

Select Biliary and Gallbladder Neoplasms

Let's decode the alphabet soup

ITPN?

IPNB?

PGA?

ICN?

ICTN?

ICPN?

*"Intracholecystic... papillo...tubulo...
one of those"*



Objective

- Become familiarized with acronyms being used in gallbladder and biliary neoplasms, based on WHO
- We will cover:
 1. Pyloric gland adenoma (PGA)
 2. Intracholecystic papillary neoplasm (ICPN)
 3. Intraductal papillary neoplasm of bile ducts (IPNB)

WHO Recognizes 4 types of Benign Tumors and Precursor Lesions in the Gallbladder and Extrahepatic Bile Ducts

Epithelial tumours

Benign epithelial tumours and precursors

Pyloric gland adenoma of the gallbladder

Biliary intraepithelial neoplasia

Intracholecystic papillary neoplasm (formerly Intracystic / intraductal papillary neoplasm)

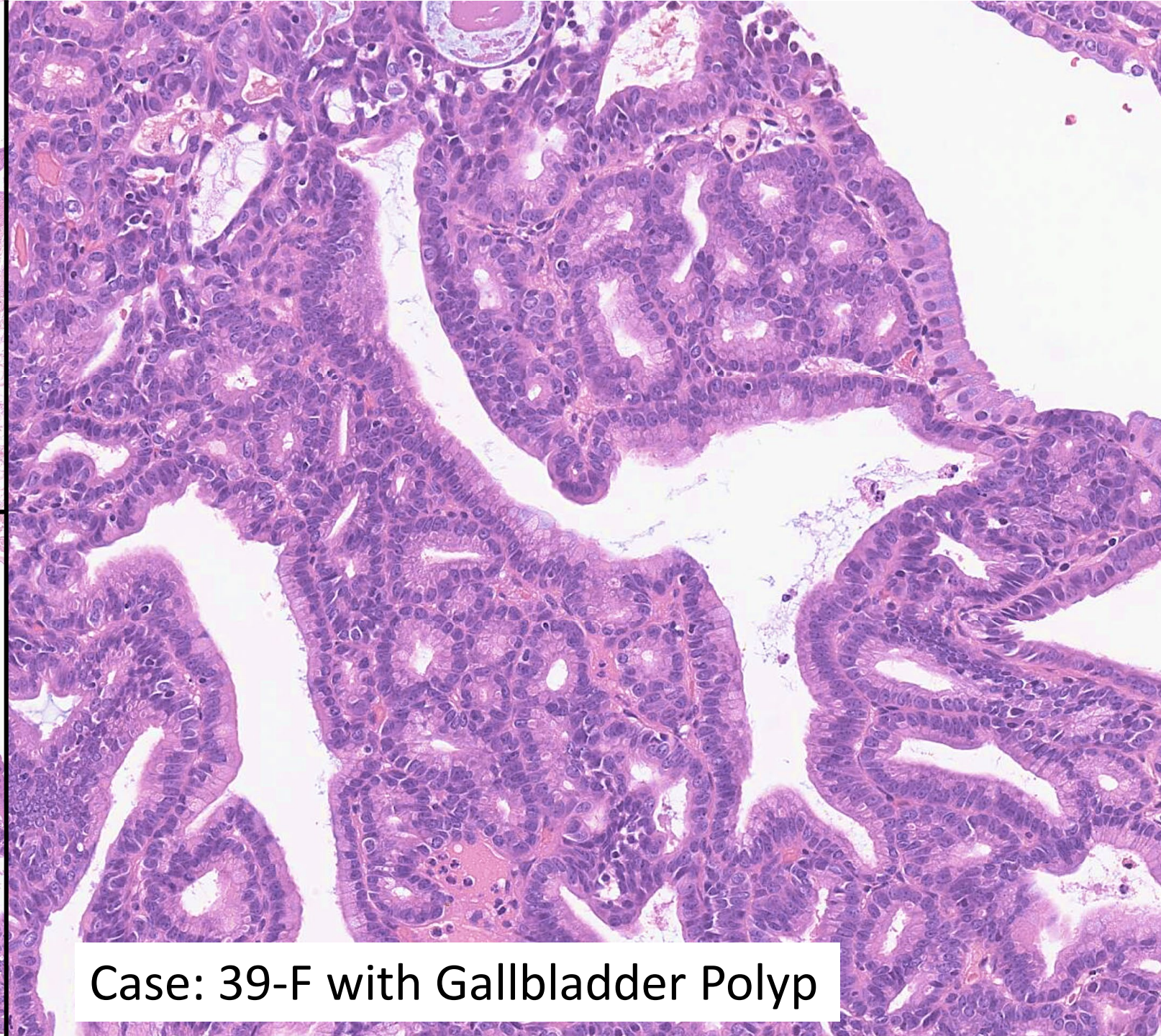
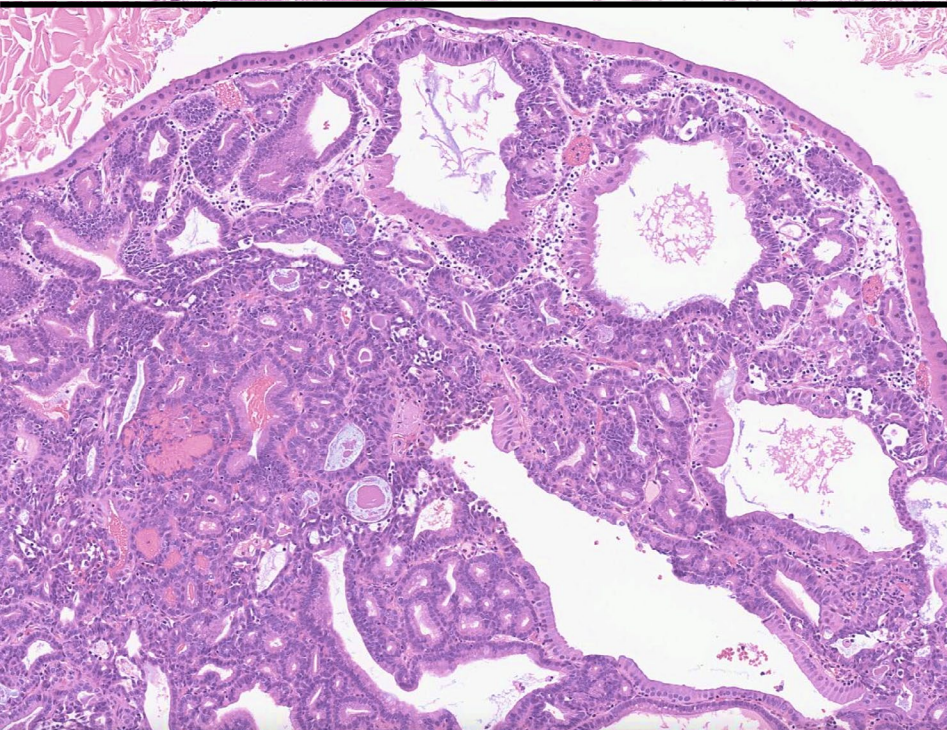
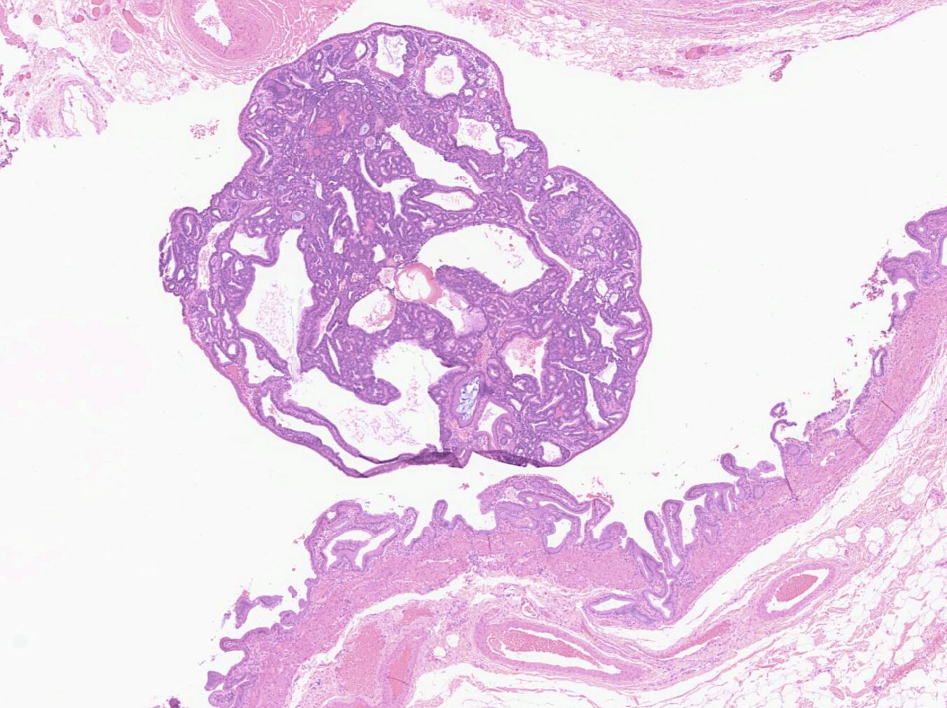
Intraductal papillary neoplasm of the bile ducts

Malignant epithelial tumours

Carcinoma of the gallbladder

Carcinoma of the extrahepatic bile ducts

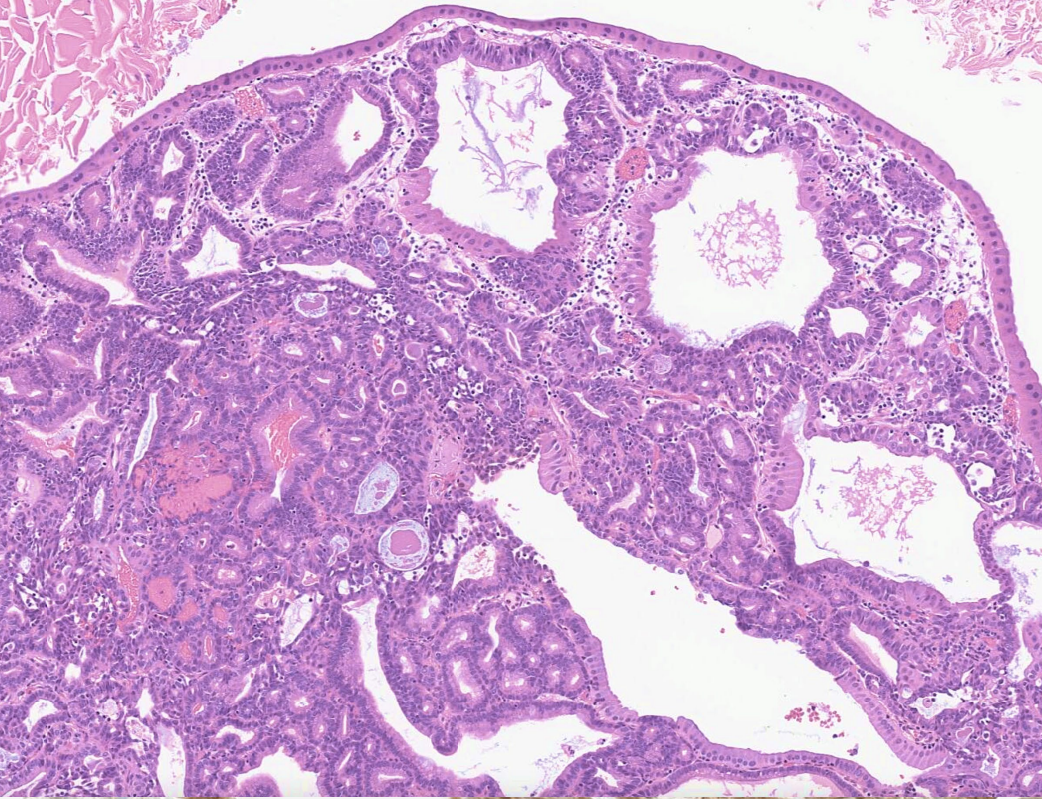
Neuroendocrine neoplasms of the gallbladder and bile ducts



Case: 39-F with Gallbladder Polyp

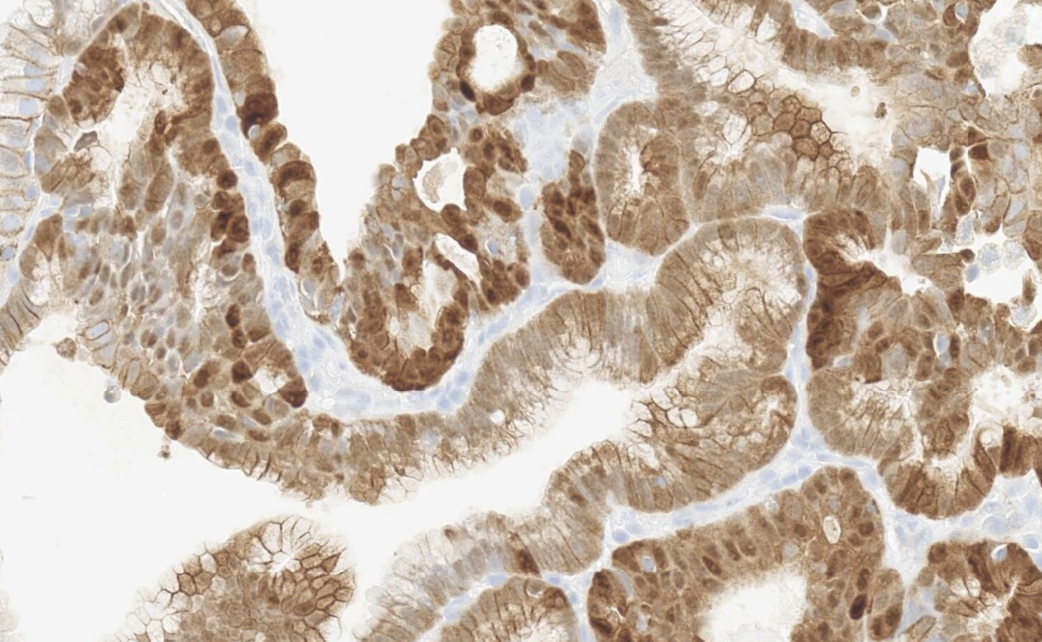
Pyloric Gland Adenoma

- Grossly visible polypoid lesion composed of pyloric-type glands
- WHO considers PGA to be related to intracholecystic papillary neoplasm; however, PGA can be separately diagnosed
 - ICPN is a precursor to gallbladder carcinoma but PGAs are seldom causative of cancer
 - WHO does not require a size criteria to diagnose PGA but states they tend to be <2 cm
- Other reports distinguish ICPN and PGA by size (ICPN is 2 cm or bigger, PGA <2 cm but >1 cm)



