Pathological classification of Hepatobiliary tumors

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Tumours of the liver and intrahepatic bile ducts: Introduction

Epithelial tumours

Benign hepatocellular tumours

- Focal nodular hyperplasia of the liver
- Hepatocellular adenoma

Malignant hepatocellular tumours and precursors

- Hepatocellular carcinoma
- Hepatoblastoma

Benign biliary tumours and precursors

- Bile duct adenoma
- Biliary adenofibroma
- Biliary intraepithelial neoplasia (See chapter 9)
- Intraductal papillary neoplasm of the bile ducts (See chapter 9)
- Mucinous cystic neoplasm of the liver and biliary system

Malignant biliary tumours

- Intrahepatic cholangiocarcinoma

Combined hepatocellular-cholangiocarcinoma and undifferentiated primary liver carcinoma

Hepatic neuroendocrine neoplasms

9. Tumours of the gallbladder and extrahepatic bile ducts

Tumours of the gallbladder and extrahepatic bile ducts: Introduction

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

Mesenchymal tumours

- Inflammatory myofibroblastic tumour

Smooth muscle and skeletal muscle tumours

- Leiomyoma
- Leiomyosarcoma
- Rhabdomyosarcoma

Vascular and perivascular tumours

- Haemangioma
- Epithelioid haemangioendothelioma
- Kaposi sarcoma
- Angiosarcoma

Tumours of uncertain differentiation

- PEComa, including angiomyolipoma
- Mesenchymal hamartoma of the liver
- Calcifying nested stromal-epithelial tumour
- Embryonal sarcoma of the liver

Leukaemia and myeloproliferative disease

- Acute leukaemias
- Hairy cell leukaemia
- Chronic leukaemias
- Chronic myeloproliferative disorders and
- myelodysplastic syndromes
- Myelomatosis/multiple myeloma

Lymphomas and lymphoreticular neoplasms

- Hodgkin lymphoma
- Non-Hodgkin lymphoma
- B-cell lymphomas
- T-cell lymphomas
- Primary hepatic lymphomas
- Hepatosplenic T-cell lymphoma
- Follicular dendritic cell tumours
- Other primary hepatic lymphomas

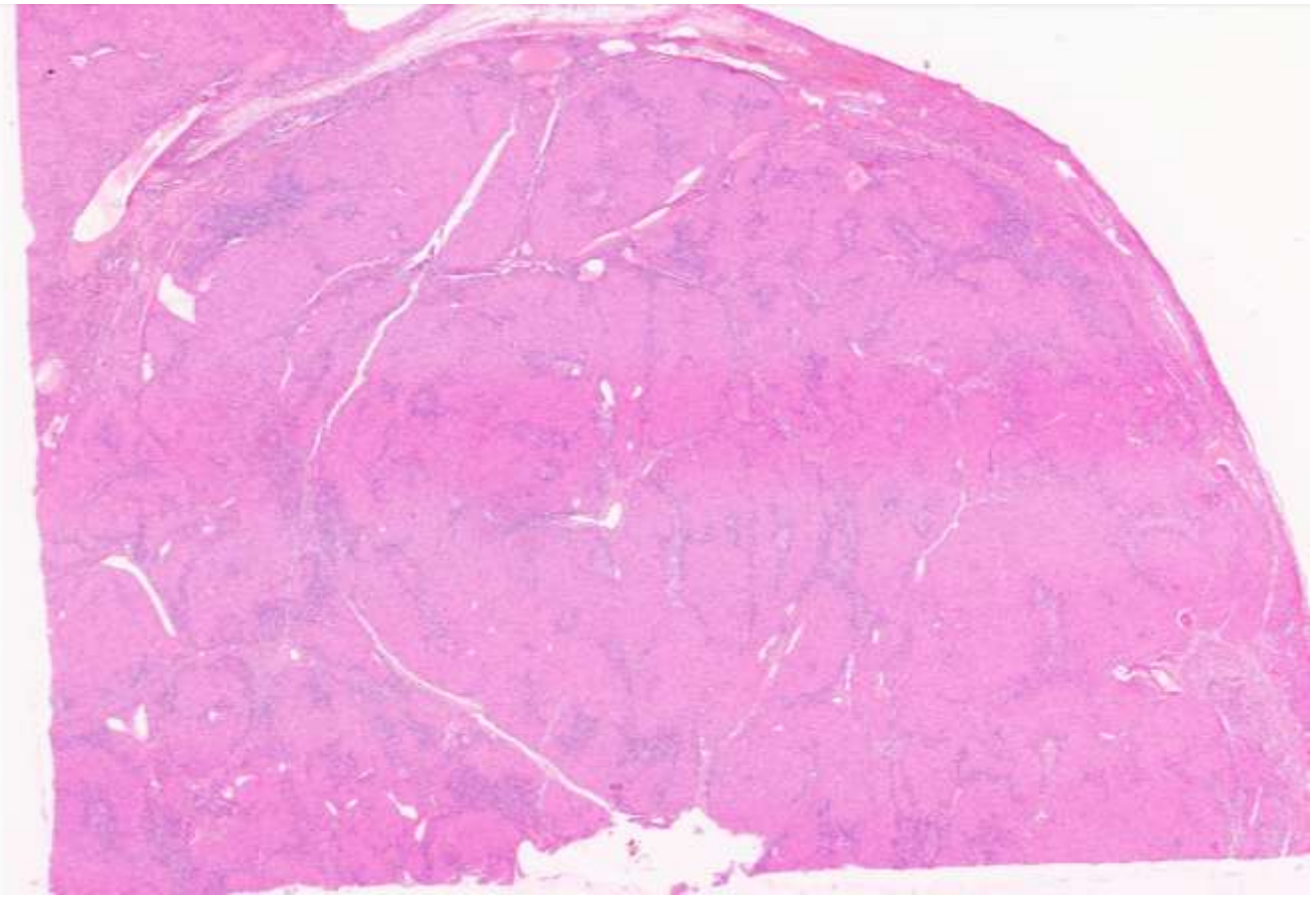
Metastatic tumours

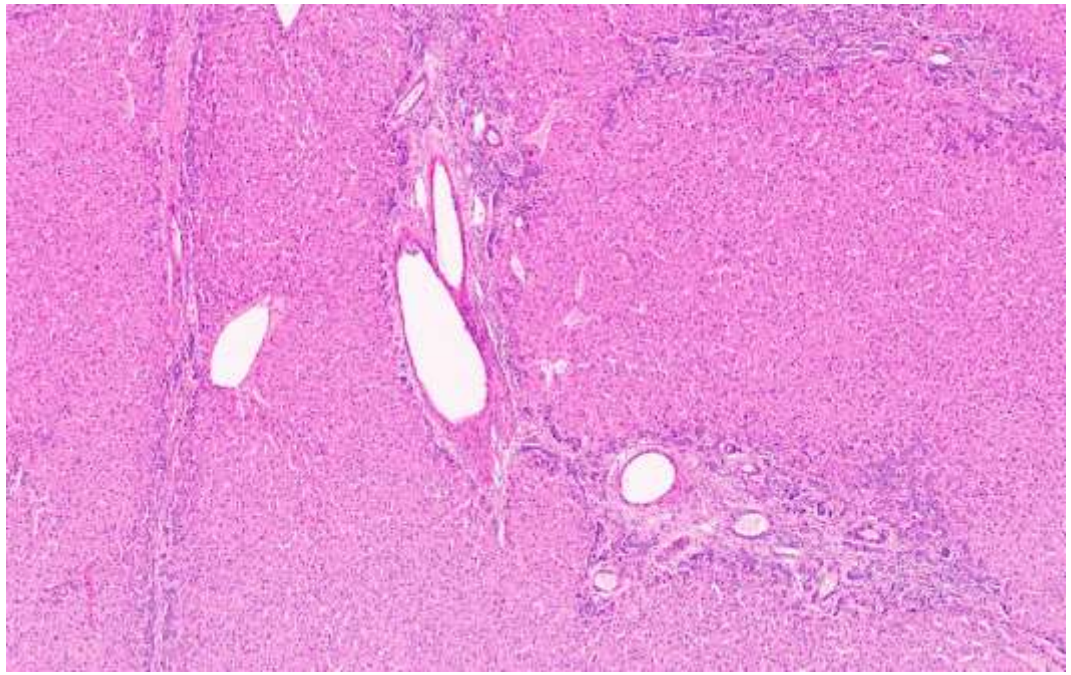
Focal Nodular Hyperplasia (FNH)

