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**CAP19**

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S1921C: Small Bites and Small Sites: Big Diagnostic Problems

# **The Latest on the Ampulla: How to Stay out of Trouble**

**Wei Chen, MD, PhD**

**Associate Director, Liver Pathology**

**The Ohio State University Wexner Medical Center**

# Agenda

## The Latest on the Ampulla: How to Stay out of Trouble

### 1. Ampulla Anatomy

### 2. Endoscopic ampullary biopsy limitations

- Small size, cautery artifact, ulcerated, reactive epithelial changes

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### 3. Helpful tips

- EUS/ERCP/Cytology correlation
- Check base of ulcer
- Small atypical glands: deepers & IHC

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### 4. Two case studies and two quizzes

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### 5. Summary

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# Definition

- **Ampulla**
  - A cavity or the dilated end of a duct
- **Ampulla of Vater**
  - AKA hepatopancreatic ampulla
  - Confluence of PD & CBD
  - Located at major duodenal papilla
  - Most common site dysplasia/ca (SB)
  - Hybrid/mixed epithelium
    - Staining for both CK7 and CK20 common
    - Intestinal CDX2/MUC2+, MUC1-
    - Pancreatobiliary CDX2/MUC2-, MUC1+

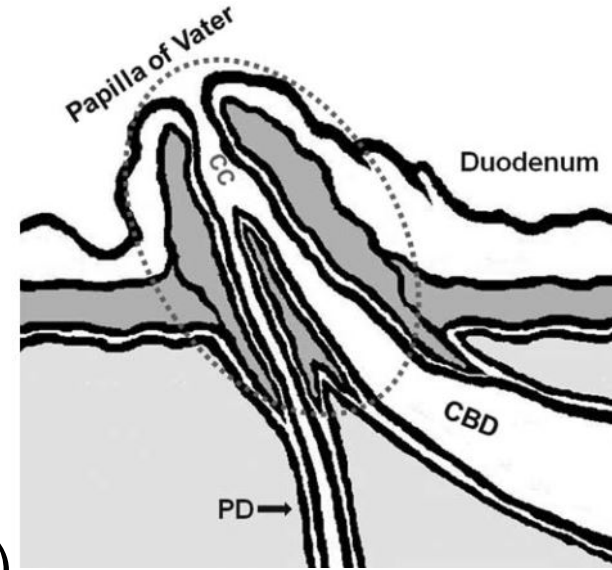
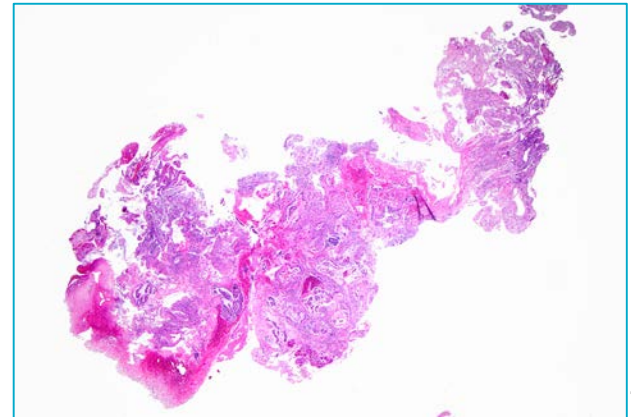
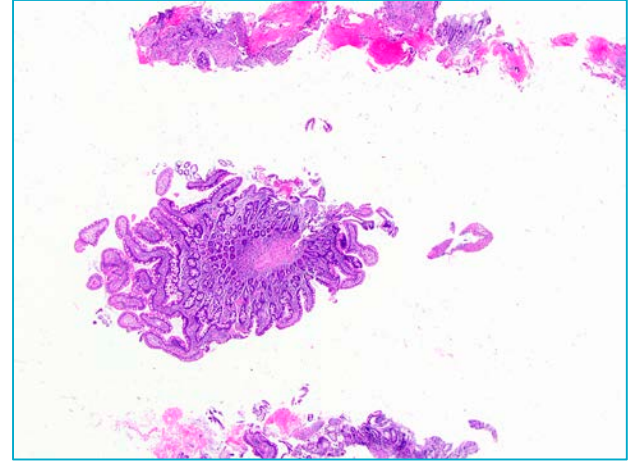


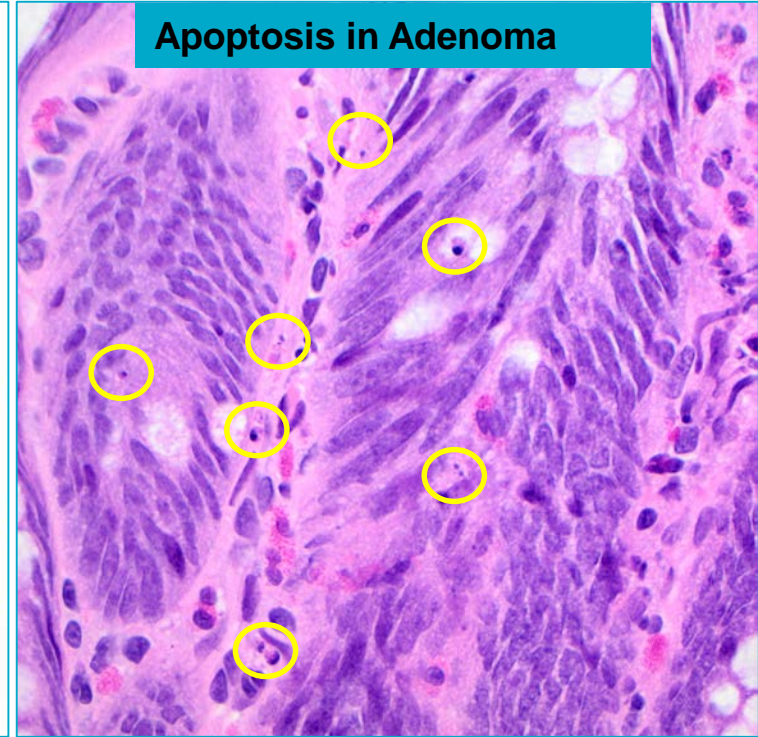
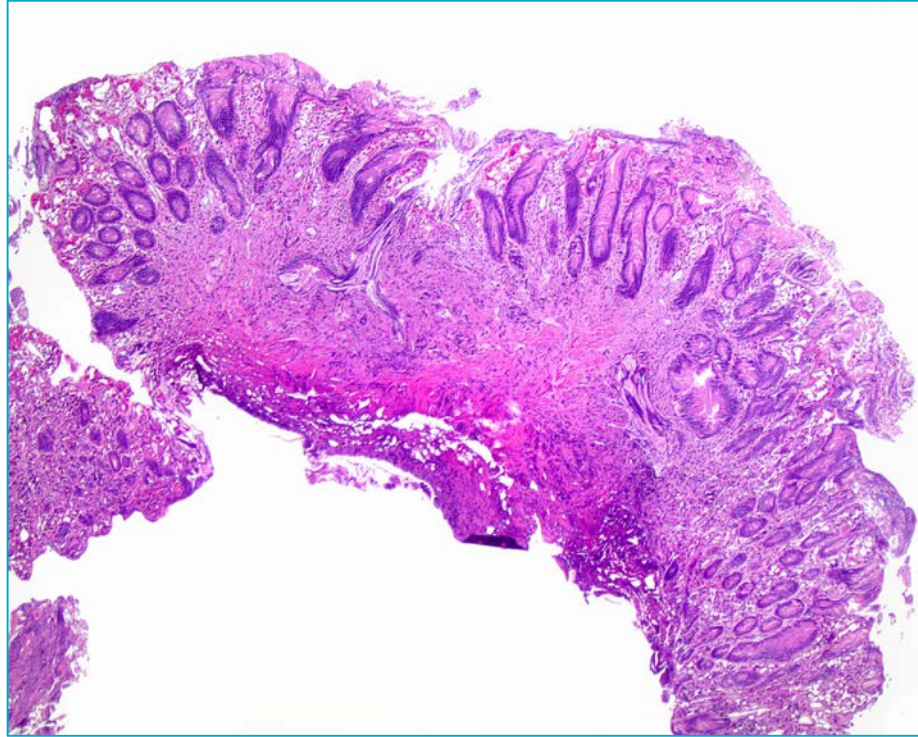
Figure from Adsay etc. *Am J Surg Pathol* 2012; 36: 1592-1608

# Endoscopic Ampullary Biopsy Limitations

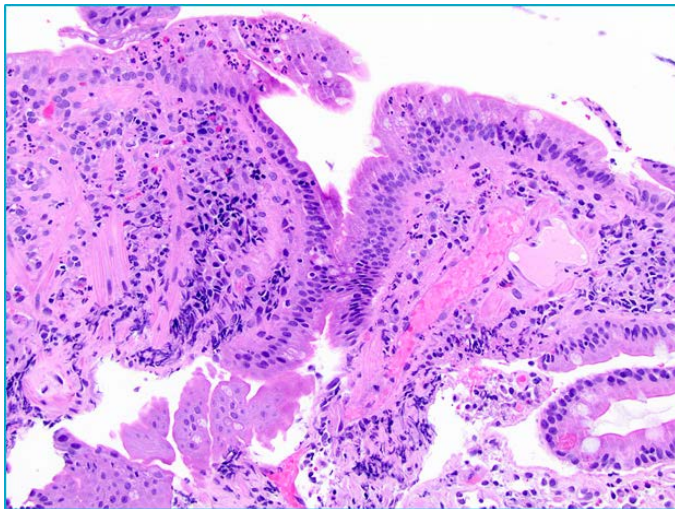
- Small size
- Fragmentation
- Crush artifact
- Cautery artifact
- Ulcerated, inflamed
- But high stakes!



# Cautery Artifact vs. Adenoma



# Reactive Epithelial Changes



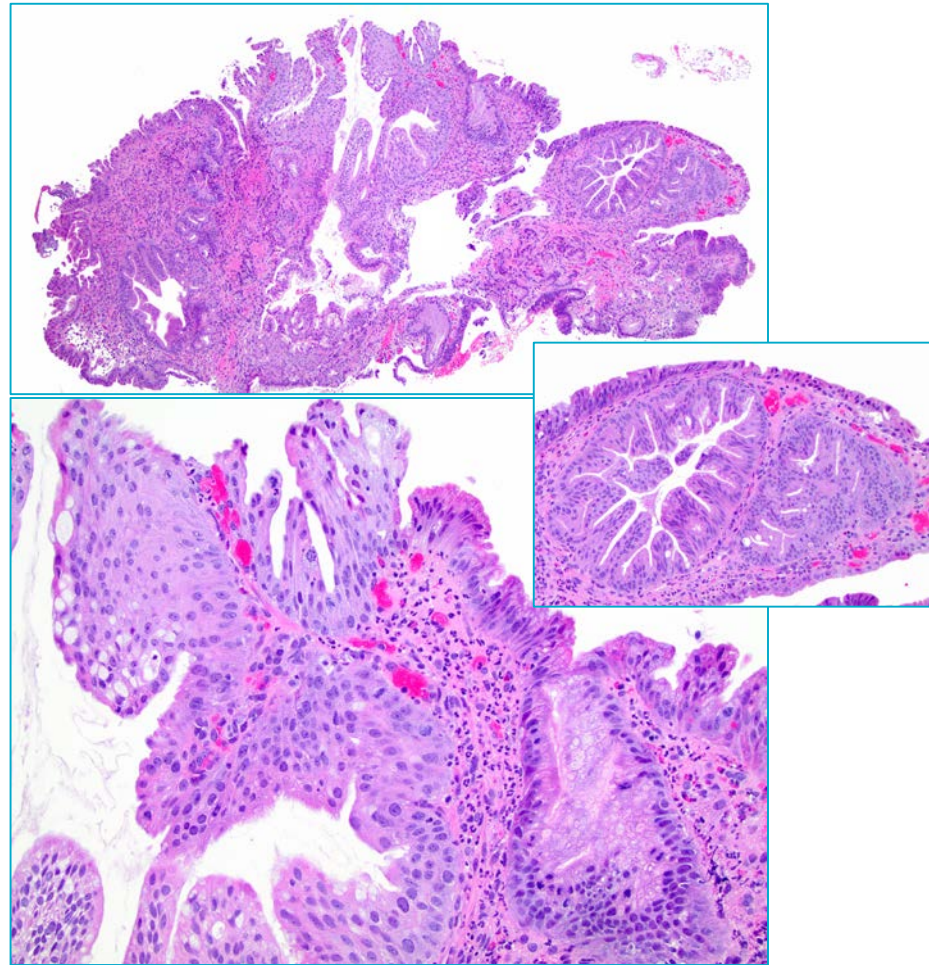
- < 3 months of prior procedure
- High interobserver disagreement
  - $\kappa = 0.24$ , no clinical data
  - $\kappa = 0.49$ , given clinical data

