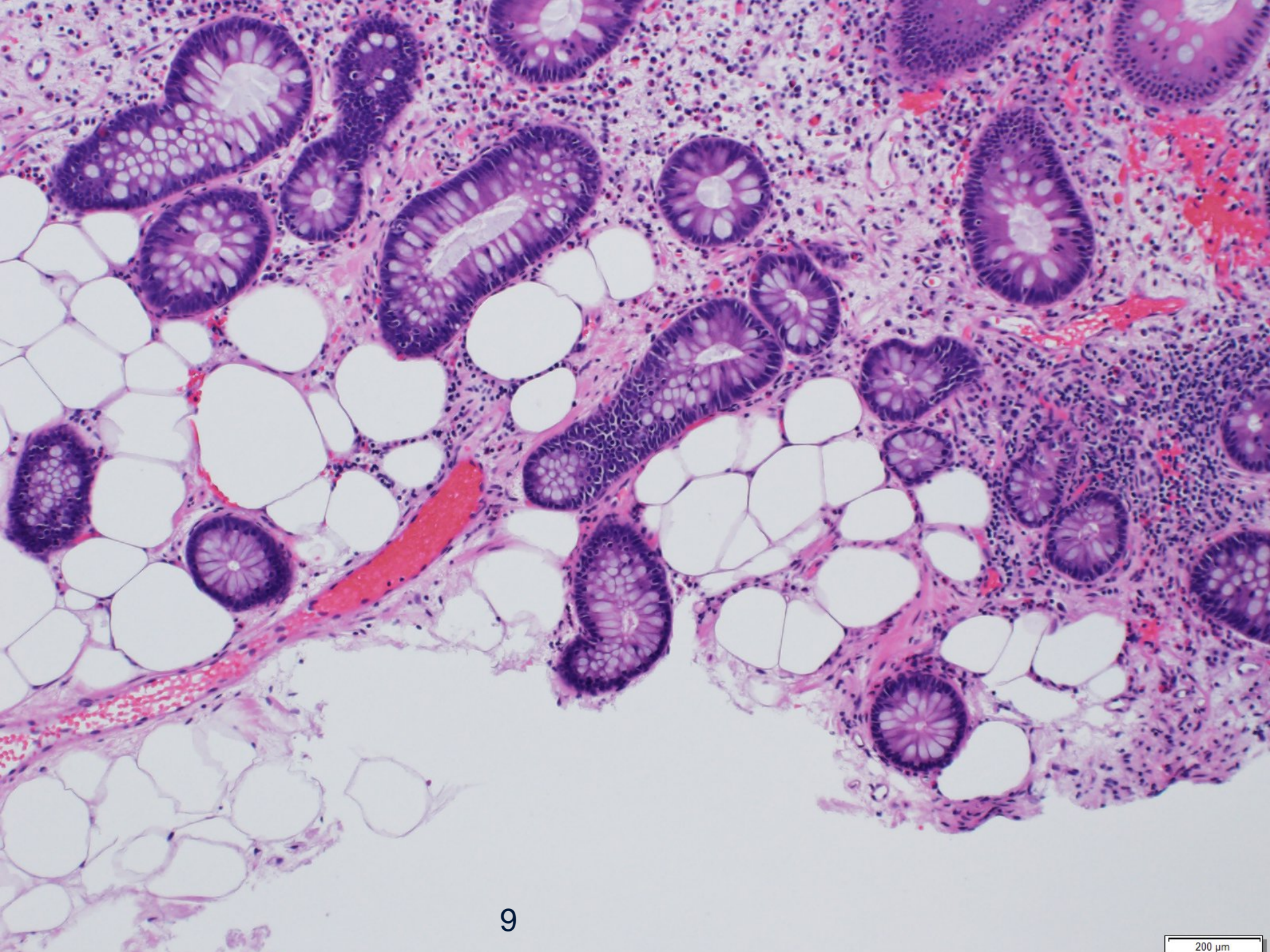




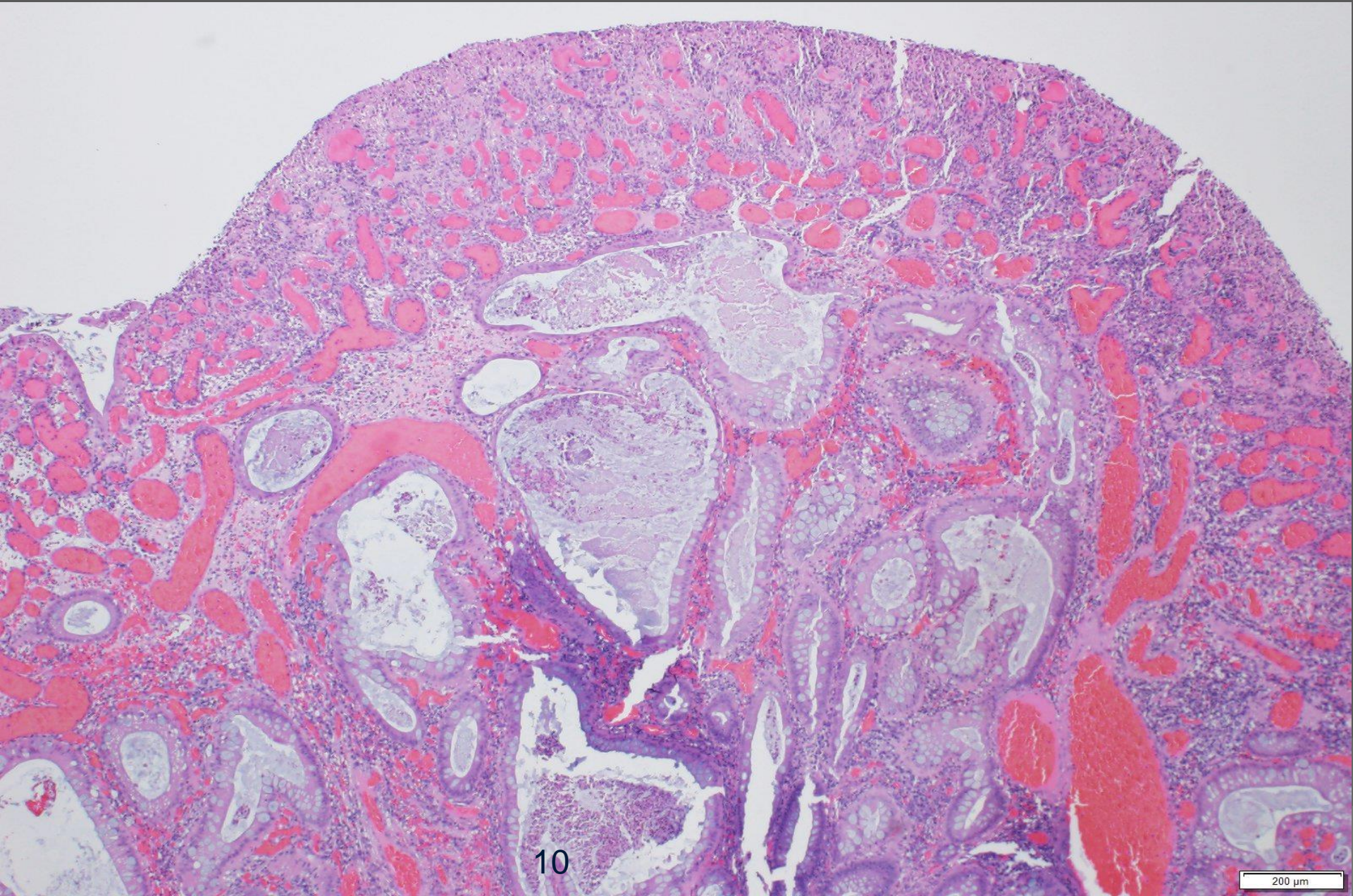


8 mm sessile trans colon polyp



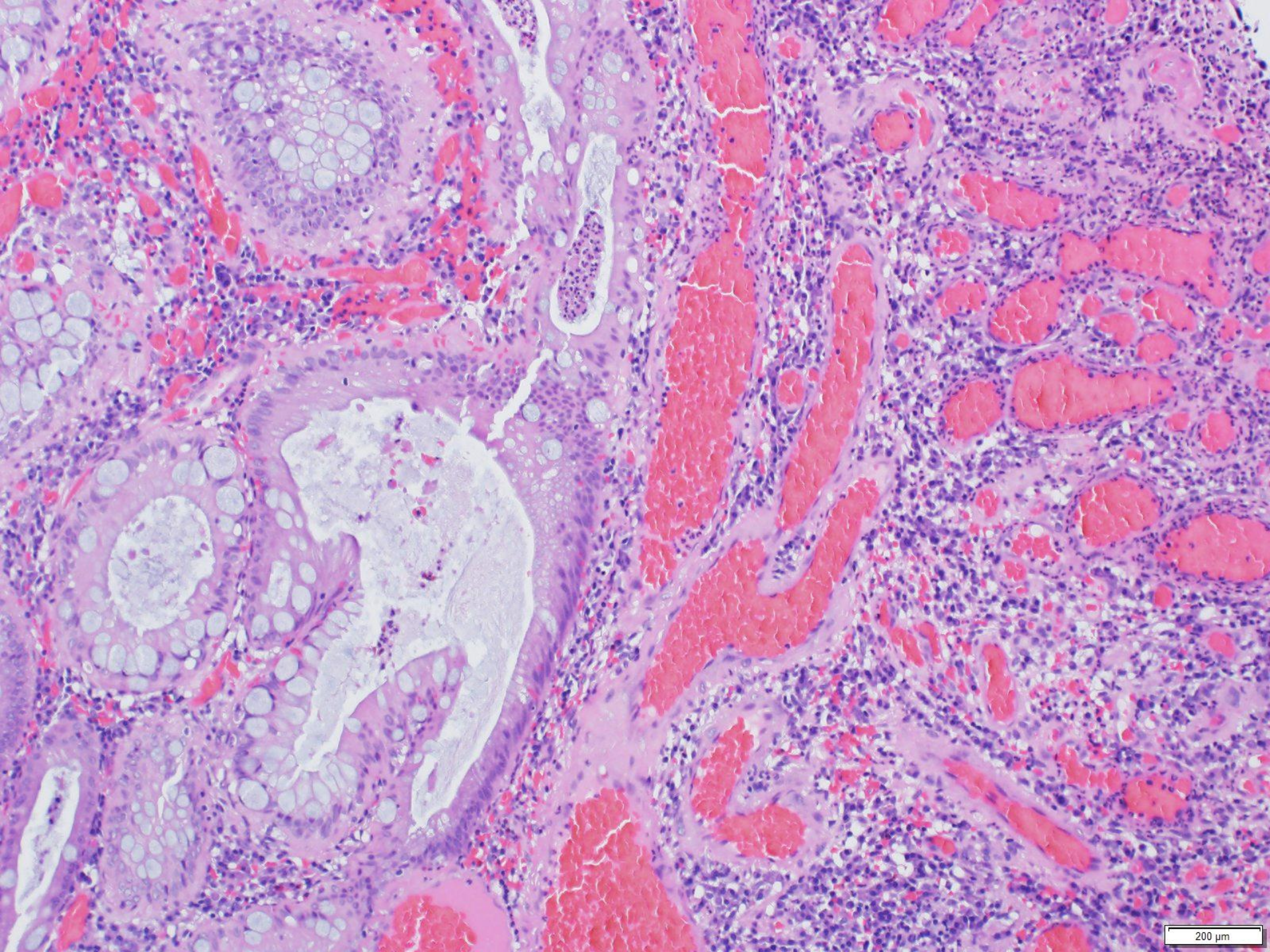


9 mm descending colon polyp



10

200 μm



200 μ m

Just a bunch of polyps?

- Lymphoid aggregate
- Tubular adenoma
- Ganglioneuroma
- Intramucosal lipoma
- Inflammatory (juvenile) type polyp

Ganglioneuroma

- Sporadic
- FAP
- Multiple endocrine neoplasia, type IIB
- Neurofibromatosis 1
- Cowden syndrome (CS)

Inflammatory (juvenile) polyp

- Sporadic (especially in children)
- Chronic injury response
 - IBD, ischemia, or chronic infections
- Juvenile polyposis
- Cowden syndrome

PTEN Hamartoma Tumor Syndrome

PTEN Hamartoma Tumor Syndrome (PHTS)