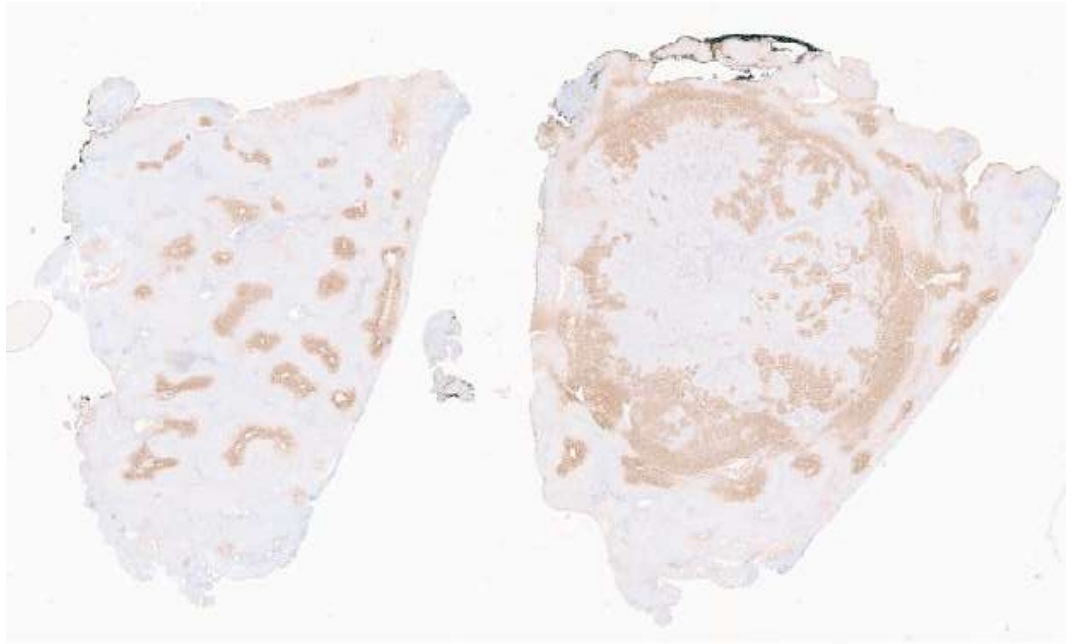
- In 80% of cases, young women, rarely in men or children
- Solitary in 80% of cases
- Most are asymptomatic, incidental findings
- Presence of unusually large vessels suggests that FNH is a nonspecific response to focally increased blood flow
- Outflow obstruction/congestive injury: parenchymal collapse and fibrosis, arteriovenous shunting, and loss of portal veins and ducts
- Increased ANGPT1:ANGPT2 ratio
- β-catenin pathway is activated

Clin Mol Hepatol. 2016 Jun;22(2):199-211.
Gastroenterology. 2003 Mar;124(3):651-9

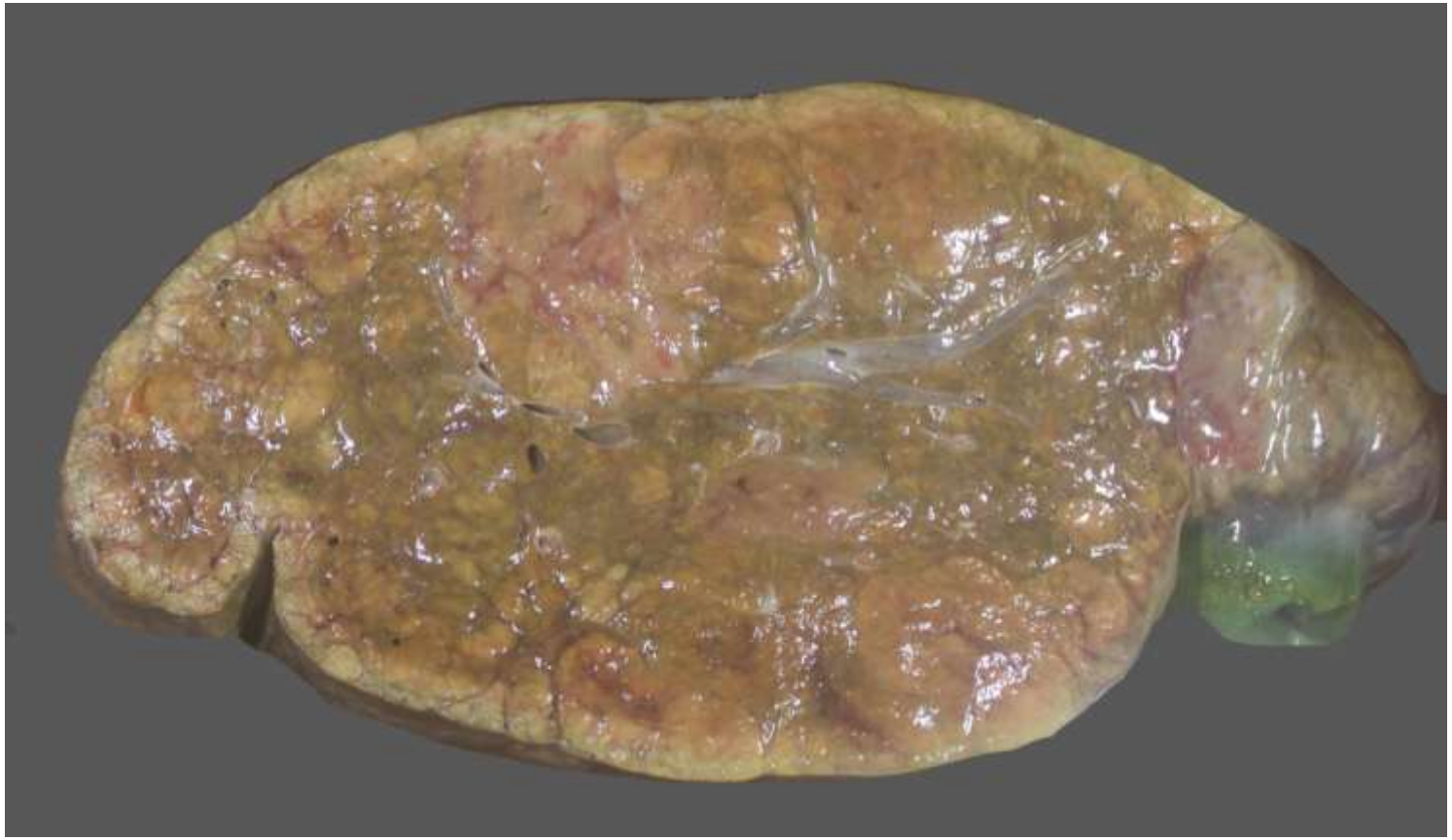
Focal Nodular Hyperplasia (FNH)







Hepatocellular adenoma (HCA)



- Benign,Monoclonal
- About 85% of HCAs occur in women of childbearing age
- Rare in children, men, > 65 years.
- Abdominal pain, palpable mass, or hemorrhage; incidental
- Single or multiple
- ≥ 10, known as adenomatosis
- Transformation to hepatocellular carcinoma (HCC) is uncommon (4–8%) and occurs mainly in men
- Risk varies with HCA subtype and is higher in some clinical settings (glycogenosis, AAS use, vascular diseases)