Pyloric gland adenoma

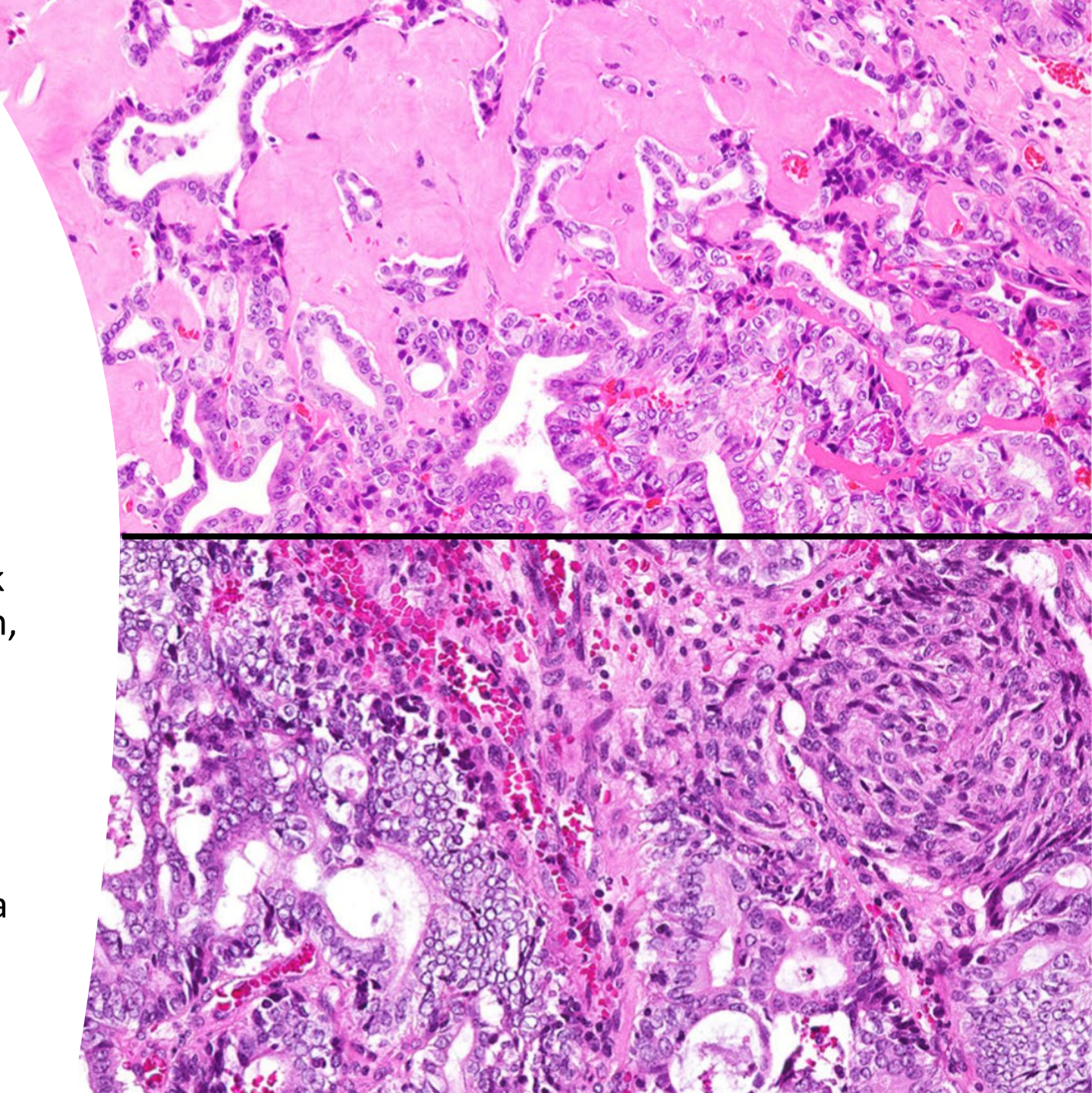
- Gross: The lesions have such thin stalks that the polyp may be detached and embedded within the gallbladder contents
- Microscopic: Lobules with rounded external contours, containing tightly packed, **bland**-appearing pyloric type or Brunner like glands with little intervening stroma.
- The tubules are lined by cuboidal epithelium with basally located nuclei, minimal cytologic atypia
- CTNNB1 mutations reported in the majority of cases, with beta catenin IHC+; however, immunohistochemistry is not needed to diagnose PGA



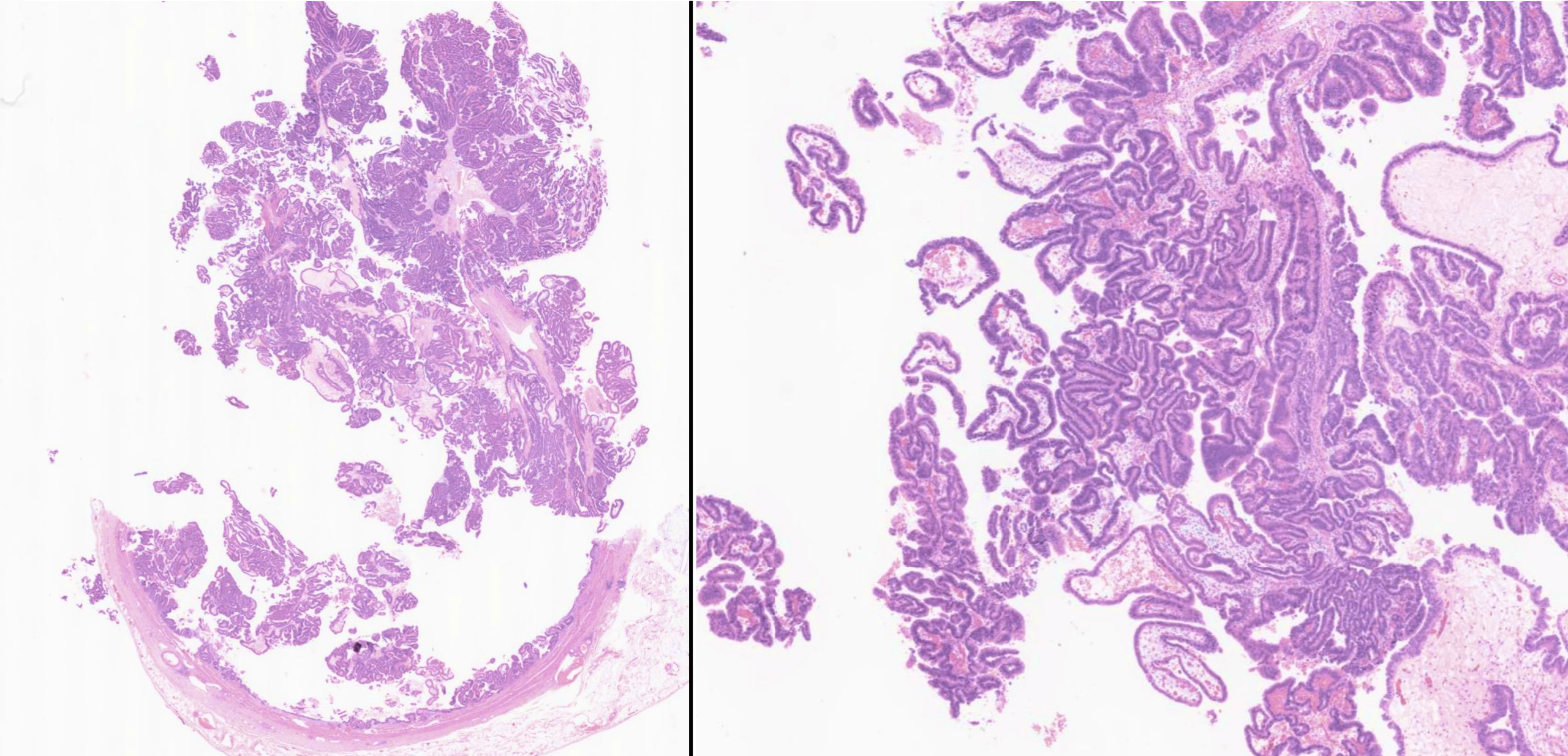
Pyloric Gland Adenoma

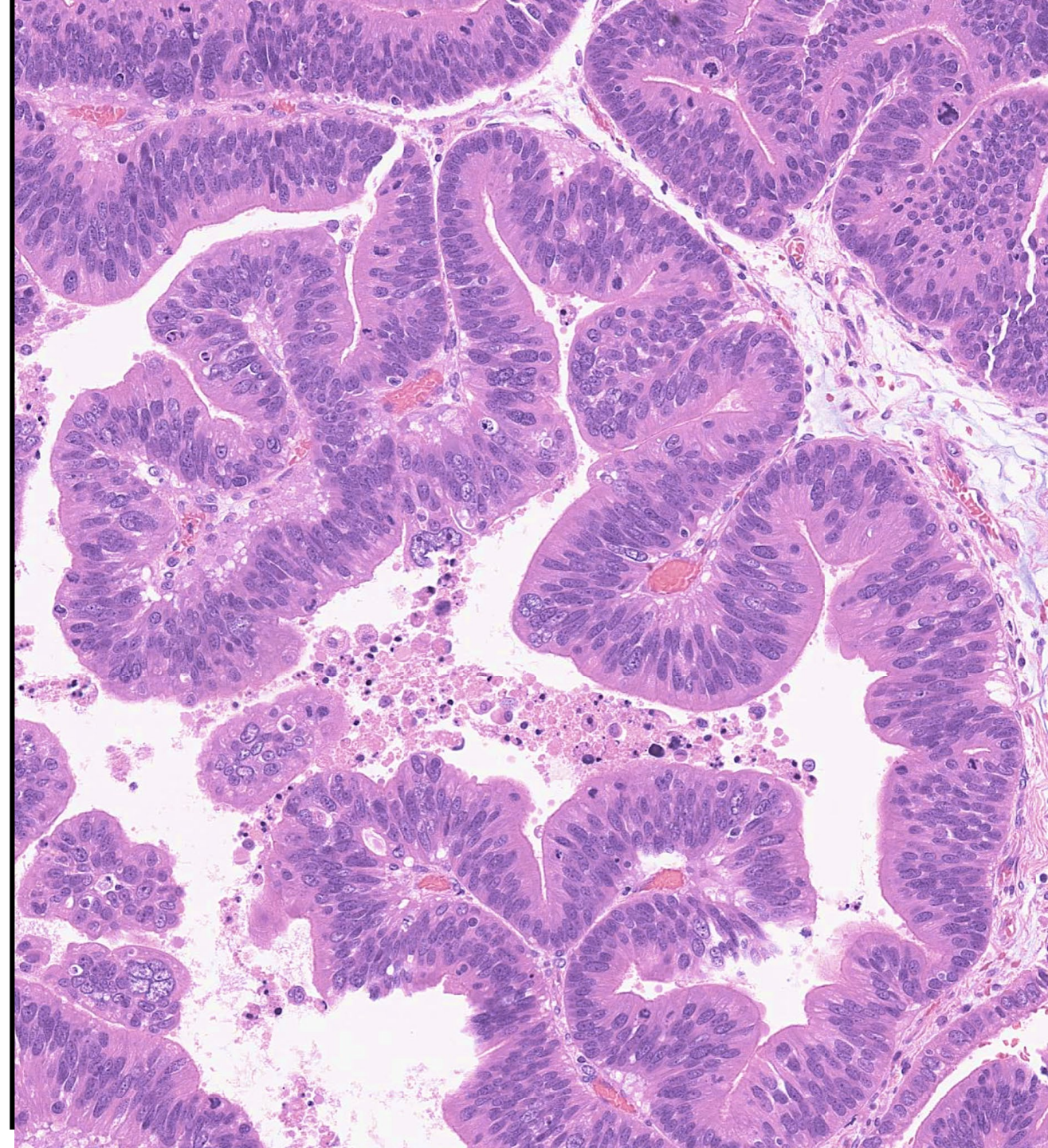
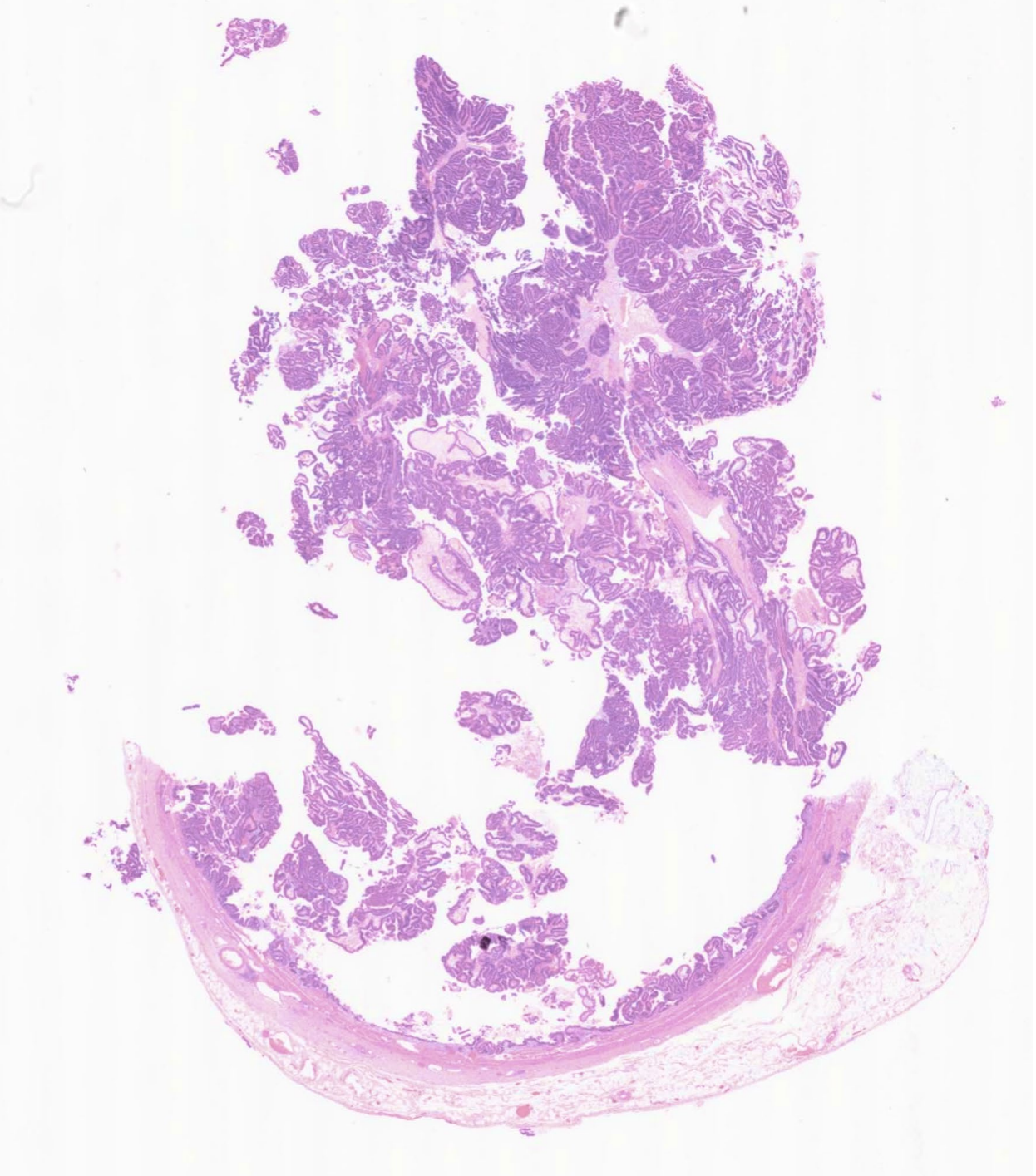
Variant “ICTN” (not in WHO)