- Unifies heterogeneous germline *PTEN* disorders
- Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), Proteus syndrome
- Multiple hamartomas and distinctive phenotypes
- *PTEN* (10q22-23) tumor suppressor gene
 - Mutated in 80% CS, 60% BRRS
- 20-30% familial, 70-80% de novo (autosomal dominant, penetrance ~80%)

CS

- CS is the only PHTS disorder associated with a documented predisposition to malignancies
 - Other PHTS with *PTEN* mutations assumed to have Cowden-associated cancer risks
- Incidence of 1 in 200,000
 - Likely underestimated
- Extra-intestinal findings predominate, 30-80% have intestinal polyps

CS Cancer Risk

- CS clinical criteria + *PTEN* mut
 - Est cumulative lifetime cancer risks:
 - 85% breast
 - 35% thyroid
 - 28% endometrial
 - 9% colorectal
 - 34% renal cell
 - 6% melanoma

Tan, MH et al. *Clin Cancer Res* 2012;18:400-407

PHTS/CS Clinical Dx Criteria (NCCN)

- Major criteria: Breast, Endometrial, Thyroid follicular cancer
 - Gastrointestinal hamartomas (≥ 3)
 - Ganglioneuromas, others but not HP's
 - Macrocephaly (≥ 97 percentile)
 - Macular pigmentation penis
 - Adult Lhermitte-Duclos disease (LDD)
 - Multiple mucocutaneous lesions
 - Trichilemmomas, acral keratoses, mucocutaneous neuromas, oral papillomas

Pilarski R et al. J Natl Cancer Inst 2013;105:1607-1616

PHTS/CS Clinical Dx Criteria (NCCN)

- **Minor criteria**

- Autism spectrum disorder
- Colon cancer
- Esophageal glycogenic acanthosis (≥ 3)
- Lipomas (≥ 3)
- Mental retardation (ie, IQ ≤ 75)
- Renal cell carcinoma
- Testicular lipomatosis
- Thyroid adenoma, multinodular goiter
- Vascular anomalies (multiple intracranial developmental venous anomalies)

Pilarski R et al. J Natl Cancer Inst 2013;105:1607-1616

Working diagnosis of PHTS/CS

EITHER/OR:

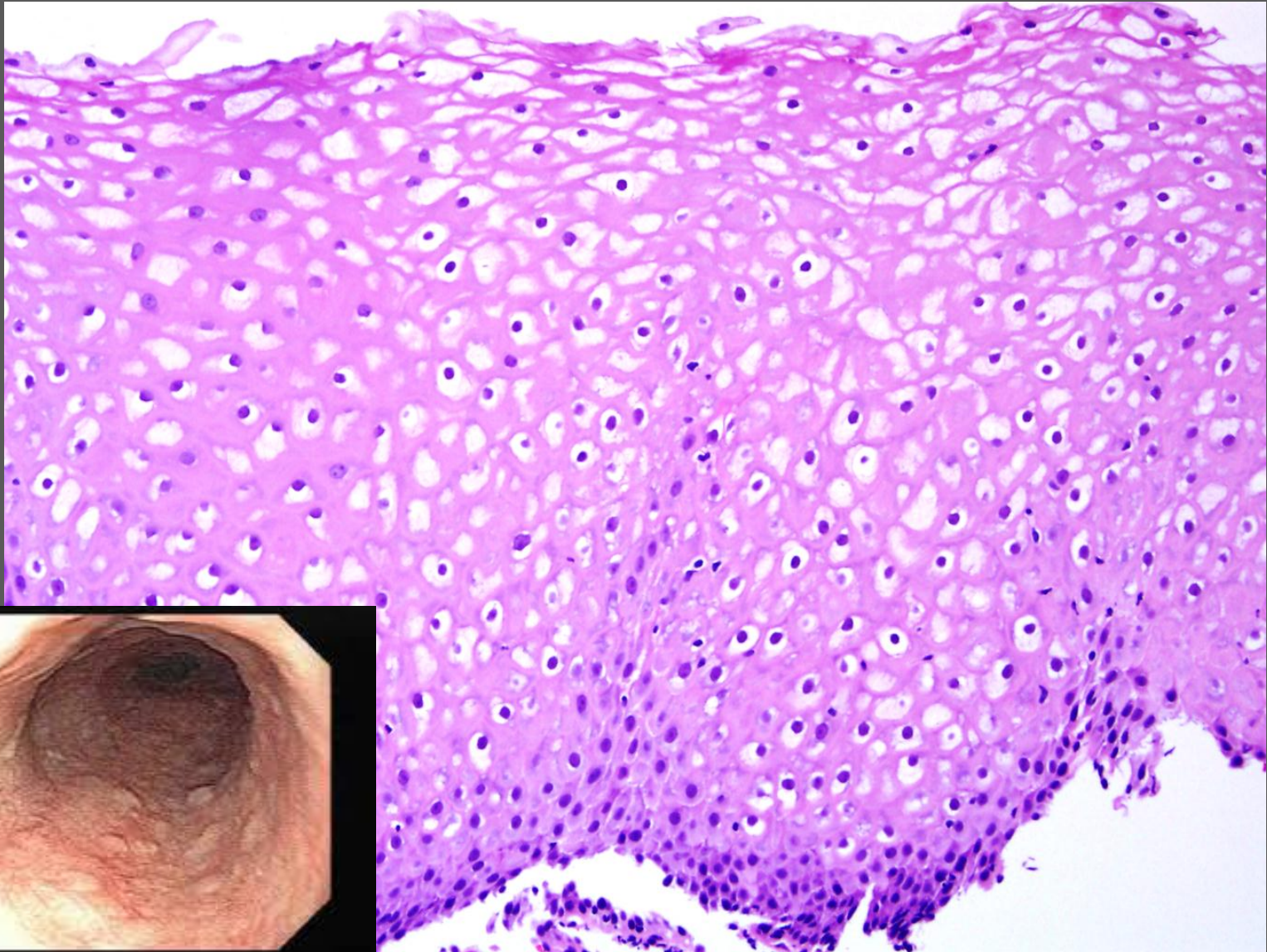
1. Three or more major criteria, must include macrocephaly, Lhermitte-Duclos disease, or GI hamartomas