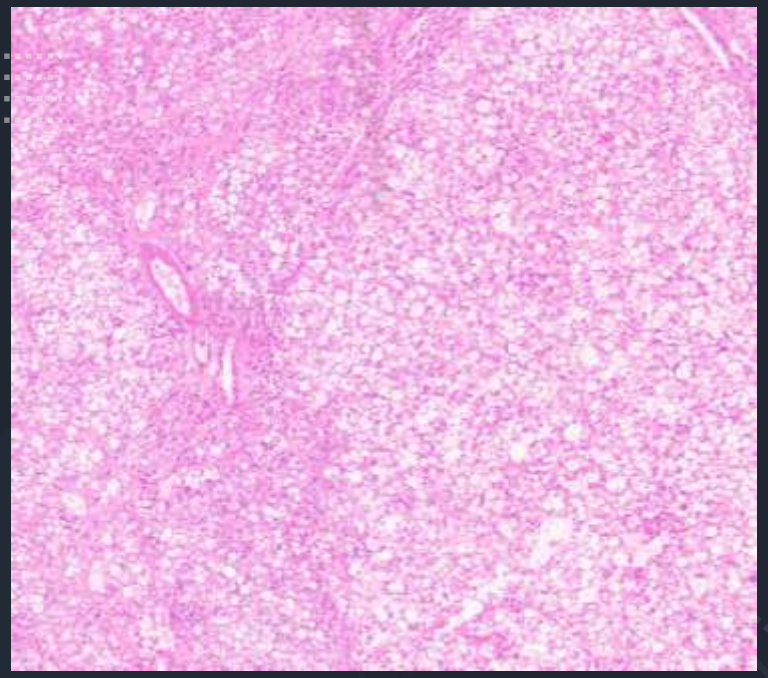
J Pathol Transl Med. 2021 May; 55(3): 171–180.

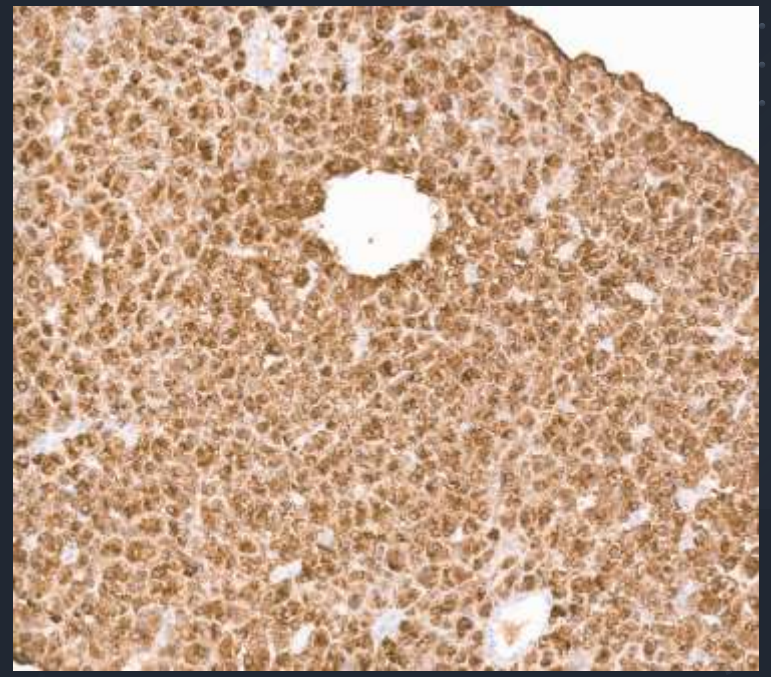
Table 1. Summary of the clinicopathological and molecular characteristics of different HCA subtypes

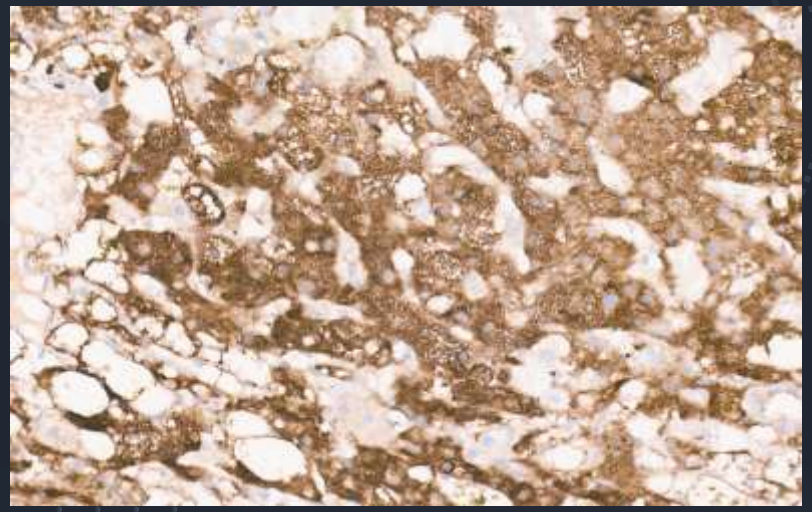
Subtype (frequency, %)	Characteristic features			
	Molecular	Clinical	Histopathological	Immunohistochemical
HNF1A-inactivated HCA (30%–40%)	*HNF1A* inactivating mutations (germline 10%, somatic 90%)	Female, obesity, MODY3, adenomatosis	Diffuse steatosis	LFABP expression loss
Inflammatory HCA (40%–50%)	gp130/*IL6ST*, *FRK*, *STAT3*, *GNAS*, *JAK1* mutations	Obesity, metabolic syndrome, alcohol, oral contraceptives	Sinusoidal dilatation Vascular proliferation Inflammatory cell infiltration Ductular reaction Focal steatosis	SAA, CRP expression
β-catenin–activated HCA (10%)				
β-catenin (exon 3)–activated HCA (7%)	*CTNNB1* exon 3 activating mutations	Male, young age, anabolic steroids, glycogen storage disease, increased risk of HCC transformation	Cytological and architectural atypia	Nuclear β-catenin expression Diffuse strong GS expression
β-catenin (exon 7,8)–activated HCA (3%)	*CTNNB1* exon 7 or 8 activating mutations	Low risk of HCC transformation	-	Absent/rare nuclear β-catenin expression GS expression: absent/weak/patchy
β-catenin–activated inflammatory HCA (5%–10%)	gp130/*IL6ST*, *STAT3*, *FRK*, *GNAS*, *JAK1* mutations + *CTNNB1* exon 3 or 7/8 mutations	Similar to inflammatory HCA Increased risk of HCC transformation (ex.3)	Similar to inflammatory HCA Cytoarchitectural atypia (ex.3)	SAA, CRP expression Nuclear β-catenin, diffuse strong GS expression (ex.3)
Sonic hedgehog–activated HCA (4%)	*INHBE-GLI1* fusion, resulting in sonic hedgehog pathway activation	Obesity, hemorrhage	Hemorrhage	PTGDS, ASS1
Unclassified HCA (<7%)	Unknown	-	-	-

HCA, hepatocellular adenoma; MODY3, maturity-onset diabetes type 3; LFABP, liver fatty acid binding protein; SAA, serum amyloid A; CRP, C-reactive protein; HCC, hepatocellular carcinoma; GS, glutamine synthetase; PTGDS, prostaglandin D2 synthase; ASS1, argininosuccinate synthase 1.