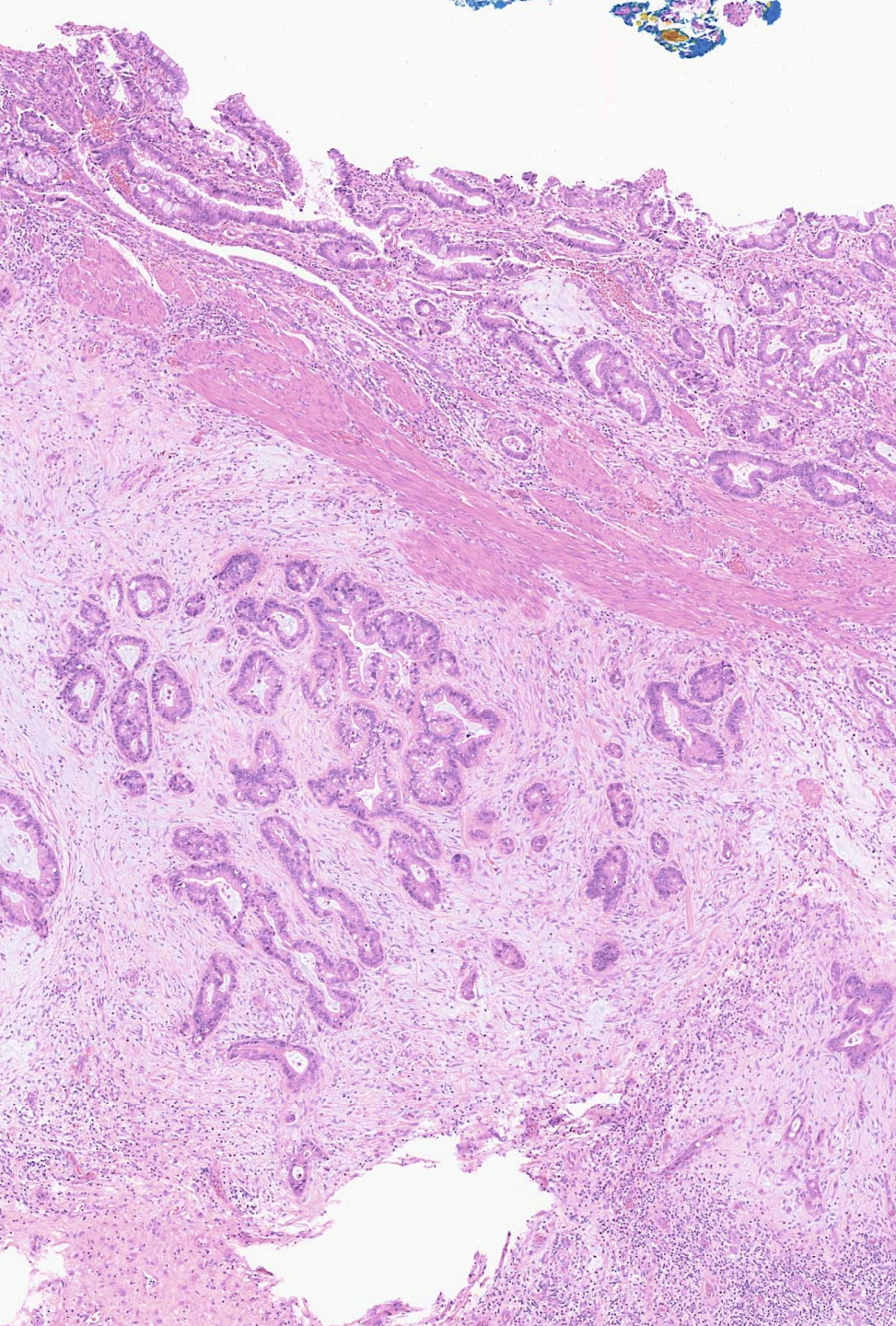
- Another variant viewed conceptually as a complex, non-mucinous version of pyloric gland adenoma:
- Intracholecystic tubular non-mucinous neoplasm (ICTN) have compact, back-to-back tubules lined by cells with minimal cytoplasm, round nuclei with prominent nucleoli, amyloid like stroma with hyalinization and squamous morules
- Like PGA, these are NOT commonly associated with invasive carcinoma despite looking high grade and also have no dysplasia in the background



Case: 62-year-old female with history of cholelithiasis. Gross exam showed detached fragments of tumor within the gallbladder contents and papillary mucosal excrescences