	Reactive Atypia	Adenoma
Adjacent ulcer, infl.	+	-/+
Surface Maturation	Yes	No
Cytoplasmic Eosinophilia	More	Less
Nuclear enlargement, macronucleoli	More	Less
Nuclear elongation, stratification	Less	More
Epithelial apoptosis	Less	More



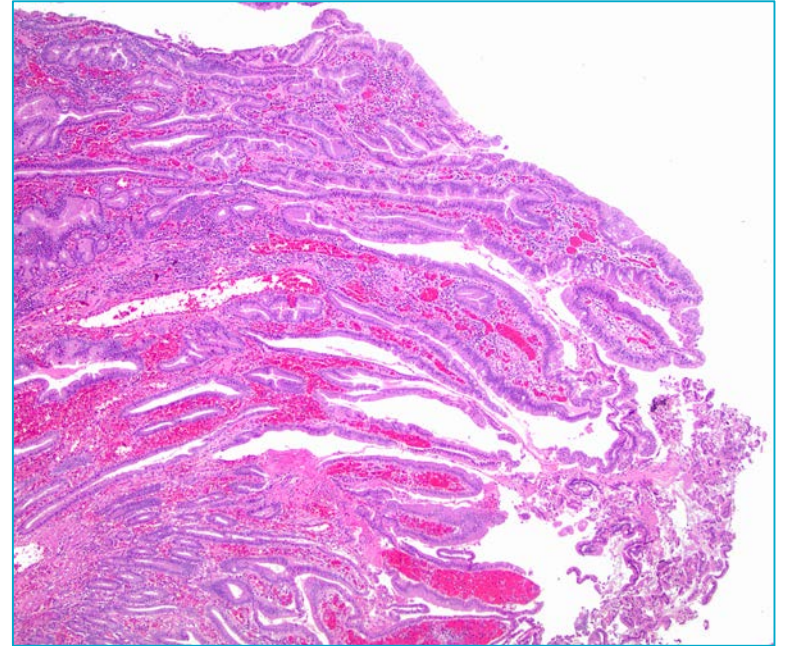
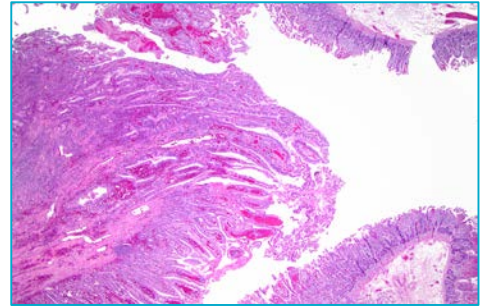
# Squamous Metaplasia

- Prior procedure/stent
- May involve underlying ampullary ductules
- Diagnostic pitfalls
  - Not HGD
  - Not invasion



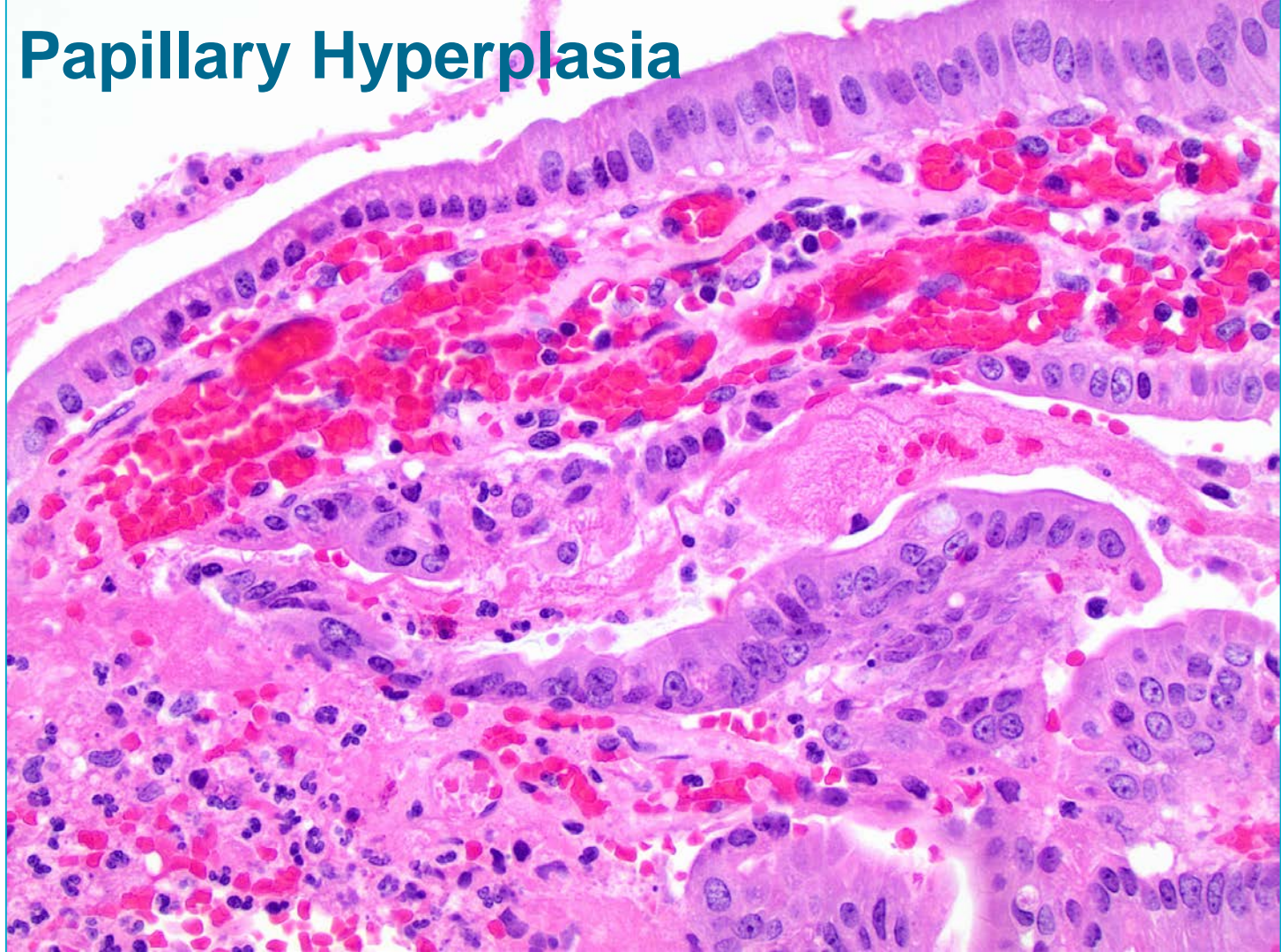
# Papillary/Reactive Hyperplasia

- Prior procedure/stent
- Adjacent to tumor
- Mimic adenoma, but show:
  - Retained maturation
  - Less nuclear elongation/stratification
  - More pink cytoplasm
  - May have macronucleoli





# Papillary Hyperplasia

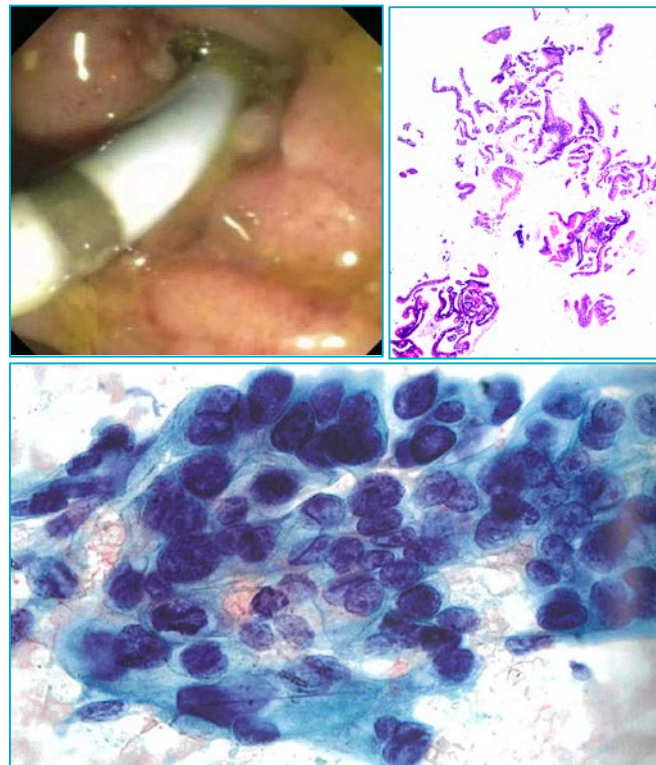


# Ampullary Biopsy Evaluation



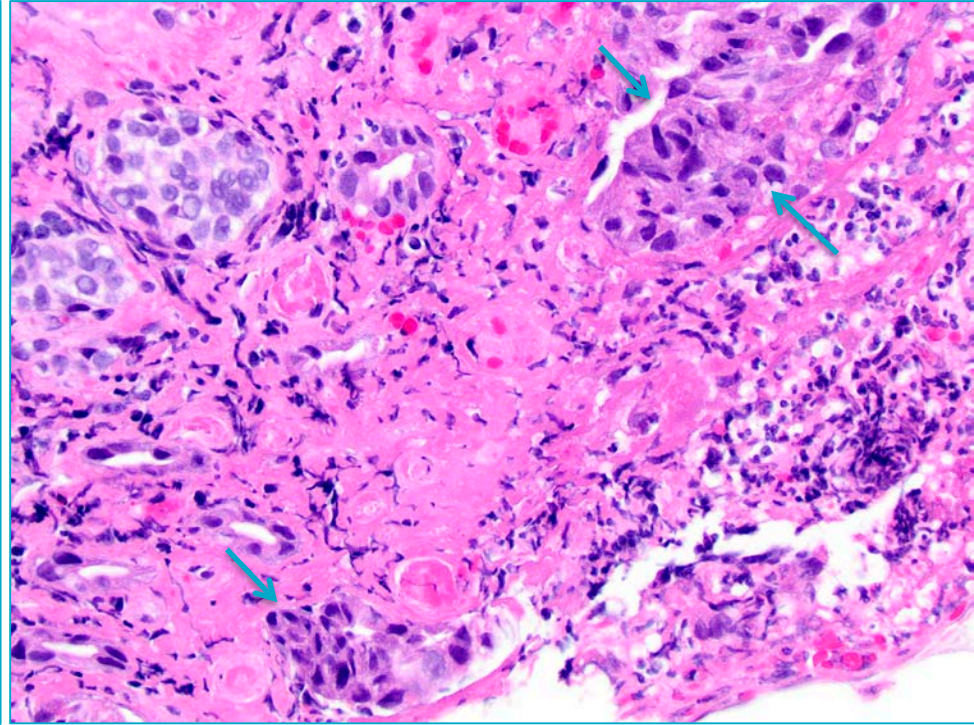
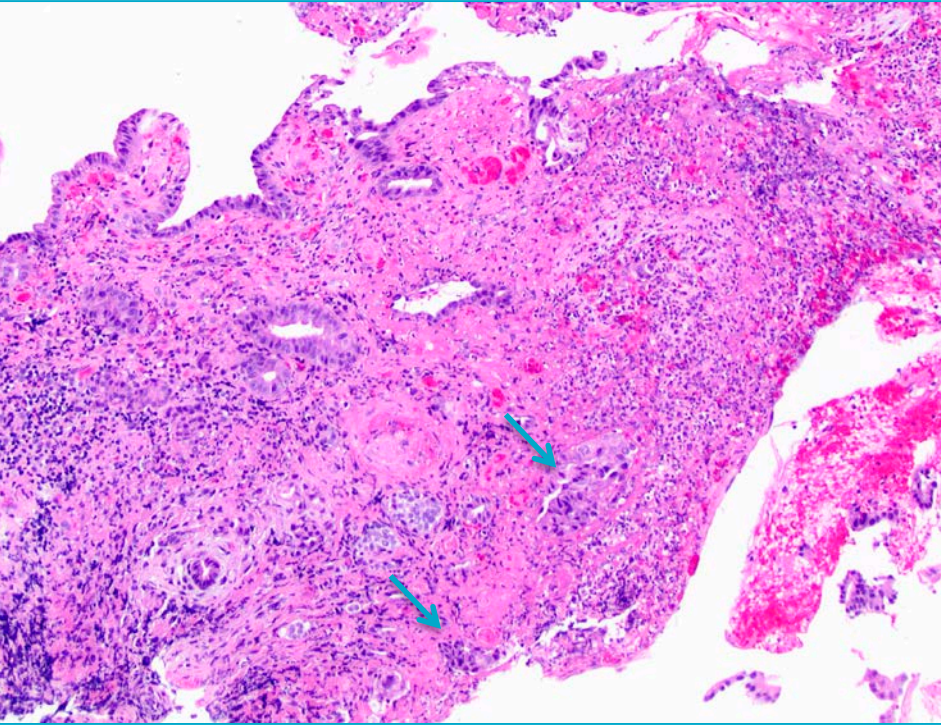
# Tip#1. Correlation, Correlation, Correlation!