journal of Pathology and Translational Medicine 2021; 55: 171-180



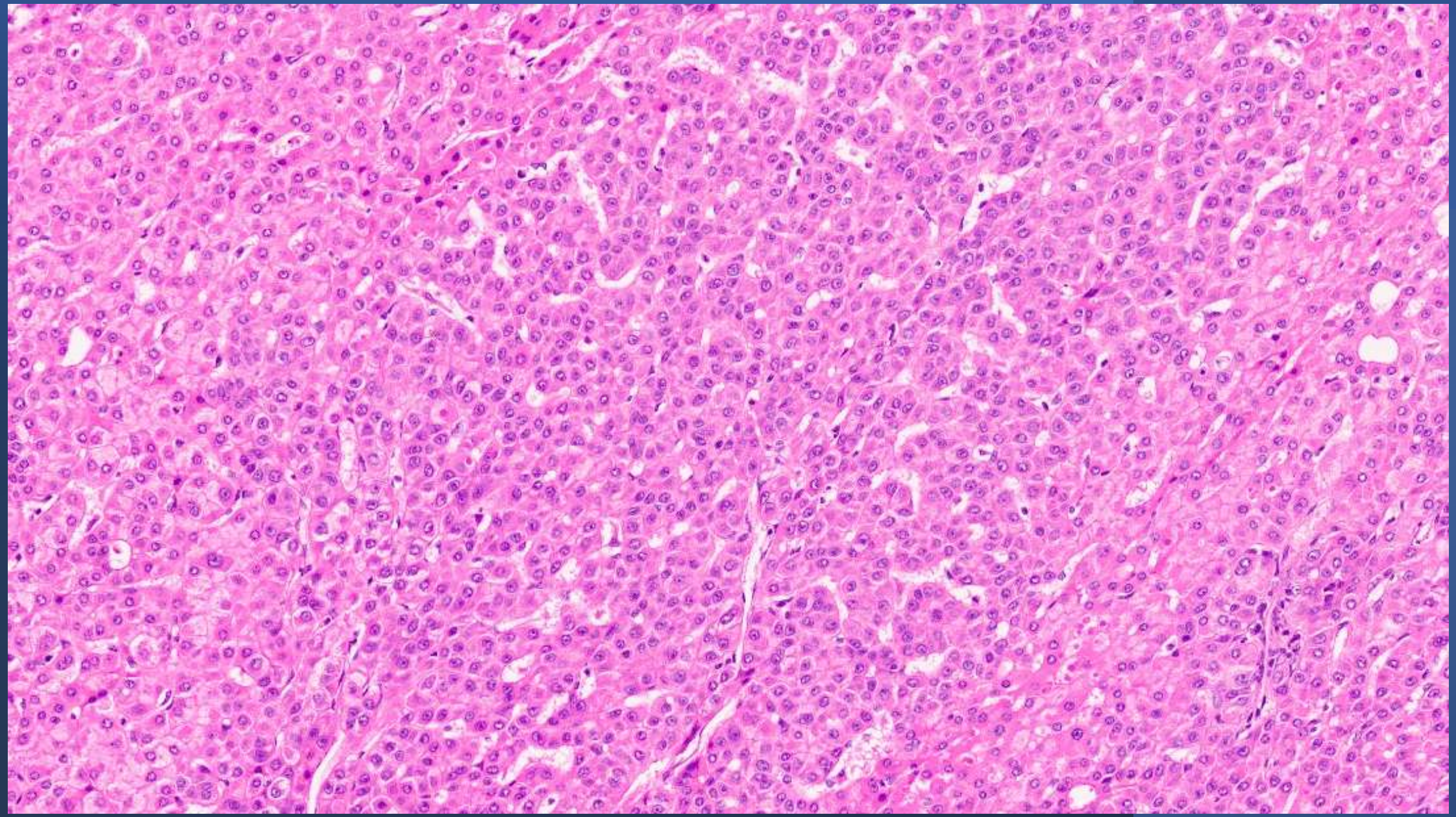




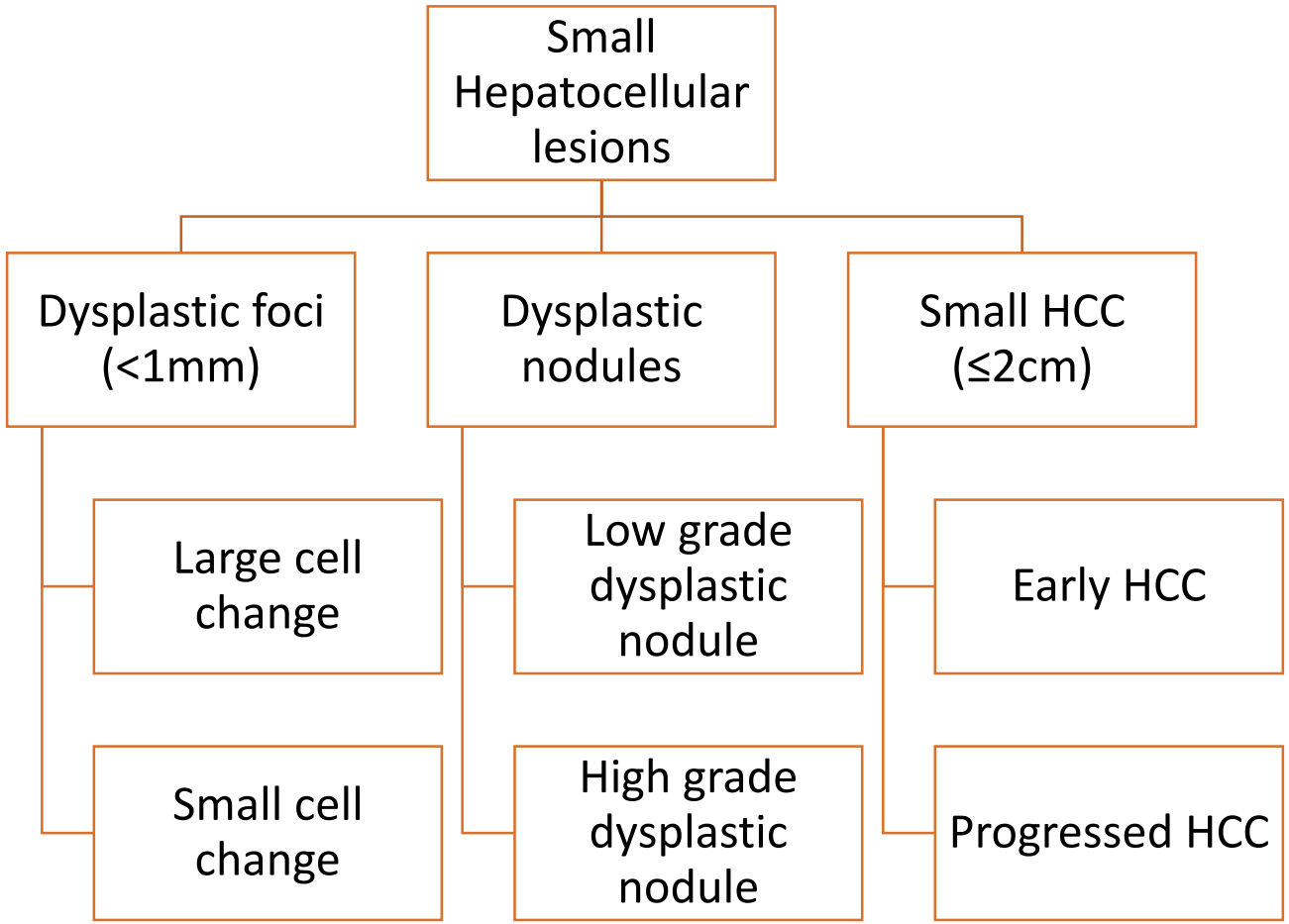
- *HNF1A*-inactivated HCA with loss of LFABP
- Diffuse strong glutamine synthetase suggesting strong β-catenin activation
- SAA staining