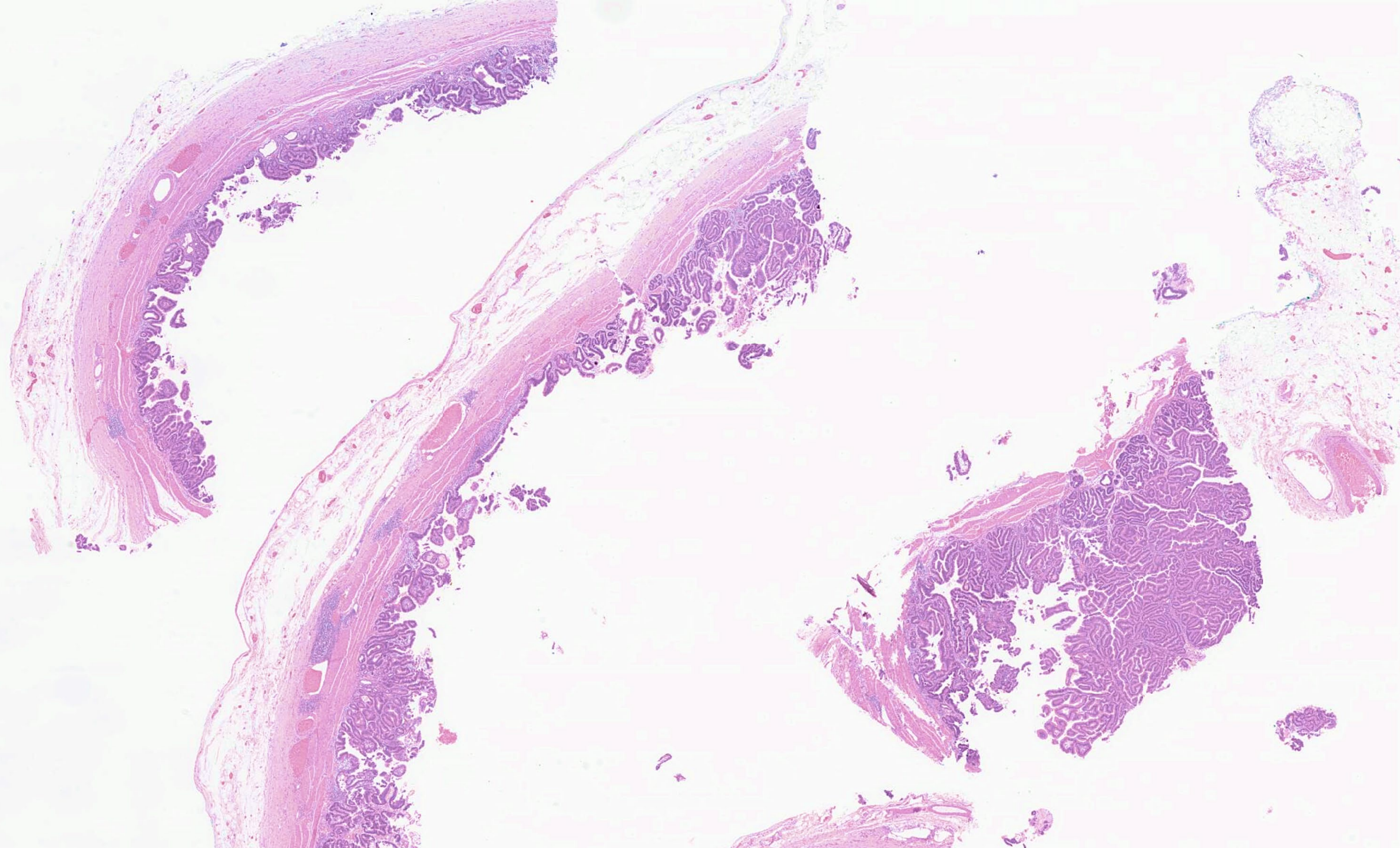


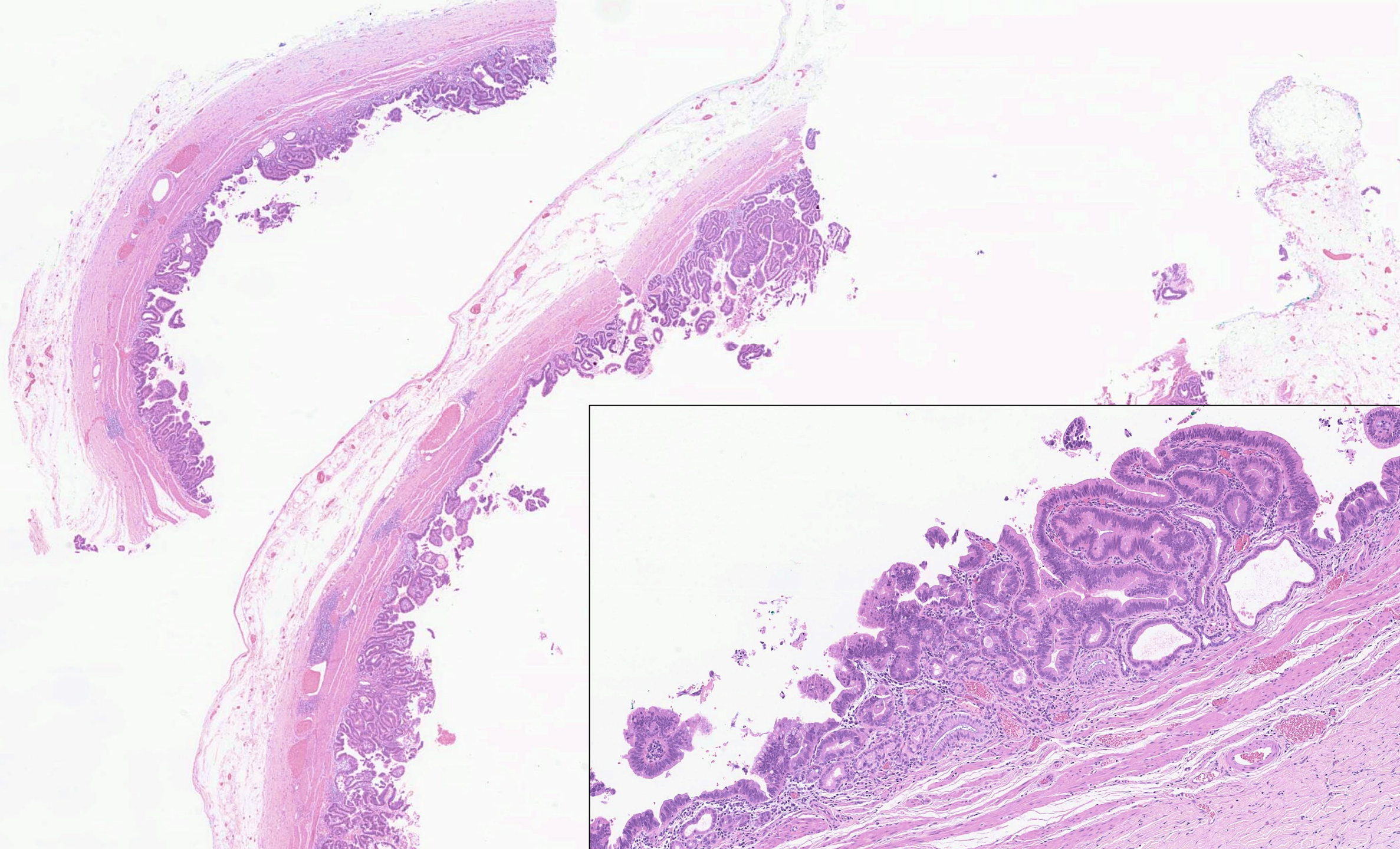
Intracholecystic Papillary Neoplasm

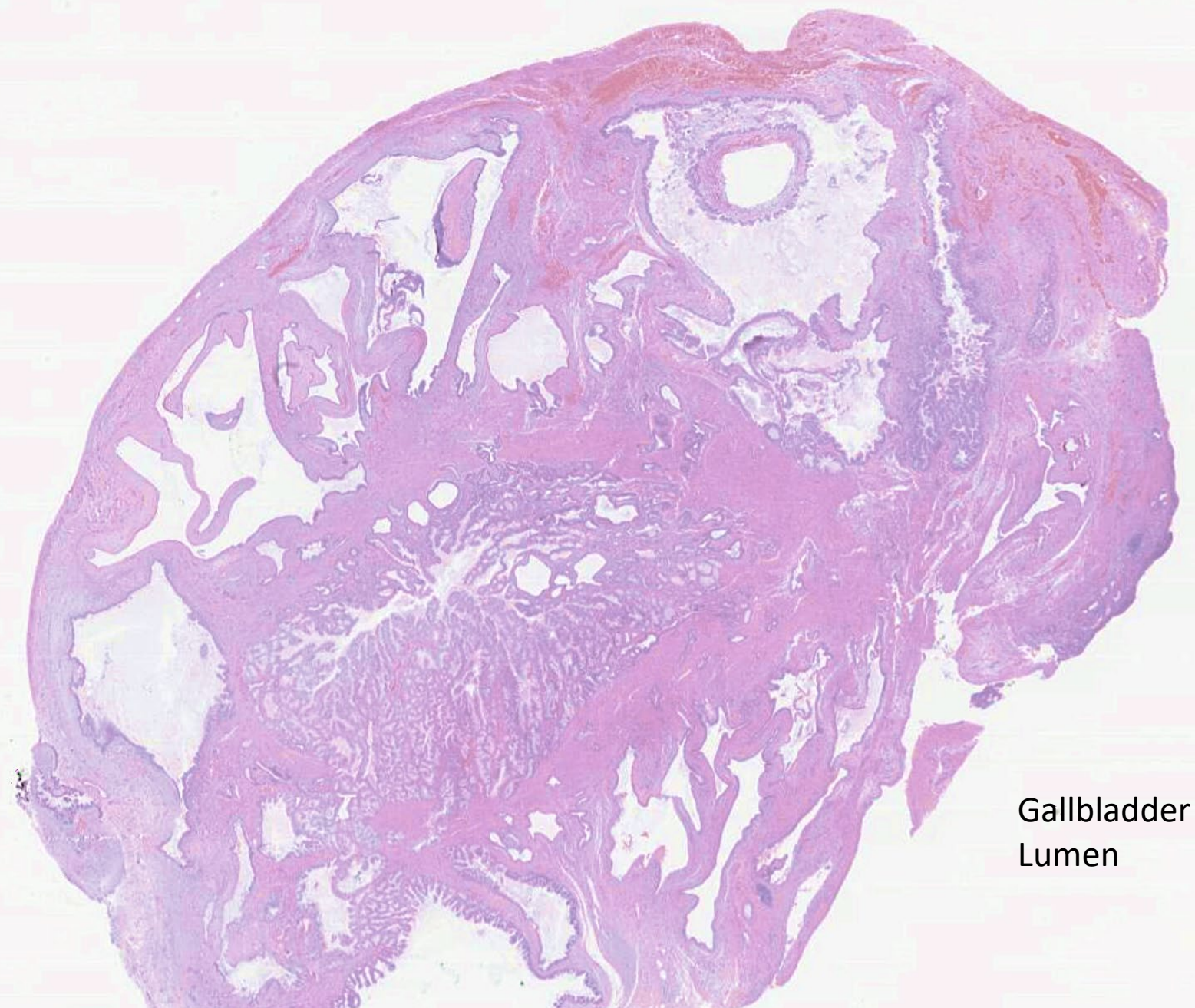
- ICPN is a mass forming intraepithelial neoplasm
- WHO does not give a size criterion to diagnose ICPN; it just states that it is grossly visible and median size is 2.2 cm
- Half of ICPNs are associated with carcinoma, which may not necessarily be within the main lesion and may be grossly indistinct. Extensive sampling is therefore important
 - Having biliary-type epithelium or HGD more likely to have cancer
- Invasive carcinoma with an ICPN component has a more favorable prognosis than invasive carcinoma without ICPN
 - Approximately 6% of gallbladder carcinomas arise in association with an ICPN

Intracholecystic Papillary Neoplasm

- ICPN has four main types: gastric, biliary, intestinal, and oncocytic, but these are very commonly intermixed within the same polyp (much more than pancreatic counterparts IPMN)
- Grade ICPN as low grade or high-grade dysplasia and state predominant phenotype
- The flat, background mucosa is often dysplastic and there is a risk of neoplasia in rest of biliary tree
- One third of ICPN are multifocal

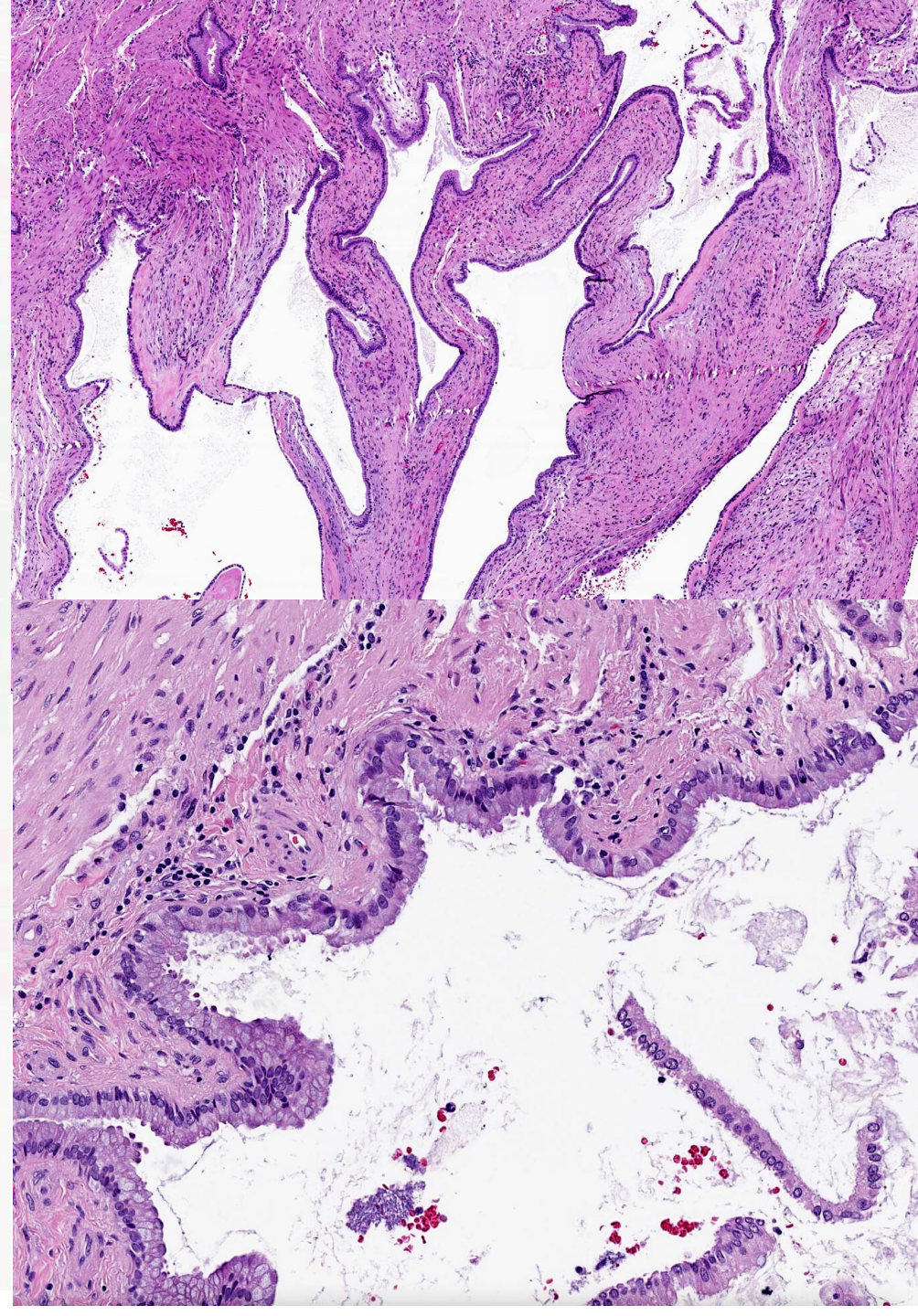






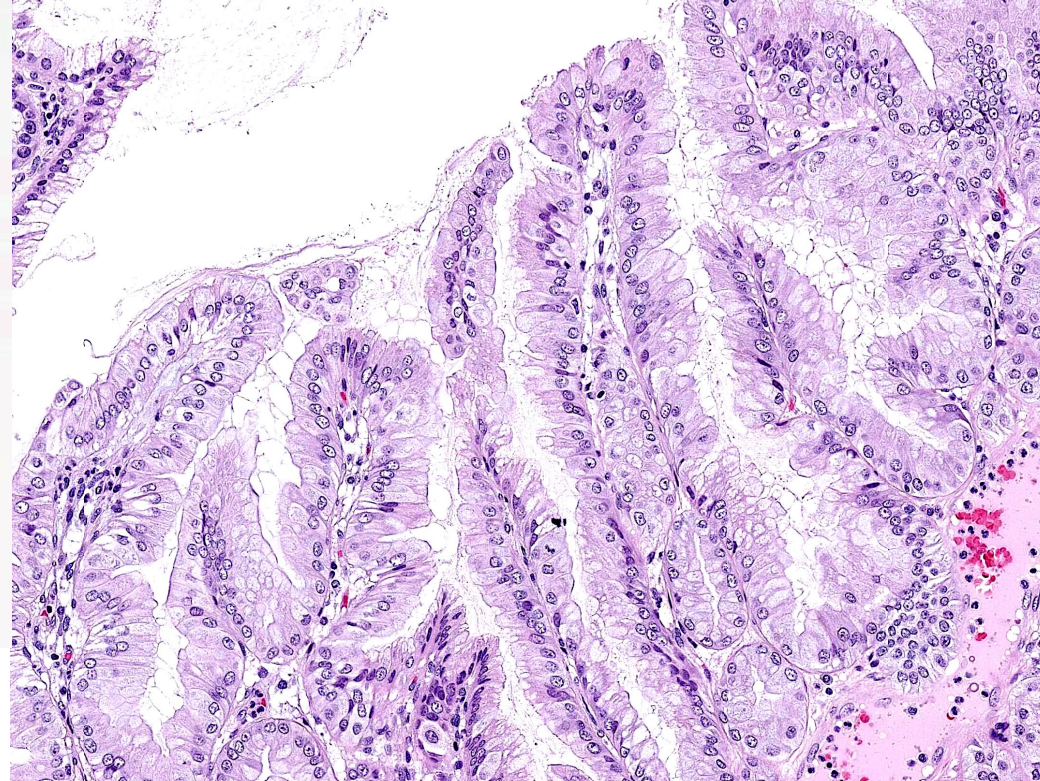
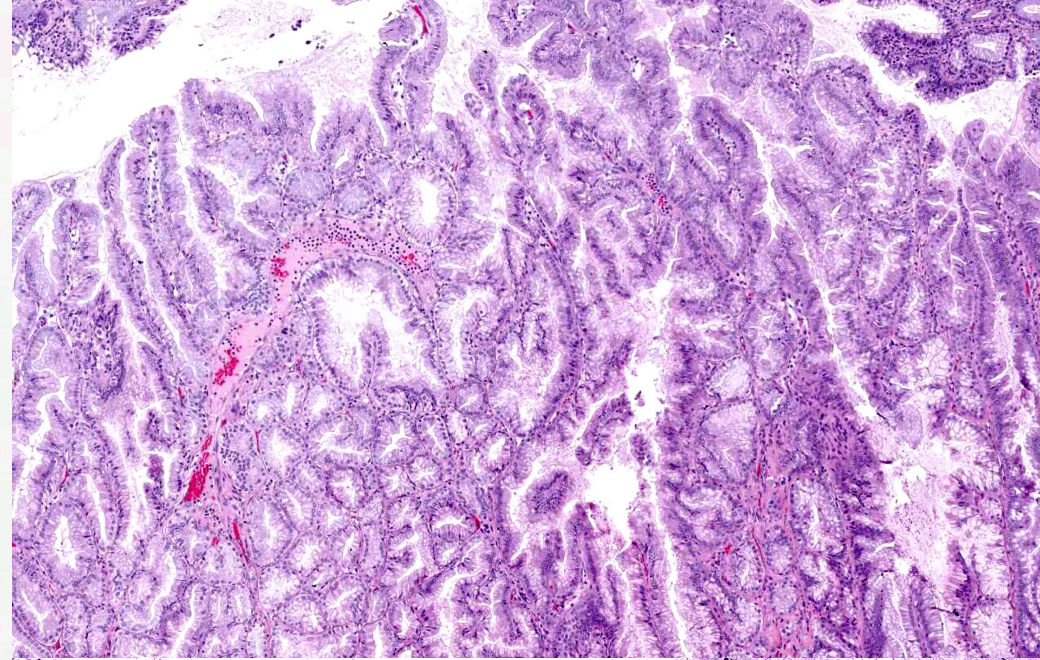
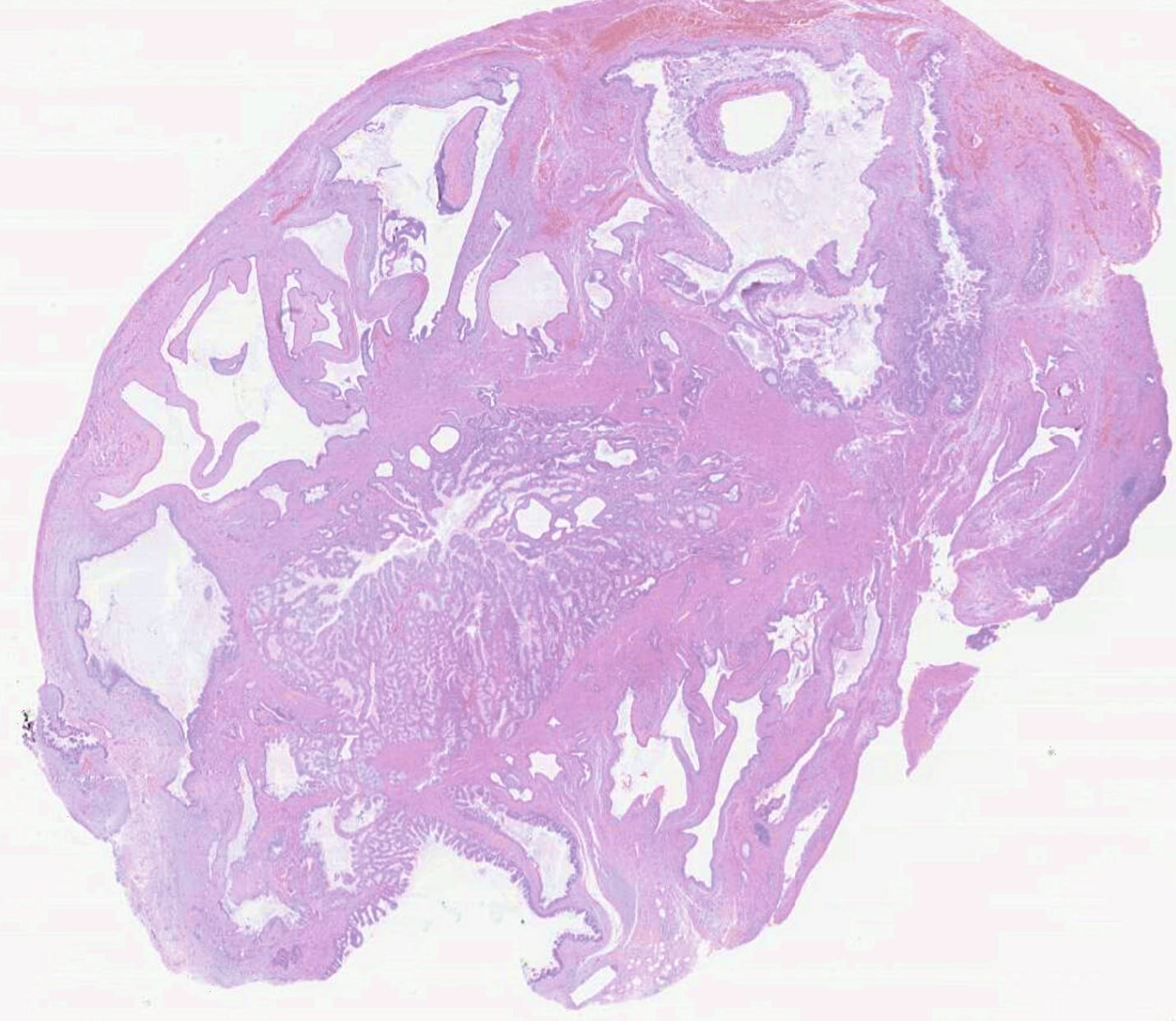
Gallbladder
Lumen

