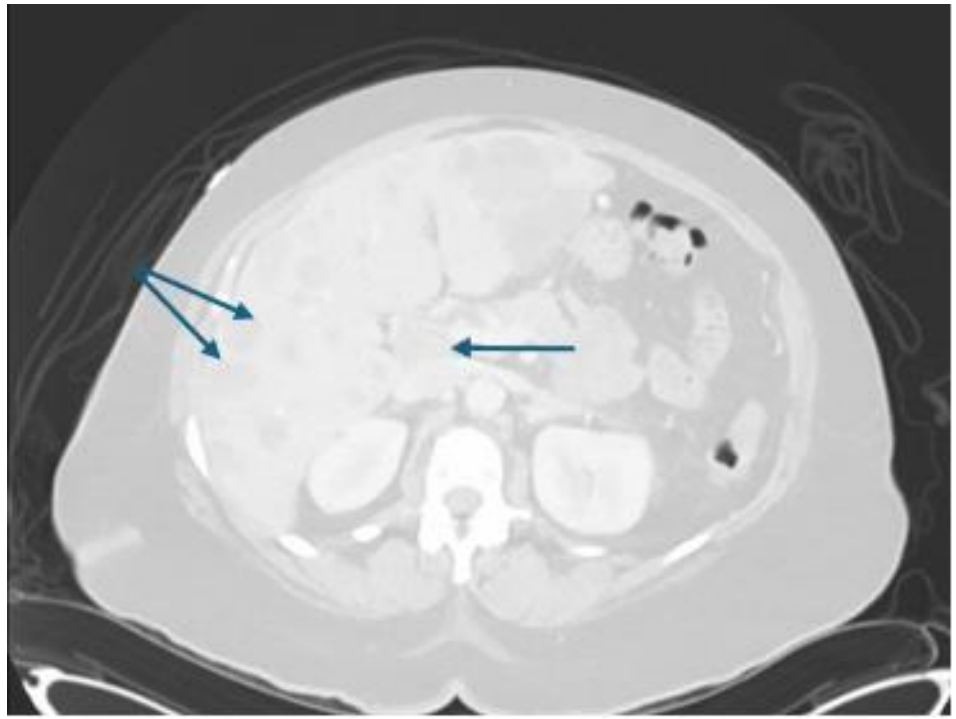
Case of the month
January 2026

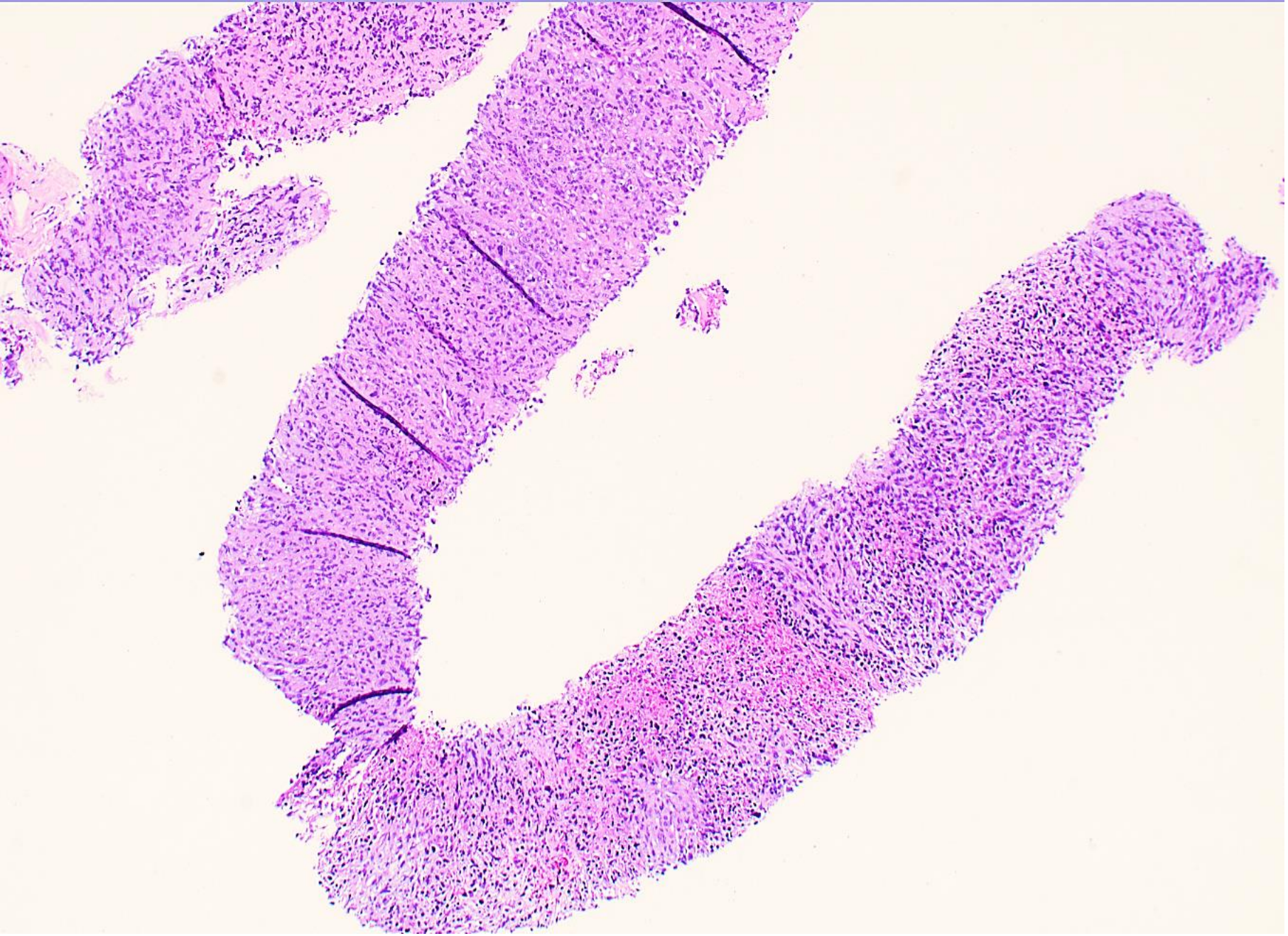
Sonal Italiya, MD (Pathology Resident, PGY-3)

Shaimaa Elzamly, MD, PhD (Assistant Professor)

Clinical Presentation

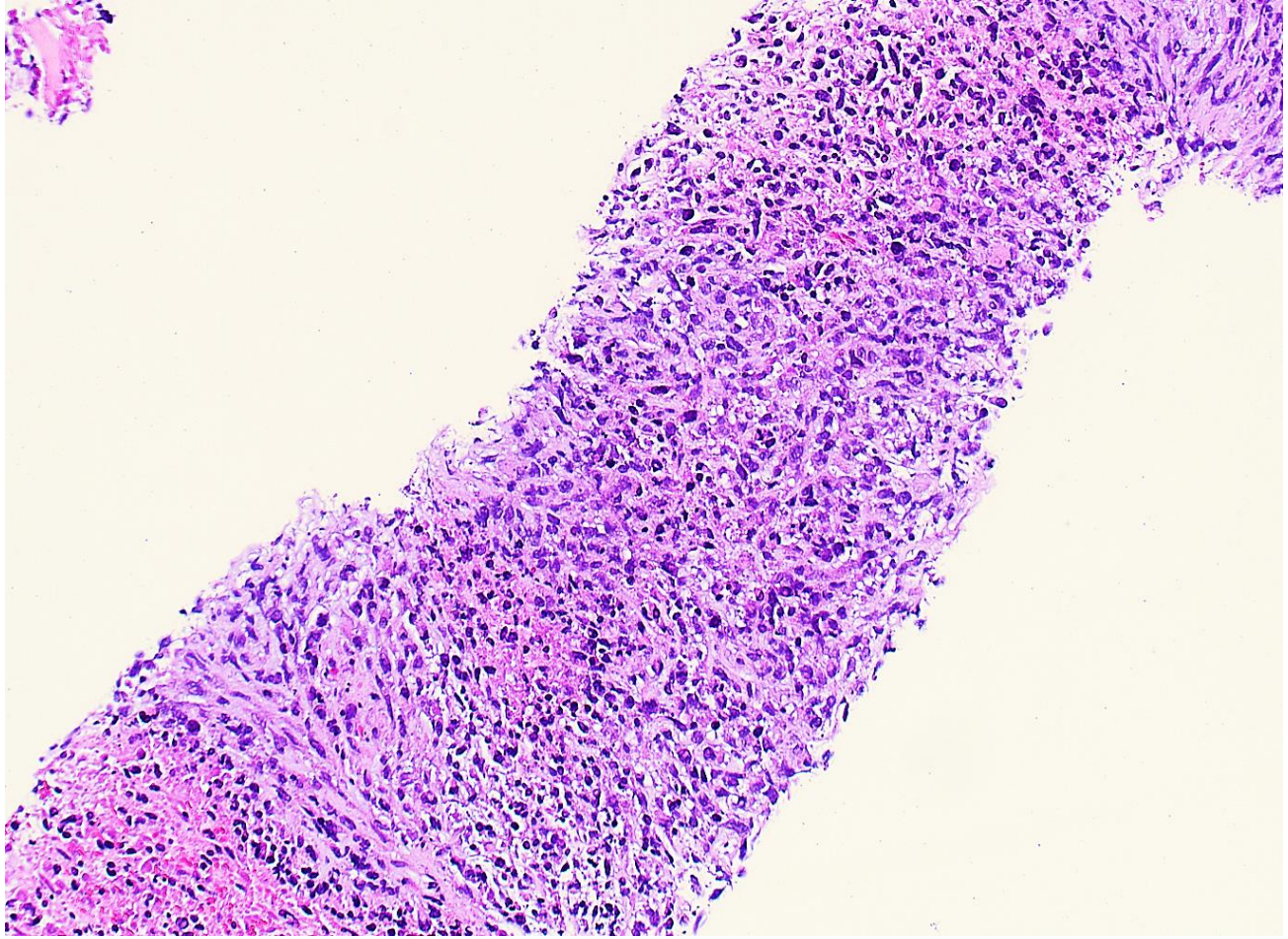
- An 80-year-old woman presented with persistent upper abdominal pain for two months, accompanied by early satiety, unintentional weight loss (10–12 lbs), occasional bloody stool, and severe weakness, without jaundice.
- An imaging revealed a large, heterogeneous mass centered in the pancreatic body, measuring approximately 6.7 × 4.0 cm, with pancreatic duct dilation.
- Additionally, splenic vein occlusion, portocaval lymphadenopathy, multiple liver metastases, and incidental pulmonary emboli were also identified. Serum CA 19-9 was markedly elevated (676,843 U/mL).
- Endoscopic ultrasound demonstrated an irregular hypoechoic mass in the body and tail of the pancreas, and a fine needle biopsy (FNB) of the pancreatic mass and liver mass was performed.

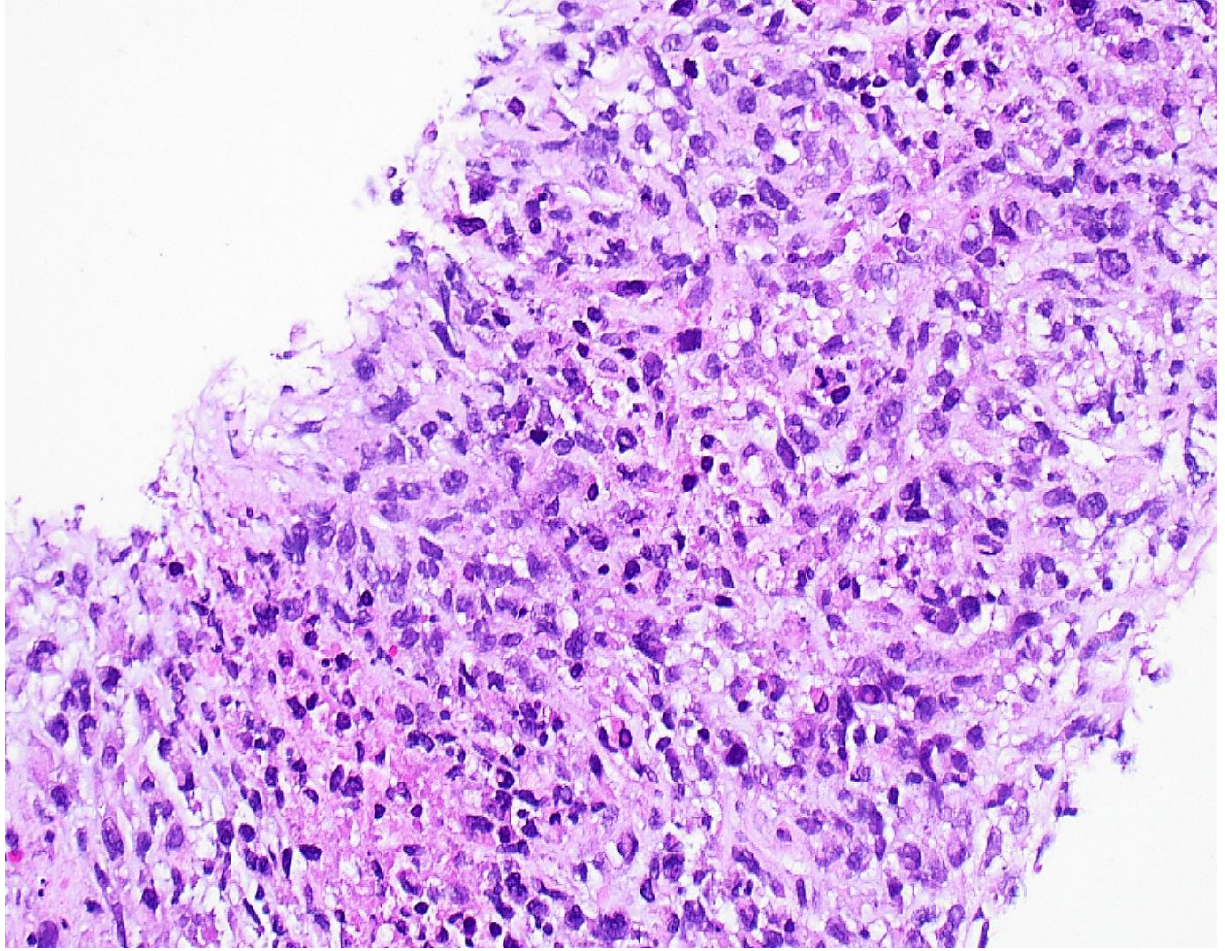




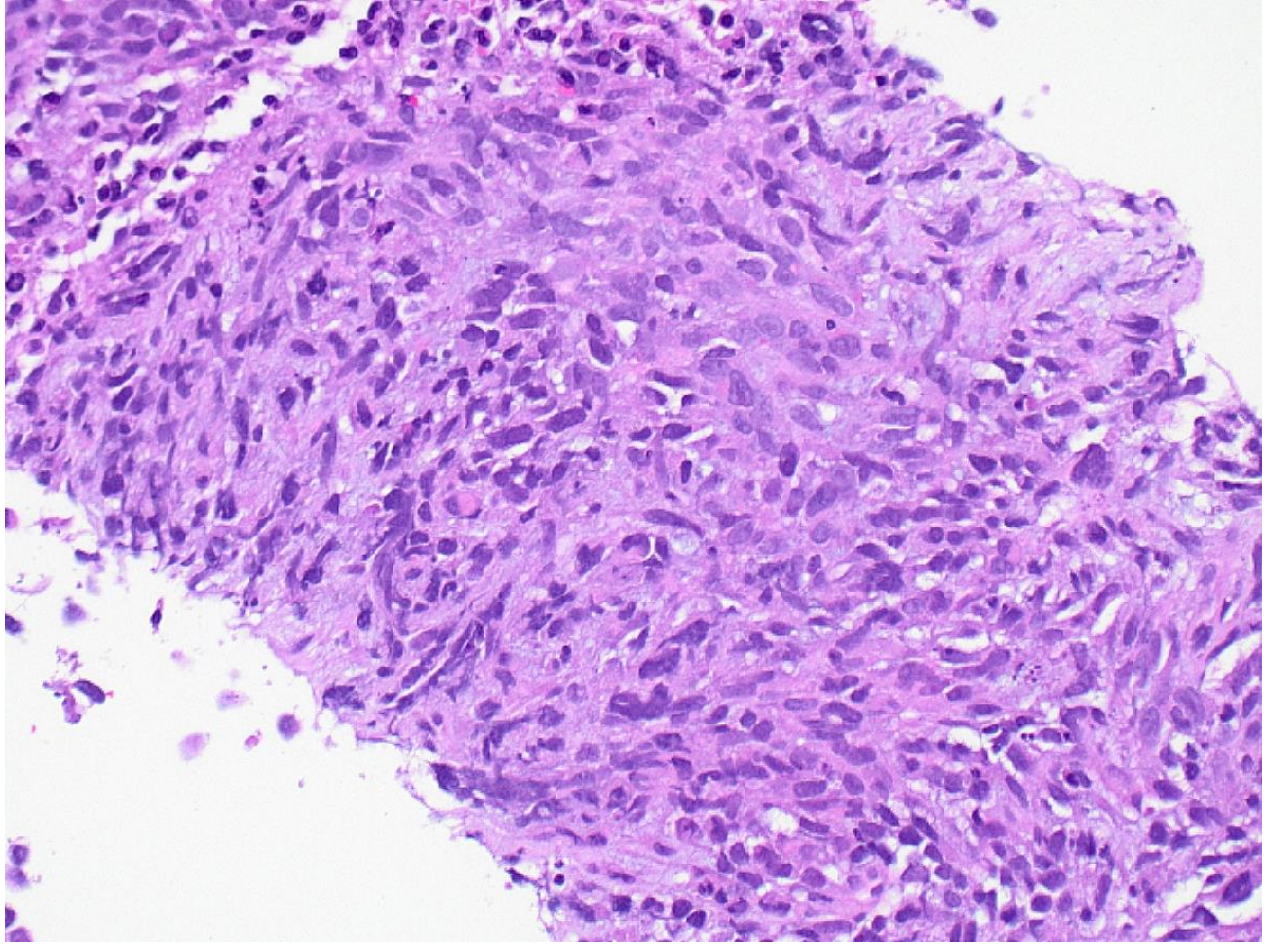
The pancreas mass biopsy (H&E,4x) shows :