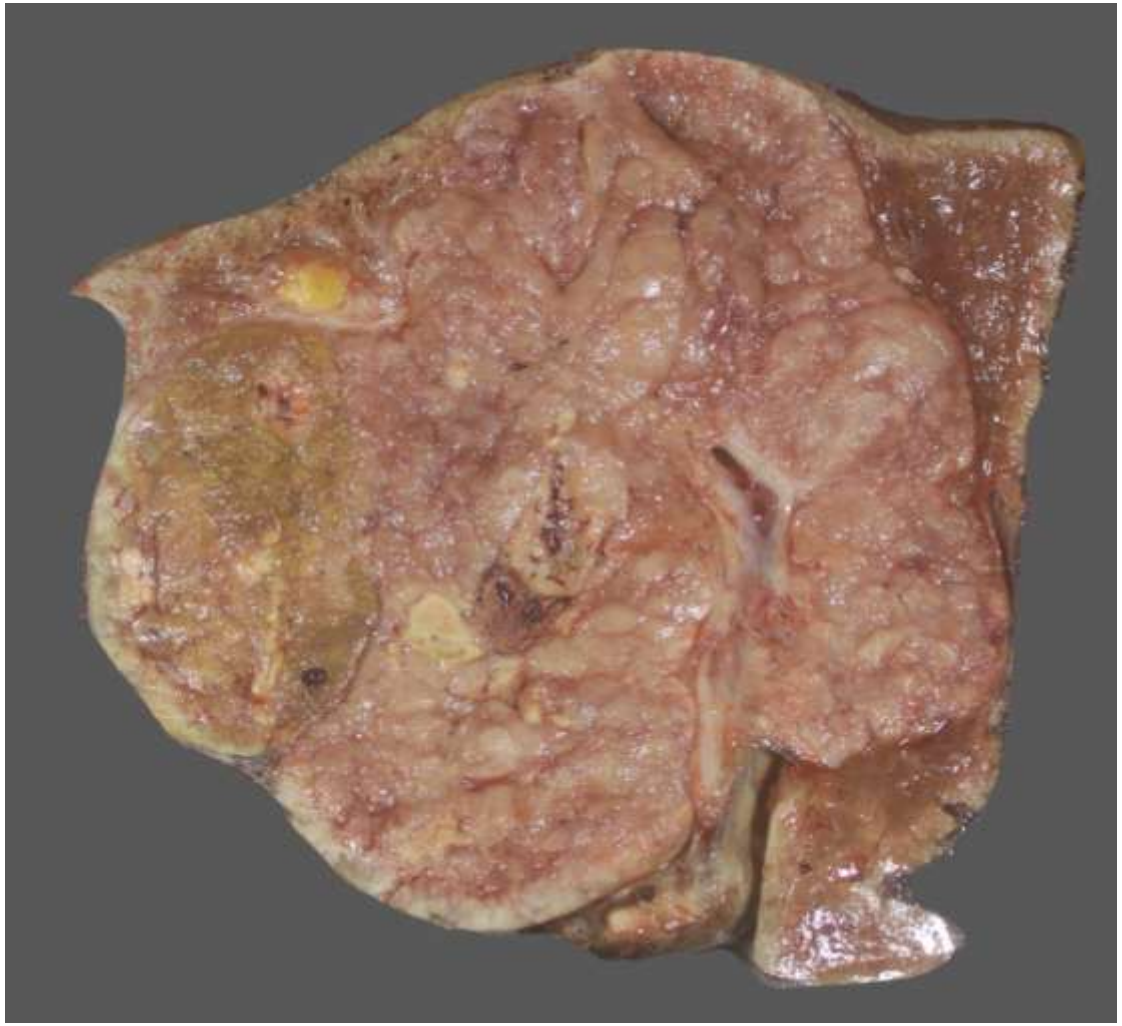
Hepatocellular carcinoma (HCC)

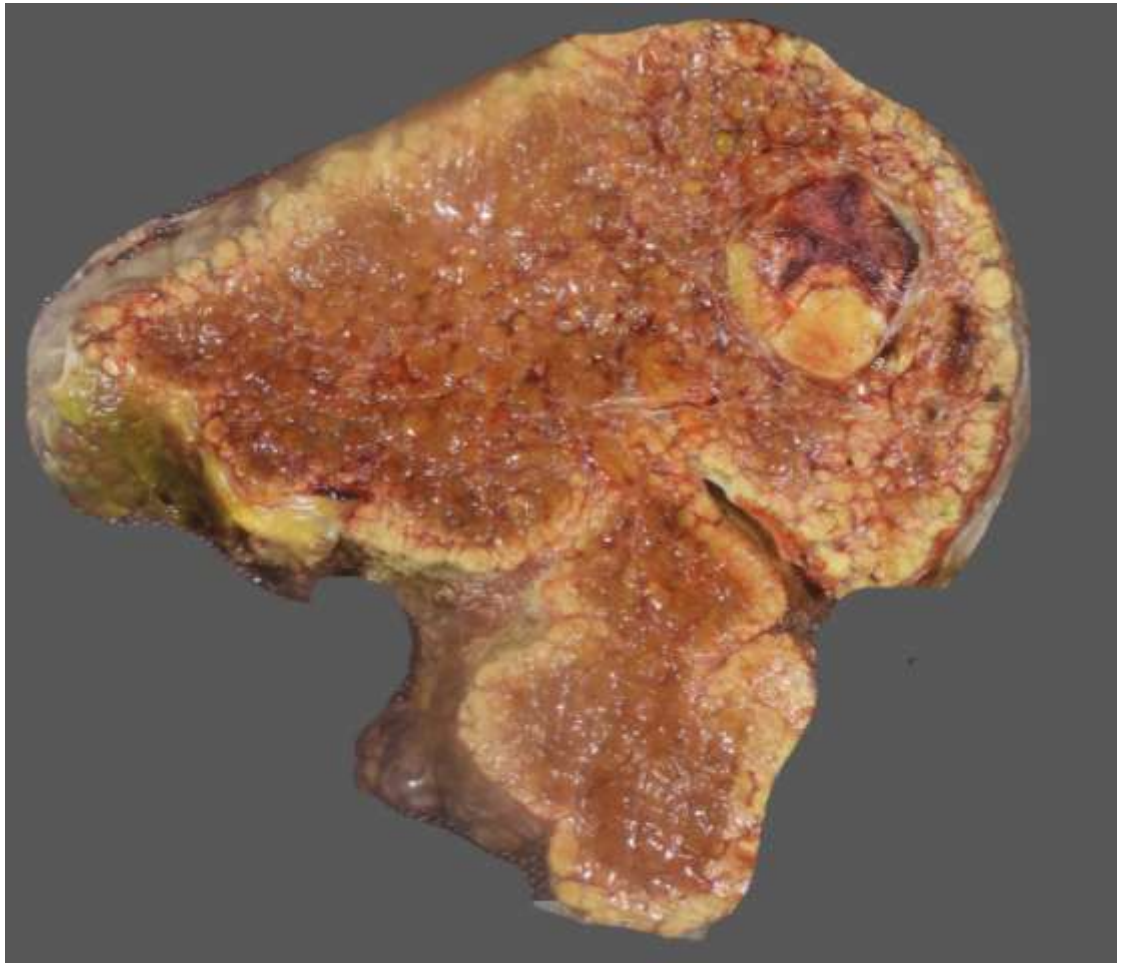
- Incidence is increasing steadily over the past two decades
- Currently ranks fifth most common cancer in men and seventh in women
- Major risk factors: HBV, HCV, chronic alcohol consumption, and NAFLD
- Majority detected at a clinically advanced stage
- Hepatocarcinogenesis is a multistep process of malignant transformation of hepatocytes through the sequential accumulation of multiple genomic and epigenomic alterations.
- HCC is a histologically and genetically diverse cancer
- Several new pathologic subtypes have been reported recently and new underlying genetic alterations have been described.
- Histological growth patterns are related to molecular alterations and oncogenic pathways.