Case: 84-year-old female with gallbladder tumor



Adenomyomatous Hyperplasia with Something Extra

- Adenomyoma typically forms a **mural nodule** and is characterized by **large, cystic tubules surrounded by muscle**
- They are thought to be non-neoplastic (malformative), but there have been reports of intracholecystic neoplasms arising from adenomyoma

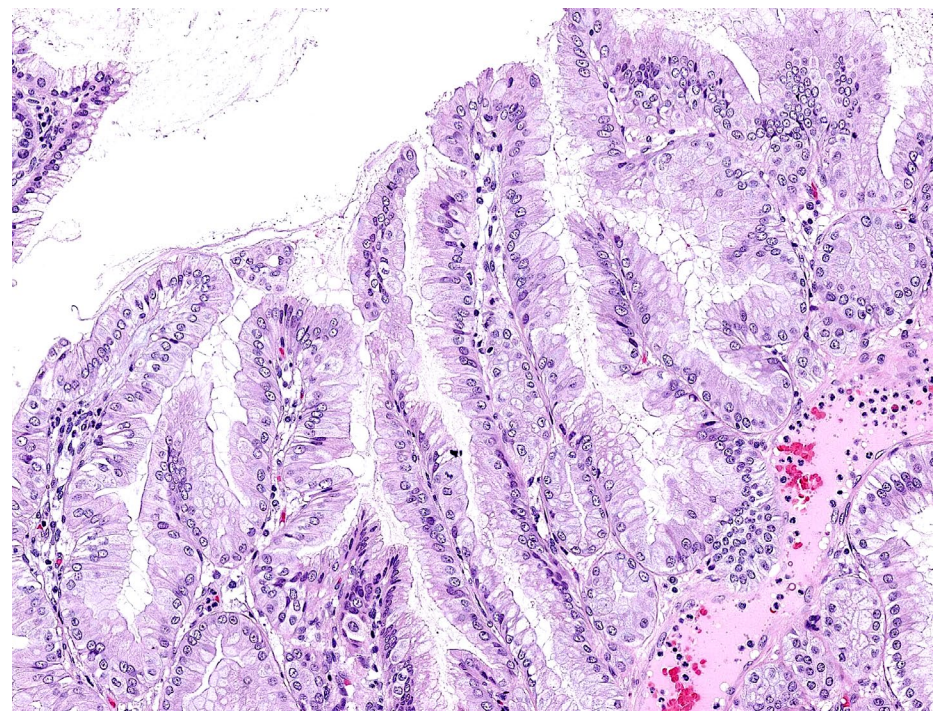
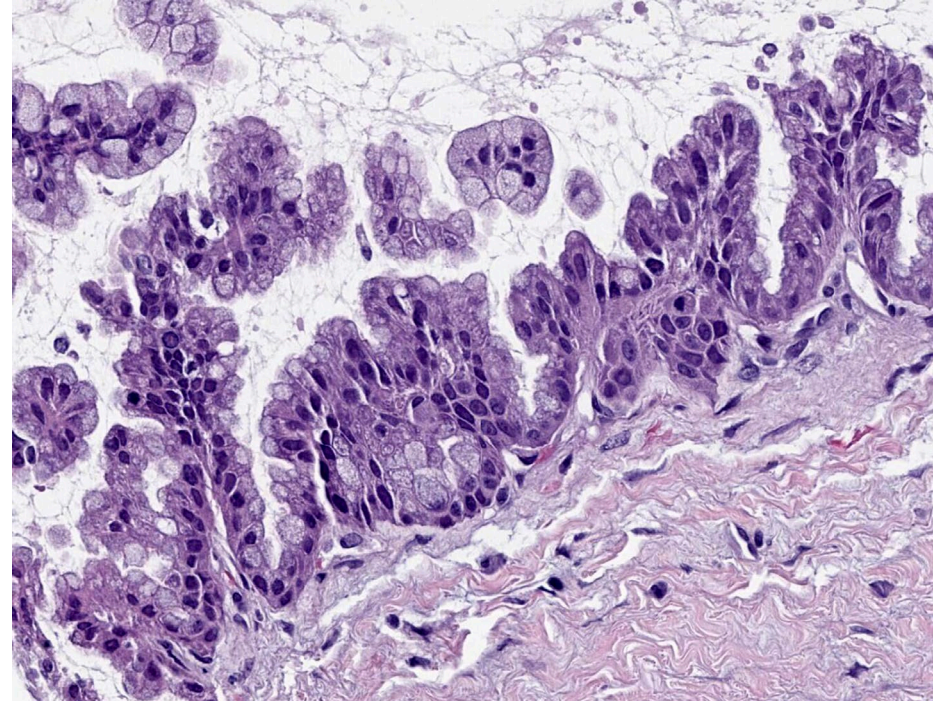
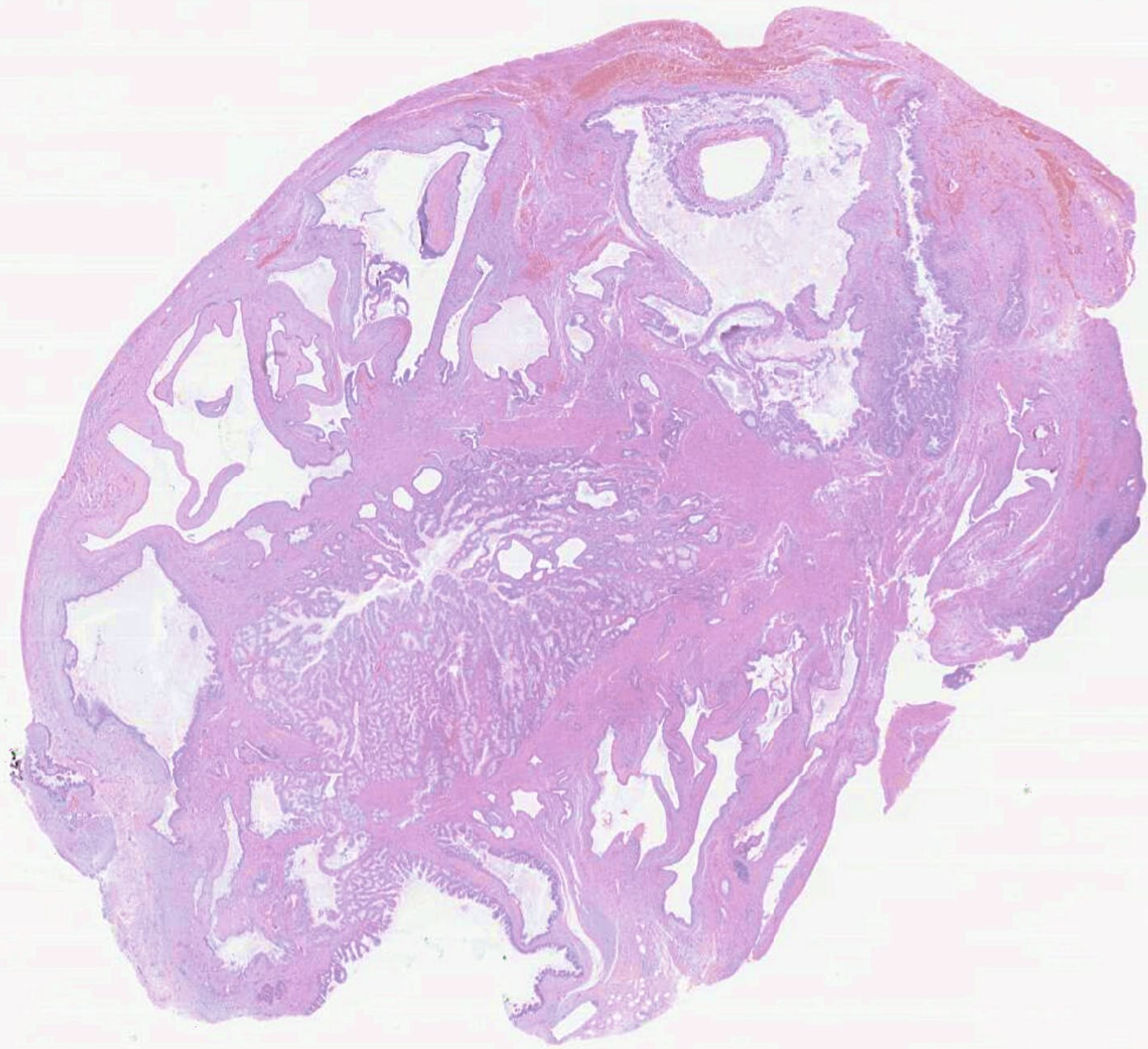


Intracholecystic Neoplasm involving Adenomyomatous Nodule

- Papillary, mucinous neoplasms involving adenomyomatous nodules
- Are biologically distinct from ICPNs in that
 - 1) the tumors are confined to the adenomyoma
 - 2) do not have dysplasia in the background gallbladder, and
 - 3) do not impart a risk for cancer in the rest of the biliary tree
- In contrast, ICPN can be multifocal, have dysplasia in the flat, background epithelium, and is associated with a “field effect” with risk of cancer in the rest of the biliary tree

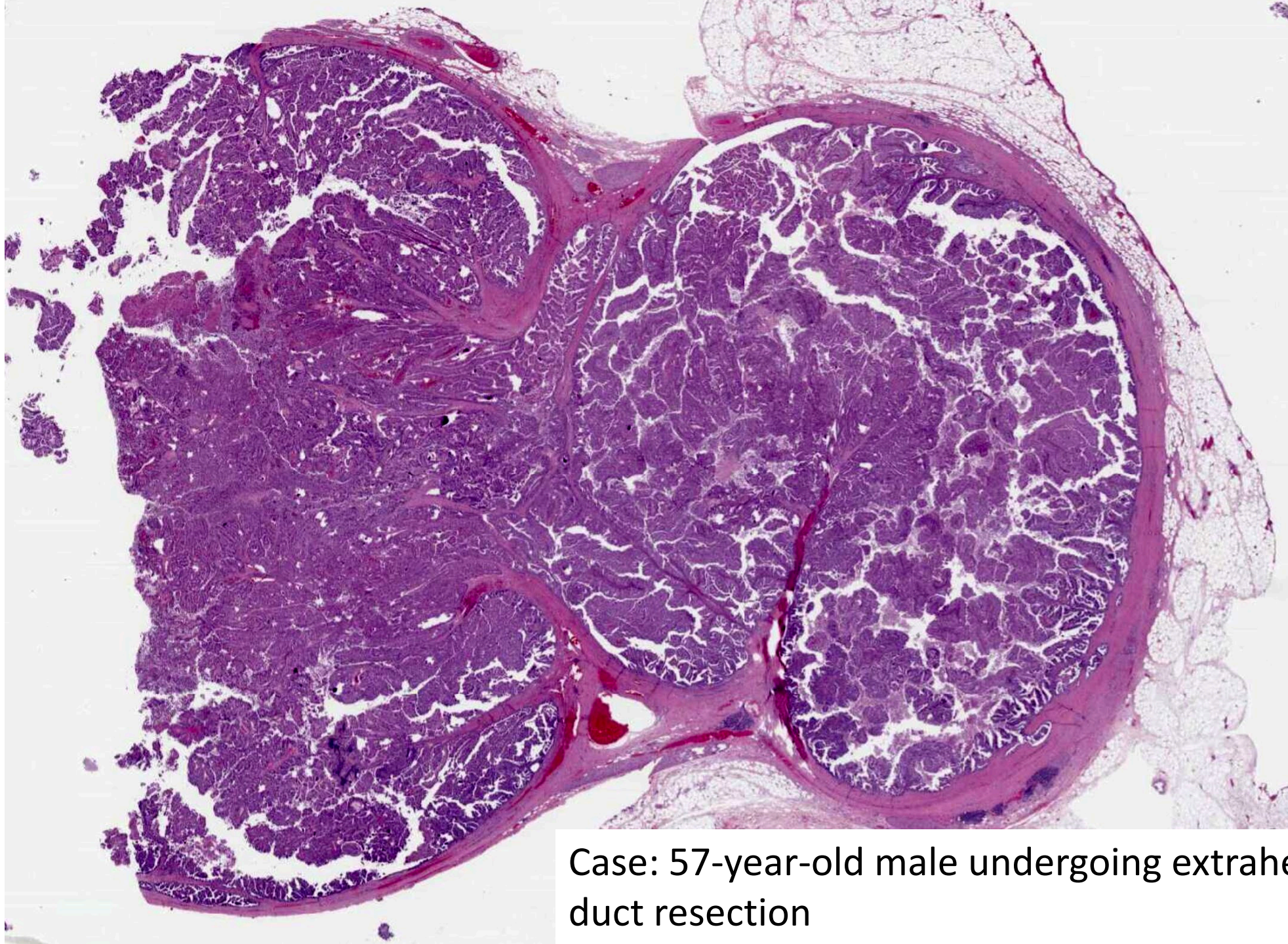
Intracholecystic Neoplasm involving Adenomyomatous Nodule