- Often limited bx material
- EUS/ERCP
  - Small vs. Large mass
  - ? Invasion (infiltrative borders, ulceration, firm texture, ductal dilatation)
- Cytology
- Bx high false negative rate
  - 16-60%
  - Acknowledge the limitations!!!

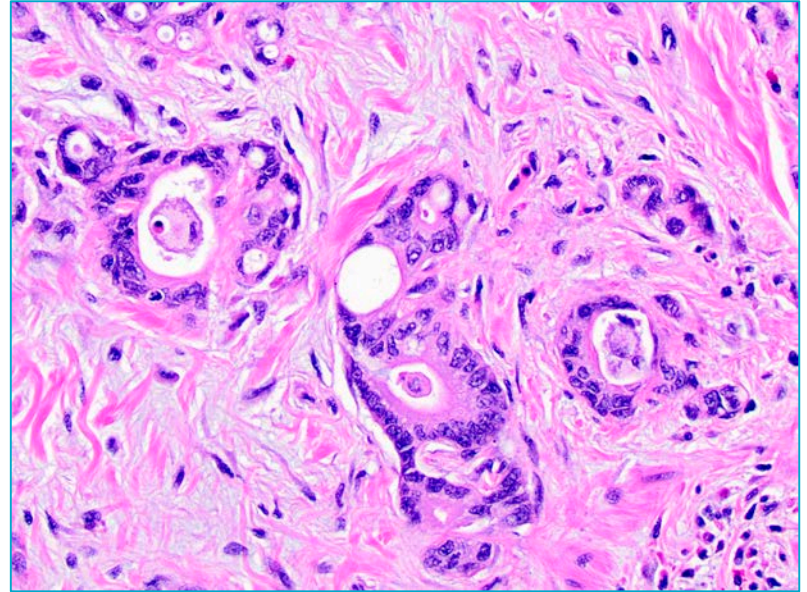
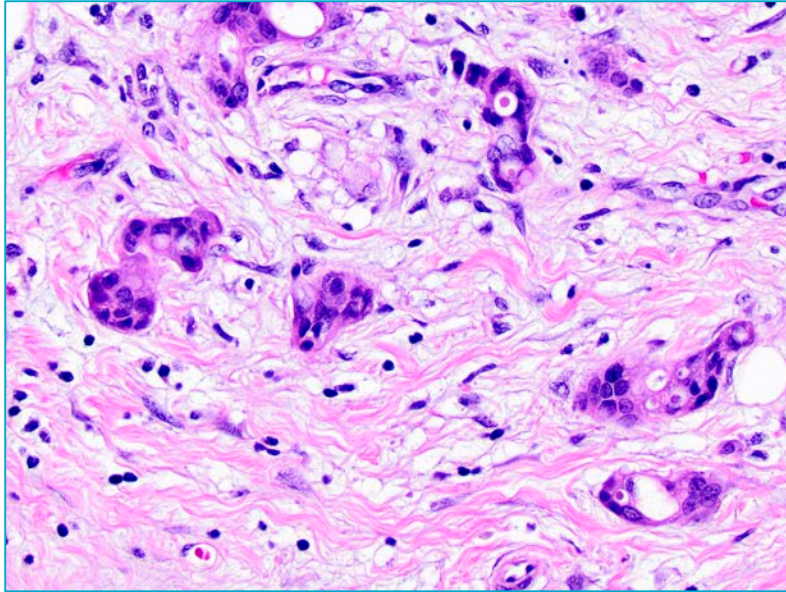




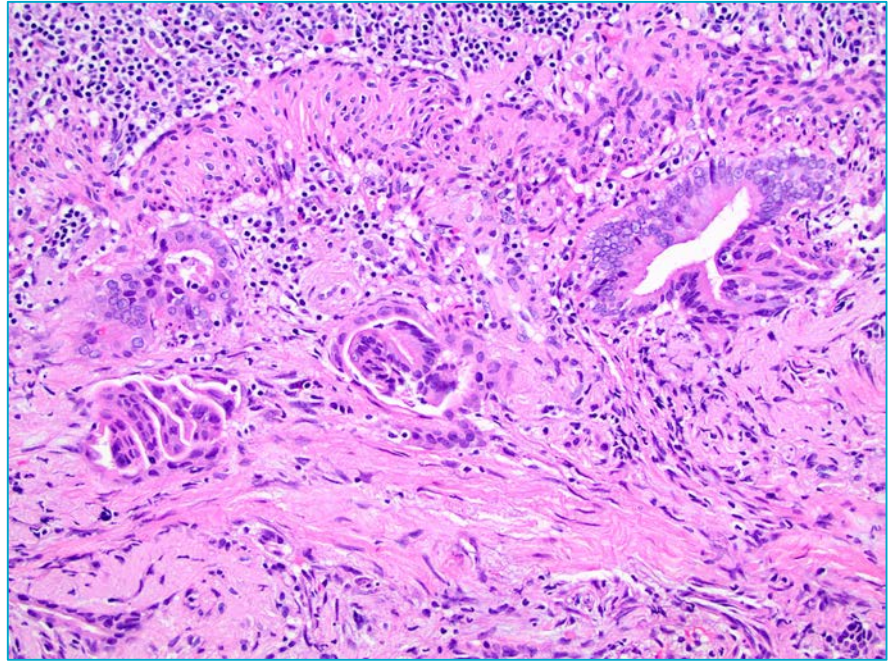
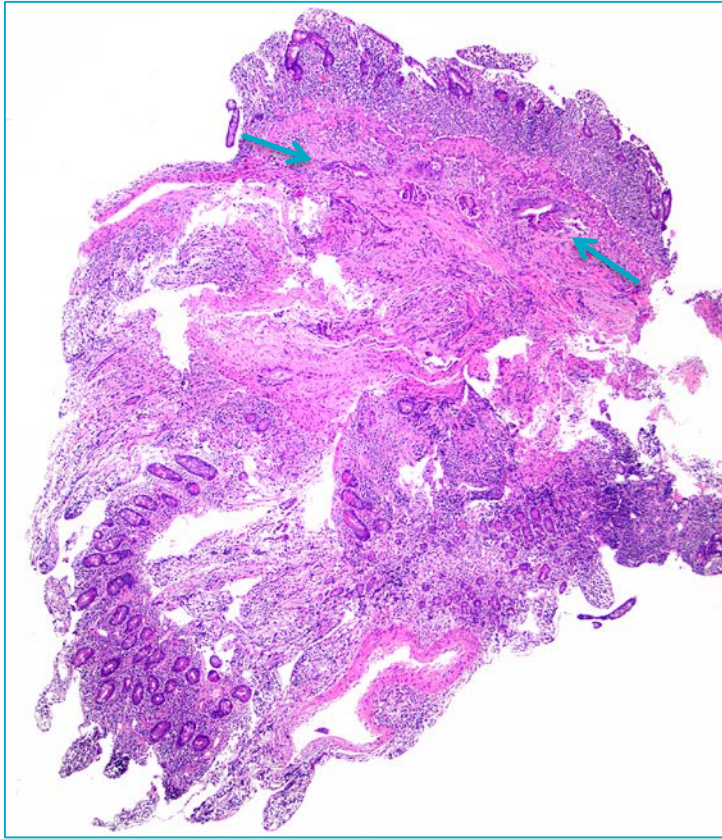
## Tip#2. Ulcer - Check Deep Edge of Biopsy