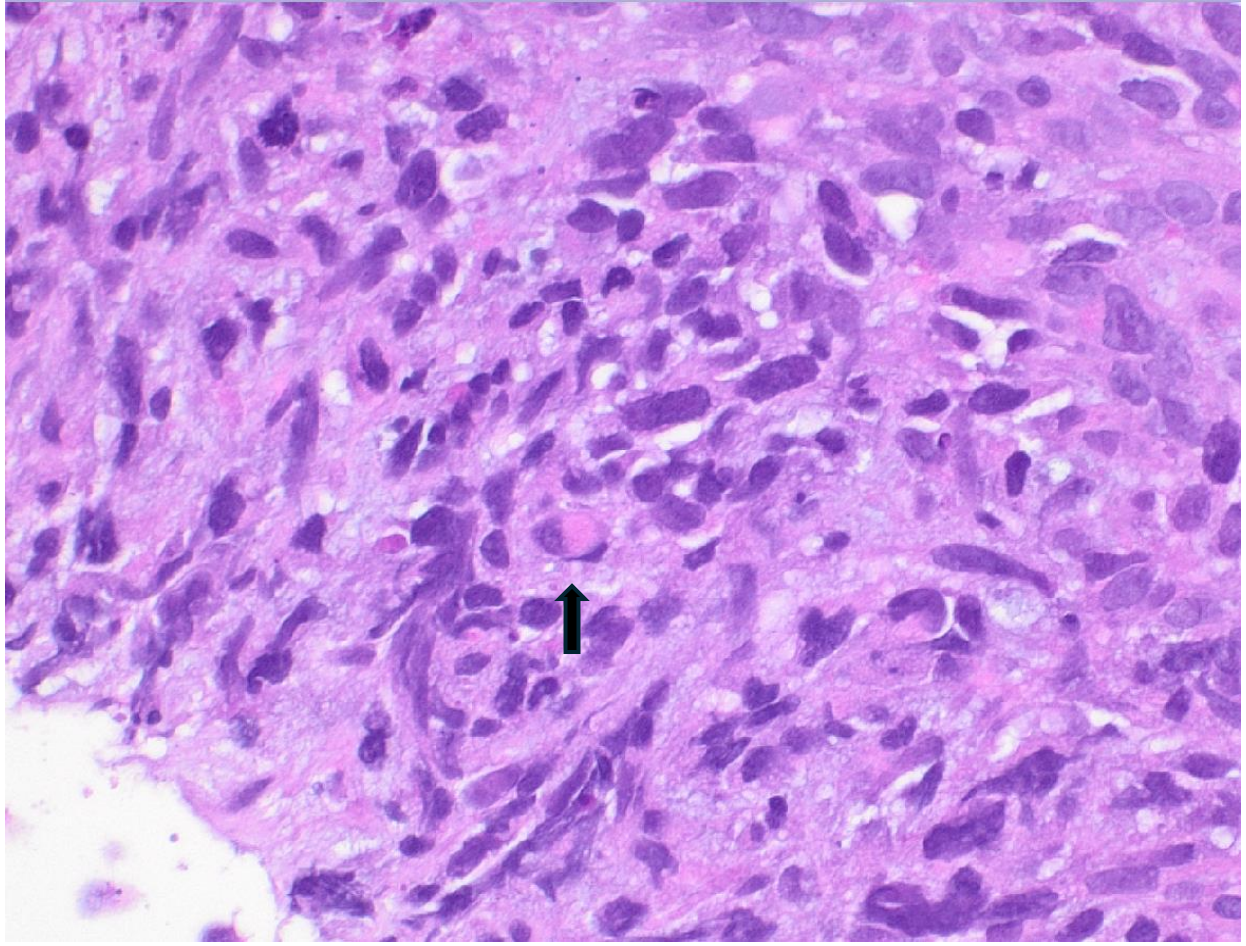
- Hypercellular tumor with a small amount of stroma
- Predominantly sarcomatoid pattern with pleomorphic undifferentiated tumor cells
- Areas with focal rhabdoid features and absence of osteoclastic giant cells



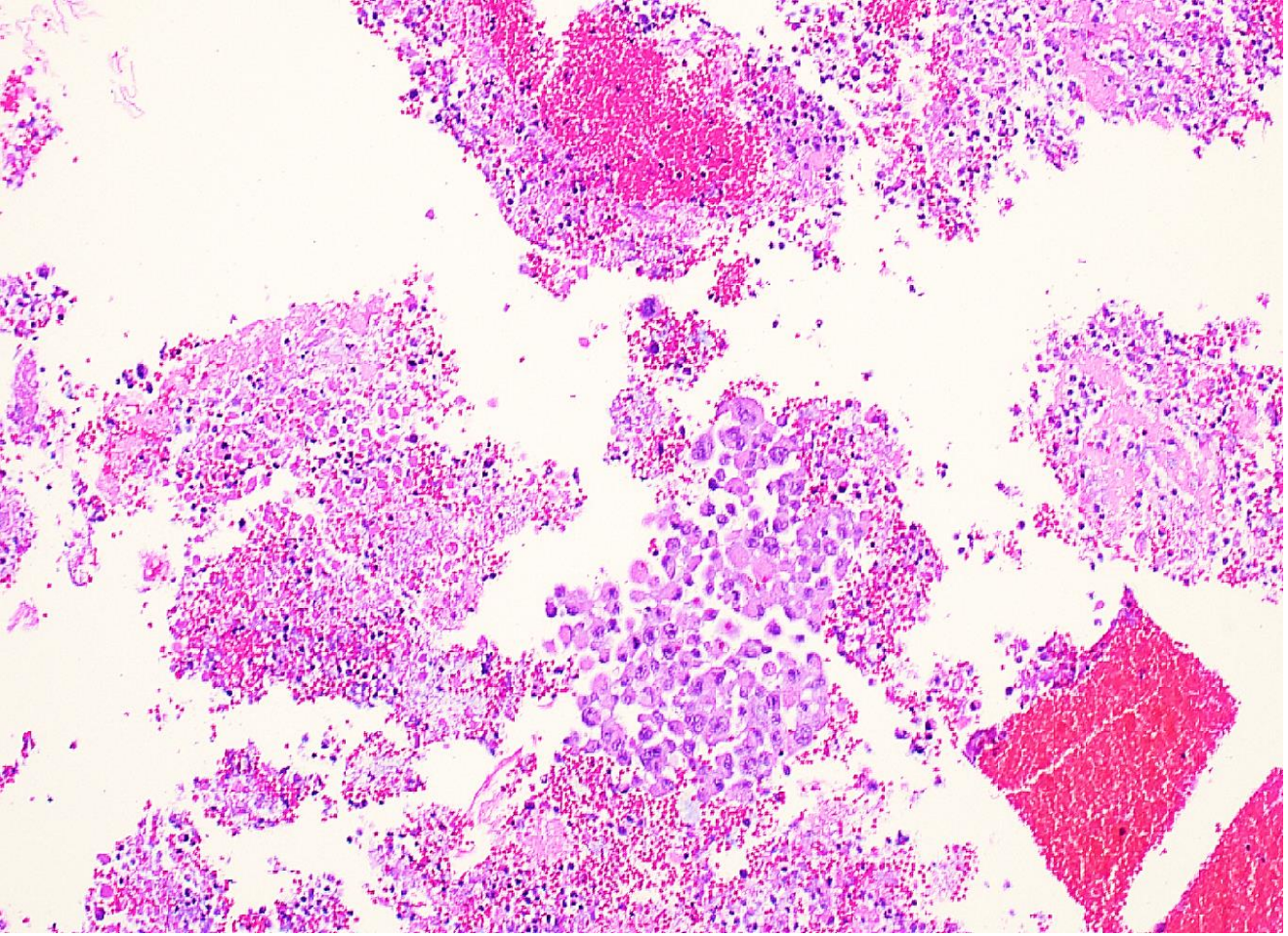


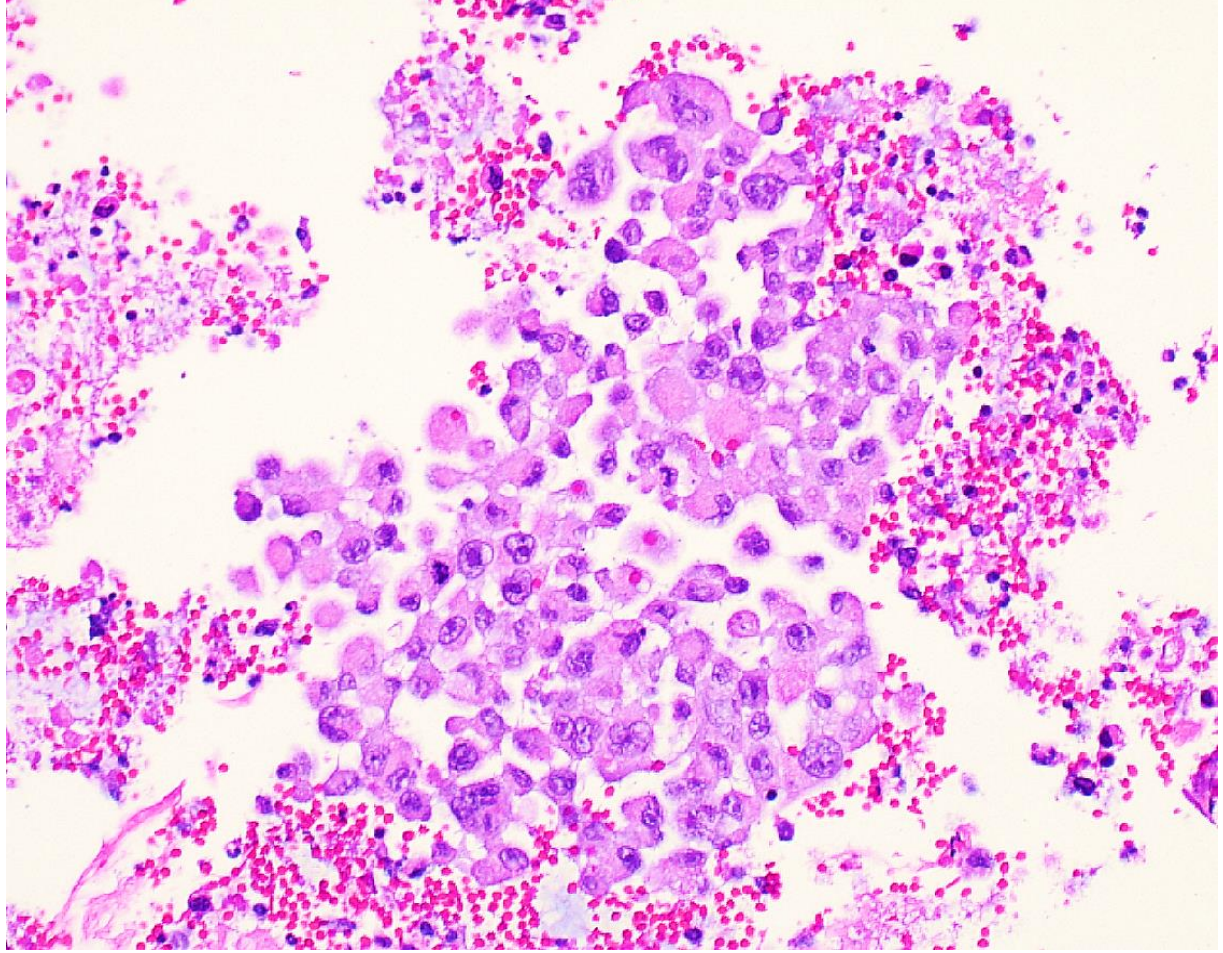
The pancreas mass biopsy (H&E,10x & 20x) shows an undifferentiated tumor with extensive necrosis and high mitotic activity



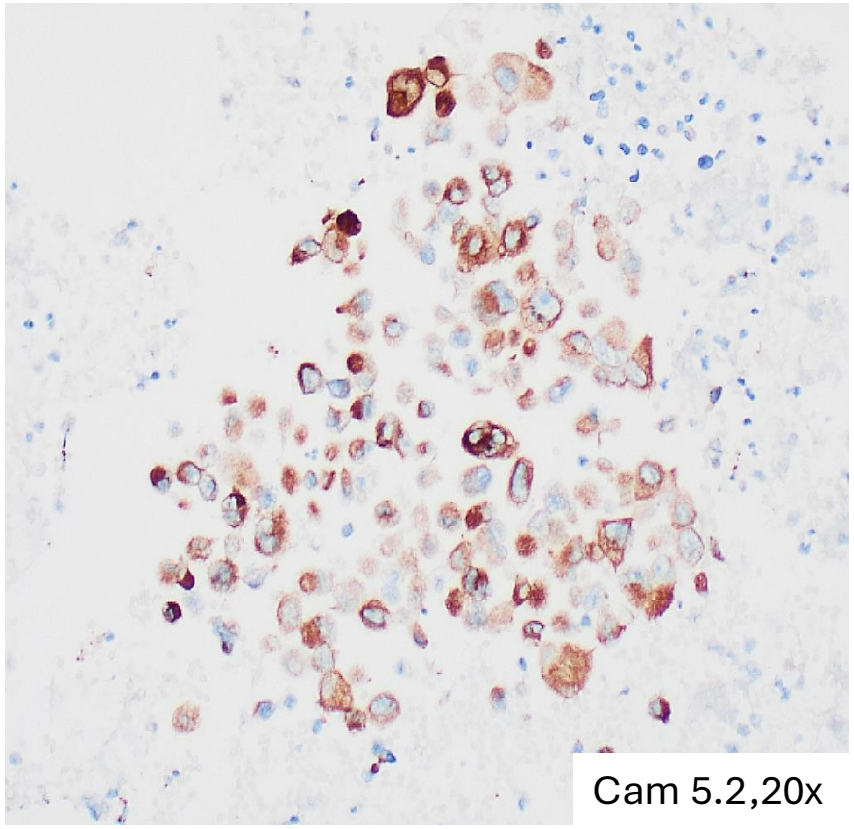


The pancreas mass biopsy (H&E,20x & 40x) shows tumor cells with focal rhabdoid morphology (arrow)

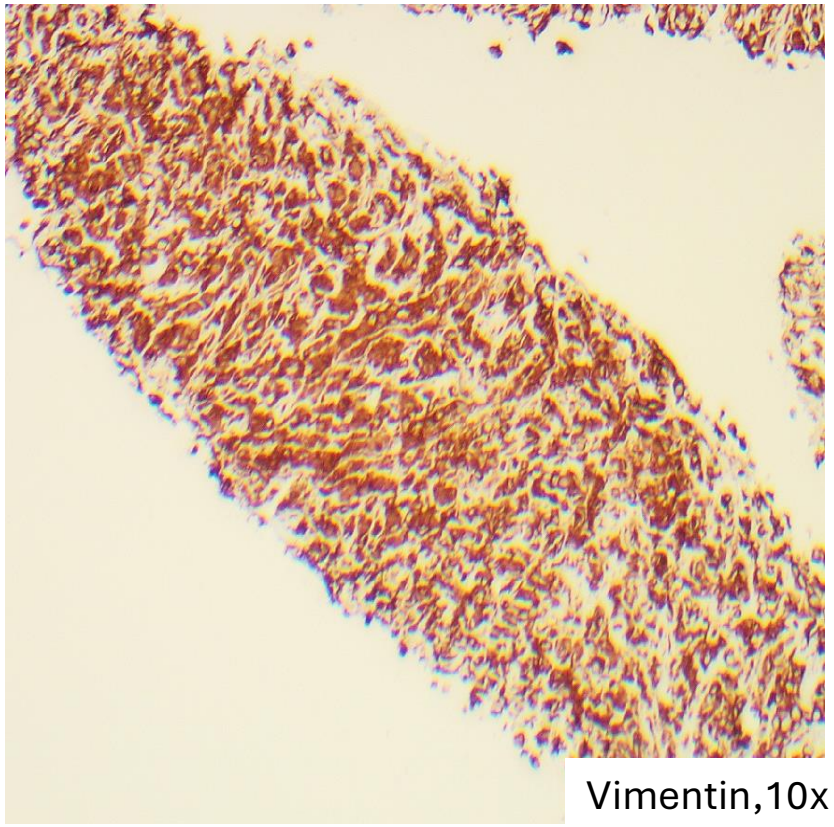




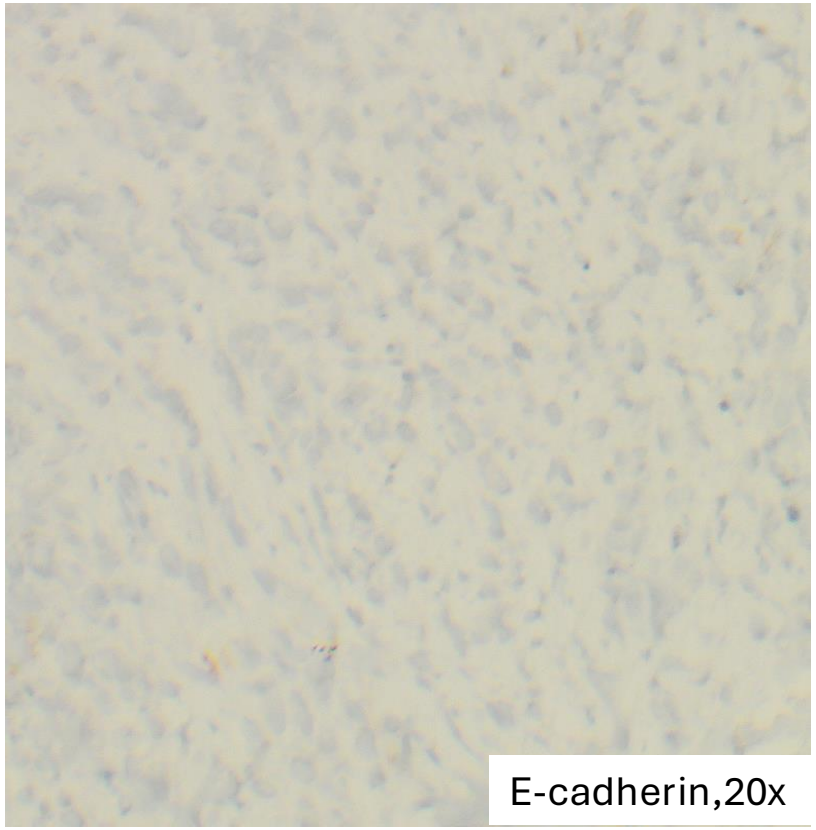
The liver mass biopsy (H&E,20x & 40x) shows tumor cells with rhabdoid features