- Microscopic: mural, papillary proliferation with mucinous epithelial lining that arises in adenomyomatous nodules and forms localized intracholecystic neoplasm
- All have some degree of cyst and papillae formation
- Gastric type of epithelium is seen in most (considered analogous to pancreatic branch duct IPMN)
 - Pale mucinous cytoplasm with peripherally placed nuclei
 - Can have varying degrees of atypia...up to high grade with cancer
 - 15% have carcinoma

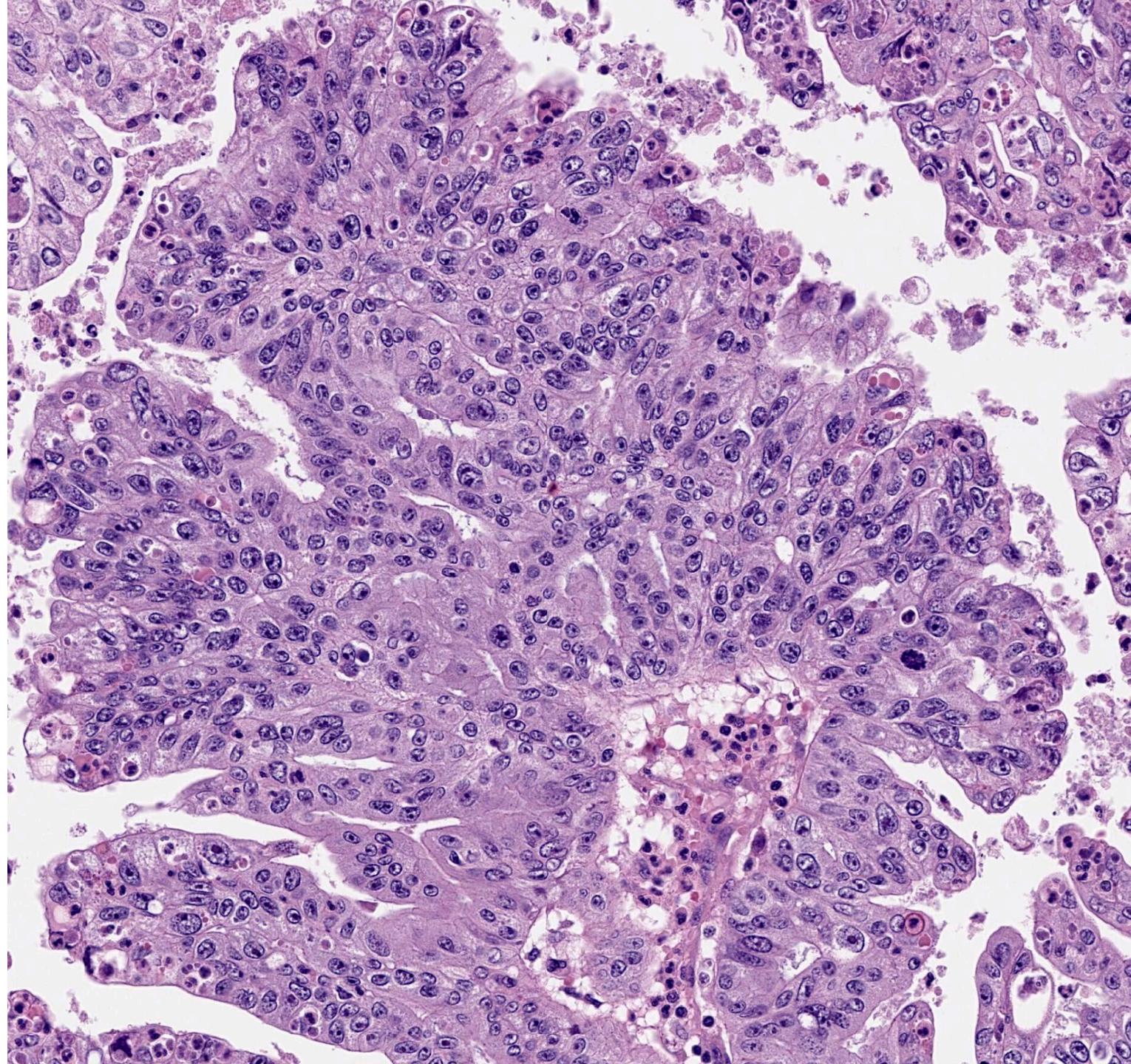
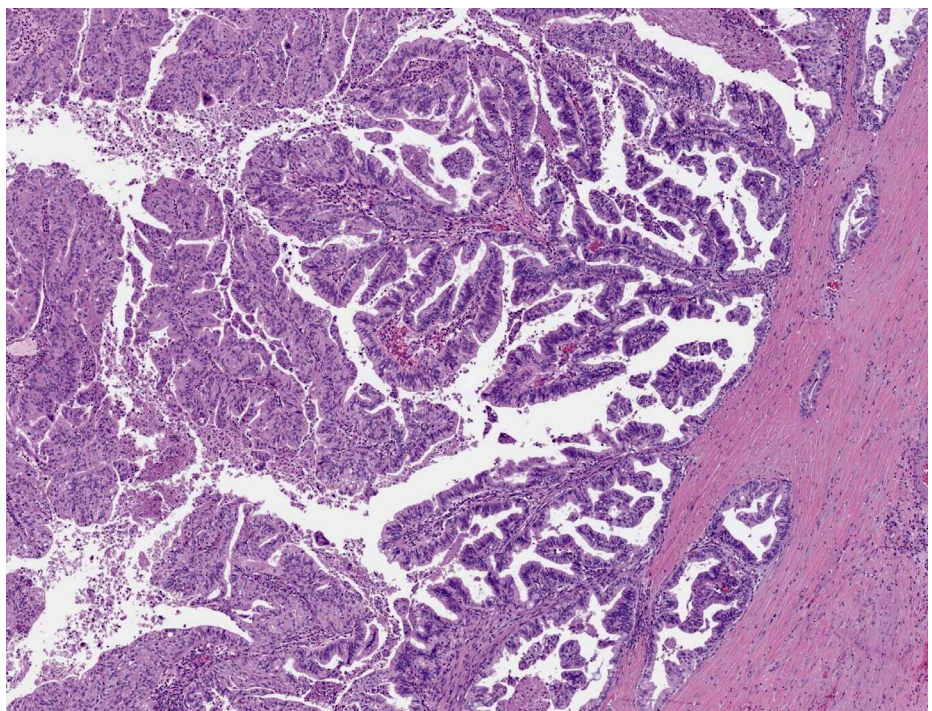
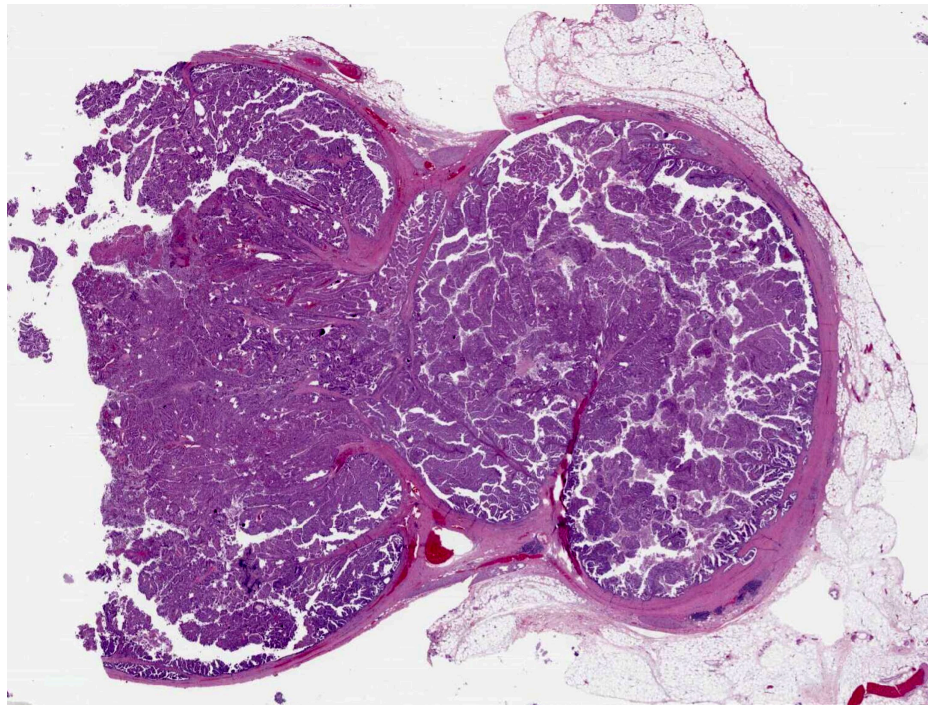


How Many Sections?

Intracholecystic papillary neoplasm (ICPN)	Submit the gallbladder entirely If very large polyp, then stepwise sampling to rule out invasive CA
Intracholecystic neoplasm arising in adenomyomatous nodule	Submit the entire lesion, together with 4 cassettes from the remaining gallbladder
Convincing low-grade dysplasia in gallbladder mucosa	Submit minimum 4–6 additional cassettes. If those reveal high-grade dysplasia, submit the gallbladder entirely
High-grade dysplasia	Submit the gallbladder entirely
Intestinal metaplasia	Submit 4 additional cassettes (thought to be part of metaplasia-dysplasia-cancer sequence; seen more commonly in GB dysplasia or carcinoma)



Case: 57-year-old male undergoing extrahepatic bile duct resection



Intraductal Papillary Neoplasm of Bile Ducts

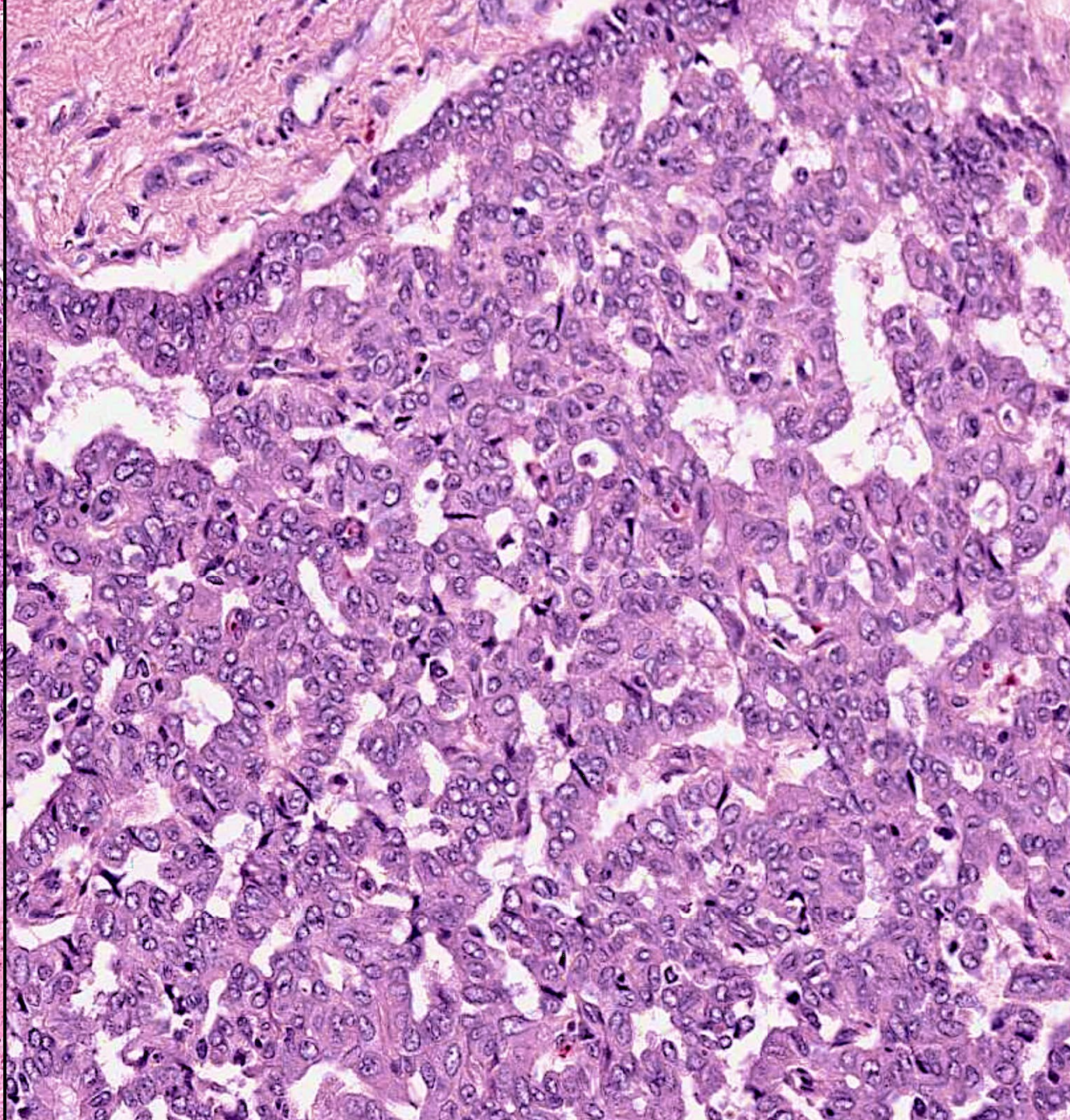
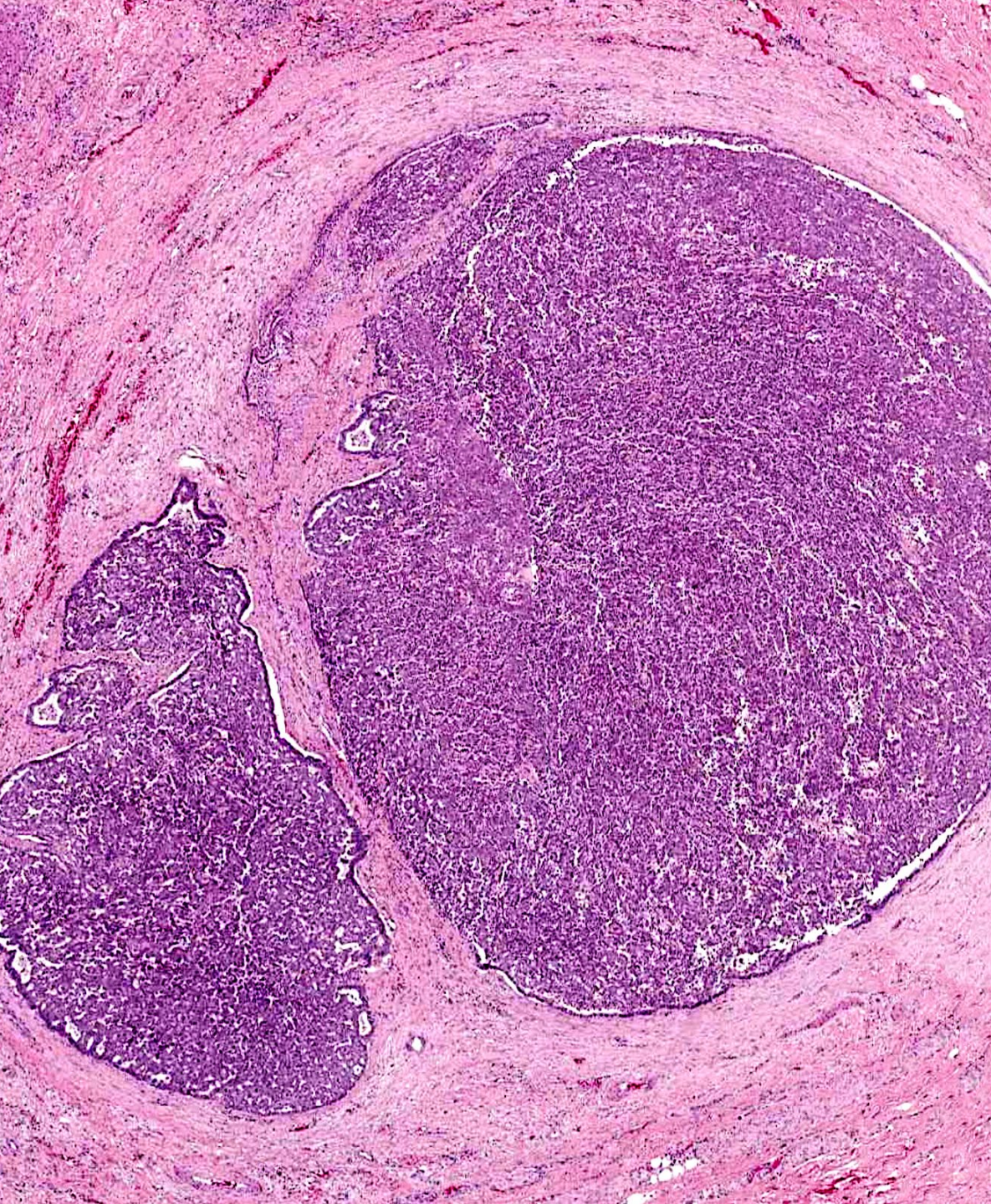
- Grossly visible neoplasm filling and dilating the bile duct
- Microscopically, there are papillary structures lined by biliary, intestinal, gastric, or oncocytic epithelium
 - Grade as low or high grade; around 40-80% can have a focal invasive component
 - Overall, **IPNB-invasive carcinoma has better prognosis than conventional cholangiocarcinoma 70% at 5 years, unless arising from the biliary type IPNB**