# Whipple Resection: Ampullary Adenocarcinoma





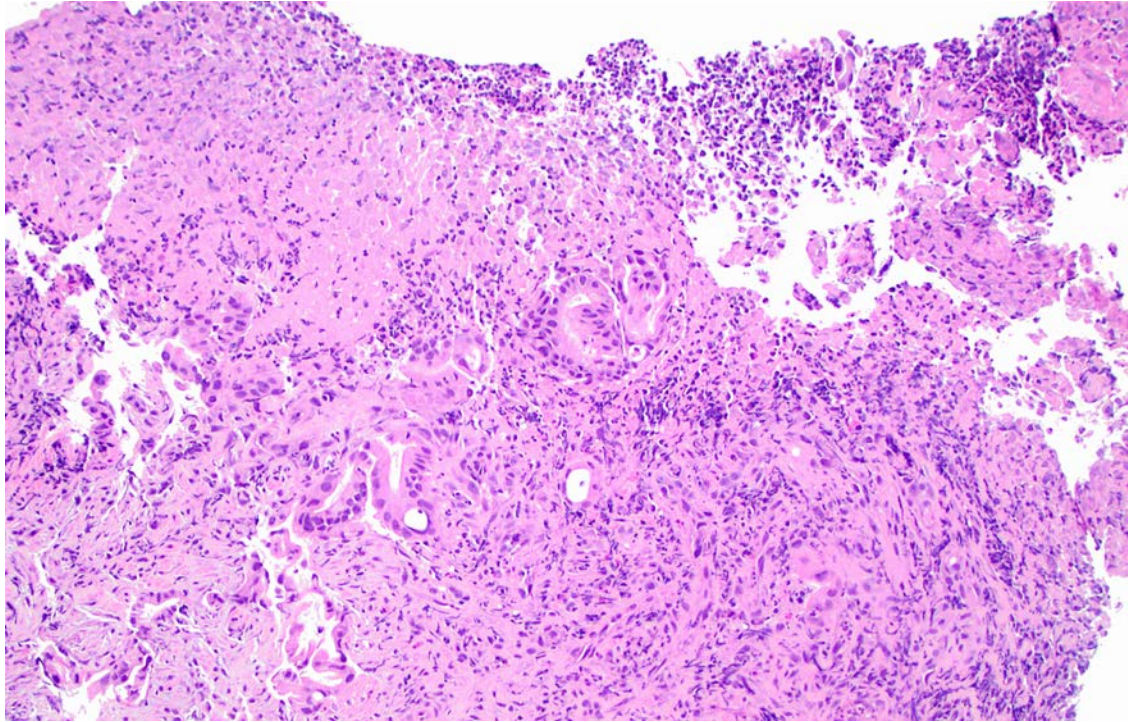


**Eroded mucosa with underlying cholangiocarcinoma**

## Tip#3. Beware Small Atypical Glands at Ampulla

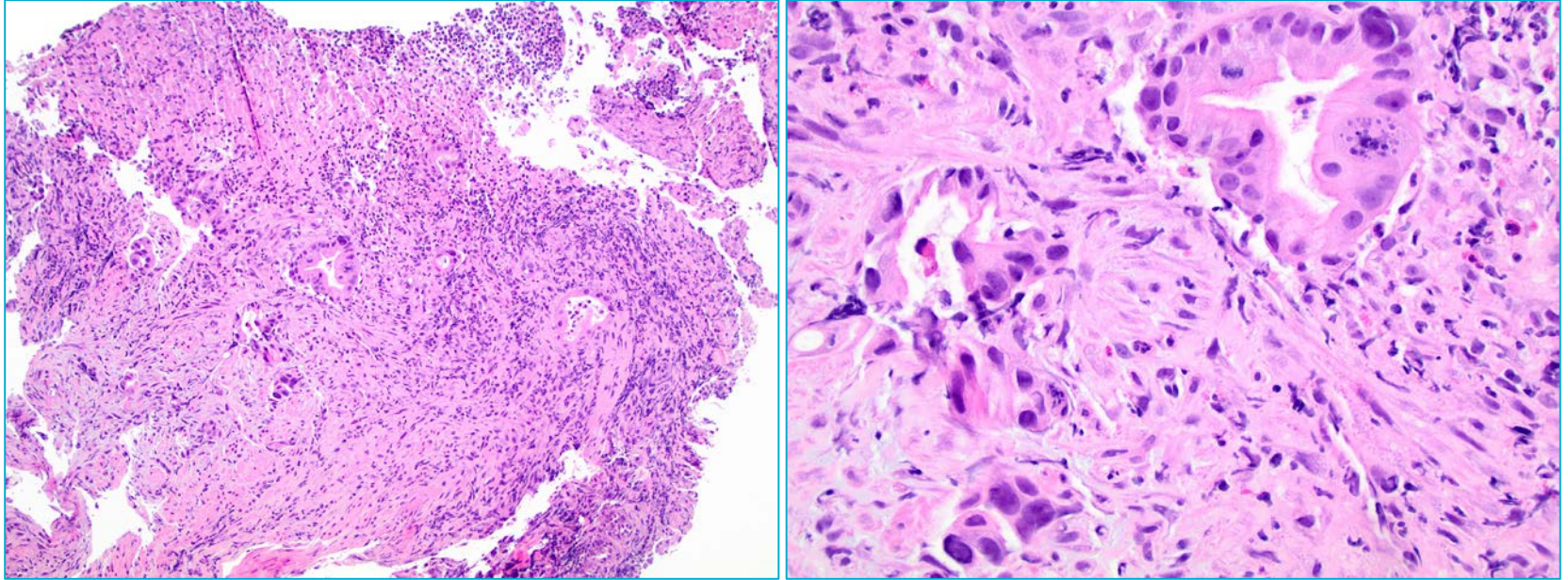
Could be invasive carcinoma from:

- Pancreas
- Ampulla
- Distal Bile Duct





## Tip#3. Small Atypical Glands: Deepers May Help



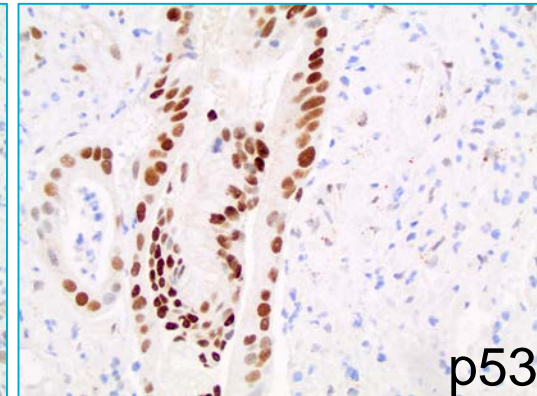
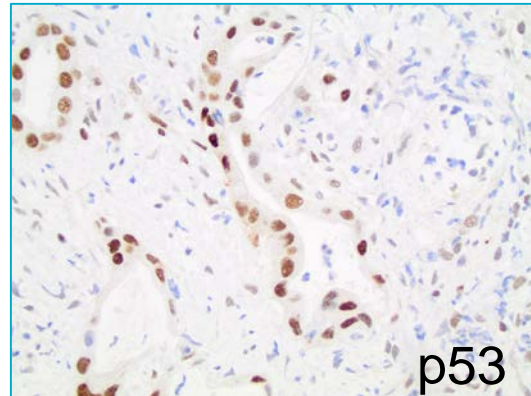
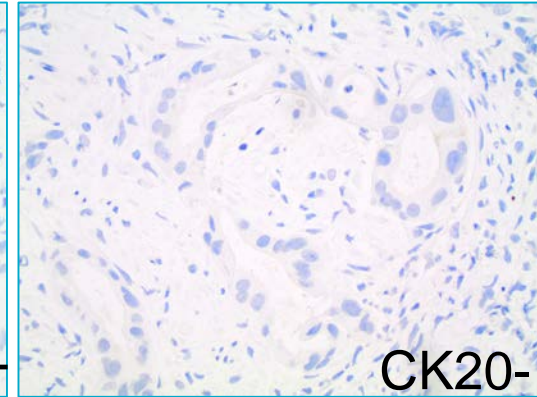
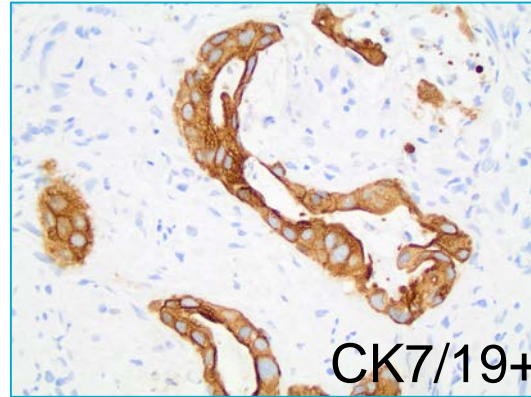
Adenocarcinoma: irregular haphazard glands, 4x anisonucleosis, stromal desmoplasia, single cell infiltration, atypical mitoses

## Tip#3. Small Atypical Glands: IHC May Help

Adenocarcinoma with pancreaticobiliary differentiation:

- \*CK7/19/MUC1+
- \*CK20/CDX2/MUC2-
- P53 ++ or null
- SMAD4/DPC4-

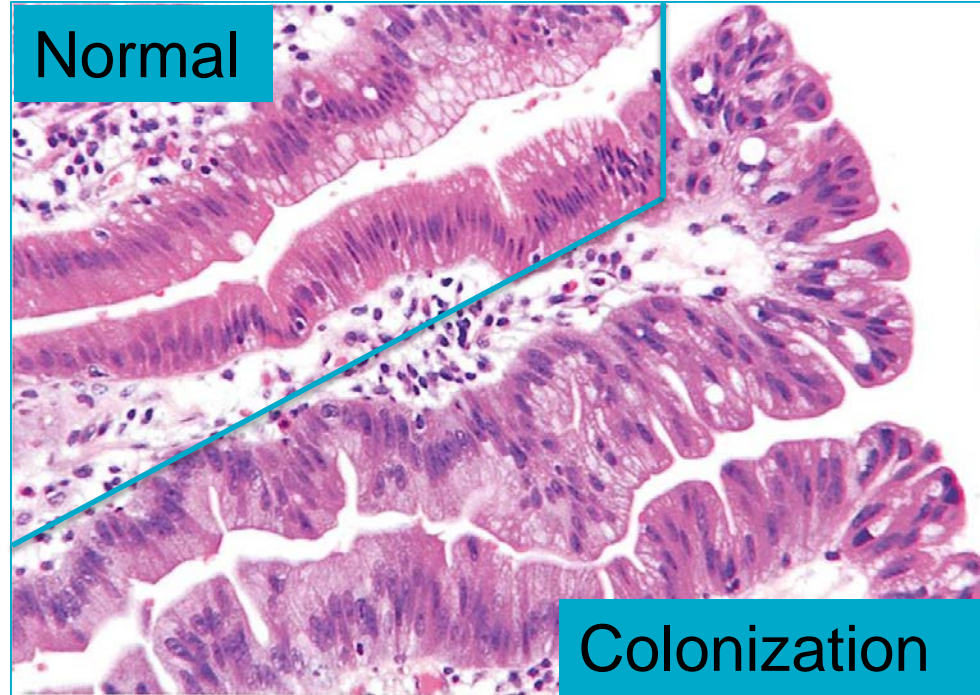
\*CK stains may be variable





## Tip#4. Colonization of Ampullary Epithelium by Underlying Carcinoma

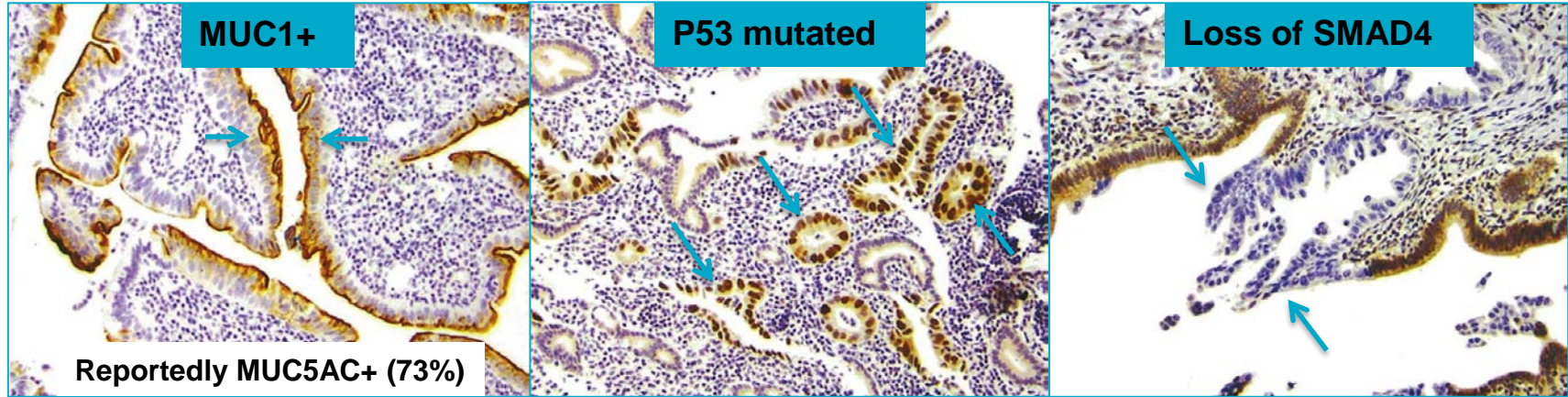
- Invasive pancreatic or cholangiocarcinoma grow along basement membrane of ampullary epithelium
  - Simulating adenoma
- IHC shows PB (not intestinal) differentiation



*Photo from Adsay and Basturk. Chap. 41. Tumors of major and minor ampulla; in book Surgical Pathology of the GI tract/liver/biliary tract/pancreas 2009, pp1126*