2. Two major and three minor criteria

PHTS/CS: Frequent GI findings

- Esophagus
 - Glycogen acanthosis 40- 60%
- Stomach
 - Fundic gland polyps, Inflammatory (juvenile) type polyps
- Colon and small bowel
 - Inflammatory (juvenile) type polyps
 - Ganglioneuromas
 - Lymphoid polyps
 - Intramucosal lipomas
 - Adenomas

Glycogen acanthosis



CS: intestinal findings

- GI polyps at U of U reviewed in CS patients
 - 12/19 had *PTEN* mutations
 - Inflammatory (juvenile) polyps most common (95%)
 - Expansive lymphoid follicles (63%)
 - Ganglioneuromas (53%)
 - Mucosal lipomas (26%)
- Two or more hamartomatous polyp types/pt: highly prevalent in Cowden syndrome

PHTS/CS Management

Women

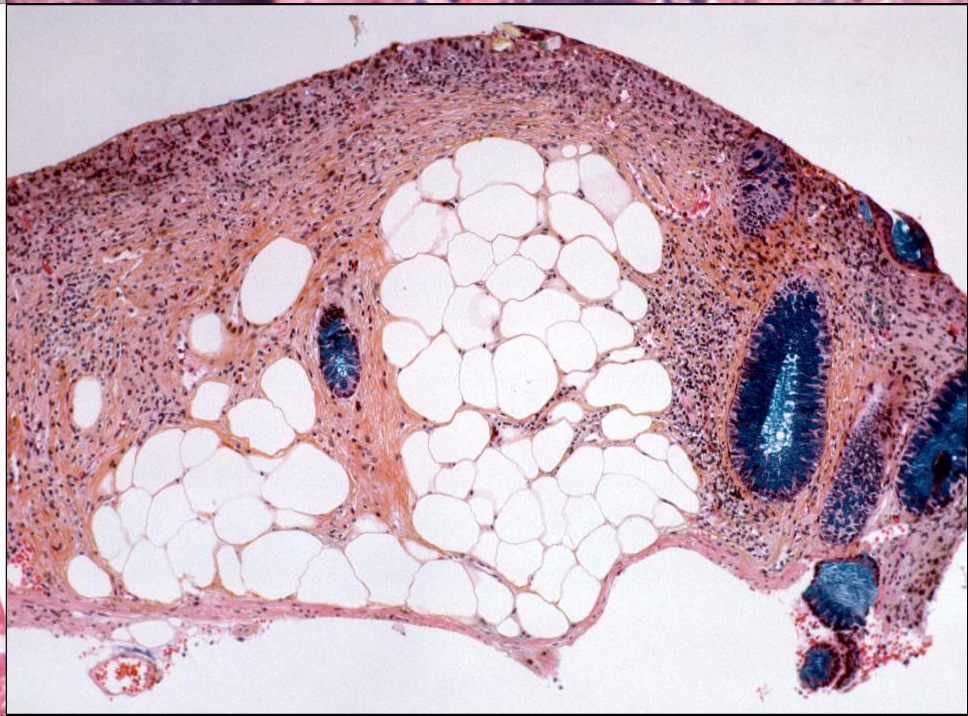
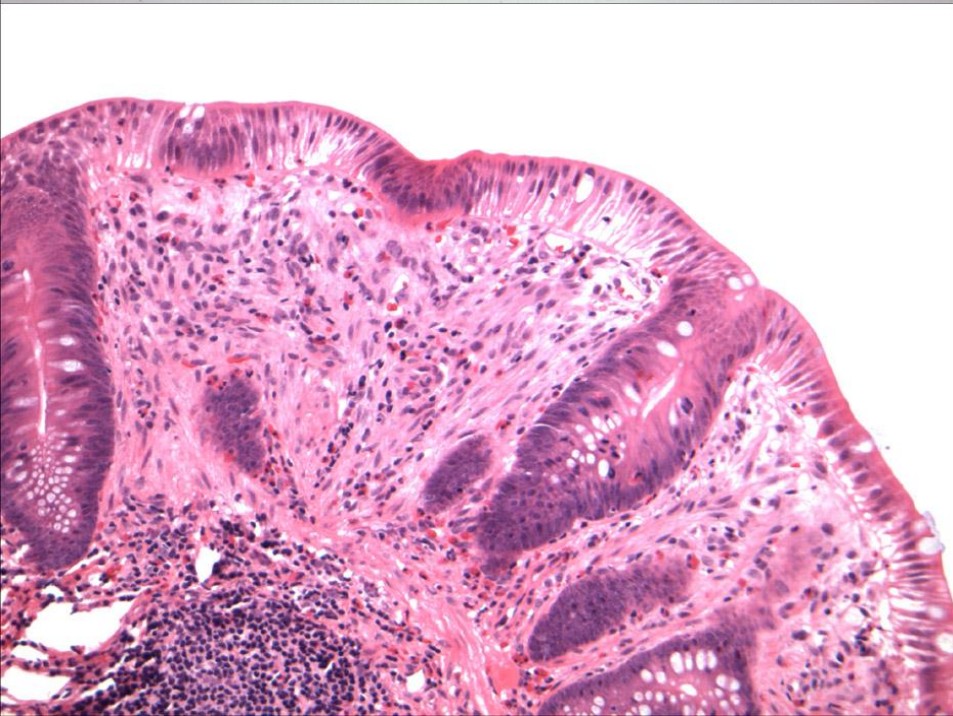
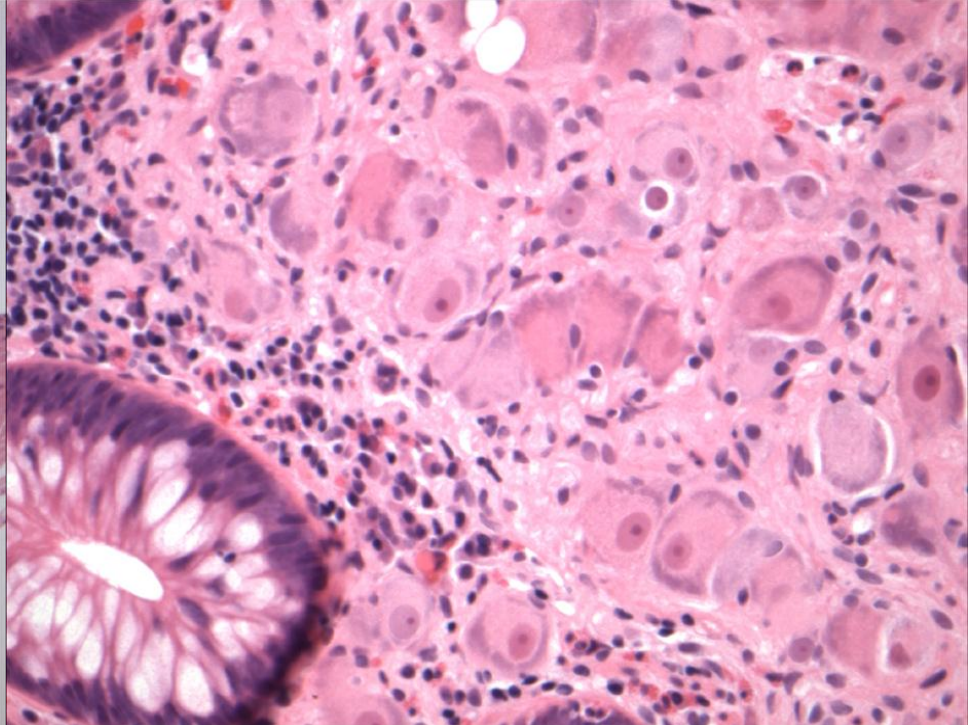
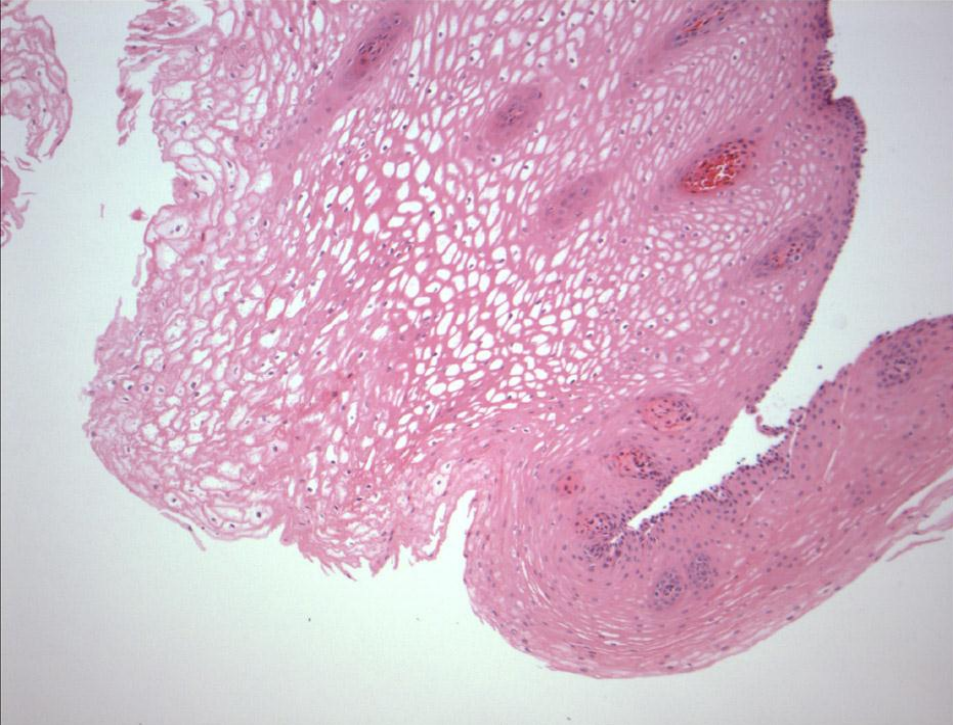
- Breast exam q 6-12 mon, starting 25yo or 5-10 years before earliest breast ca in family
- Annual mammogram and breast MRI screening starting 30-35yo
- Consider annual endometrial bxs and/or US starting 30-35yo
- Discuss risk reduction mastectomy, hysterectomy

Men and Women

- Annual PE starting 18yo
- Annual thyroid US starting 18yo
- Colonoscopy, starting 35yo, then q5 yr or more
- Consider renal US starting 40yo, they q1-2 yr

When to raise suspicion for PHTS in your pathology report?

- Multiple gastrointestinal hamartomas
 - Combinations of inflammatory (juvenile) polyps, ganglioneuromas, mucosal lipomas distributed throughout the GI tract
- Diffuse esophageal glycogenic acanthosis



Thanks for your attention!



Department of Pathology

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