Cam 5.2,20x

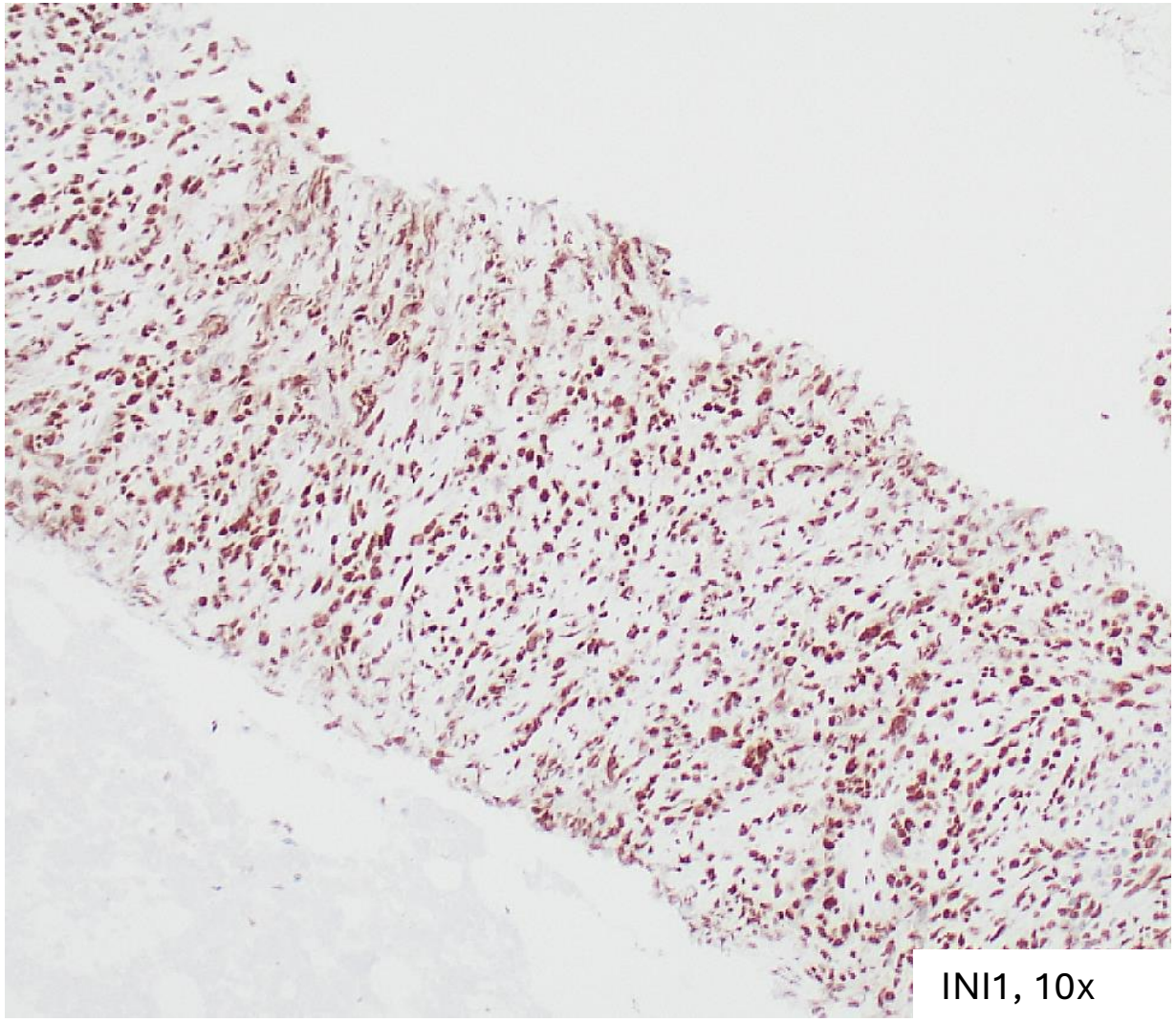


Vimentin,10x

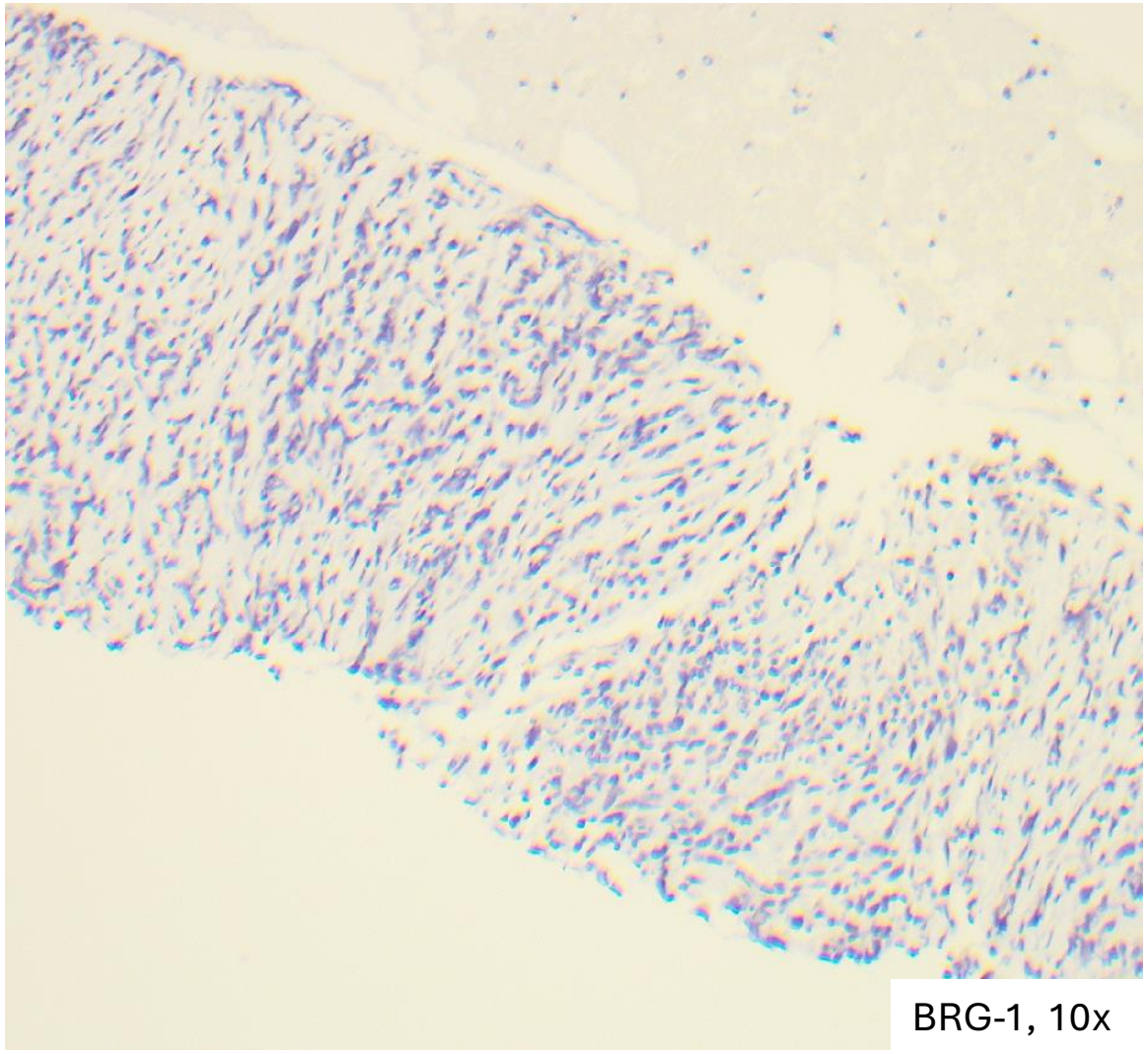


E-cadherin,20x

Pancreas mass biopsy shows tumor cells are diffusely positive for CAM5.2 and vimentin.
E-cadherin is lost.



INI1, 10x



BRG-1, 10x

Pancreas mass biopsy shows tumor cells with retained INI1 and loss of BRG-1 expression

Q: An 80-year-old woman undergoes fine-needle biopsy of a pancreatic mass. Which of the following statements accurately describes SMARCA4-deficient undifferentiated pancreatic carcinoma?

A) It lacks gland formation, has minimal stroma, and exhibits more aggressive behavior
B) It is strongly associated with rhabdoid morphology
C) It carries the worst prognosis and is highly prone to recurrence and metastasis
D) Novel therapeutic options include immune checkpoint inhibitors, EZH2 inhibitors, and SMARCA2 degraders
E) All of the above.

Answer: E) All of the above.

Explanation: SMARCA4-deficient undifferentiated pancreatic carcinoma (UPC) is an exceptionally rare and poorly understood subtype of pancreatic cancer, defined by loss of the SMARCA4 gene, which encodes the BRG1 protein, and characterized by highly aggressive behavior.

Please see the attached images for more context.

- Undifferentiated pancreatic carcinoma (UPC) is a rare, aggressive epithelial malignancy lacking glandular differentiation or desmoplastic reaction. It frequently exhibits rhabdoid morphology.
- According to the WHO classification, UPC subtypes include anaplastic, rhabdoid, sarcomatoid, and carcinosarcoma subtypes.
- Unlike classic pancreatic ductal adenocarcinoma (PDAC), UPC typically demonstrates scant stroma, frequent KRAS-wild-type status, and a significantly worse prognosis.
- Recent research emphasizes the role of SWI/SNF (Switch/Sucrose Non-Fermentable) chromatin remodeling complex, particularly SMARCA4 loss, in driving tumorigenesis and contributing to poor clinical outcomes.

- However, SMARCA4-deficient UPC remains extremely uncommon, with limited case documentation, highlighting the need for increased recognition and development of targeted therapies.
- Current management relies primarily on surgery and conventional chemotherapy, which offer limited benefits. Emerging evidence suggests potential responsiveness to immune checkpoint inhibitors in PD-L1–high tumors, especially in SWI/SNF-deficient cancers. Investigational strategies include EZH2 inhibitors and SMARCA2 degraders.
- Routine immunohistochemical staining for SMARCA4, SMARCA2, and SMARCB1 is recommended in pancreatic tumors with rhabdoid morphology to identify SWI/SNF-deficient variants.
- Future research should aim to clarify the molecular basis of site-specific differences, investigate the interactions among co-occurring mutations, and evaluate the therapeutic potential of other members of the SWI/SNF family.

References:

1. Yavas A, Ozcan K, Adsay NV, Balci S, et al; SWI/SNF Complex-Deficient Undifferentiated Carcinoma of the Pancreas: Clinicopathologic and Genomic Analysis. Mod Pathol. 2024 Nov;37(11):100585. doi: 10.1016/j.modpat.2024.100585. Epub 2024 Jul 31. PMID: 39094734; PMCID: PMC11585460.

2. Armstrong SM, Dickson BC. SMARCA4 / BRG1 . PathologyOutlines.com website.https://www.pathologyoutlines.com/topic/stainssmarca4brg1.html.

3. Pang, Chaoyua; Fan, Zhiyaoa; Su, Pengb; et al. An unrecognized undifferentiated tumor of the pancreas: a case report. Journal of Pancreatology 6(4):p 225-227, December 2023. | DOI: 10.1097/JP9.0000000000000132.

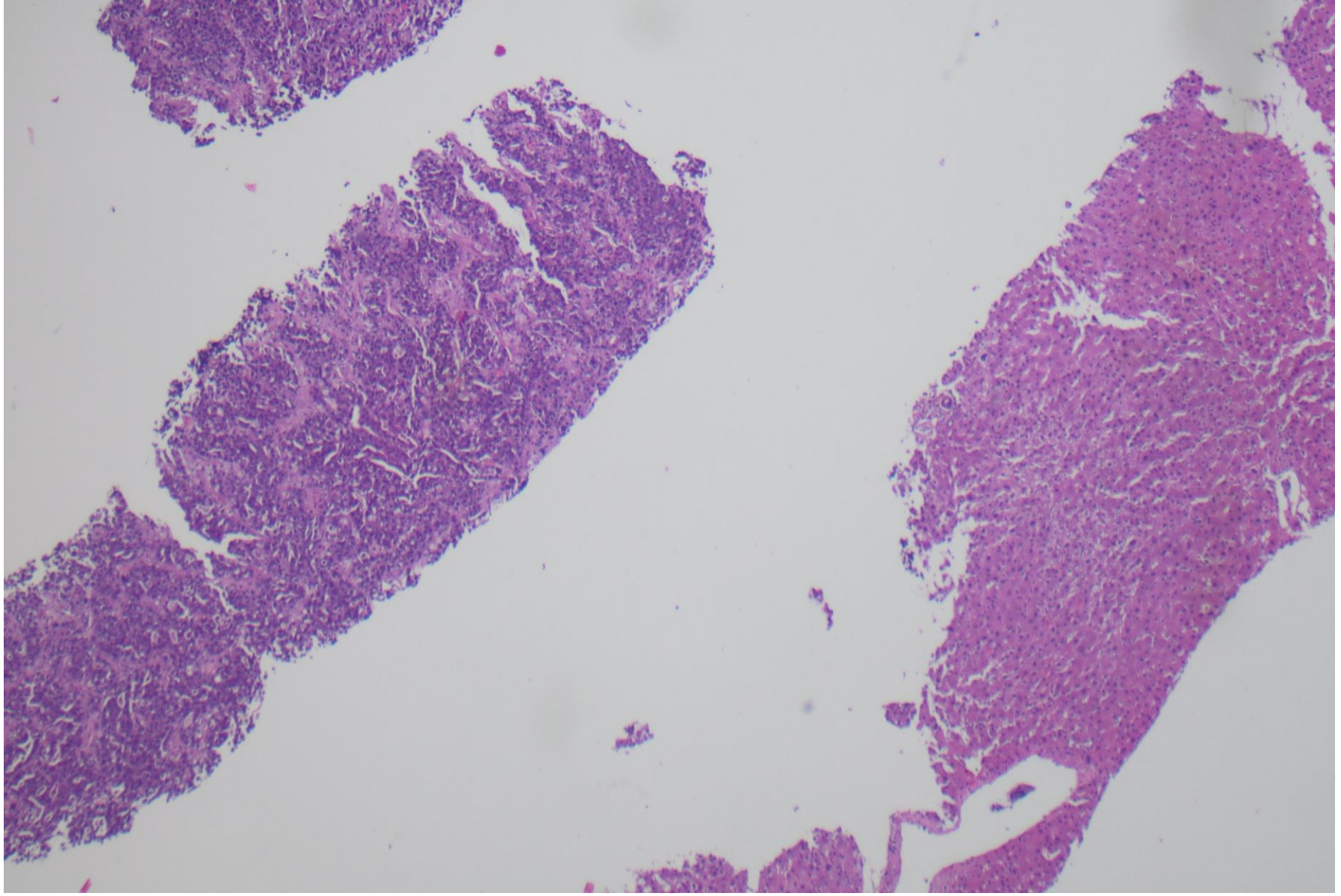
4. An HR, Kim HD, Ryu MH, Park YS. SMARCA4-deficient undifferentiated gastric carcinoma: a case series and literature review. Gastric Cancer. 2024 Sep;27(5):1147-1152. doi: 10.1007/s10120-024-01510-9. Epub 2024 May 22. PMID: 38772975.

Case of the month
February 2026

Hareem Hamza, MD (PGY2)