# IHC: Invasive Pancreatic Ca Colonizing Ampulla



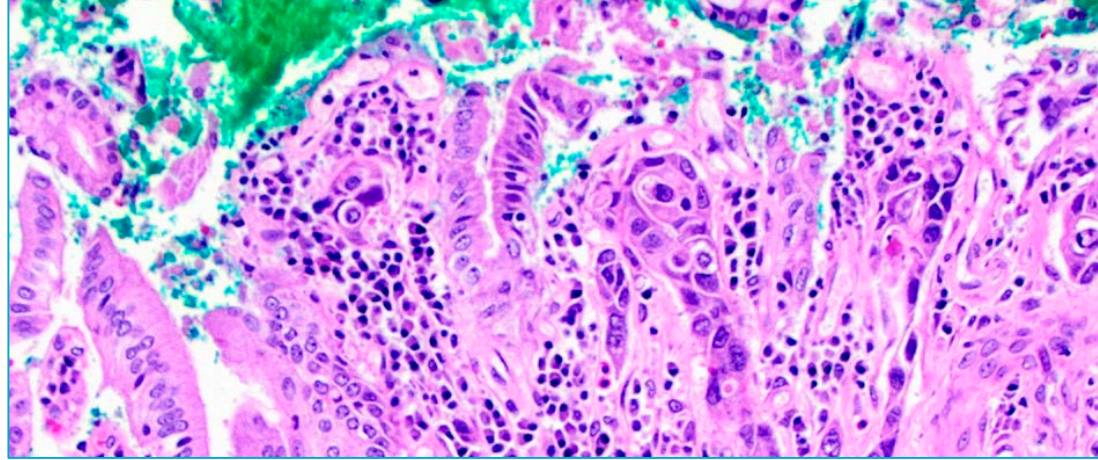
**PB differentiation**

**Mutations of tumor suppressors**

*Photos from Chap 18. Preinvasive neoplastic lesions of the vaterian system; in AFIP Fascicle 23: Tumors of the gallbladder, extrahepatic bile ducts, and Vaterian system 2015, pp456-457*

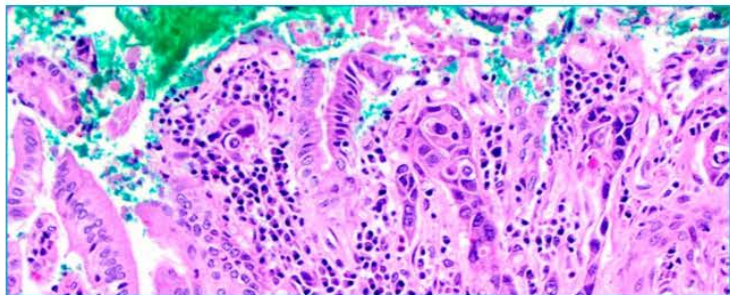
## Quiz 1

Ampullary biopsy, what's your diagnosis?



- A. Squamous metaplasia
- B. High-grade dysplasia
- C. Low-grade dysplasia
- D. Carcinoma colonization of ampullary epithelium

# Ampullary biopsy, what's your diagnosis?

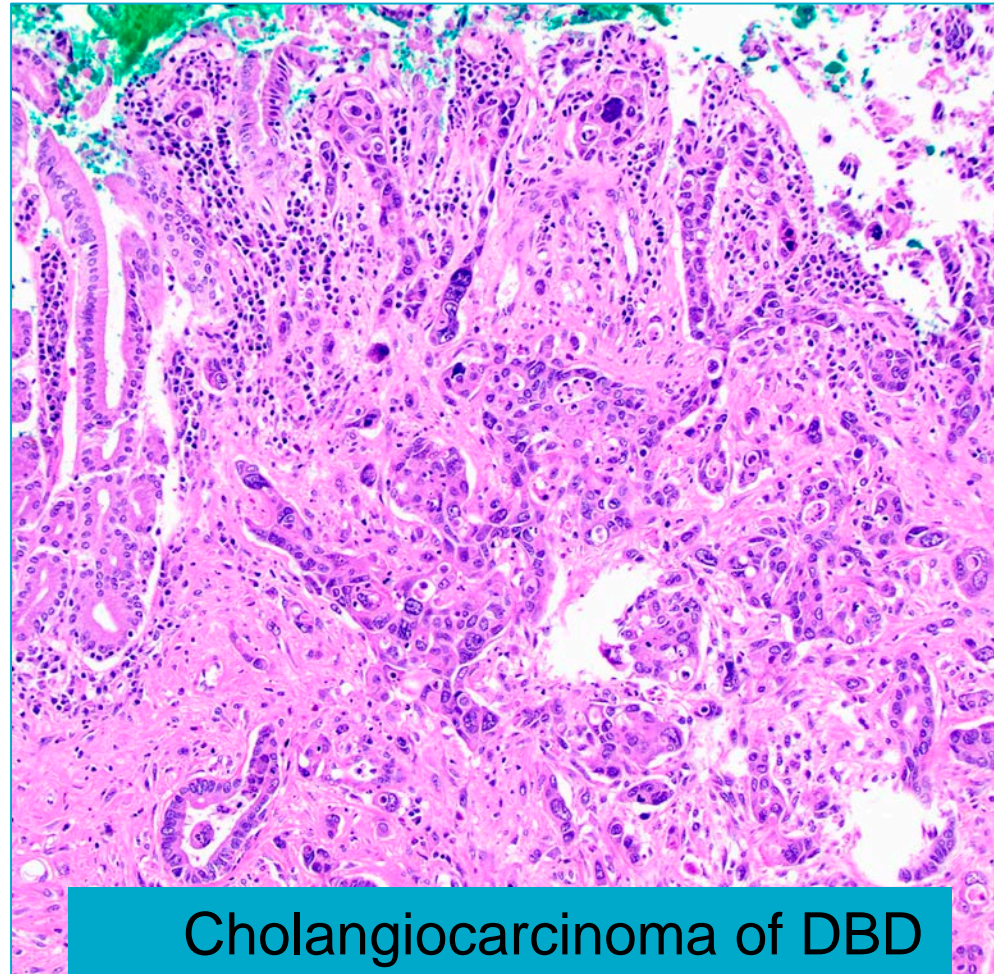


- A. Squamous metaplasia
- B. High-grade dysplasia
- C. Low-grade dysplasia
- D. Carcinoma colonization of ampullary epithelium



# Quiz 1 Answer

- A. Squamous metaplasia
- B. High-grade dysplasia
- C. Low-grade dysplasia
- D. Carcinoma colonization of ampullary epithelium



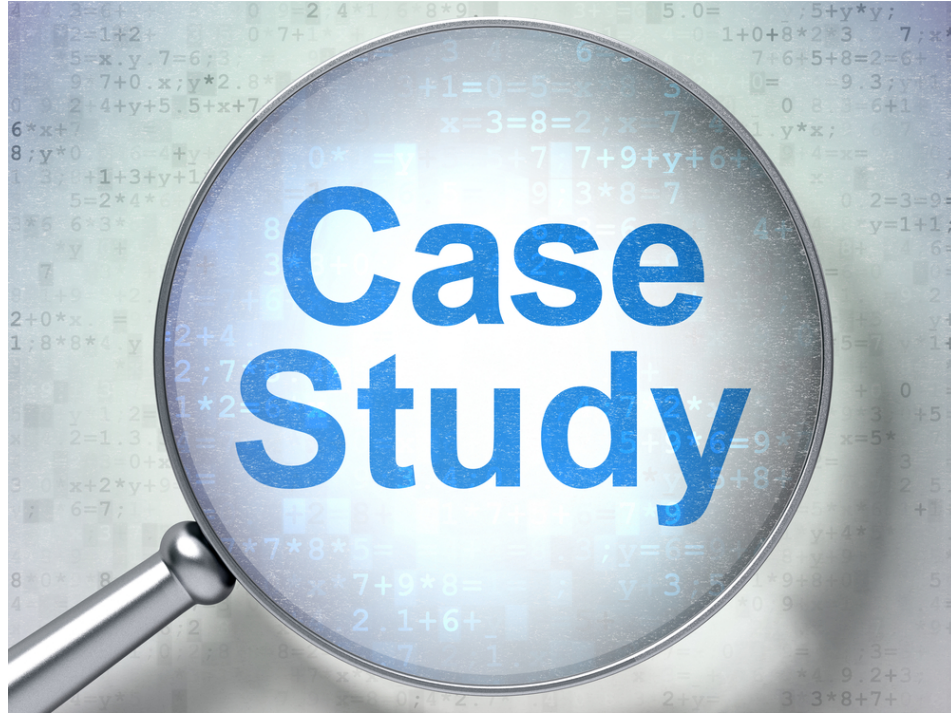
Cholangiocarcinoma of DBD

# Summary Ampullary Biopsy Evaluation

- Complex anatomy & histomorphology
- Correlation ERCP/EUS/Cytology
- Reactive changes post instrumentation
- Ulcer – ? tumor, check deep edge
- Abnormal epithelium – ? colonization by carcinoma
- Small atypical glands – Get deepers & IHC