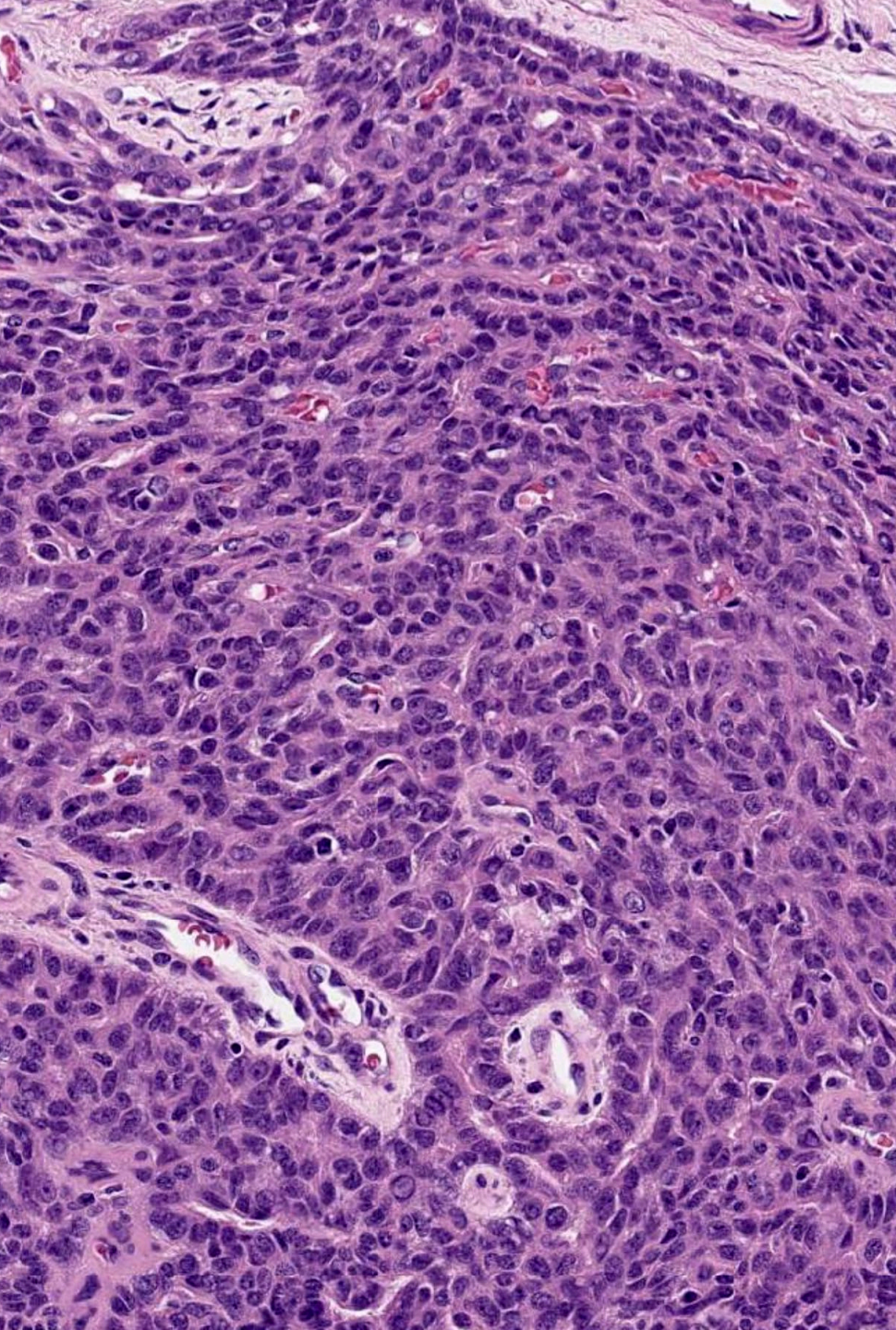
Intraductal Papillary Neoplasm of Bile Ducts

- Japanese and Korean experts have classified IPNB into two types:
 - Type 1 resembles pancreatic IPMN, intestinal or gastric, can have gross mucin production, and involves intrahepatic bile ducts
 - Type 2 involves extrahepatic bile ducts, has a more complex architecture with irregular papillae and branching, are biliary or intestinal, and is highly associated with carcinoma