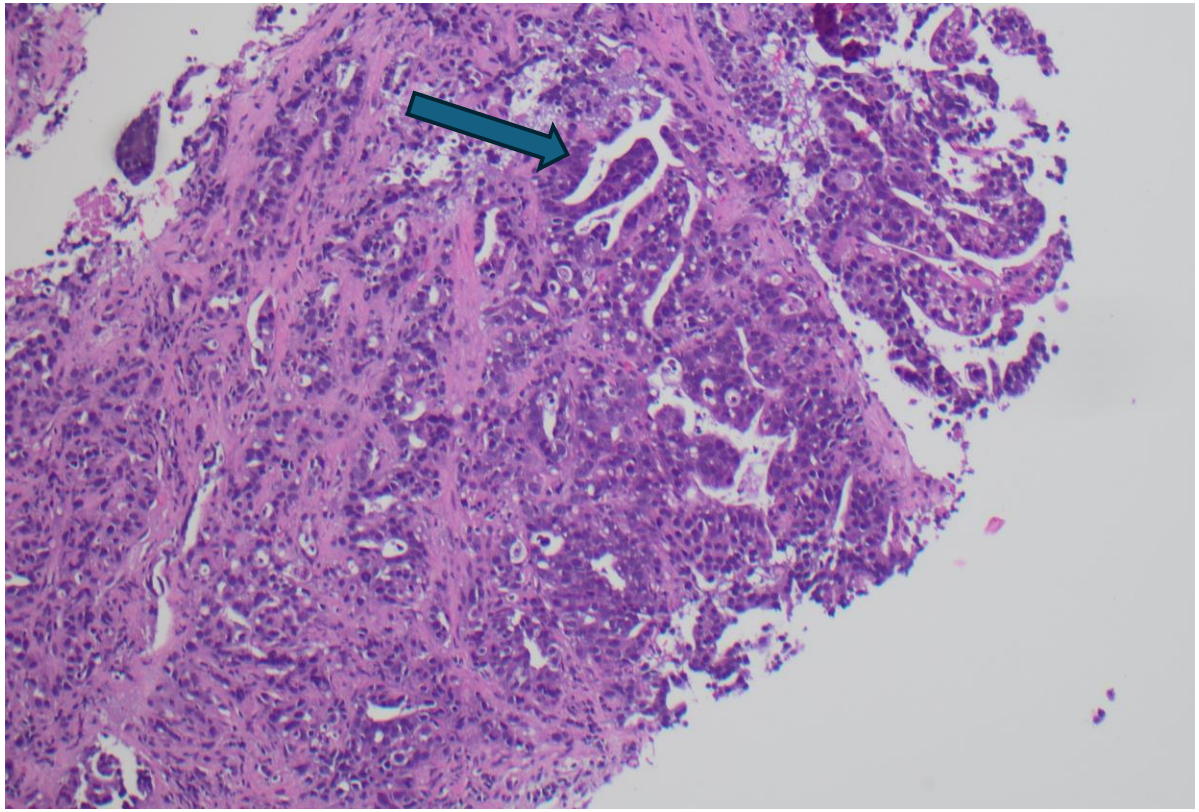
Celia Marginean, MD

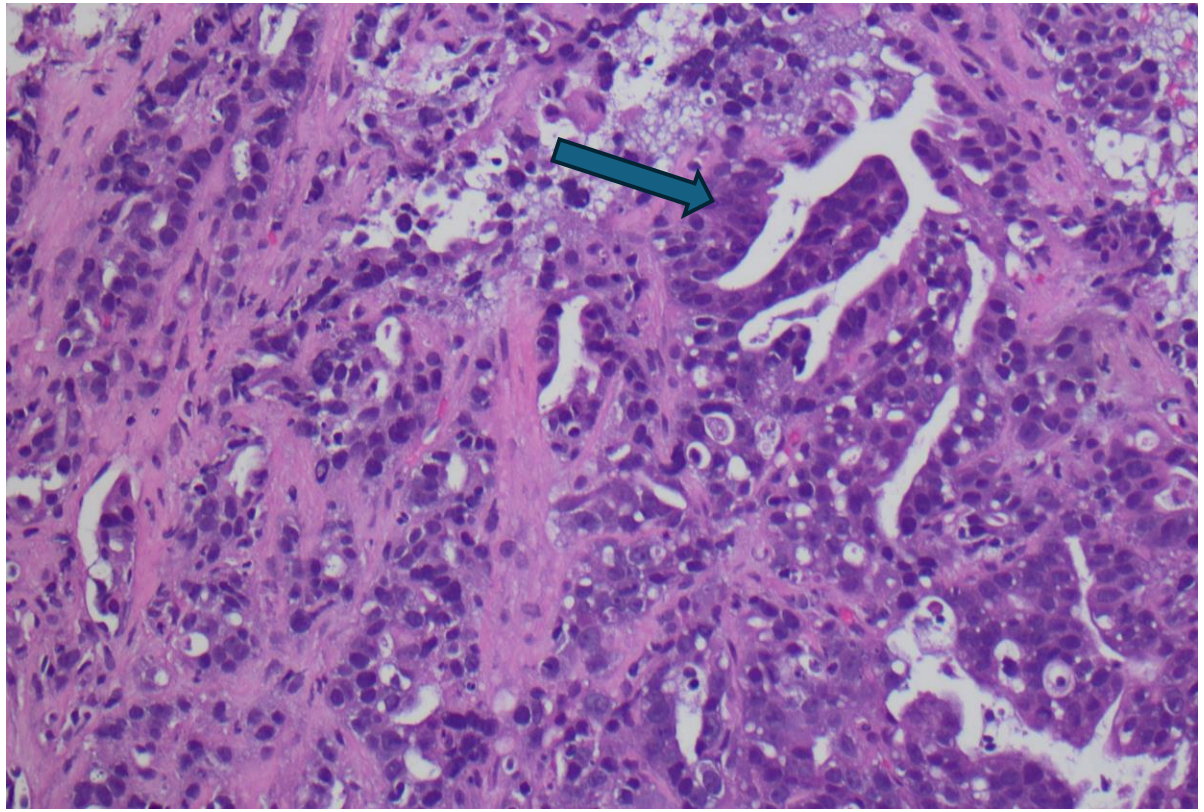
Baylor St. Lukes Hospital



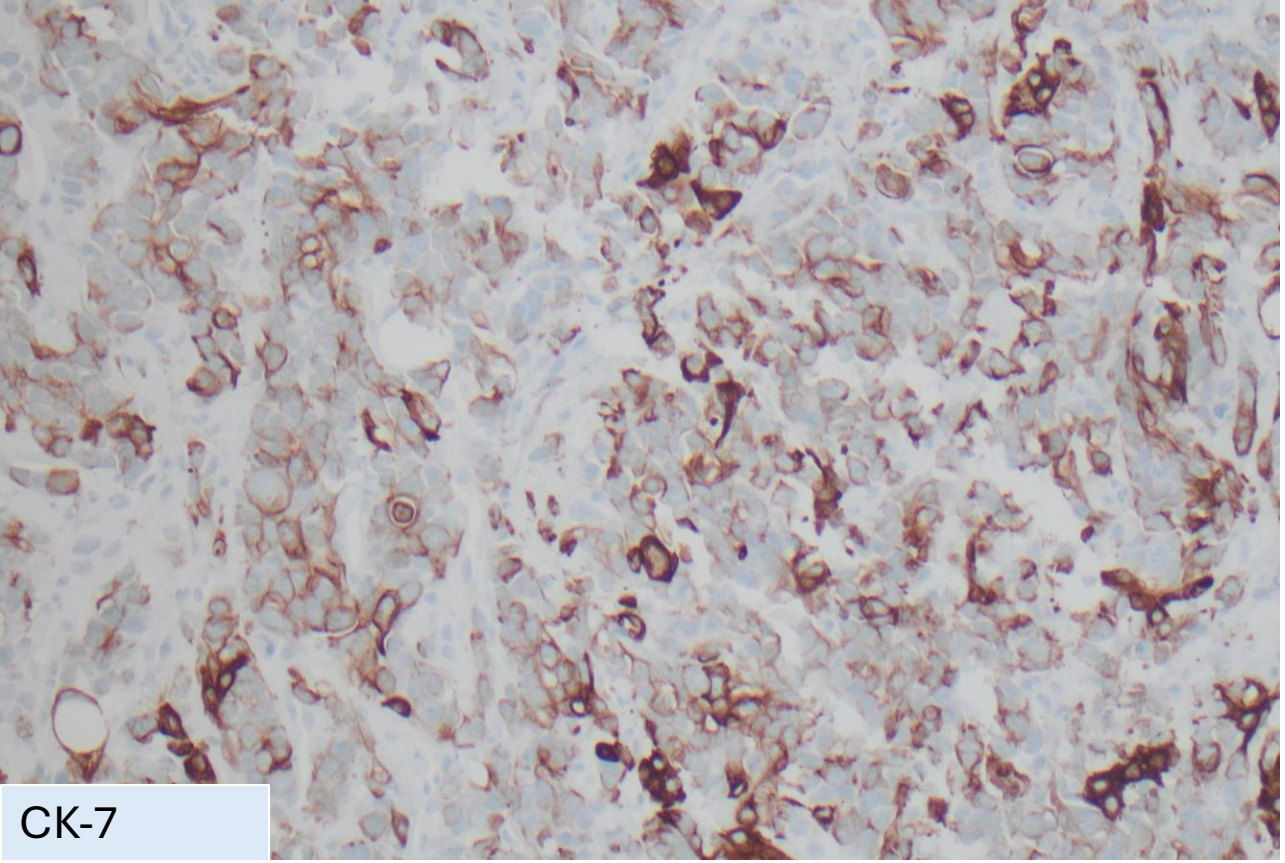
Ultrasound guided liver mass biopsy

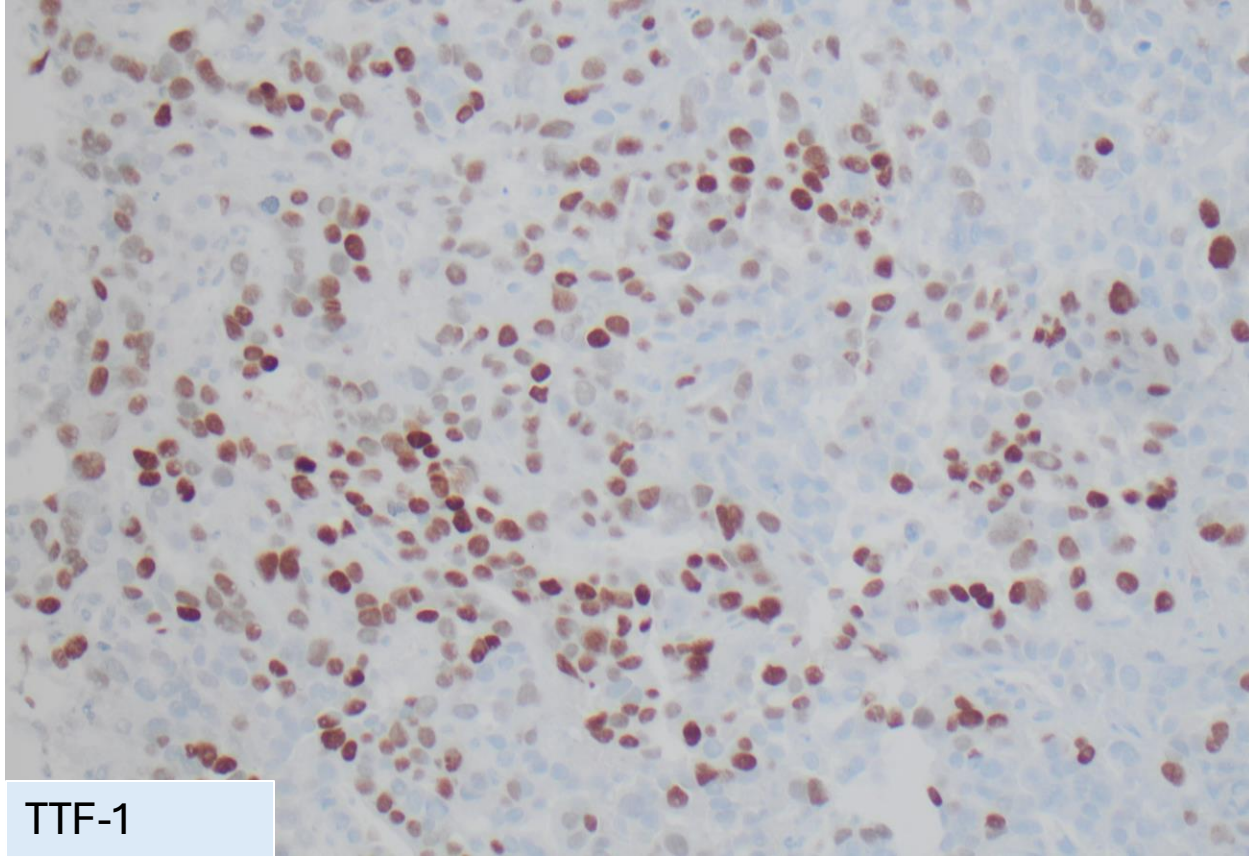
- *Liver mass biopsy (H&E, 4x): Infiltrative tumor with glandular architecture and background benign liver parenchyma*





Liver mass biopsy (H&E,10x and20x): On higher magnification the
mass show moderately differentiated adenocarcinoma, with focal papillary features (solid blue arrow)





Immunohistochemically the tumor shows moderate CK7 and TTF-1 expression in approximately 30% of tumor cells.

Final Diagnosis

- *Adenocarcinoma, moderately differentiated with focal papillary features*
- *IHC: CK7 (patchy) and TTF-1 (moderately positive in 30% of tumor cells)*

Comment:

- *Based on the immunohistochemical profile and morphologic features, the findings favor metastatic disease of pulmonary origin, supported by the moderate TTF-1 positivity. However, a metastasis from a pancreatobiliary primary (including extrahepatic cholangiocarcinoma) or from a gastrointestinal primary cannot be definitively excluded. Clinicoradiologic correlation is recommended, including upper and lower endoscopy as well as dedicated pancreatic imaging.*

Interval History

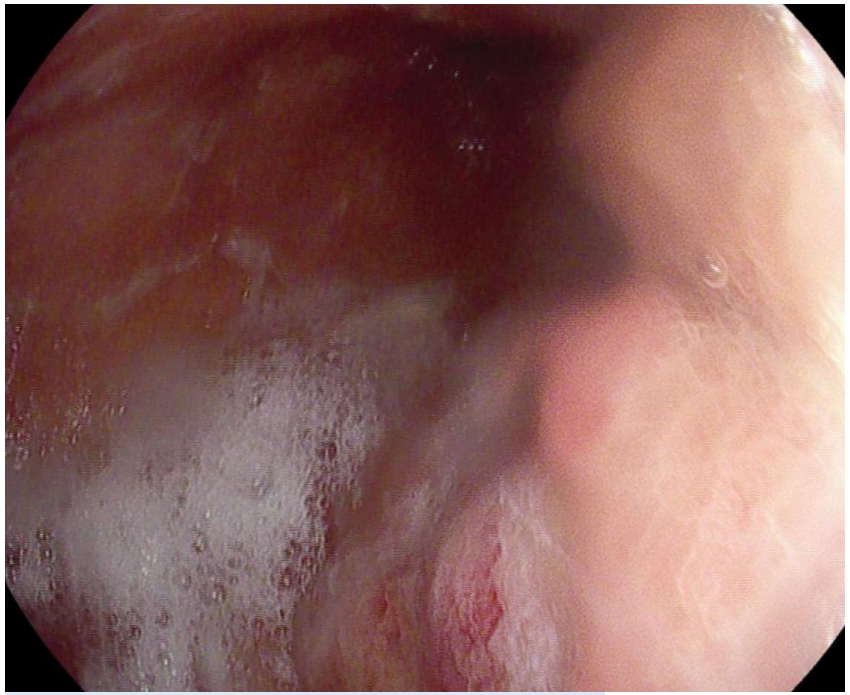
- Several days later, the patient presented to the emergency department with severe, intractable abdominal pain.

- The patient reported occasional dark specks in the stool but denied melena or hematochezia. He also endorsed a history of constipation.

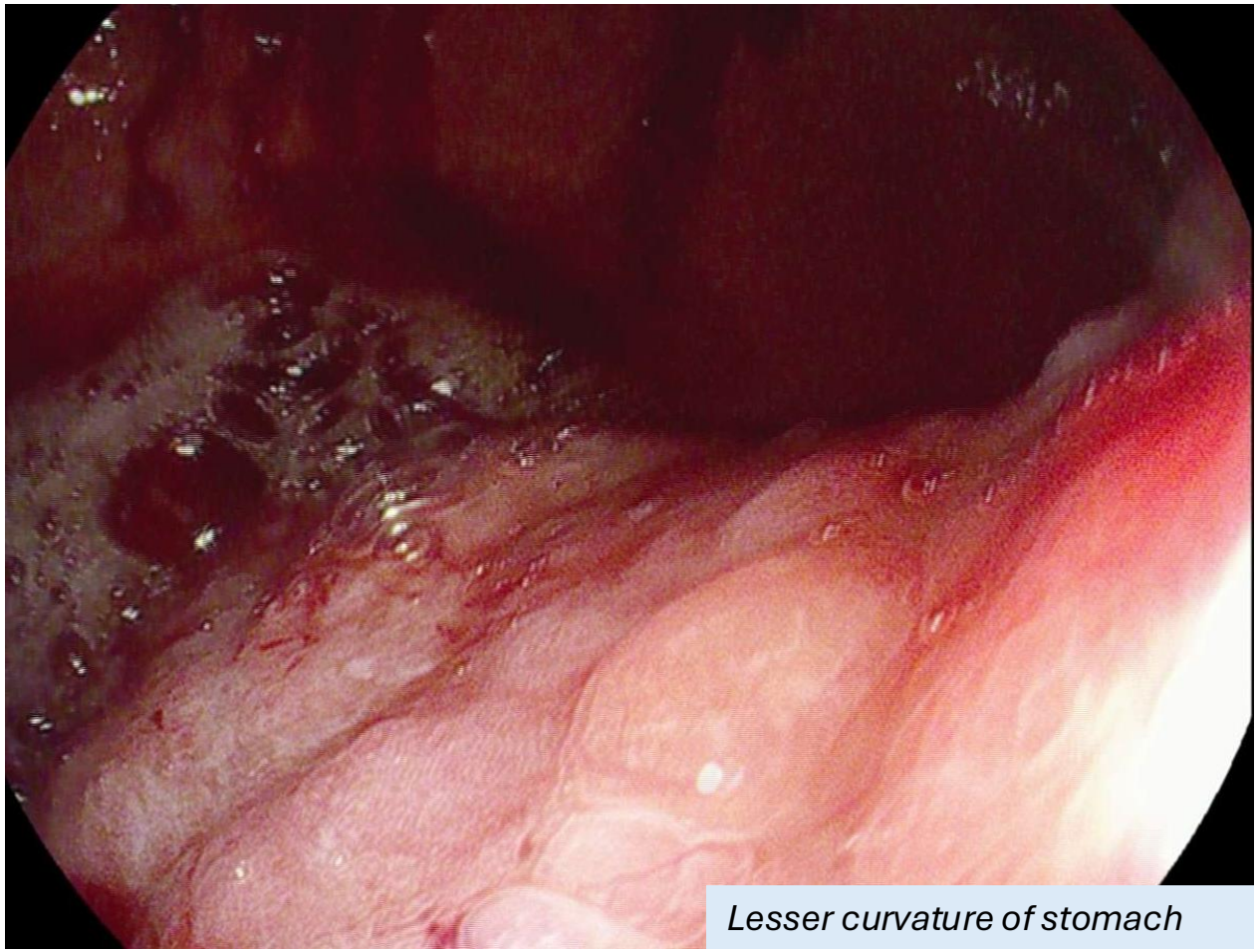
- Gastroenterology was consulted at the request of oncology for esophagogastroduodenoscopy (EGD) and colonoscopy to evaluate for a potential primary malignancy.

- ***Upper GI Endoscopy:***

A large, infiltrative, non-circumferential mass was identified along the lesser curvature of the stomach.