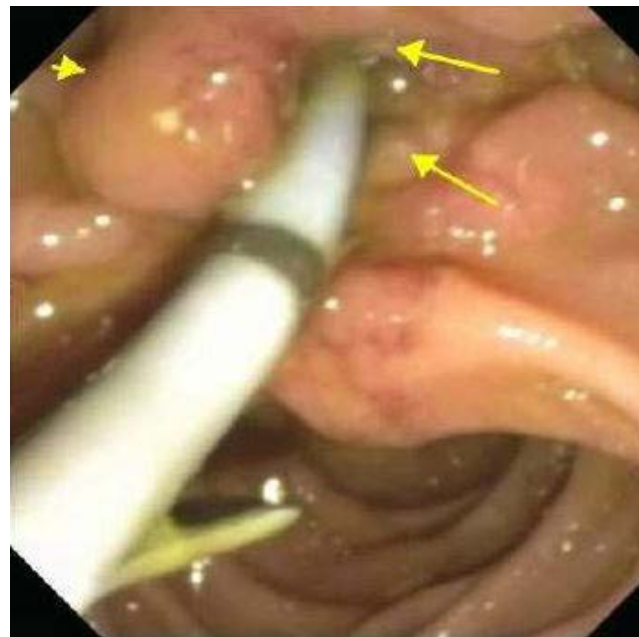


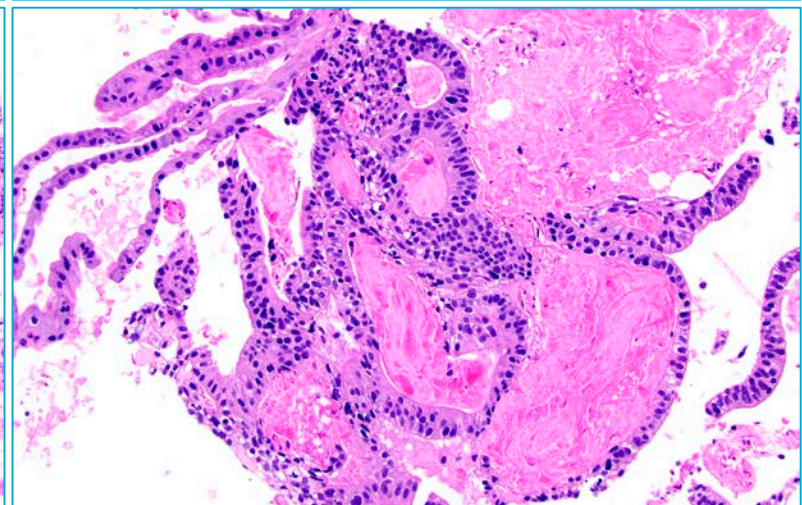
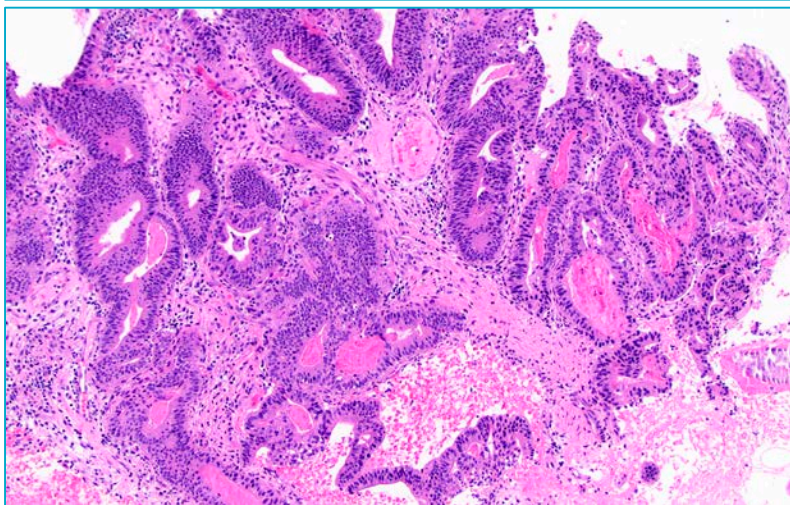
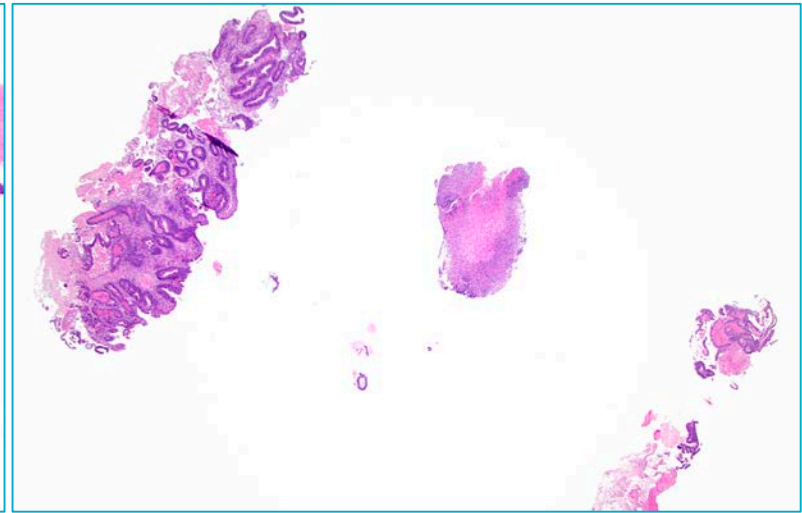
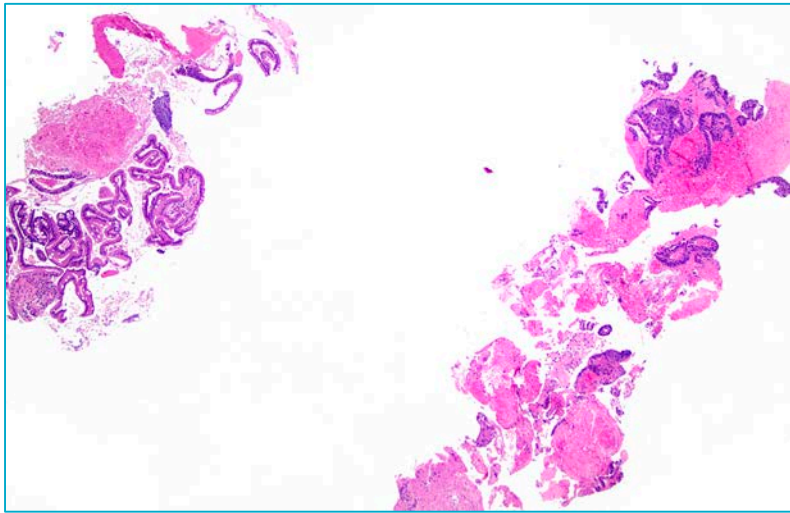
# Ampullary Biopsy



# Case 1

- 81 y.o. F jaundice
- EUS: Distal biliary stricture and ampullary mass
- Endoscopic ampullectomy





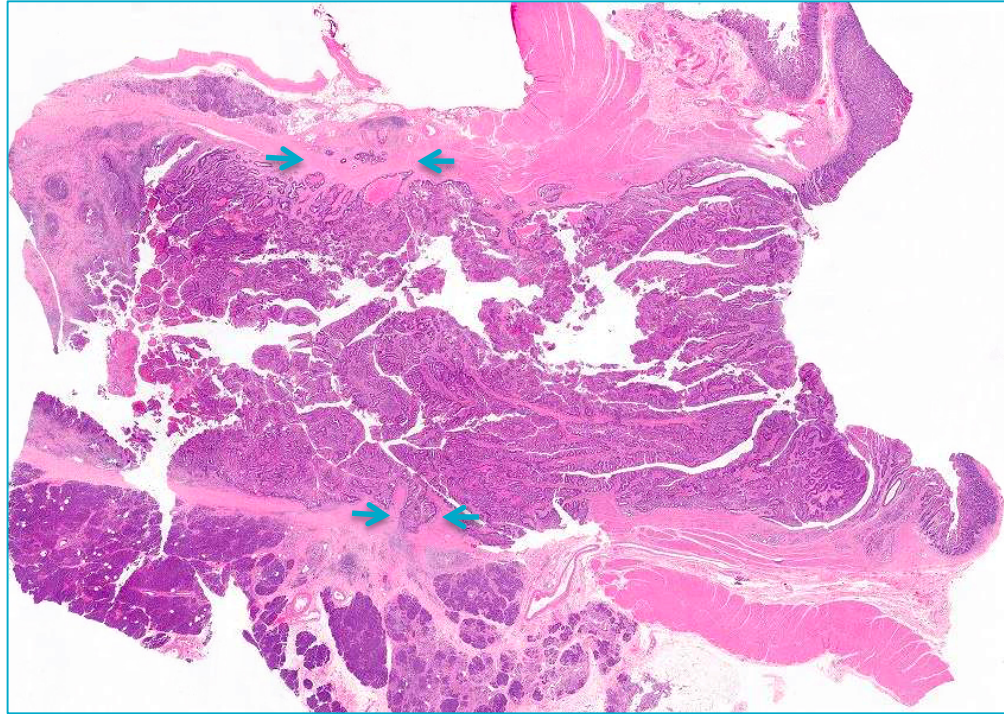
# Case 1. Ampullary Biopsy Diagnosis

- **Fragments of ampullary adenoma with focal necrosis, see note.**
- **Adjacent small intestinal mucosa with ulcer and acute inflammation.**

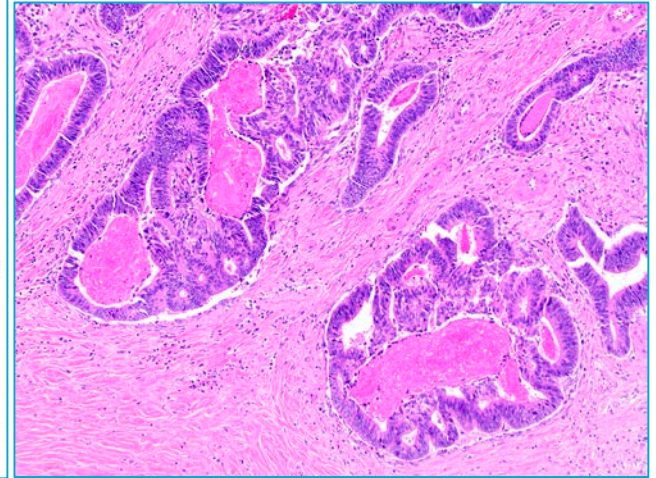
*Note: Focal necrosis, prominent nuclear changes, atypical cells and glands were seen in fibrotic tissue fragments. Deeper sections obtained show similar findings with no definitive evidence of invasion. Caution should be exercised as the fragmented superficial biopsy material may not be representative of the clinically concerning lesion, an invasive carcinoma cannot be completely excluded. Correlate with clinical and radiologic findings and rebiopsy are recommended if clinically indicated. The slides have been reviewed by Dr. XXX.*



# Case 1. Whipple Resection



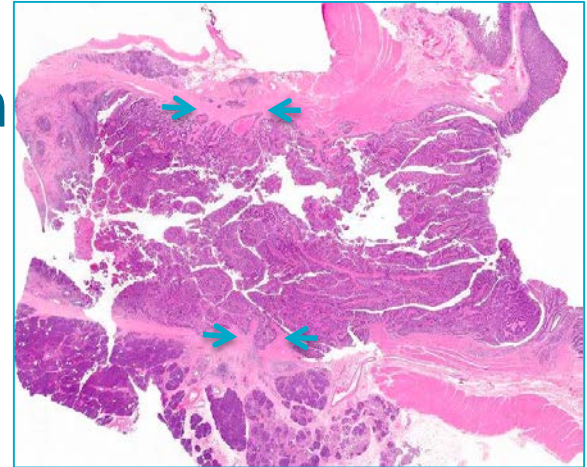
**Intra-Ampullary Papillary-Tubular Neoplasm (IAPN) with associated invasive carcinoma**





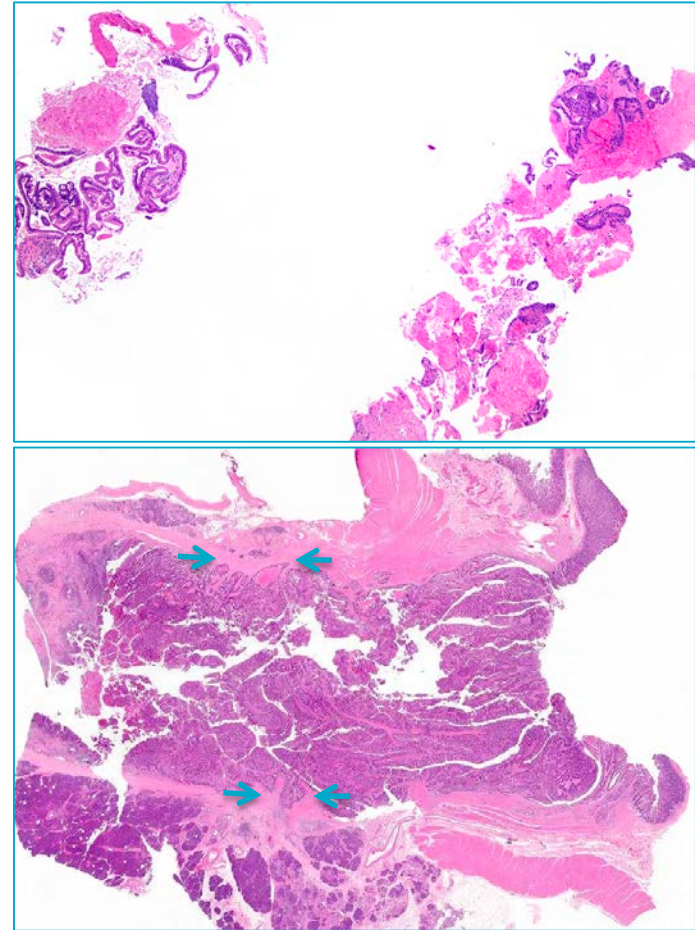
# Intra-Ampullary Papillary-Tubular Neoplasm

- **Preinvasive, intra-ampullary, exophytic**
  - Minimal/no involvement of BD, PD, or duodenal papilla
  - Analogous to ITPN of pancreas/BD
- **75% has invasive carcinoma on resection**
  - Invasion subtle - hidden in crevices underneath polypoid areas
  - **Missed by biopsy**
- **Biologically indolent**
  - Even when invasive significantly better prognosis than invasive ampullary ca unaccompanied by IAPNs



# Case 1. Summary

- **Ampullary mucosal biopsy:**
  - Fragments of adenoma with ulcer, necrosis (\*careful note\*)
- **Pancreaticoduodenectomy:**
  - Small foci of invasive adenocarcinoma, arising in IAPN
  - pT2N1
- **Discordance due to limitation of mucosal bx**