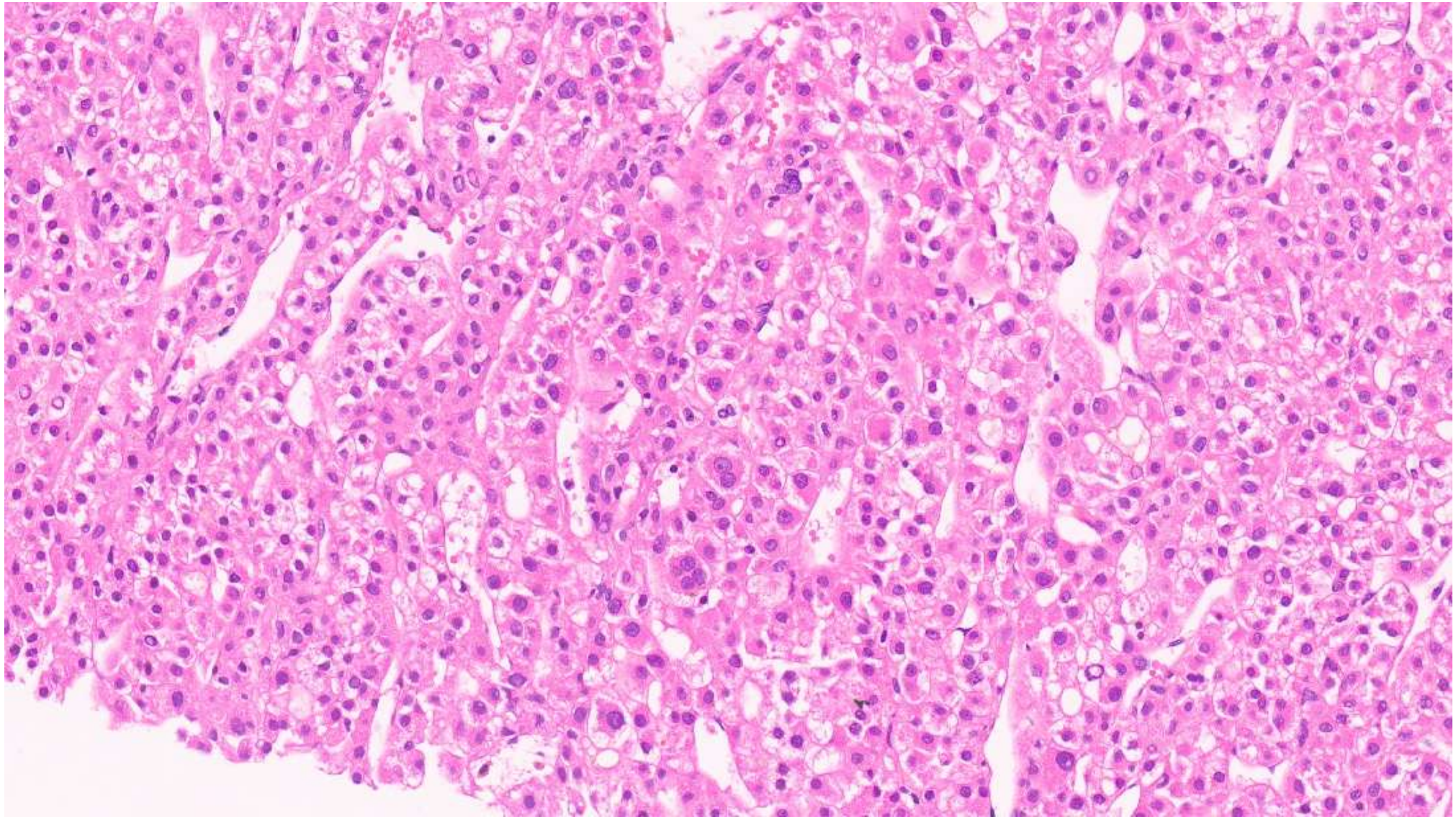
International consensus group for hepatocellular neoplasia classification of small hepatocellular lesions