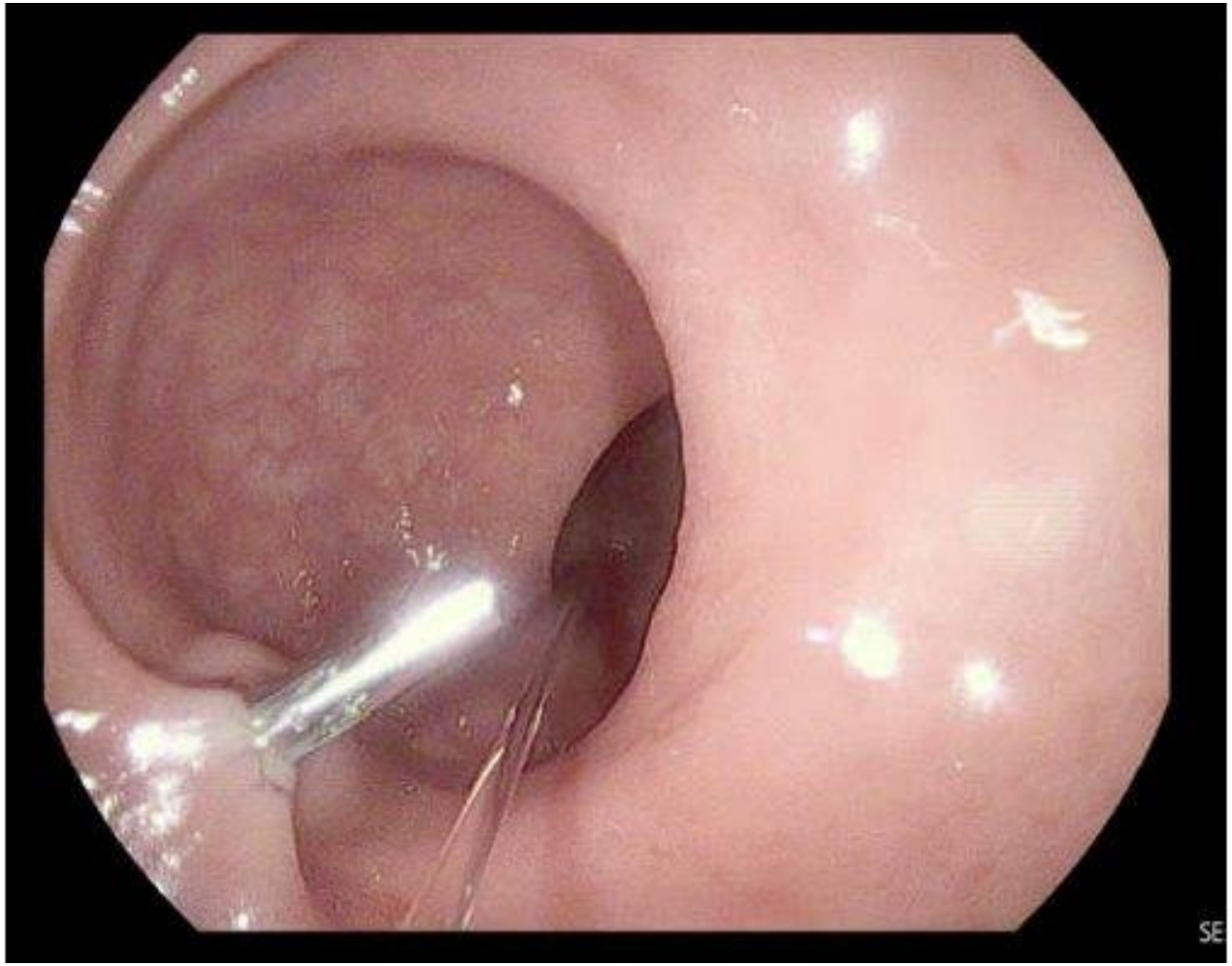
Lesser curvature of stomach



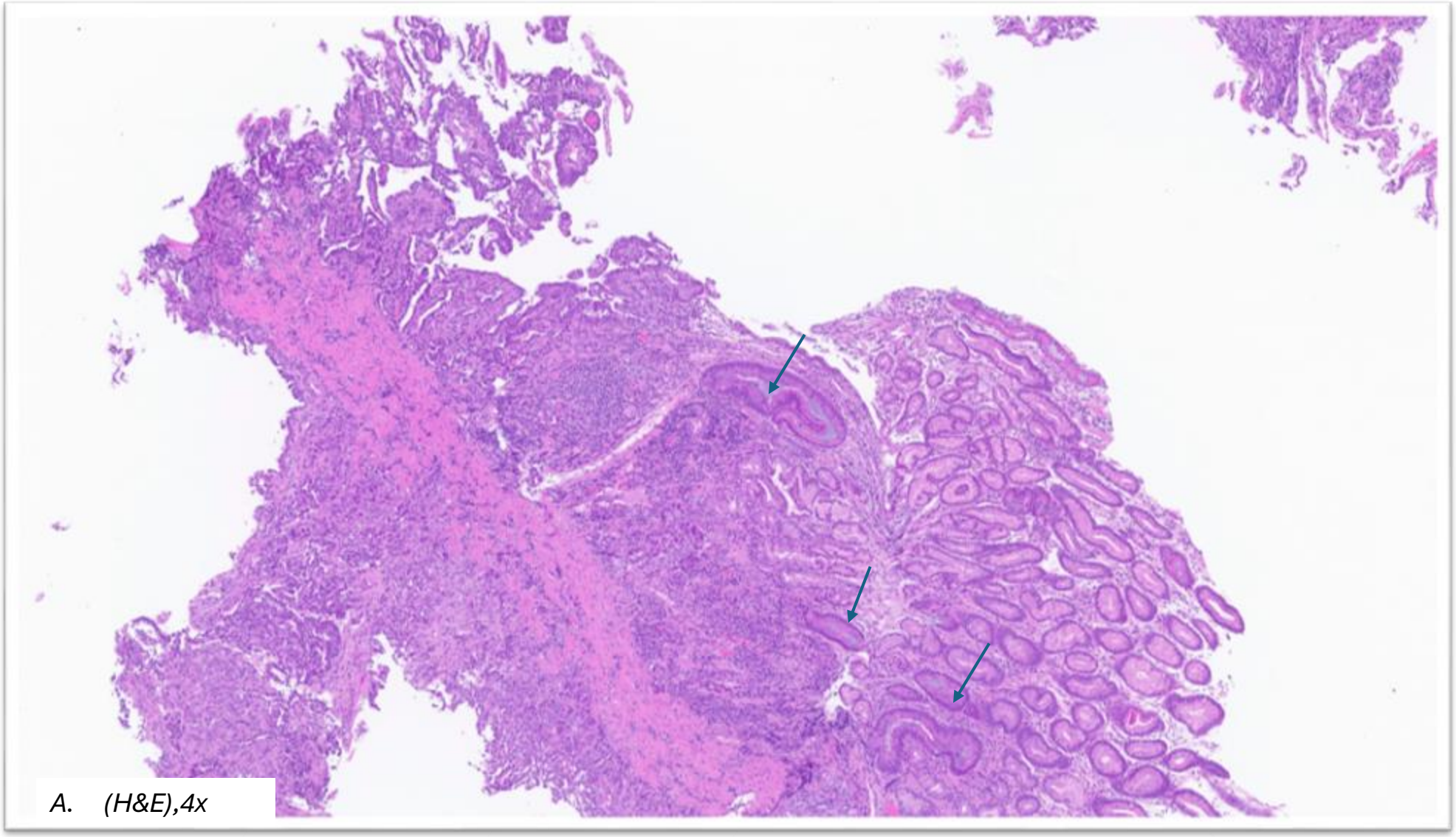
Lesser curvature of stomach

- ***Colonoscopy:***

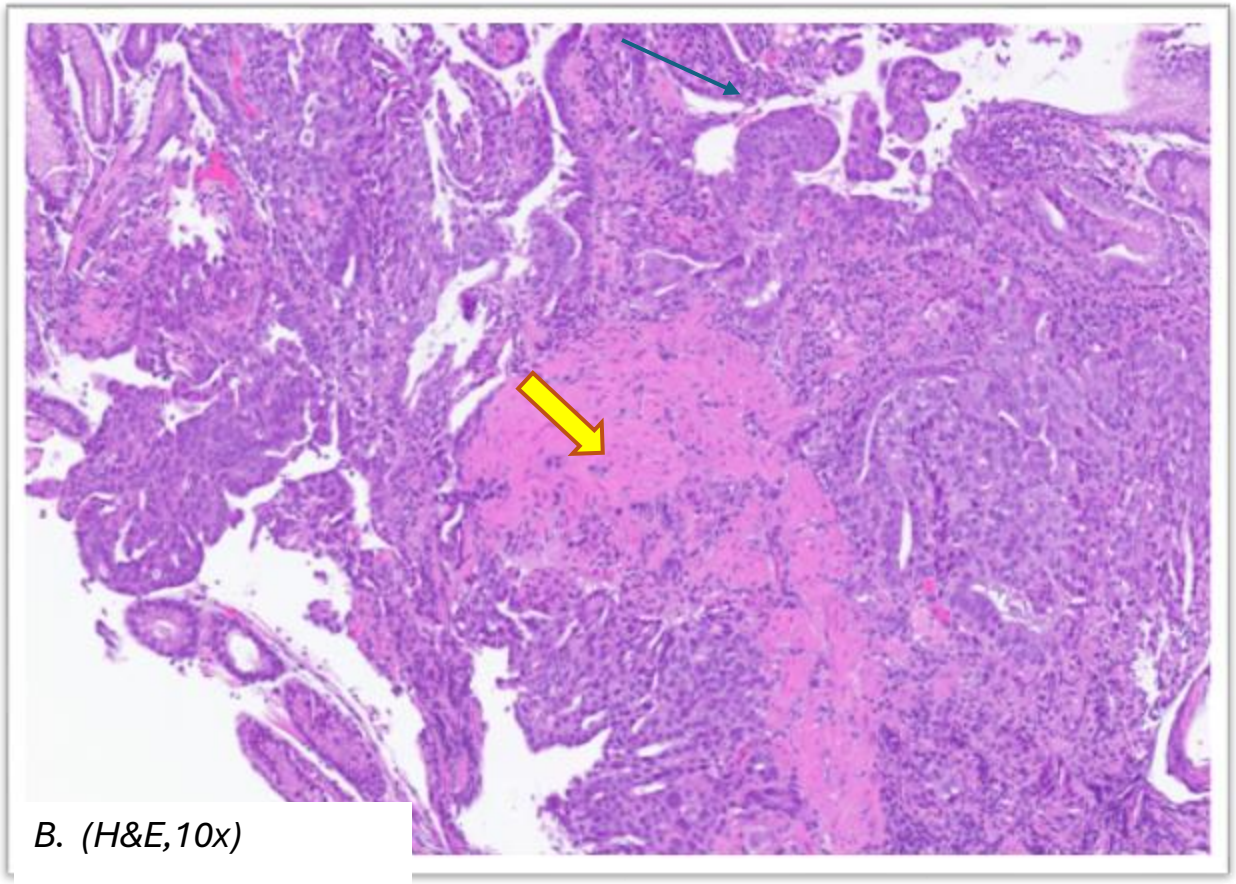
A 10 mm semi-pedunculated polyp was identified in the rectum.



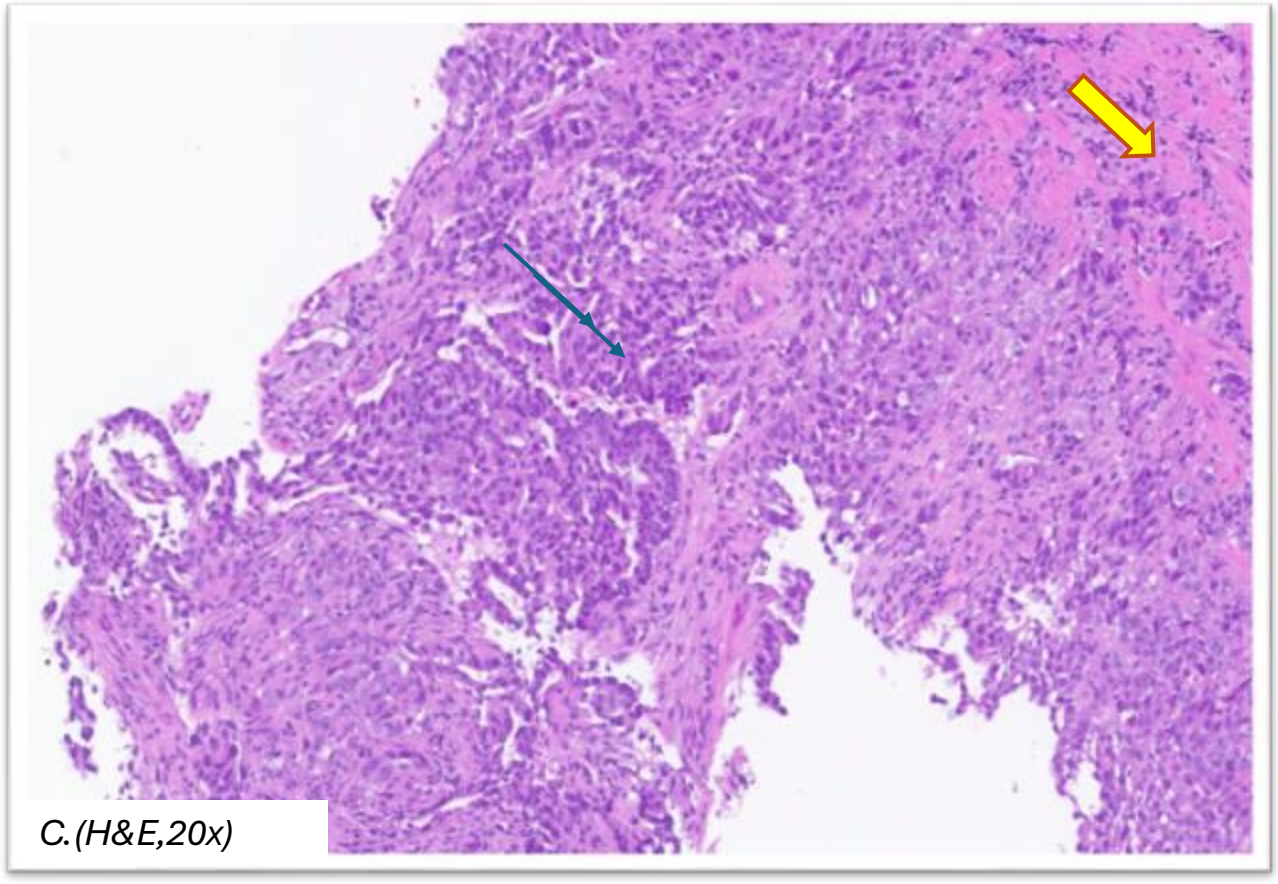
Stomach mass biopsy



A .*The biopsy of the body mass shows an infiltrating tumor arising in a background of intestinal metaplasia (Blue arrow). The tumor infiltrates below muscularis mucosae into submucosa (at least).*

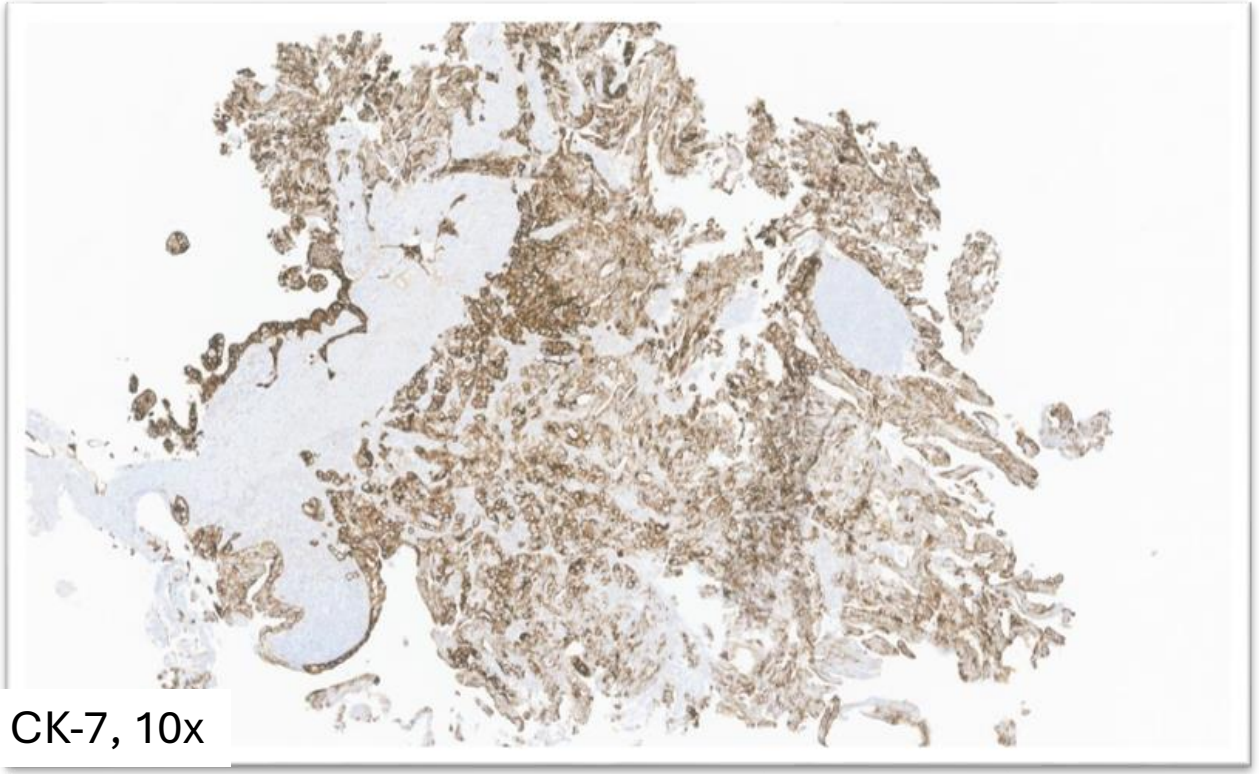


B. (H&E,10x)

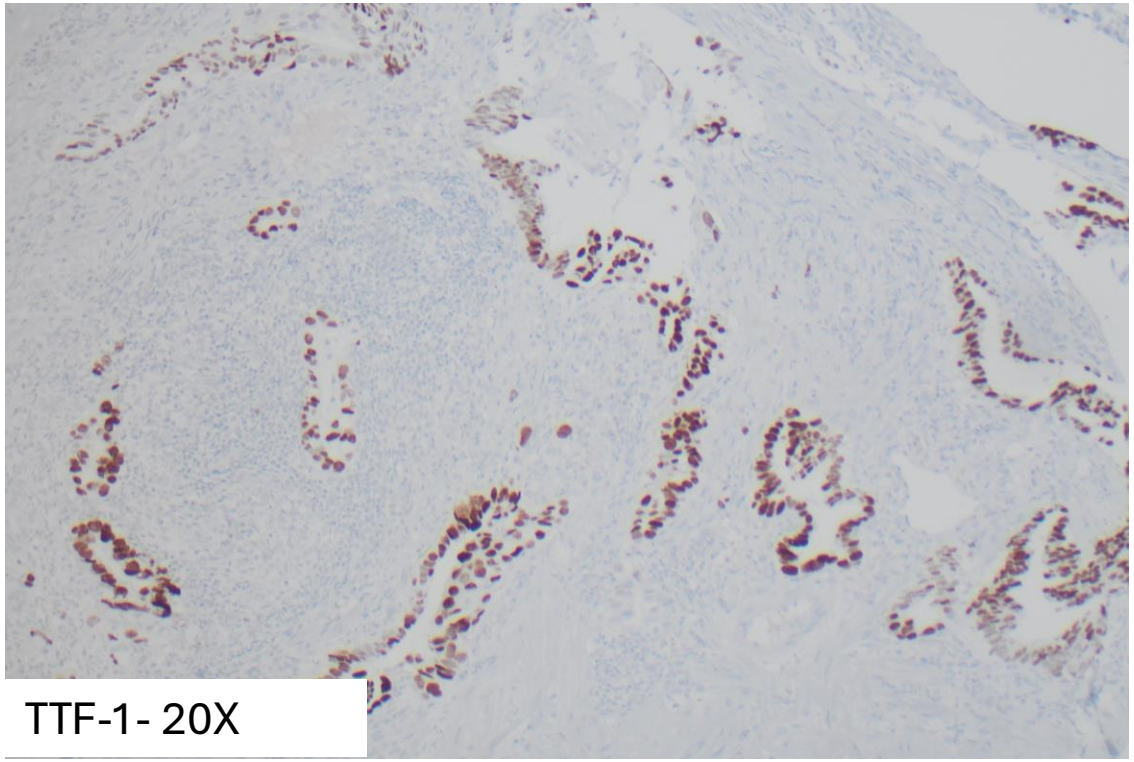


C.(H&E,20x)

B and C: On higher magnification, the mass shows features similar to those of the liver lesion; an invasive moderately differentiated adenocarcinoma with focal papillary architecture (blue arrow).
The tumor infiltrates through muscularis mucosae at least into the submucosa (yellow arrows).