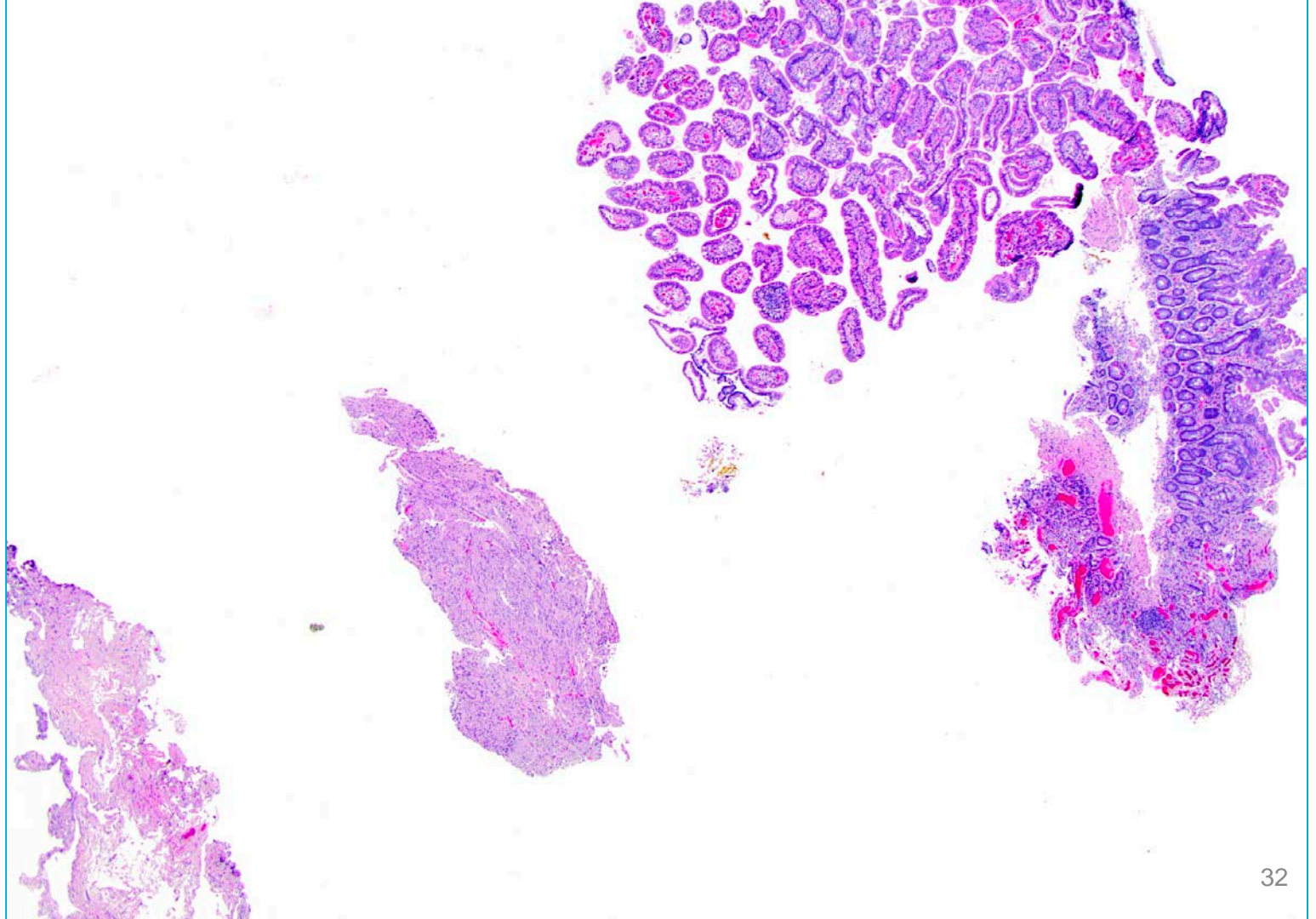
## Case 2

- 63 y.o. M painless jaundice
- ERCP: CBD dilation, stent placed
- EUS: 2.9 cm lesion biopsied



Mass in the duodenal wall obstructing the bile duct and invading the pancreas



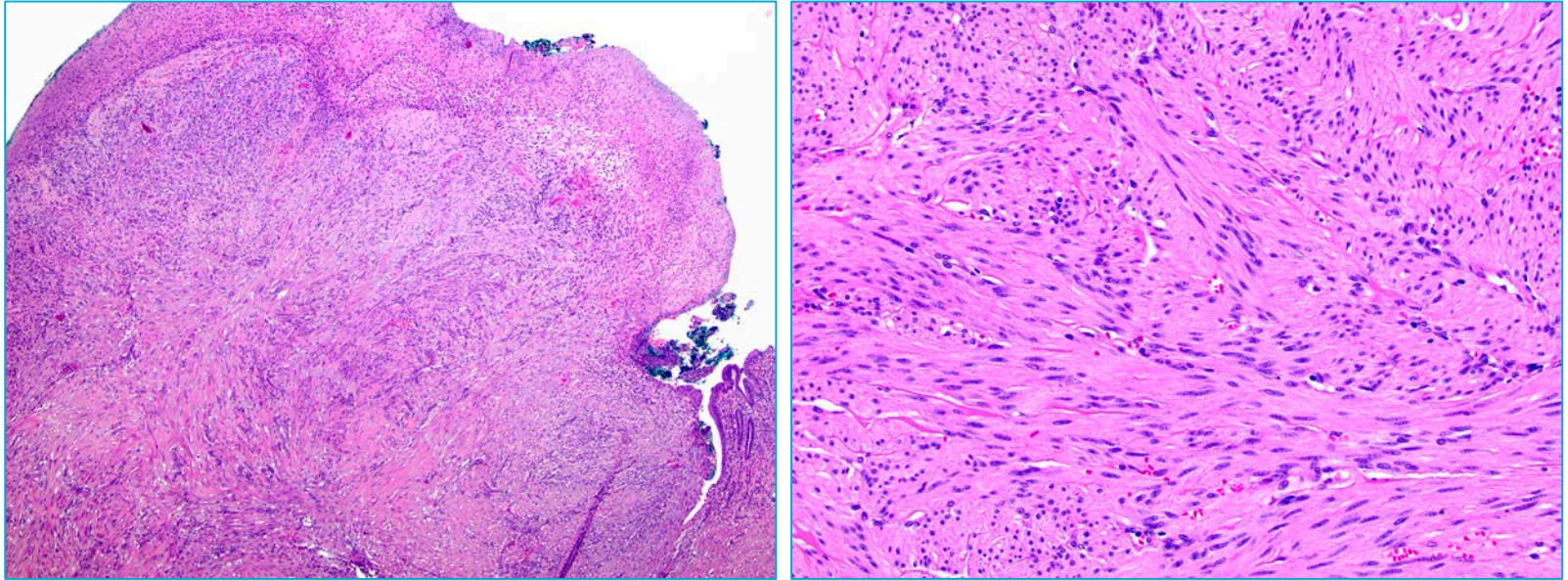


## Case 2. Ampullary Biopsy Diagnosis

- **Ampullary mucosa with no diagnostic abnormality, see note.**

*Note: An AE1/3 is negative for an infiltrating process. Deeper sections are examined. If the lesion remains clinically concerning, repeat sampling is a consideration.*

## Case 2. Whipple Resection



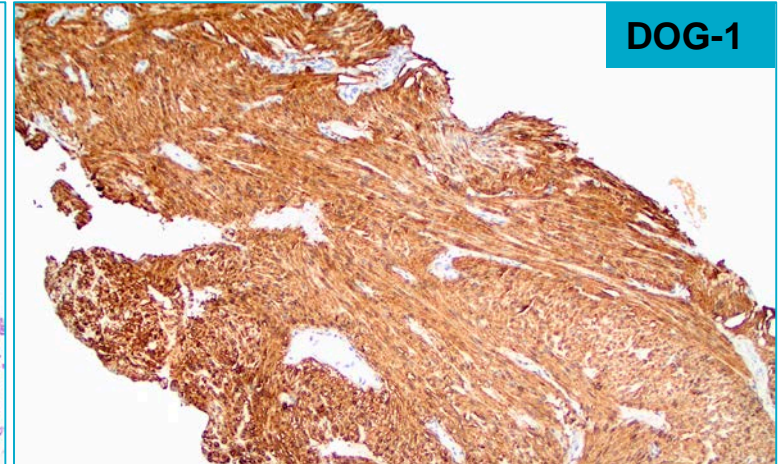
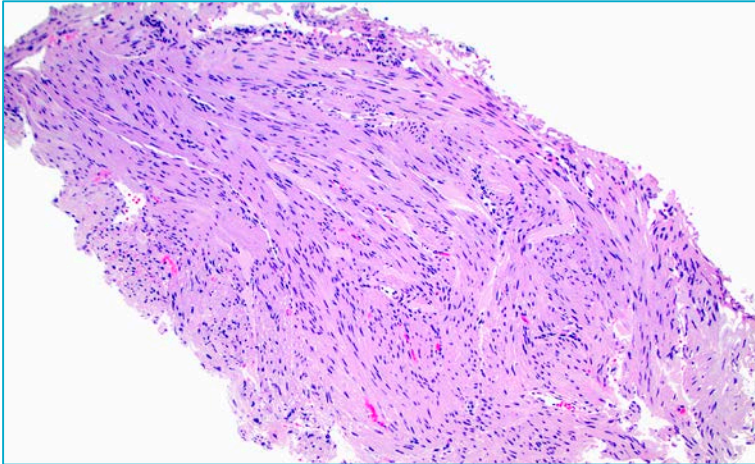
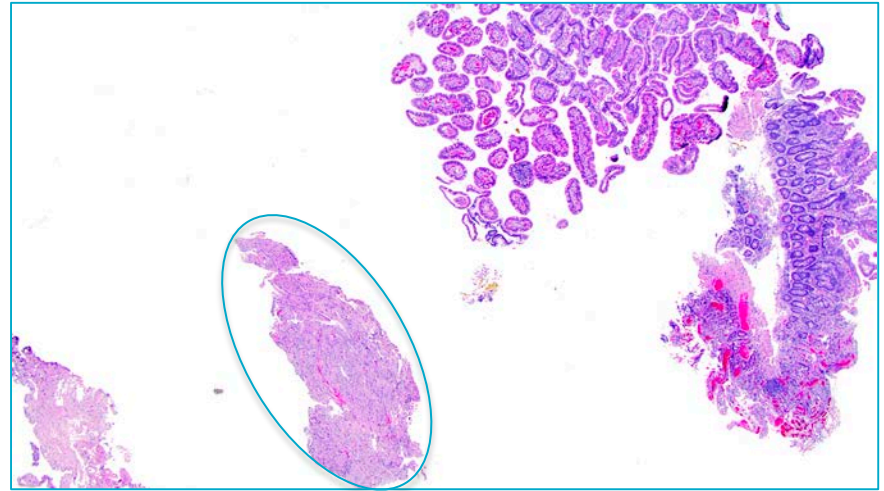
**Low-grade GIST, duodenum**