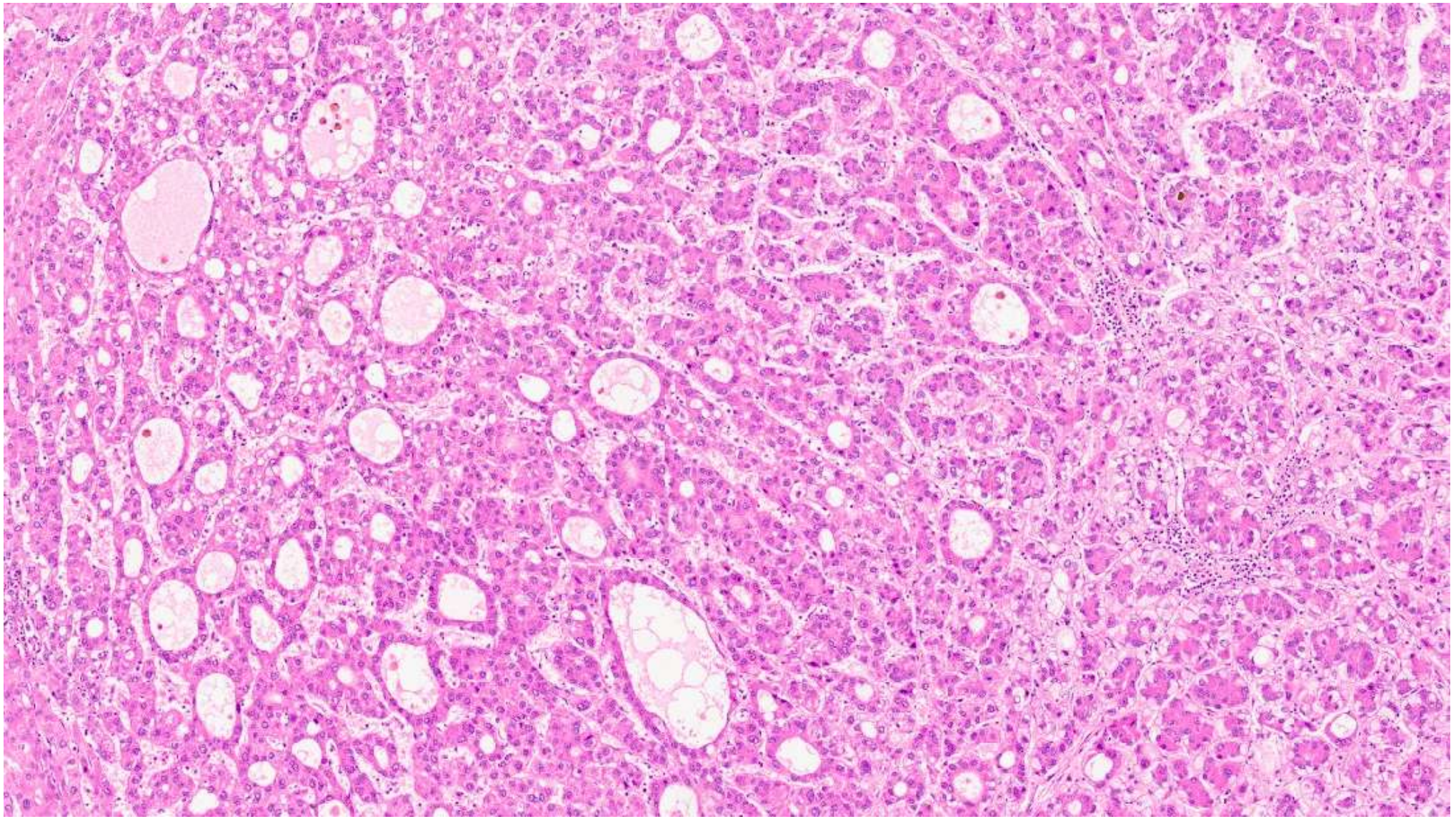




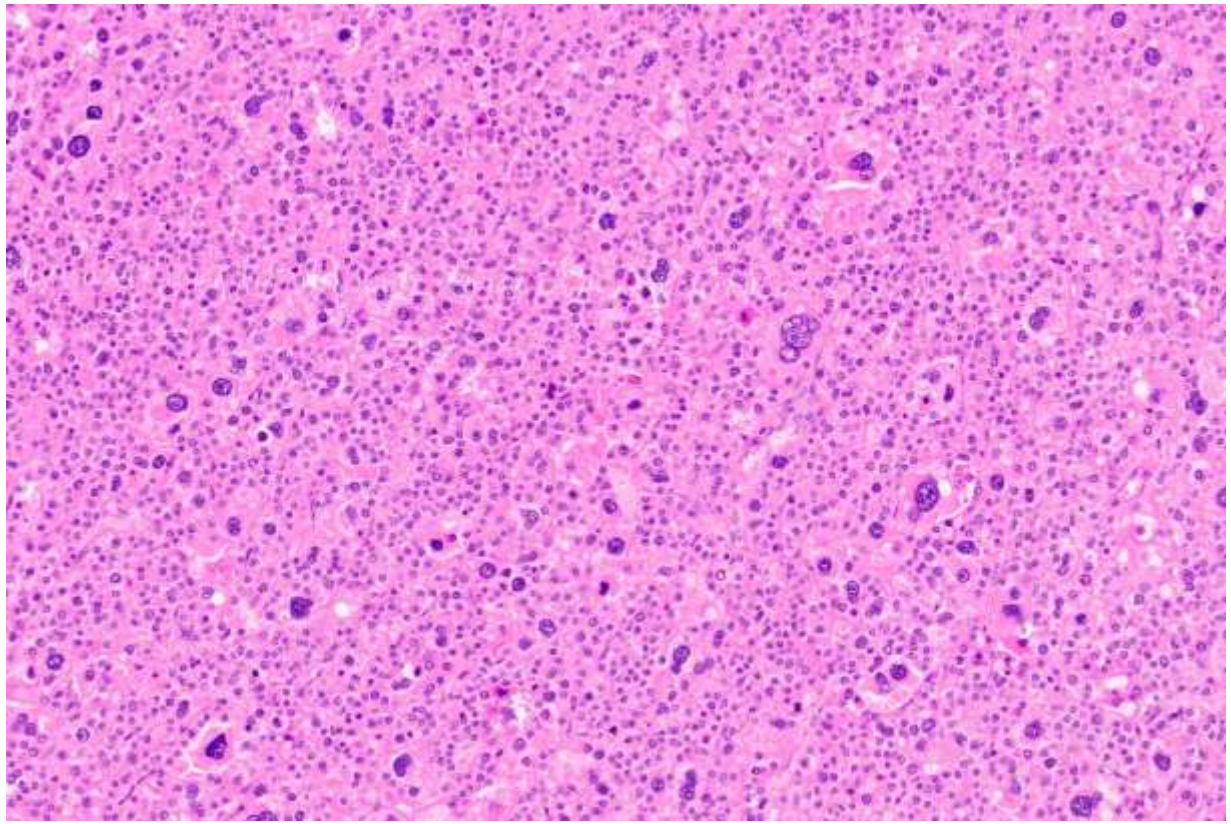
Trabecular growth pattern

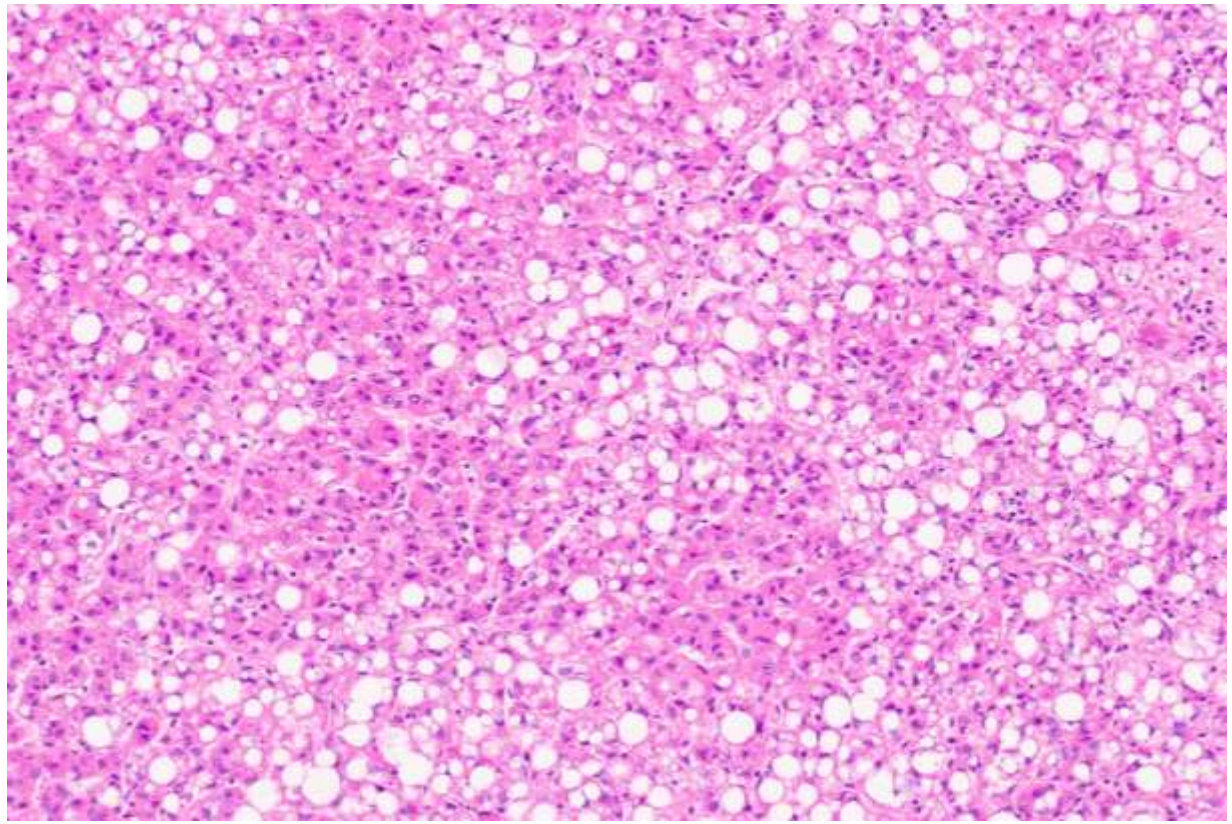


Pseudoacini growth pattern



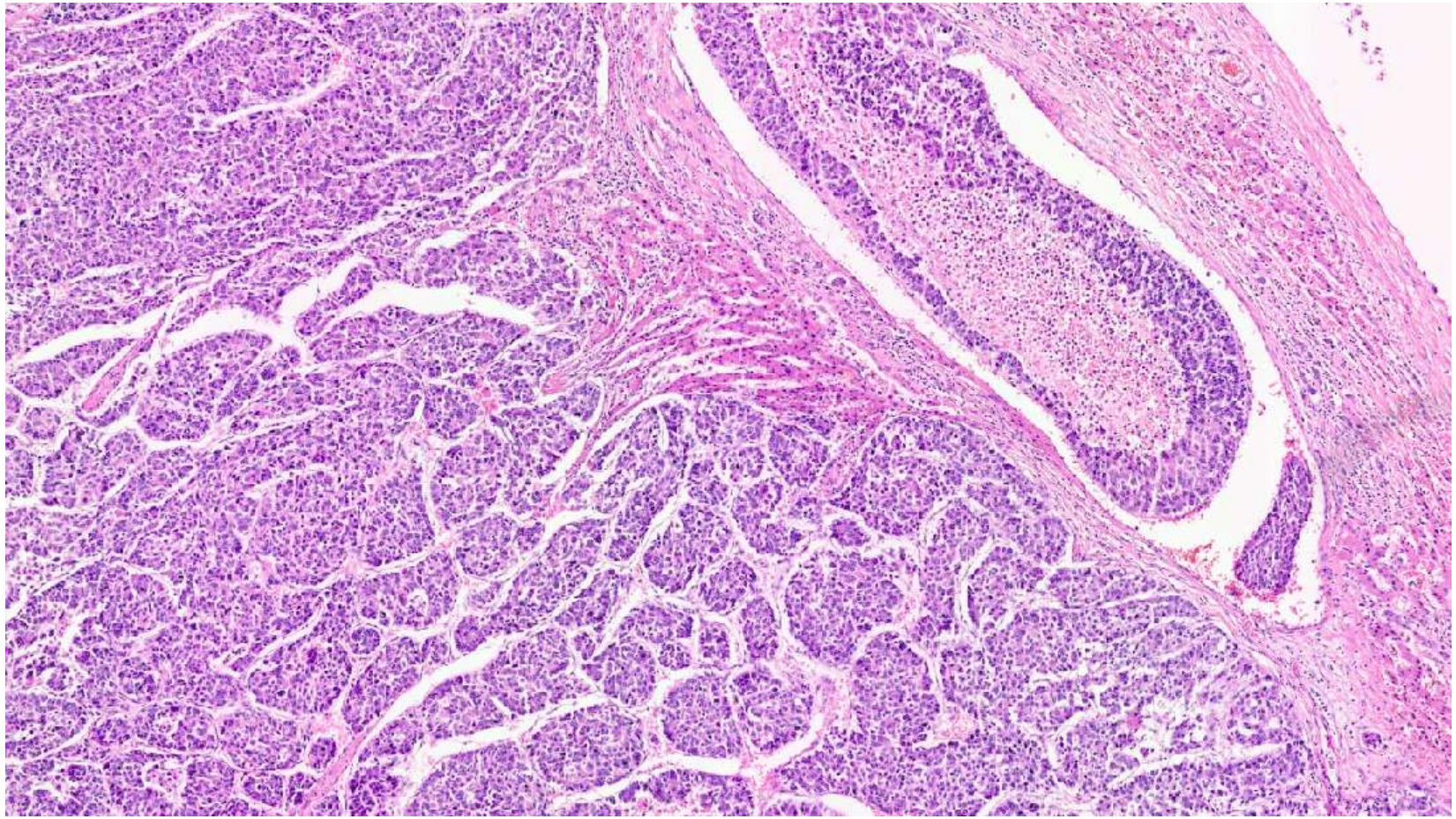
Solid sheets with pleomorphism and steatosis