CK-7, 10x



TTF-1- 20X

Tumor is diffusely and strongly positive for CK-7 and moderate and patchy positive for TTF-1

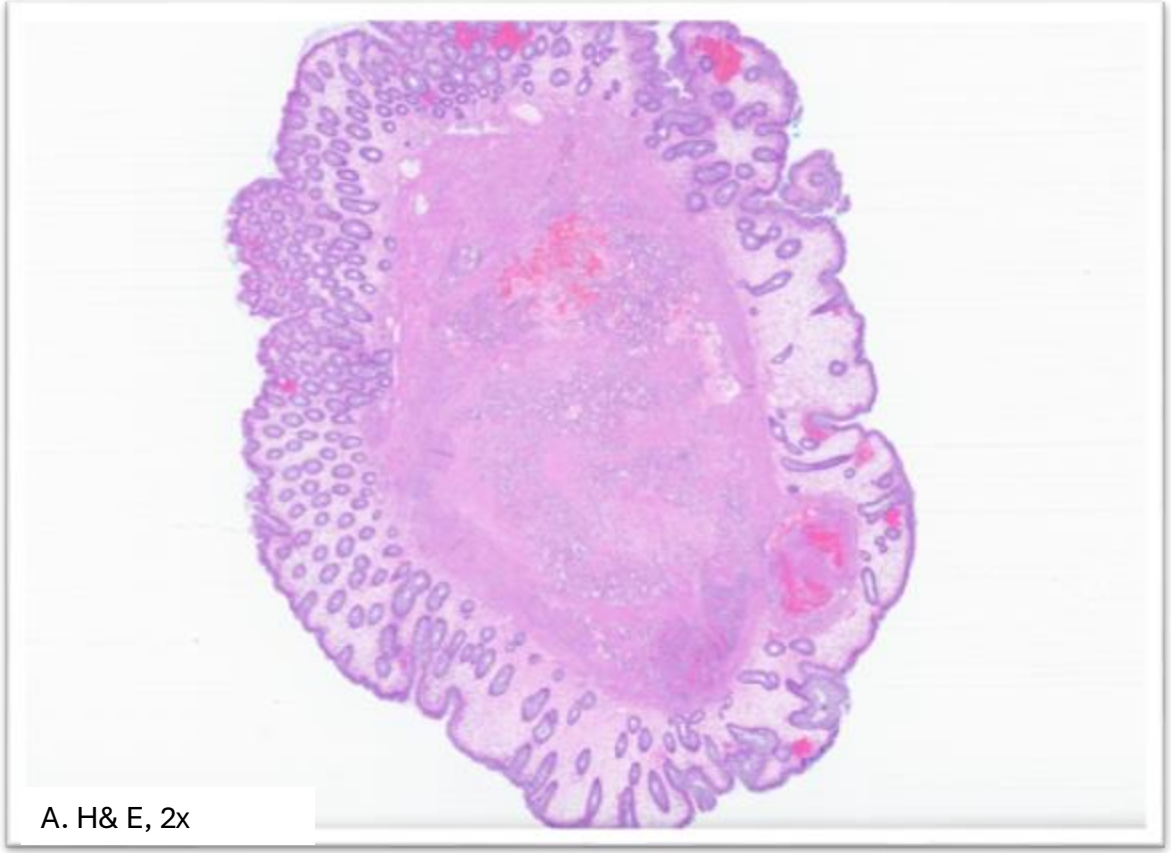
Final diagnosis

-***Invasive moderately differentiated adenocarcinoma*** *arising in a background of atrophic gastritis with intestinal metaplasia*

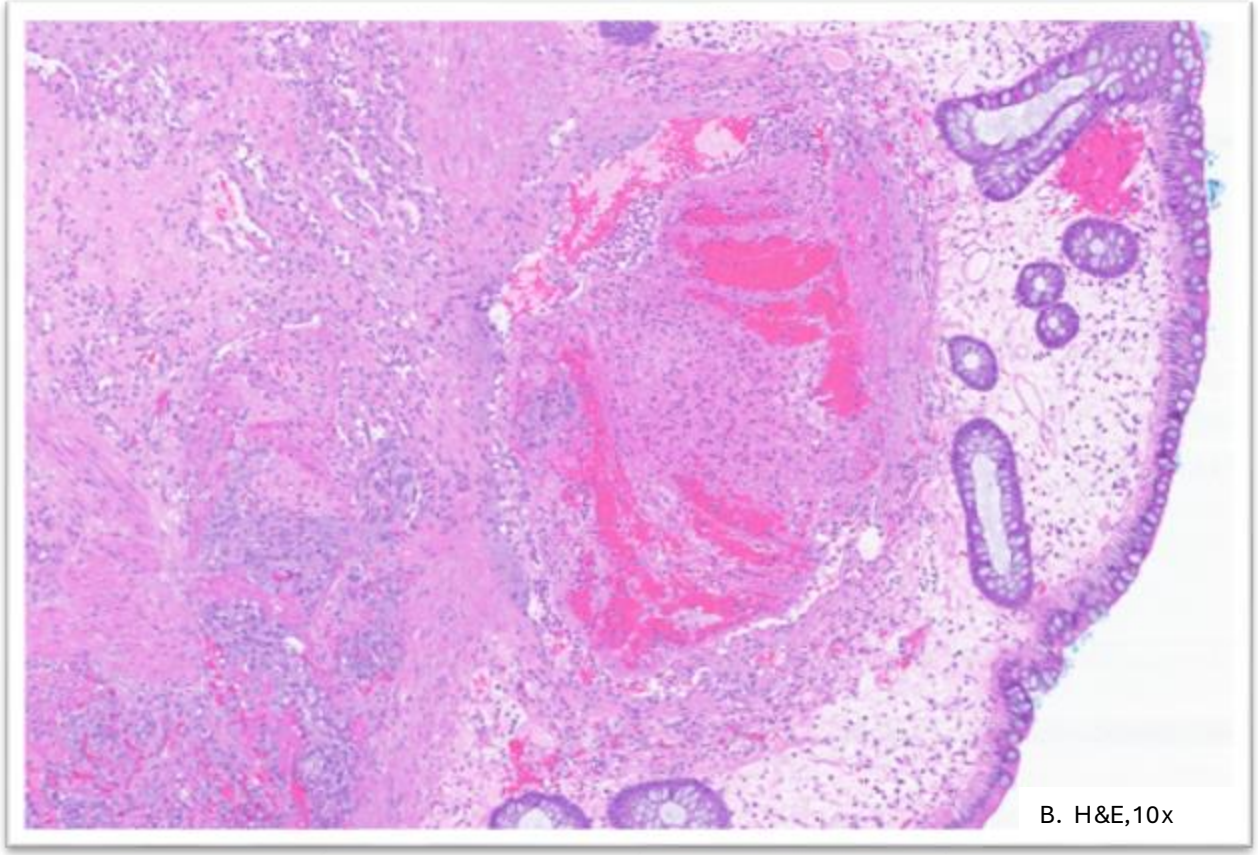
- The tumor infiltrates through muscularis mucosae, at least into submucosa

- Positive for lymphovascular invasion

Rectal Polyp



A. H& E, 2x

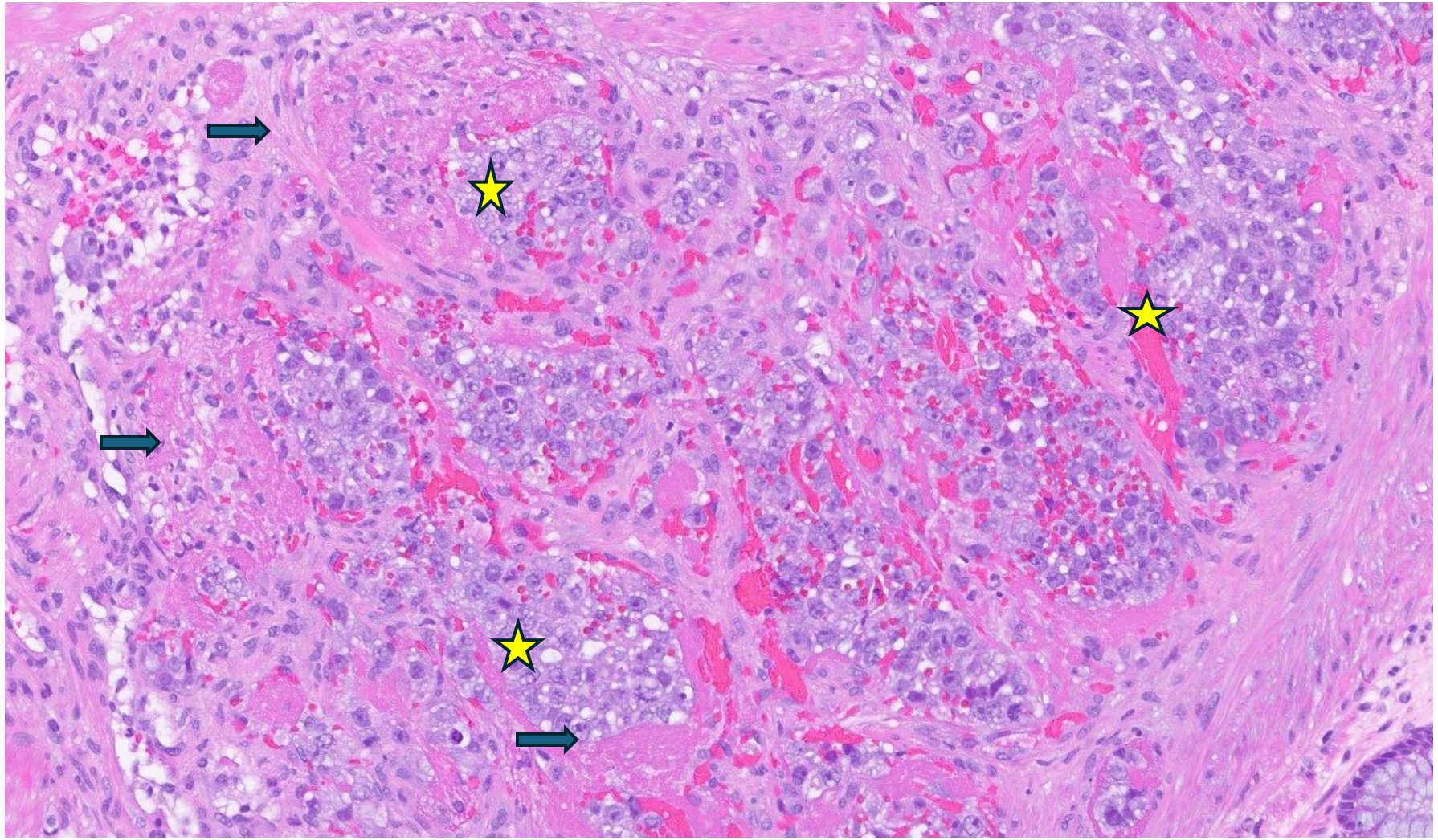


B. H&E,10x

A and B Rectum biopsy : The biopsy of the rectal polyp shows a submucosal vascular proliferation consistent with a pyogenic granuloma.The mucosa shows no dysplasia

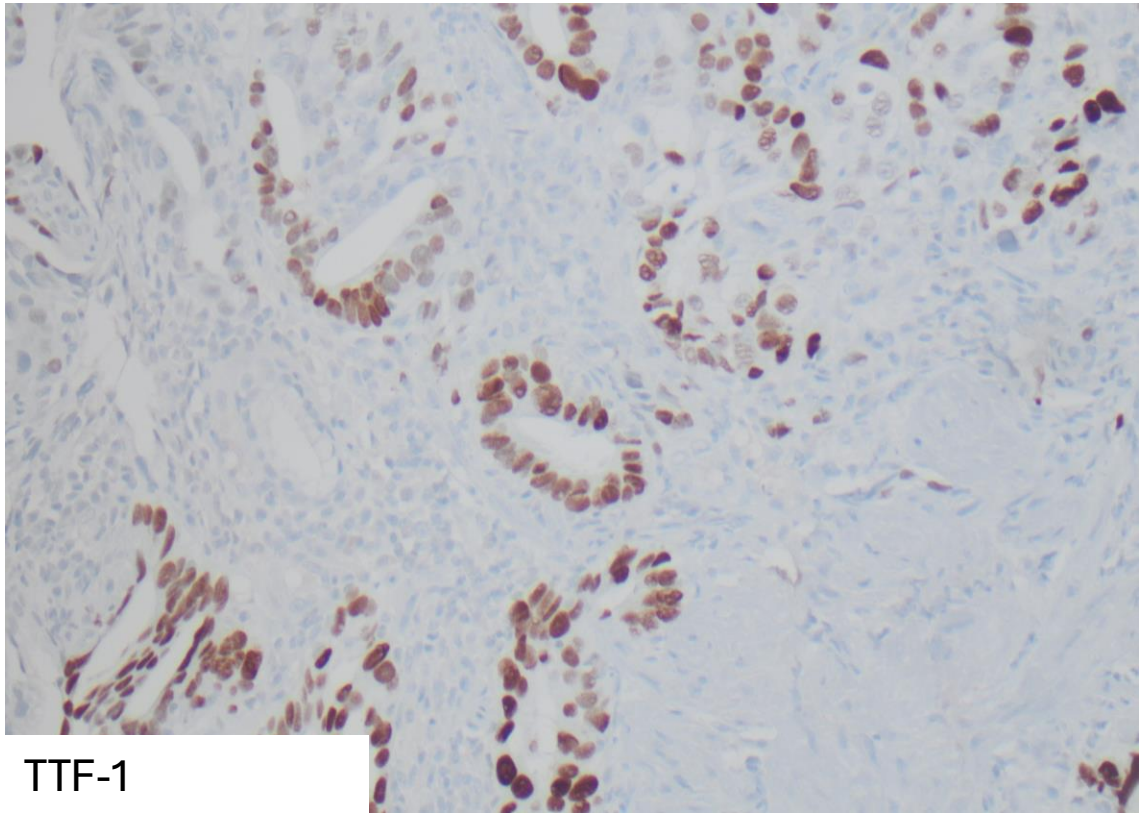
Rectal Polyp

C

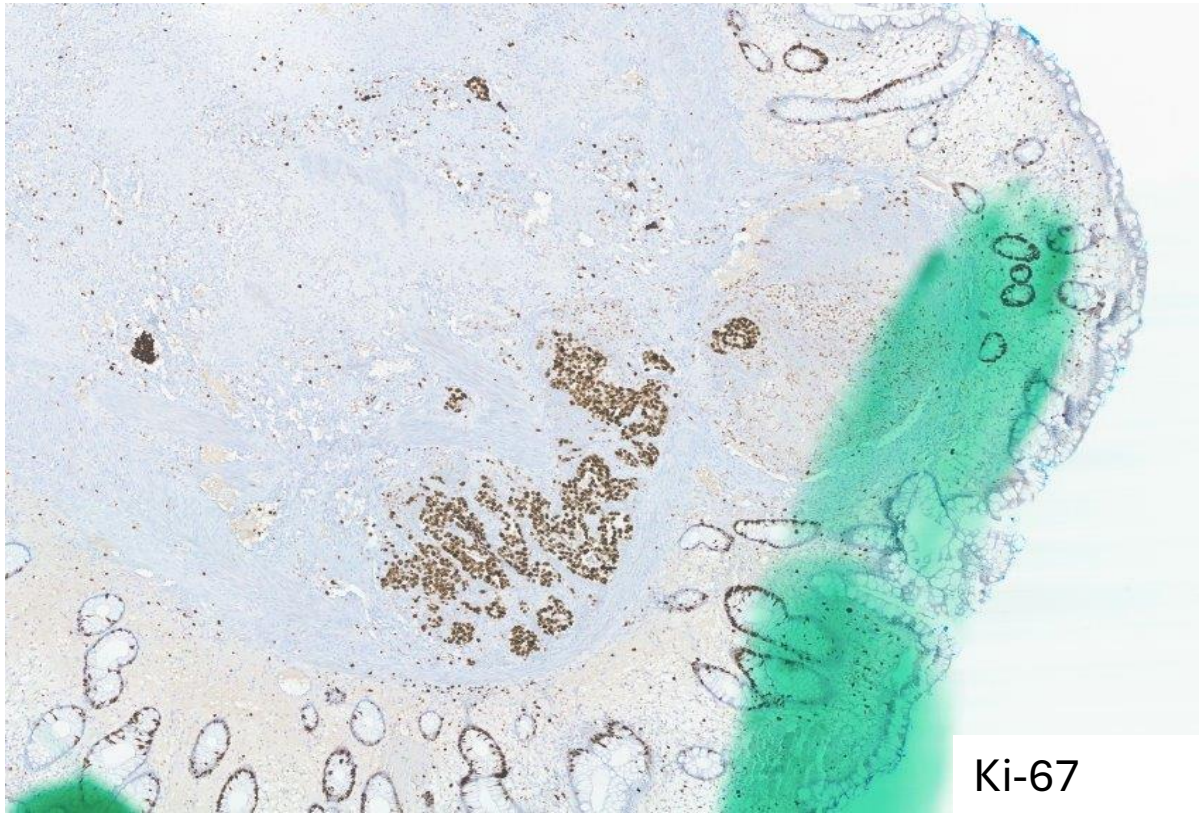


C Rectum polyp (H& E 2x): On higher magnification, the submucosa shows a prominent vascular proliferation containing numerous intravascular fibrin thrombi (➡) and tumor emboli (☆) that are morphologically identical to the gastric primary. The lymphangitic carcinomatosis within the submucosa, consistent with metastatic involvement.