## Case 2. Summary

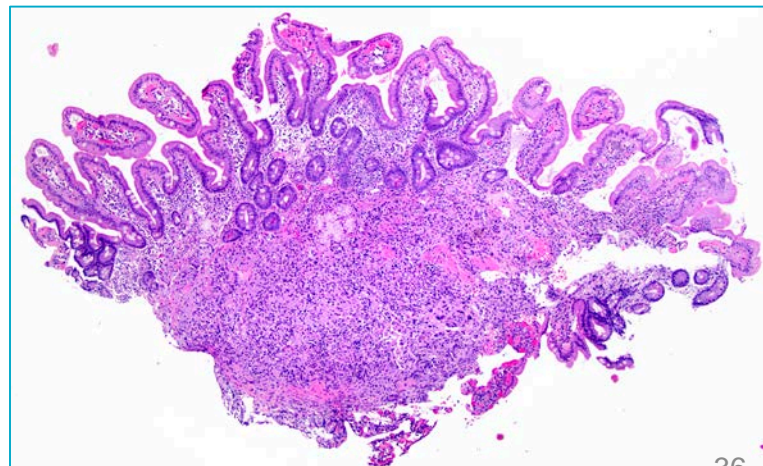
Retrospectively stained Bx

- One fragment DOG1+
- NOT MM – too thick
- NOT MP – superficial Bx



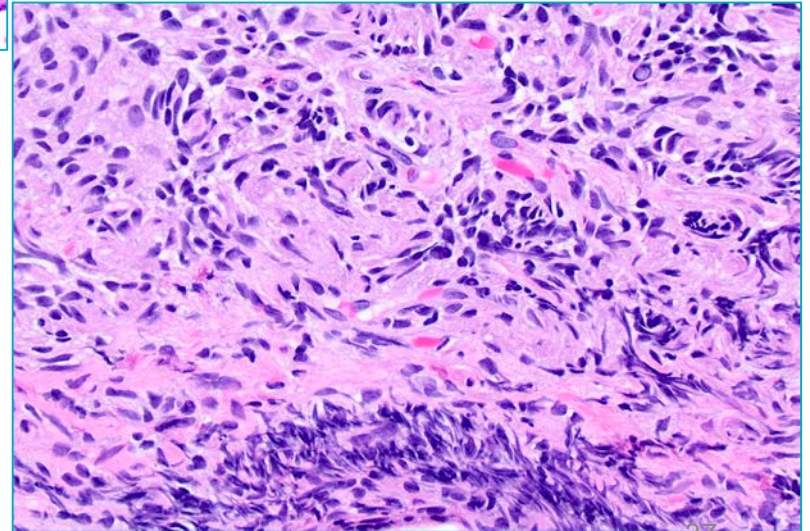
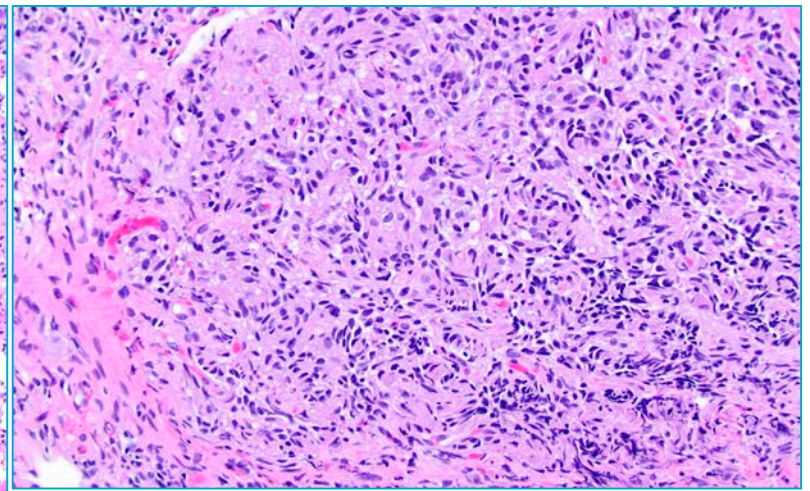
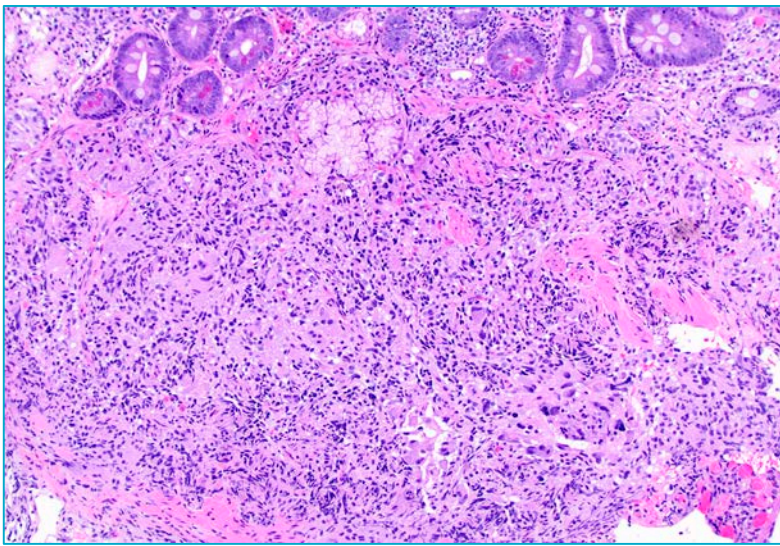
## Quiz 2

- 44 y.o. male
- EUS: 1.2 cm ampullary mass
- Biopsied





## Quiz 2

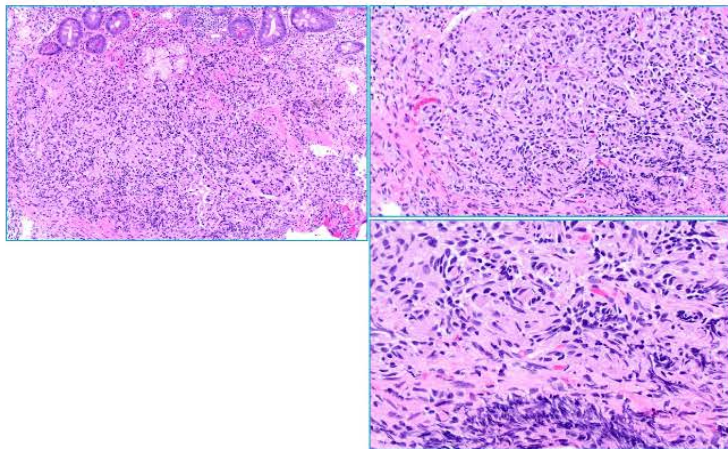


**What's your diagnosis?**

- A. Adenocarcinoma
- B. GIST
- C. Pancreatic heterotopia
- D. Neuroendocrine tumor



# What's your diagnosis?



A.  
Adenocarcinoma

B. GIST

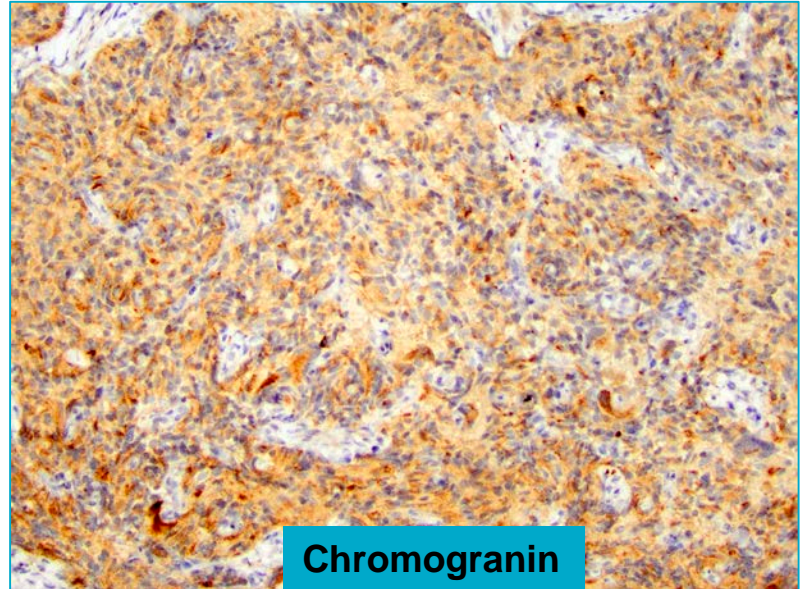
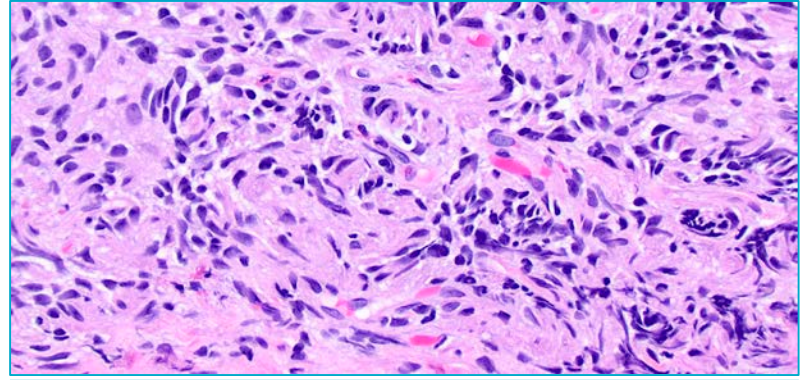
C. Pancreatic  
heterotopia

D.  
Neuroendocrine  
tumor

## Quiz 2 Answer

**What's your diagnosis?**

- A. Adenocarcinoma
- B. GIST
- C. Pancreatic heterotopia
- D. Neuroendocrine tumor**



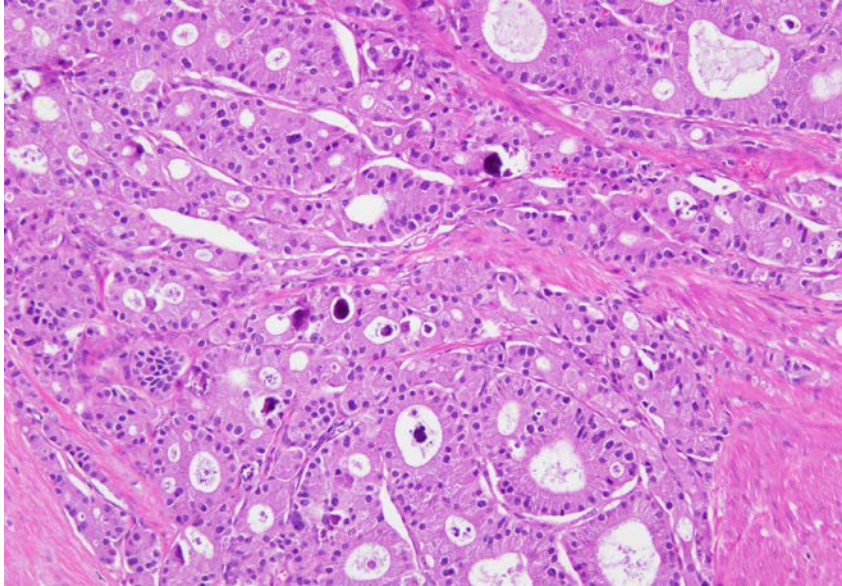
**Chromogranin**

# Ampullary Neoplasms: Other Than Adenoma/Adenocarcinoma

Epithelial	Mesenchymal
Neuroendocrine Neoplasms	GIST
• Somatostatinoma	Lipoma
• Gangliocytic Paraganglioma	Neurofibroma, ganglioneuroma
MINEN	Rhabdomyosarcoma, Kaposi sarcoma

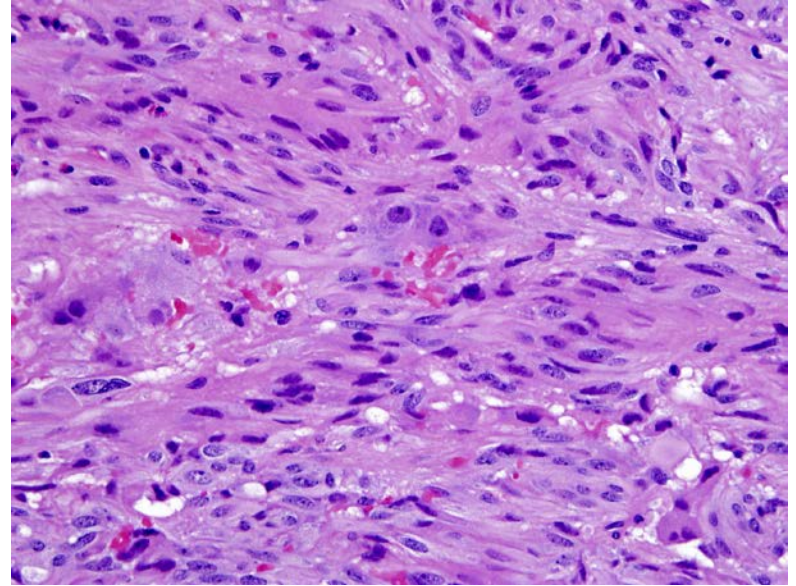


# Ampullary NEN with Distinctive Features



**Somatostatinoma**

*Photo courtesy of Dr. Christina Arnold, Ohio State University*



**Gangliocytic  
paraganglioma**

# Pearls from Ampullary Bx Case Studies

- **Recognize other tumors near ampulla – GIST, NEN, etc**
  - Keep broad differentials more than adenoma/adenocarcinoma
- **Write careful note to ampullary mass bx diagnosis**
  - Acknowledge limitations (fragmentation, crush/cautery artifacts, prior procedure changes)
  - May not be representative of the entire lesion
  - Deepers, IHC, show around
  - Ask for clinical correlation

# References

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