49-year-old male with intrahepatic bile duct tumor

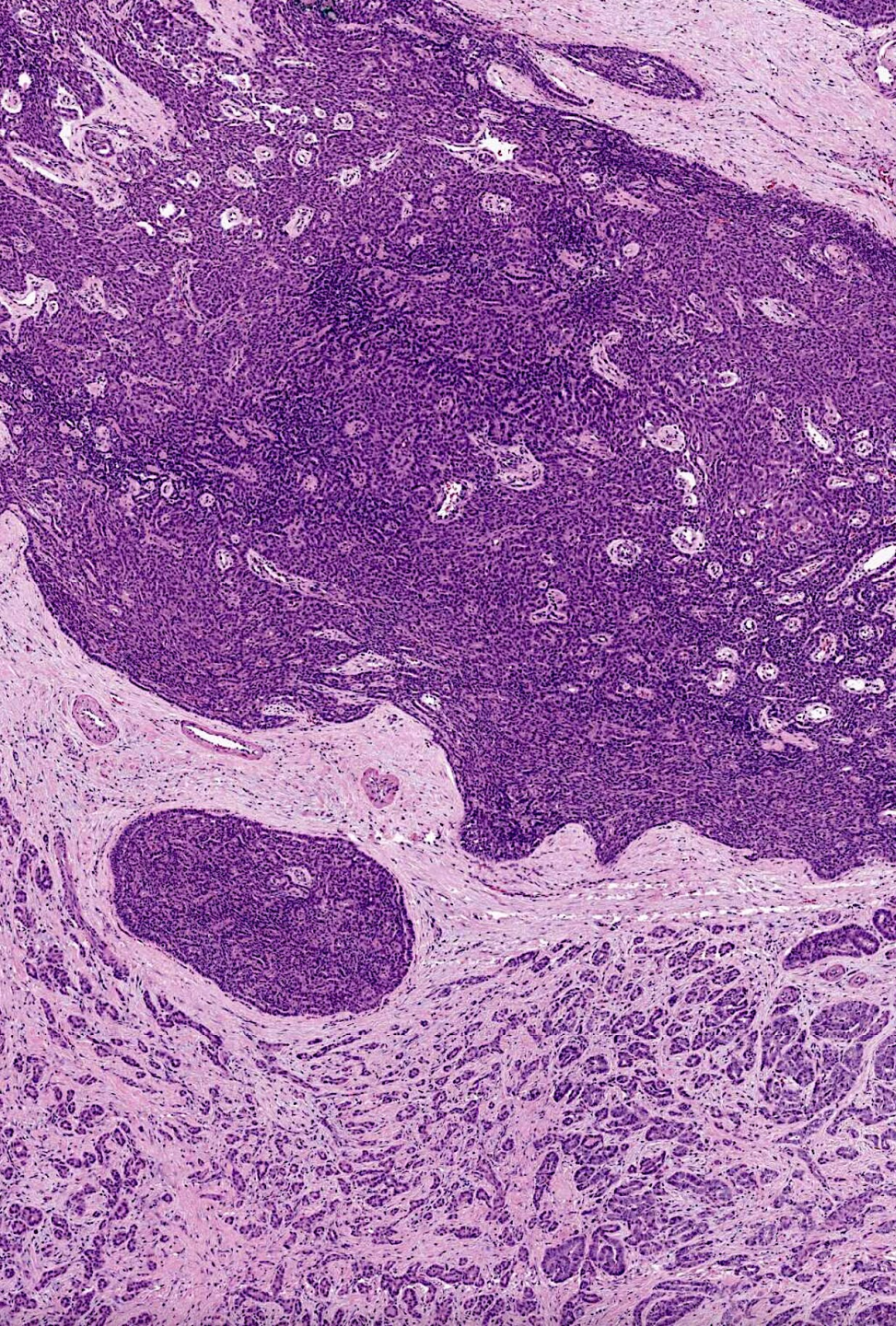






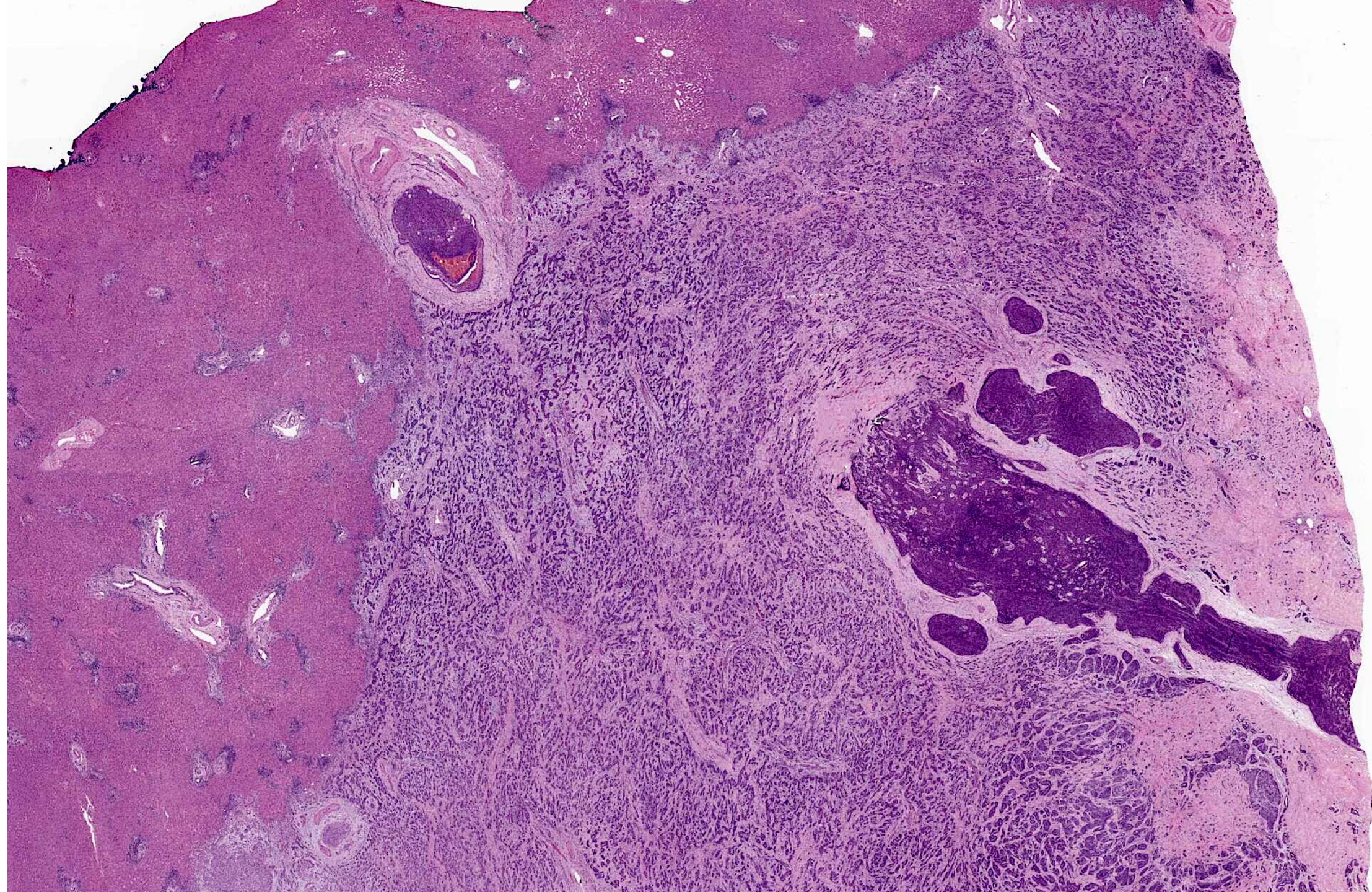
IPNB, Tubulopapillary Pattern

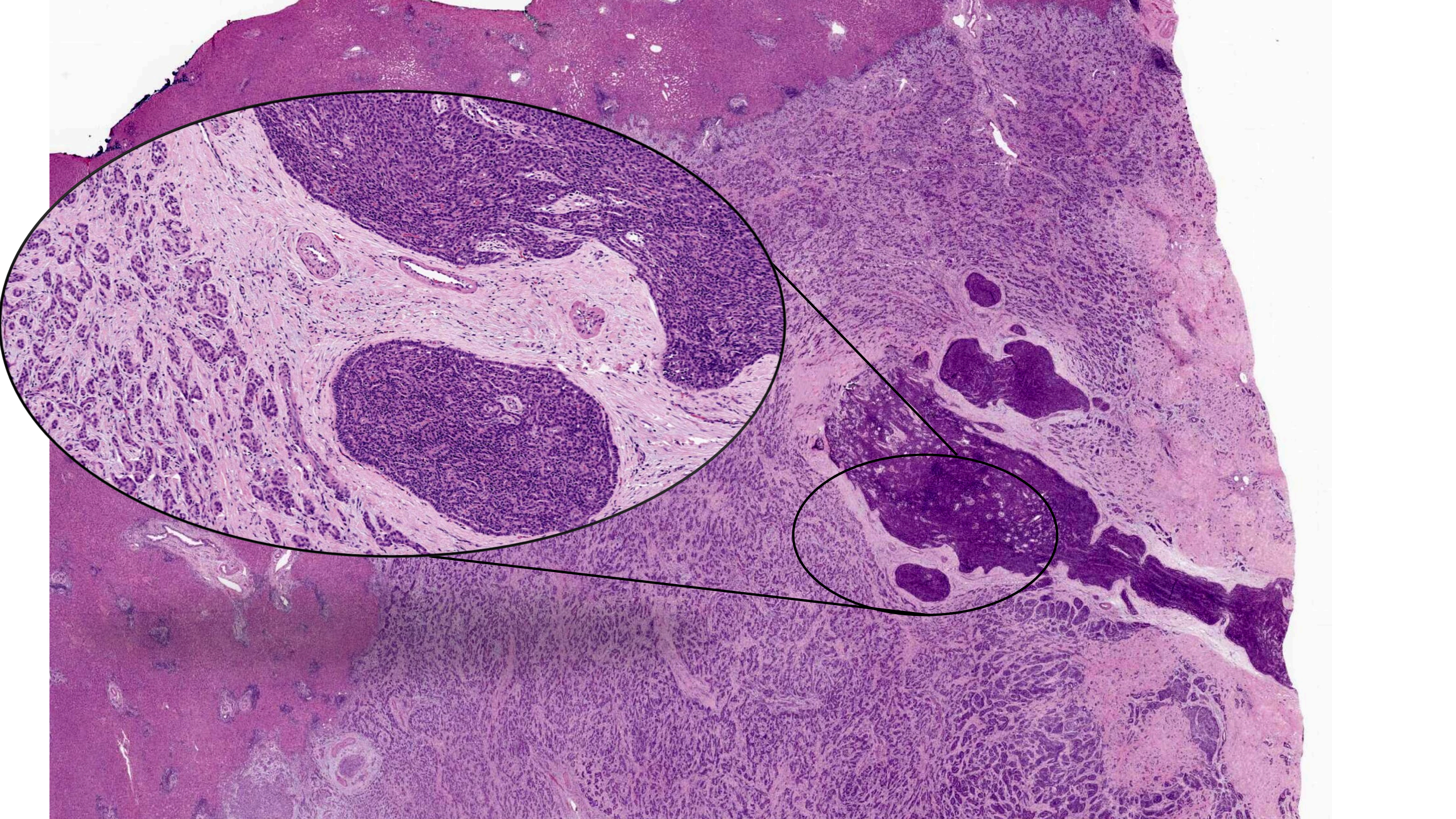
- The bile duct counterpart to the intraductal tubulopapillary neoplasm (ITPN) of the pancreas, but is still under the umbrella of IPNB in WHO
- Is characterized by densely packed neoplastic tubules filling up the duct with high grade dysplasia
- **Compared to other IPNB, it has a more solid, tubular growth pattern with less papillary frond formation and mucin production**
- The ITPN variant of IPNB affect the **intrahepatic** bile ducts in half of cases, followed by perihilar bile ducts (30%) and extrahepatic bile ducts (17%).
- Tumors tend to be larger, with a median size of 5.3 cm

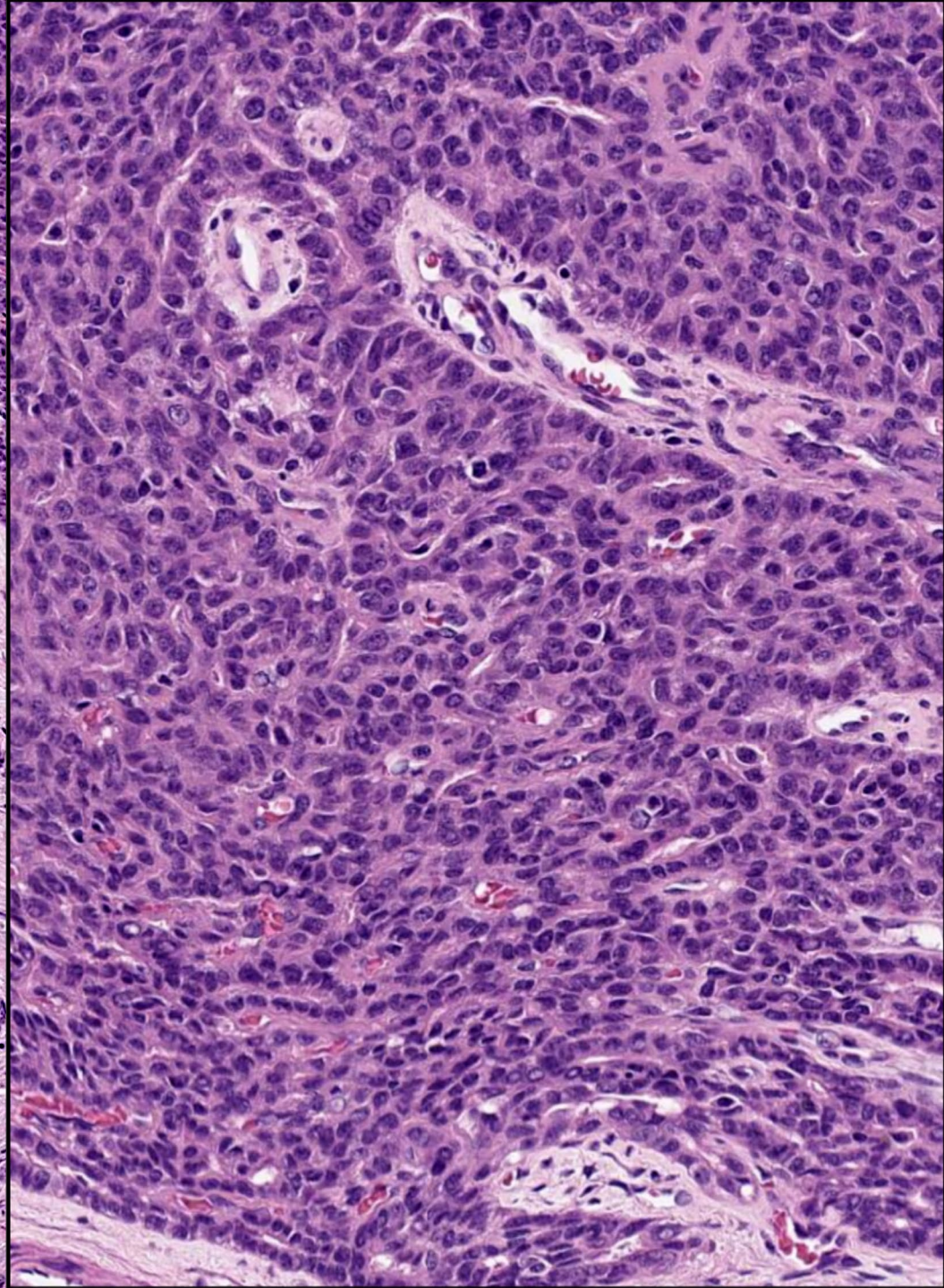
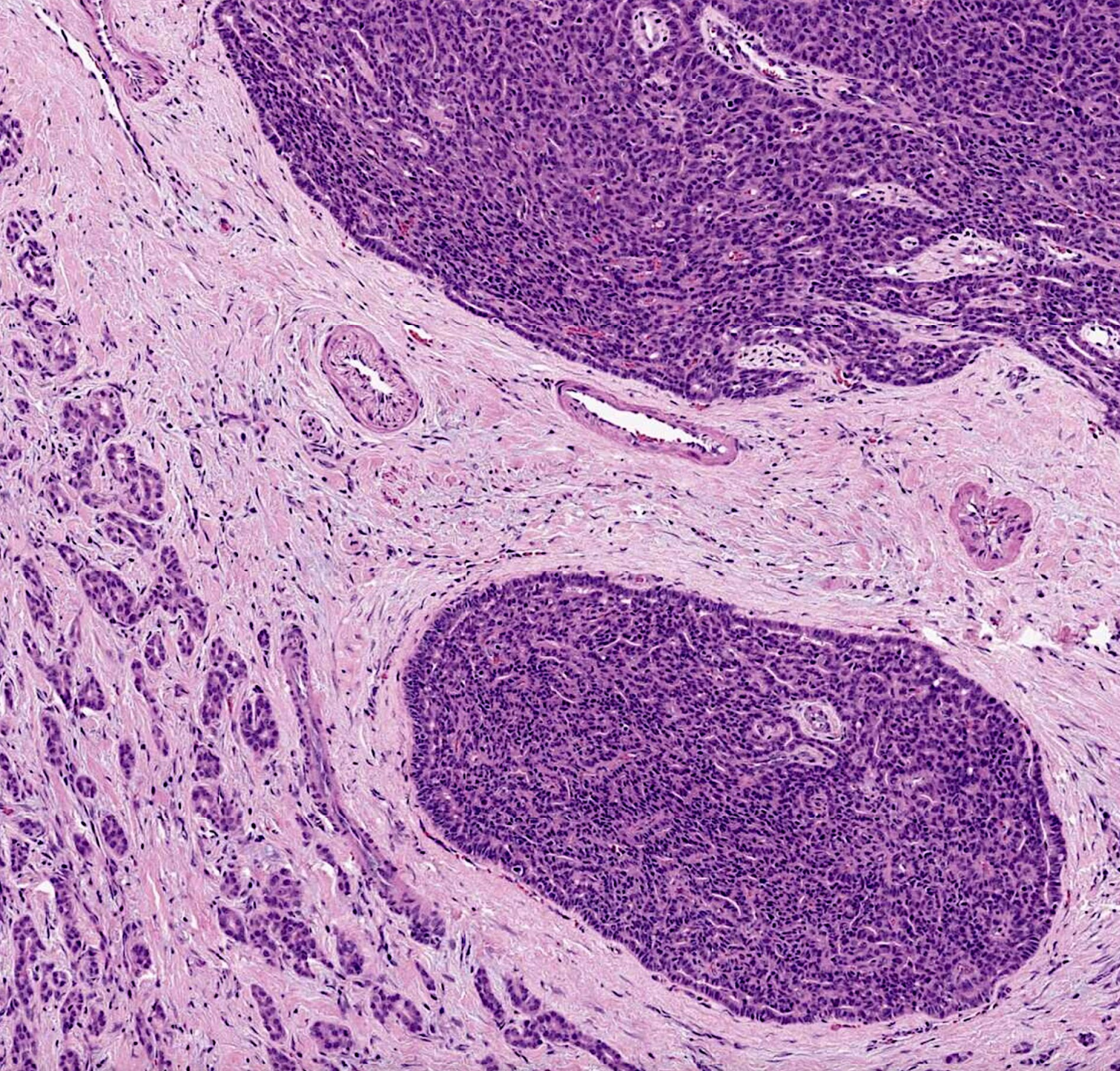


IPNB, Tubulopapillary pattern

- Have cancer associated with them in up to 80% of cases
- Therefore must undergo formal oncologic resection even if it is technically a premalignant neoplasm; this includes partial hepatectomy if intrahepatic
 - Despite the high association with cancer, these have excellent prognosis
 - These have FGFR2 fusions, as is seen in small duct intrahepatic cholangioCA;
 - There are FGFR inhibitors that pts may benefit from if necessary
 - SWI/SNF complex protein encoding gene mutations such as SMARCA5, ARID1a mutations also found







Summary

Pyloric gland adenoma

- <2 cm, >1 cm, grossly visible, composed of pyloric-type glands, seldom progress to cancer

Intracholecystic papillary neoplasm

- Carcinoma present in >50%, may not be within the lesion
- Background flat epithelium dysplastic
- Grade as low or high grade and state predominant epithelial type

Intraductal papillary neoplasm of bile duct

- Grossly visible tumor filling up intrahepatic or extrahepatic bile duct
- Grade as low or high grade
- Many have cancer associated with it, but have good prognosis unless biliary phenotype

Thank You

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