Rectal Polyp



TTF-1



Ki-67

Tumor cells are positive for TTF-1. Ki-67 is positive in 100% of the tumor emboli.

Final Diagnosis

- *Metastatic gastric adenocarcinoma in a rectal pyogenic granuloma*

Case of the month

Feb 2026

Hareem Hamza, MD (PGY2)

Celia Marginean, MD

Case presentation

A 53-year-old man with a history of type 2 diabetes mellitus presented with several weeks of subacute abdominal pain, unintentional weight loss, and poor oral intake.

Evaluation revealed acute bilateral pulmonary emboli and widely metastatic malignancy of unknown primary, with extensive hepatic and lung metastases, peritoneal carcinomatosis, and malignant ascites.

A biopsy of the liver was performed, see images in ppt.

Question 1 : A liver mass biopsy shows adenocarcinoma with **TTF-1 positivity in ~30% of tumor cells and CK-7 positivity**. Imaging reveals a dominant gastric mass with nodal disease. Which of the following statements is **MOST accurate** regarding interpretation of these findings?

A. Expression of TTF-1 is essentially specific for primary lung adenocarcinoma and excludes a gastrointestinal primary.

B. TTF-1 positivity with clone SPT24 is highly specific for lung and thyroid carcinomas and rarely occurs in other tumors.

C. Gastric adenocarcinomas can show focal TTF-1 positivity, particularly with clone SPT24, and metastatic deposits may retain this expression, potentially mimicking lung origin.

D. Clone 8G7G3/1 is more sensitive than SPT24 and would be expected to show stronger staining in gastric adenocarcinoma.

E. TTF-1 immunostaining alone is sufficient to determine the primary site in carcinoma of unknown origin.

- **Correct Answer: C**
- **Explanation:**

TTF-1 expression is clone dependent. The SPT24 clone is more sensitive but less specific, detecting TTF-1 in a subset of non-pulmonary tumors, including gastric adenocarcinomas, where up to 25% of cases may show focal positivity.

Metastatic sites can retain this staining pattern, and some cases may also express Napsin A, creating a strong false impression of pulmonary origin.

In contrast, clone 8G7G3/1 is more specific but less sensitive. Therefore, TTF-1 (especially with SPT24) must be interpreted in the context of morphology, clinical findings, and a broader immunohistochemical panel, as reliance on this marker alone can lead to misclassification of tumor origin.

This case underscores two important diagnostic pitfalls.

- **First**, TTF-1 expression, although classically associated with pulmonary and thyroid primaries, is not entirely specific and can be seen in a subset of gastric adenocarcinomas and other gastrointestinal malignancies, as well as occasionally in pancreatobiliary tumors such as cholangiocarcinoma. Therefore, reliance on a single immunohistochemical marker may lead to misclassification of the primary site. Accurate diagnosis requires integration of morphology, a comprehensive immunohistochemical panel, clinical history, and radiologic findings.
- TTF-1 expression varies significantly among antibody clones, with clone 8G7G3/1 demonstrating higher specificity but lower sensitivity for lung adenocarcinoma compared with SPT24 and SP141. A subset of nonpulmonary tumors, particularly colorectal carcinomas, may also show TTF-1 positivity, especially with the latter clones. Therefore, TTF-1 expression alone cannot reliably distinguish primary lung cancer from pulmonary metastasis. Accurate diagnosis requires correlation with morphology, a broader immunohistochemical panel, and clinical findings.
- Autoimmune metaplastic atrophic gastritis (AMAG)–associated gastric adenocarcinomas show significantly higher patchy TTF-1 and Napsin A immunoreactivity compared with adenocarcinoma not associated with atrophy. This staining may mimic metastatic lung adenocarcinoma, highlighting the need for careful interpretation (4).
- **Second,** Metastatic disease can occasionally present in highly unusual locations. Tumor involvement within a rectal polyp or vascular lesion may mimic a primary colorectal neoplasm or even a benign process. Recognition of lymphovascular tumor emboli, along with correlation to a known primary malignancy, is essential to

avoid diagnostic error. Careful attention to histologic features—such as the absence of surface dysplasia, evidence of mucosal cancerization, or prominent submucosal lymphangitic spread—should raise suspicion for metastasis. Accurate classification relies on judicious, targeted immunohistochemistry of limited biopsy material, interpreted within the context of clinical history, endoscopic findings, and imaging evidence of widespread disease.

References

- Choi, S. M., Furth, E. E., & Zhang, P. J. (2016). Unexpected TTF-1 Positivity in a Subset of Gastric Adenocarcinomas. Applied Immunohistochemistry & Molecular Morphology, 24(8), 603–607. https://doi.org/10.1097/PAI.0000000000000244
- Noack, P., Grosse, C., Eschemann, S., Dislich, B., & Langer, R. (2025). Immunohistochemical TTF-1 and Napsin a Expression in Gastrointestinal Adenocarcinomas—Low Frequency but an Important Pitfall. Diagnostics (Basel), 15(12), 1490. https://doi.org/10.3390/diagnostics15121490
- Vidarsdottir, H., Tran, L., Nodin, B., Jirström, K., Planck, M., Mattsson, J. S. M., Botling, J., Micke, P., Jönsson, P., & Brunnström, H. (2018). Comparison of Three Different TTF-1 Clones in Resected Primary Lung Cancer and Epithelial Pulmonary Metastases. American Journal of Clinical Pathology, 150(6), 533–544. https://doi.org/10.1093/ajcp/aqy083
- Toussieng, T., Kozak, M., Burch, M., Gangi, A., Gong, J., Guindi, M., Lai, K. K., Hutchings, D. A., Larson, B. K., & Waters, K. M. (2026). Pulmonary immunohistochemical markers may be positive in gastric adenocarcinomas associated with autoimmune metaplastic atrophic gastritis. Histopathology, 88(3), 729–735. https://doi.org/10.1111/his.15526

March 2026

No Case of the Month

GI Case of the Month

April 2026

Dr. Dorsay Sadeghian, MD, PGY3

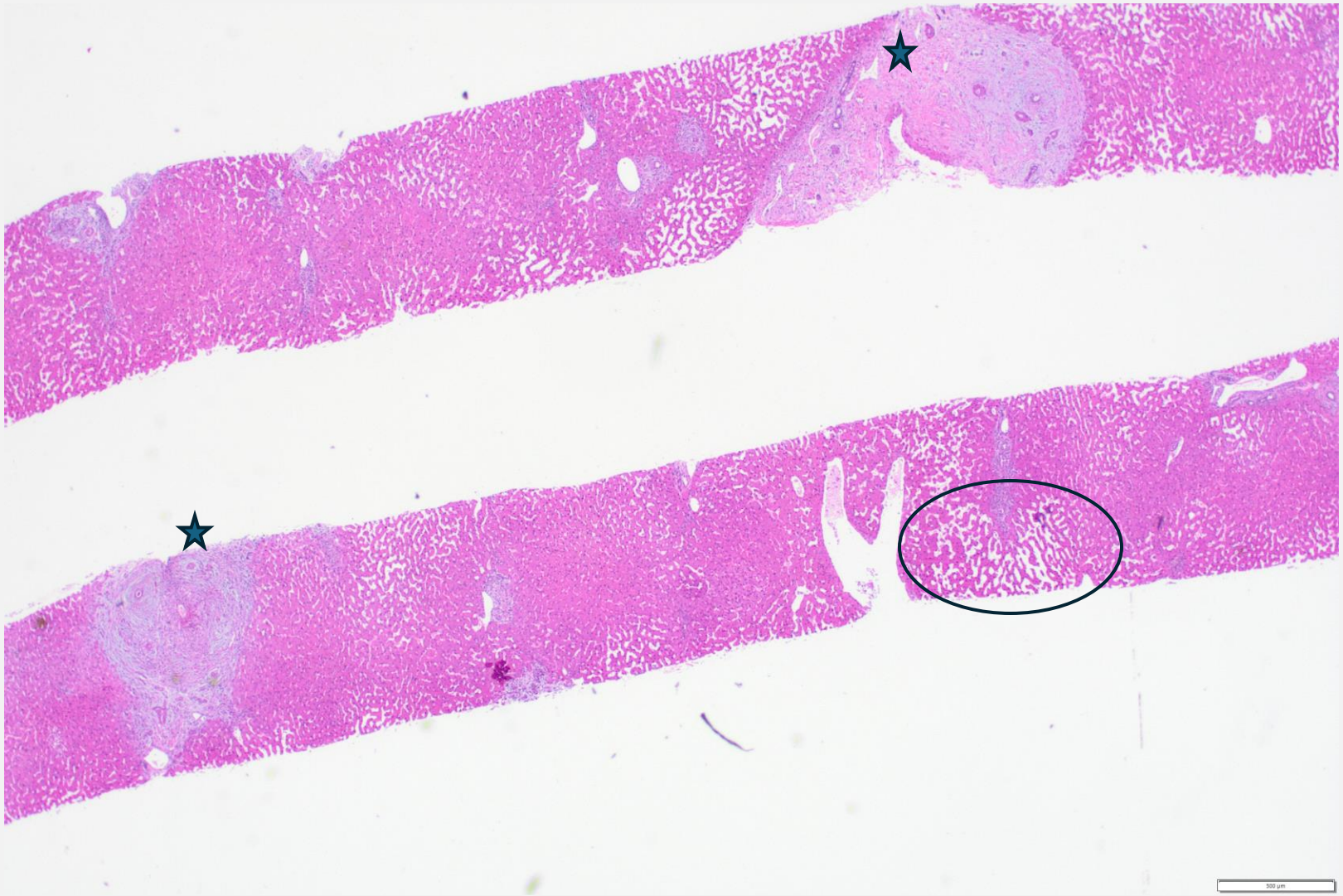
Dr. Shilpa Jain, MD, Associate Professor

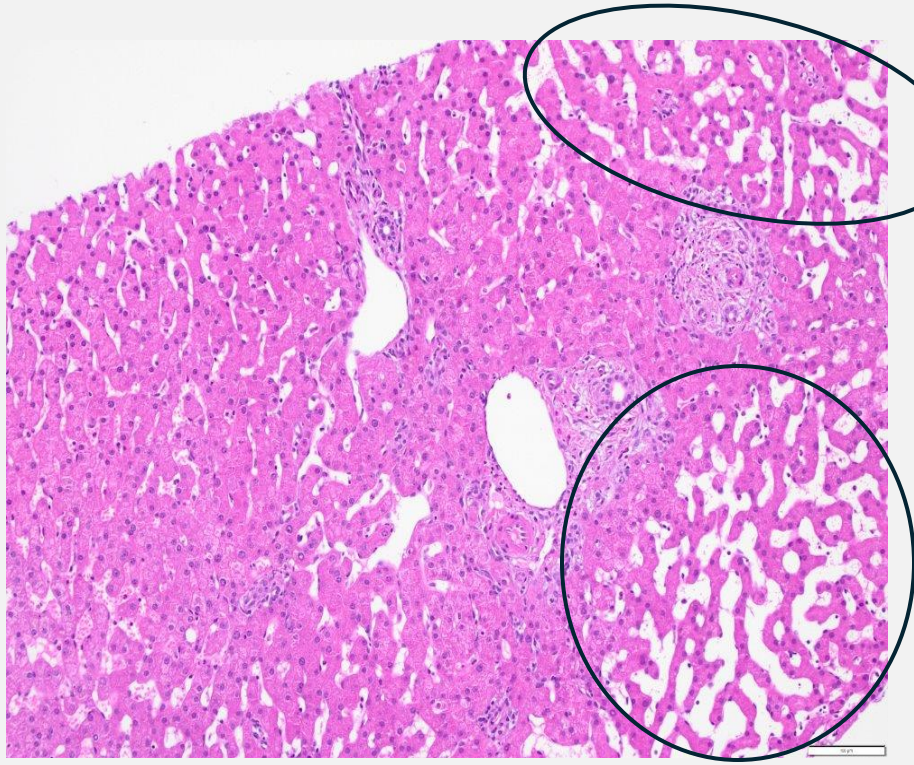
Clinical History:

- A 49 y/o female, presented with an increasing right upper quadrant abdominal pain.
- The past medical history of the patient was significant for hypothyroidism.
- Negative serologic markers (ANA, AMA, ANCA, anti-LKM1, ASMA, C3, C4)
- MRCP: Unremarkable extra and intrahepatic bile ducts.
- Liver biopsy was performed for further evaluation.

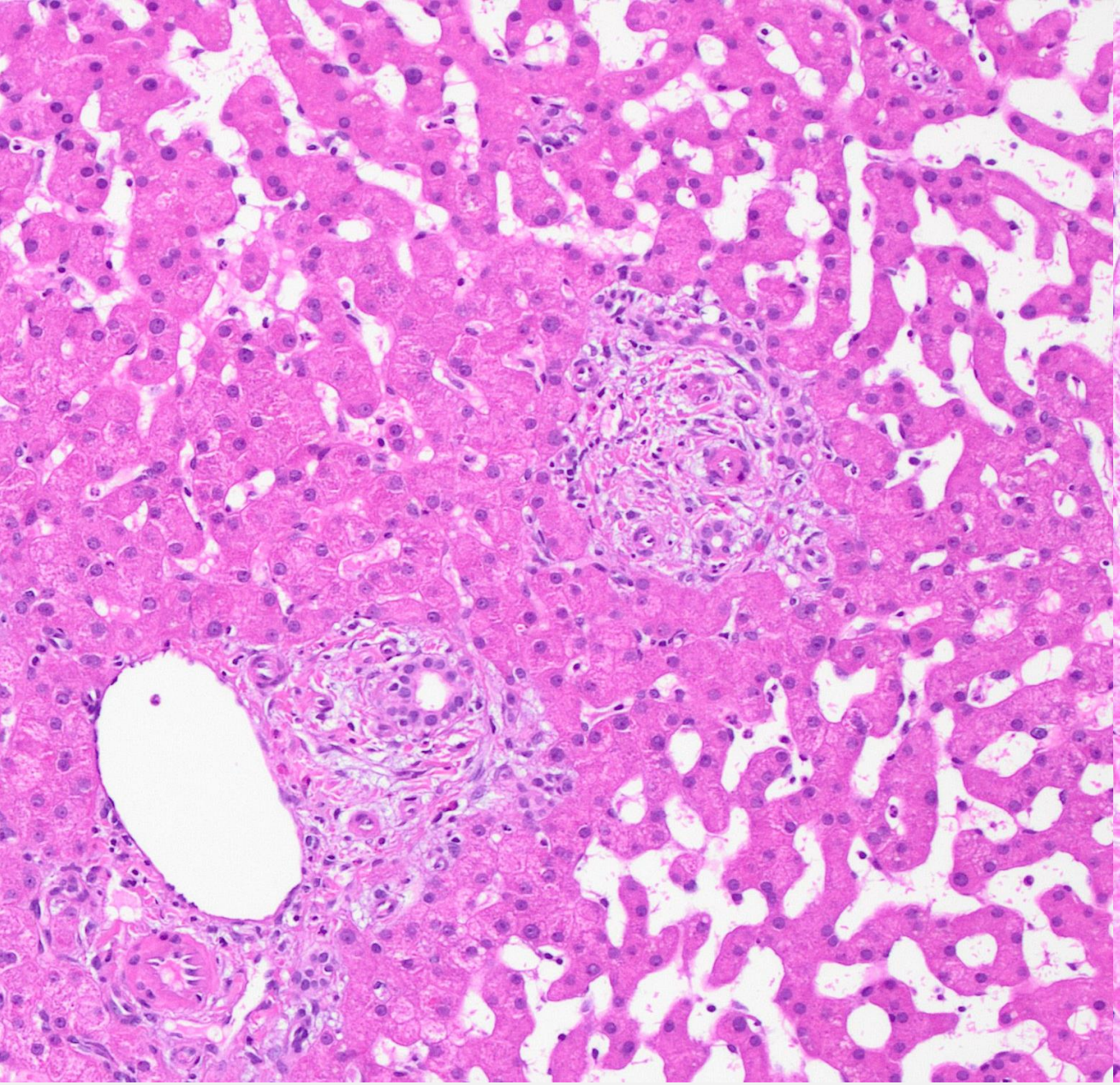
AST: 58 U/L, ALT: 108 U/L	Increased ESR and CRP
ALP: 1450 U/L, GGT: 252 U/L	Negative viral markers
Normal Bilirubin	Normal IgG

Initial Biopsy

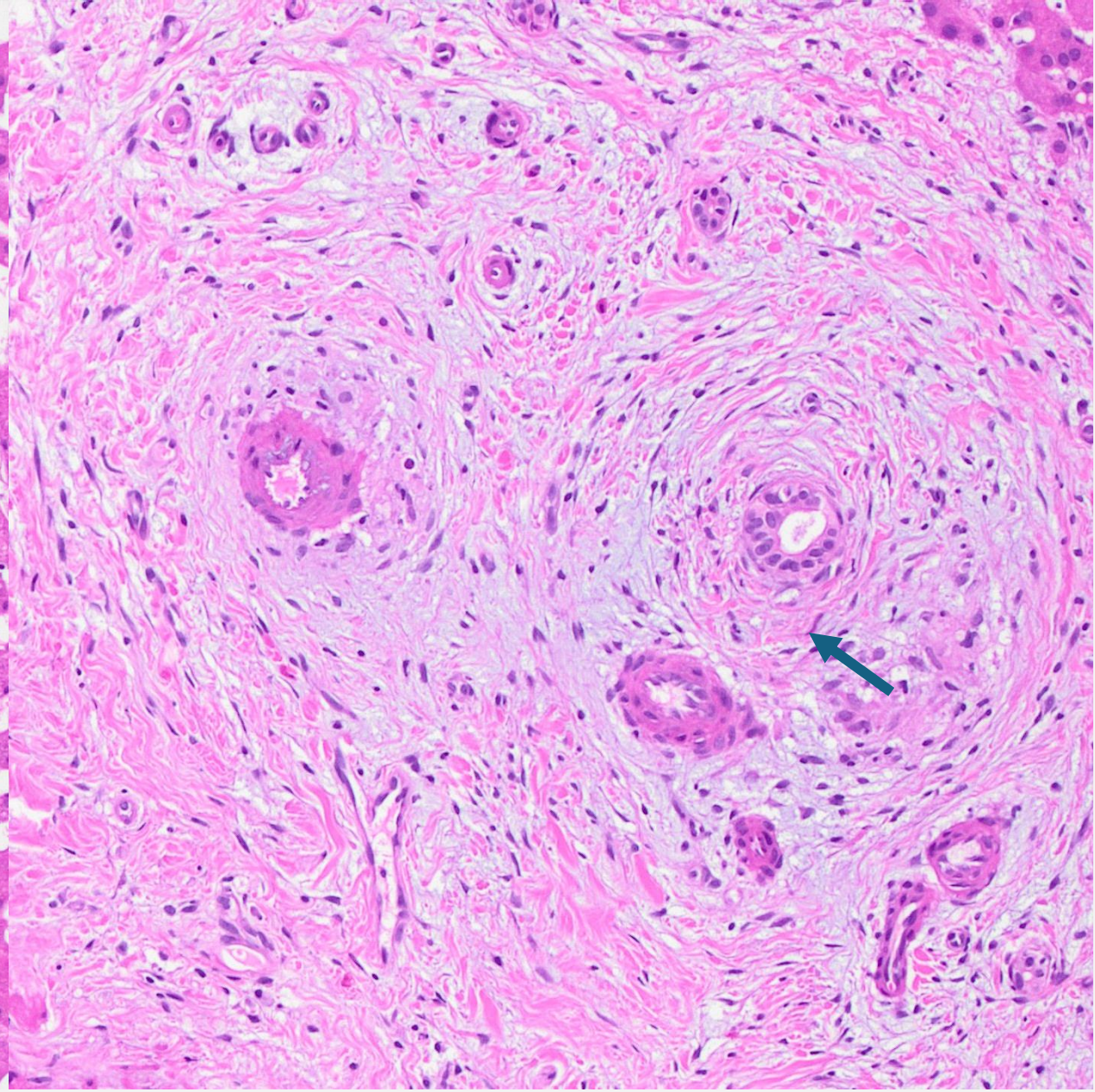




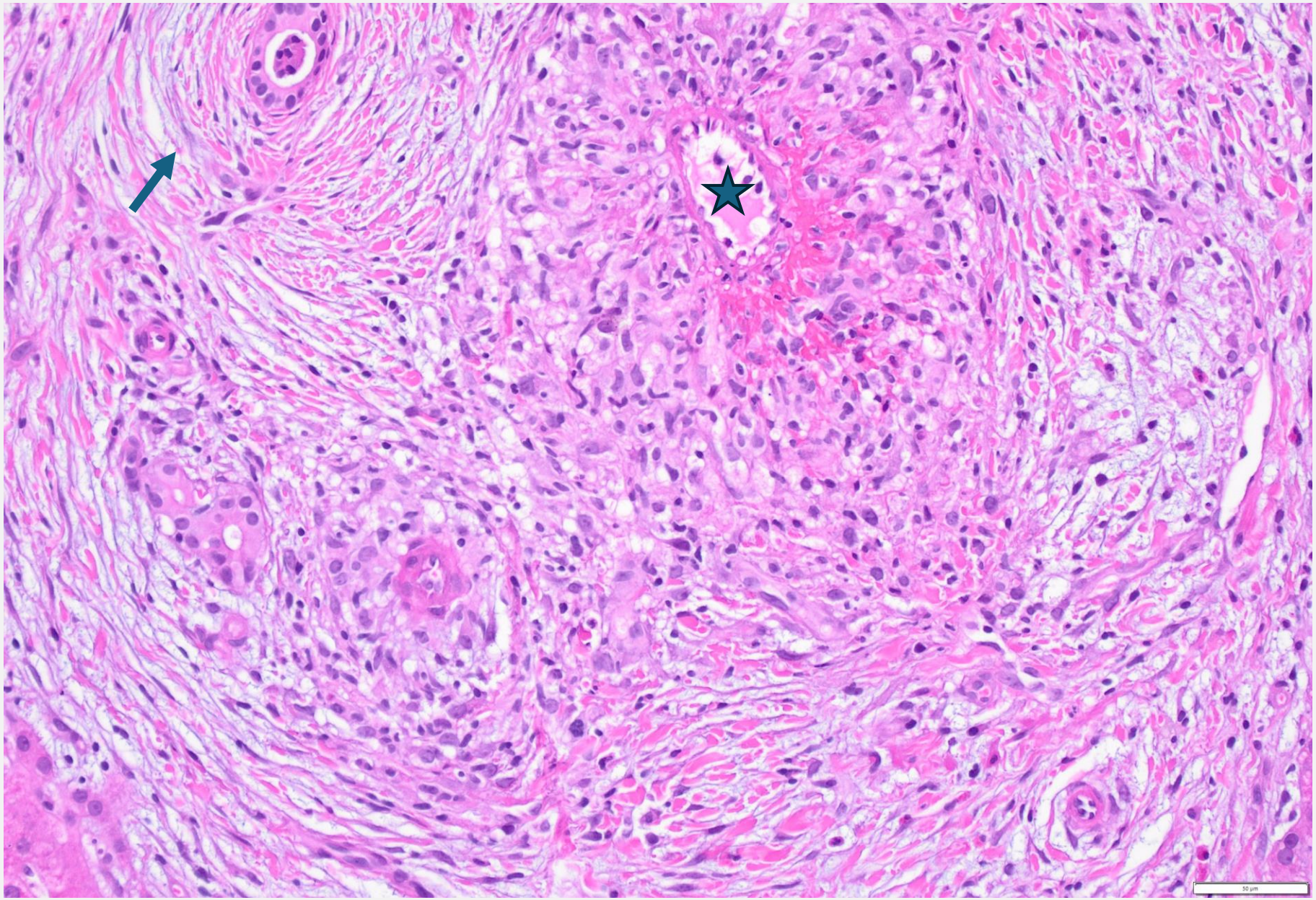
Two liver core biopsies with adequate portal tracts. Low-power examination shows portal expansion and edema in a few portal tracts (asterisk). The annotated areas demonstrate prominent centrilobular sinusoidal dilatation associated with lobular atrophy.



Most portal tracts show minimal lymphocytic inflammation, admixed with rare eosinophils



Portal edema with mild periductal fibrosis



Focal necrotizing granulomatous arteritis is identified (asterisk). Layered periductal fibrosis is present in small bile ducts adjacent to the area of granulomatous inflammation (arrow).

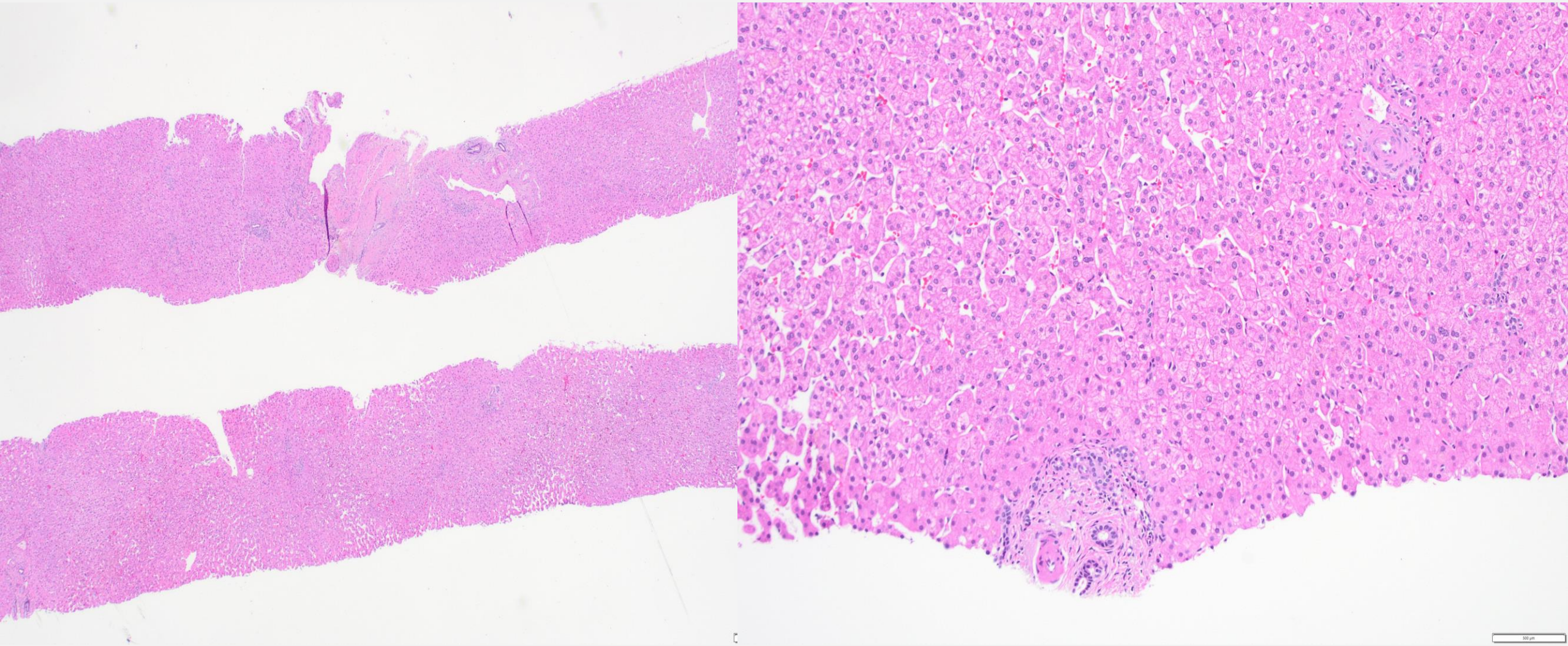
Final Diagnosis:

- Intra-hepatic acute necrotizing and granulomatous arteritis (Mild sclerosing cholangitis
- Centrilobular sinusoidal dilatation and hepatocyte atrophy

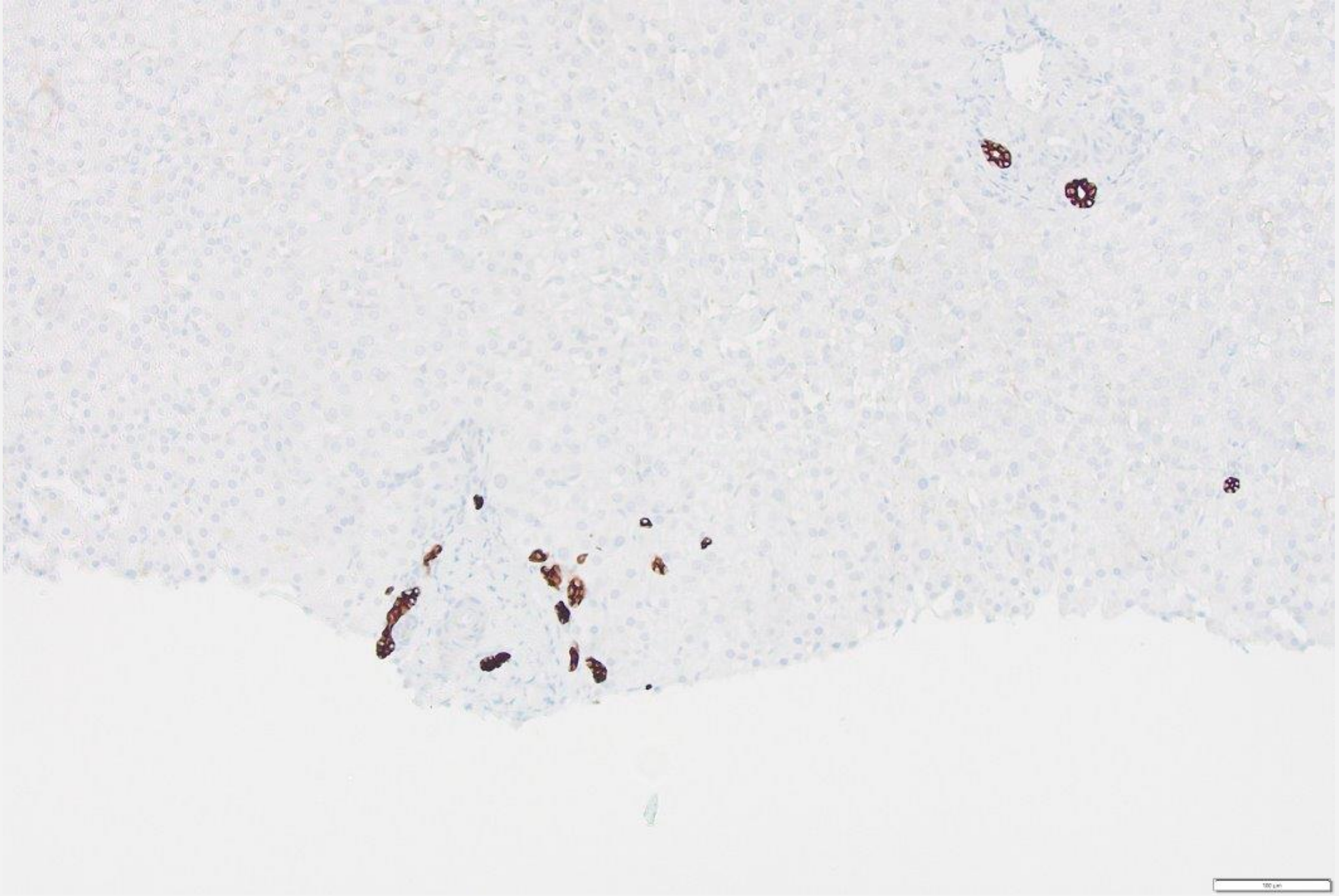
Special Stain Interpretation (Images not included):

- Trichome stain: Expanded portal triads with areas of periductal fibrosis associated with small ducts
- No increased iron
- No hyaline globules on PAS-D

Post-immunosuppressive Treatment Biopsy



???? How long and what treatment ? Post-immunosuppressive treatment liver biopsy revealed marked improvement in comparison with initial biopsy with less bile duct damage and less extensive sinusoidal dilatation



Presence of mild chronic cholestasis is supported by CK7 staining

Case history:

A 50-year-old patient presented with high alkaline phosphatase with normal bilirubin, AST and ALT (cholestatic pattern). Liver biopsy shows concentric fibrosis around affected bile ducts with onion-skin appearance resembling primary sclerosing cholangitis (PSC). Granulomatous vasculitis of hepatic vessels is also noted. Which feature most strongly supports ischemic cholangiopathy secondary to granulomatous vasculitis rather than primary sclerosing cholangitis?

A. Presence of biliary strictures on imaging
B. Chronic cholestatic laboratory pattern
C. Association with inflammatory bowel disease
D. Presence of vasculitis and reversibility with immunosuppressive therapy
E. Onion skin periductal fibrosis on histology

Correct Answer: D. Potential reversibility with immunosuppressive therapy

A. The presence of biliary strictures on imaging can result from a variety of causes. Although rare, ischemic cholangiopathy and vasculitis may lead to strictures. More commonly, etiologies include:
   - **Malignancies:** cholangiocarcinoma, pancreatic, gallbladder, or ampullary adenocarcinoma
   - **Benign inflammatory or autoimmune causes:** primary sclerosing cholangitis (PSC), IgG4-related sclerosing cholangitis
   - **Iatrogenic or traumatic causes:** prior surgery, instrumentation, or radiation
   - **Infectious causes:** parasitic infections, recurrent pyogenic cholangitis

B. Chronic cholestatic laboratory patterns are defined below and can be seen in a wide variety of clinical conditions.
   - **Alkaline phosphatase (ALP)**: Markedly elevated (typically ≥2 - 3× upper limit of normal)
   - **Gamma-glutamyl transferase (GGT)**: Elevated (supports hepatic origin of ALP)
   - **Bilirubin**: may be elevated, mainly direct (conjugated)
   - **AST and ALT**: Normal or only mildly elevated (usually <2 - 3× ULN)

C. Primary sclerosing cholangitis (PSC) has a well-established association with inflammatory bowel disease (IBD), particularly ulcerative colitis (UC). Approximately 60–80% of patients

with PSC have coexisted with UC. However, only 2–7% of patients with UC develop PSC, reflecting the overall rarity of this condition.

D. The patient's symptom improvement marked alkaline phosphatase reduction, and resolution of vasculitis on liver biopsy after treatment support ischemic cholangiopathy secondary to granulomatous vasculitis. The differential for hepatic granulomatous vasculitis is broad, including systemic vasculitis (e.g., granulomatosis with polyangiitis, polyarteritis nodosa), immune-mediated conditions (e.g., sarcoidosis), and infections (e.g., mycobacterial or fungal). In this case, the absence of infectious organisms, lack of systemic vasculitis features, localized vascular involvement, and negative serologies favor a primary granulomatous vasculitis confined to the liver.

E. Presence of onion-skin, concentric fibrosis can be seen either primarily in PSC or secondary to various conditions, including but not limited to long-standing stricture, vascular and ischemic injuries and recurrent cholangitis.

Summary:

Granulomatous vasculitis of the liver is rare and a diagnostic challenge, due to its broad differential and risk of ischemic injury. Ischemic cholangiopathy typically arises from hepatic artery thrombosis, prolonged hypotension, or post-transplant complications, presenting acutely with bile duct necrosis. Any disruption of hepatic blood flow—such as granulomatous vasculitis of medium-sized arteries—can cause similar injury. Chronic or indolent vascular compromise may mimic histologic features of primary sclerosing cholangitis (PSC), but unlike PSC, these changes may be reversible with immunosuppressive therapy. In this case, long-term infliximab treatment led to a marked reduction in alkaline phosphatase and improvement of liver biopsy.