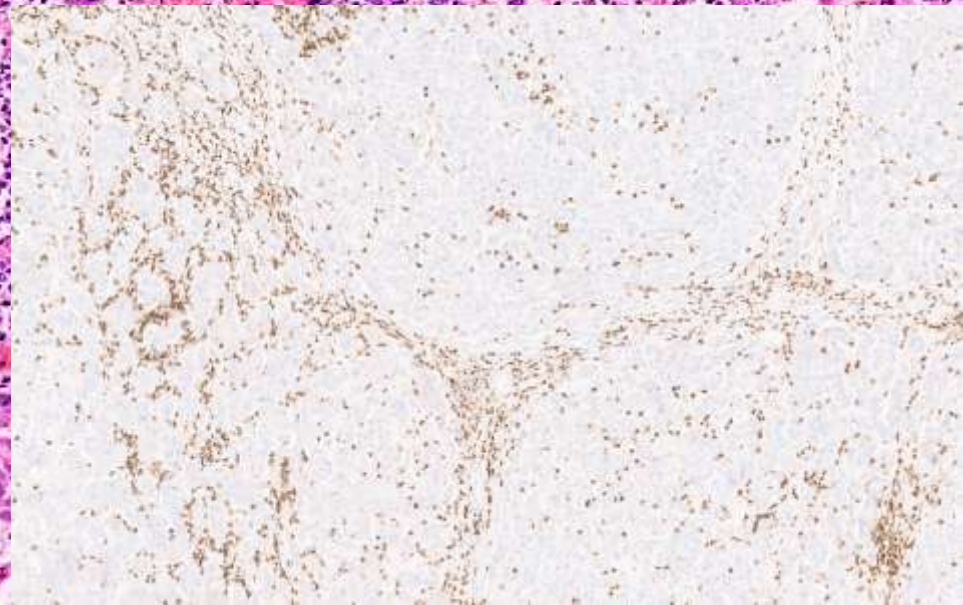


Macrotrabecular-Massive (MTM-HCC)

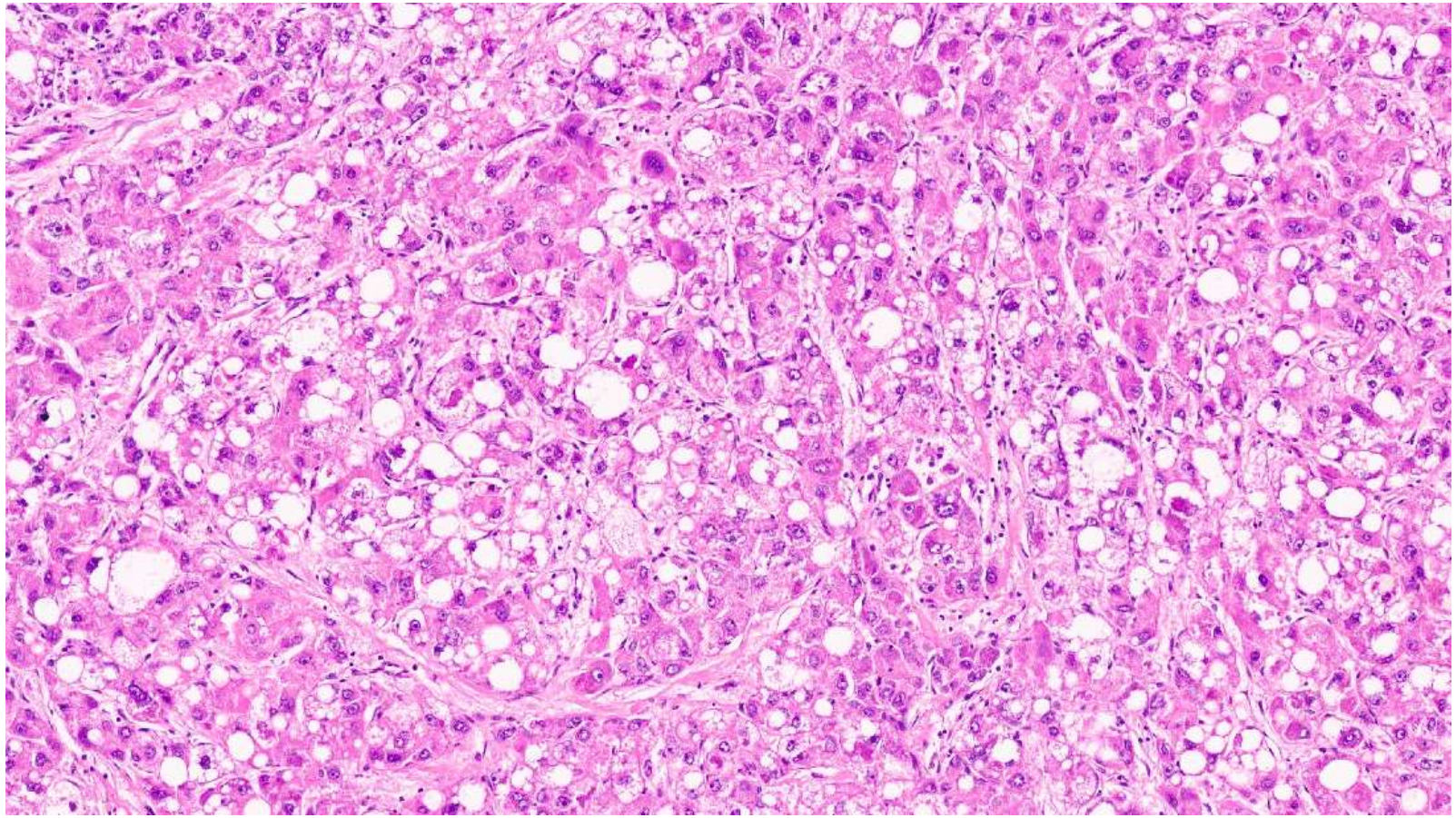
- HBV
- High AFP levels
- Very aggressive phenotype
- Frequent satellite nodules and vascular invasion
- Angiogenesis activation is a hallmark feature
- Both angiopoietin 2 and VEGFA overexpression



Lymphoepithelioma-like Hepatocellular Carcinoma (LEL-HCC)/Lymphocyte rich hepatocellular carcinoma

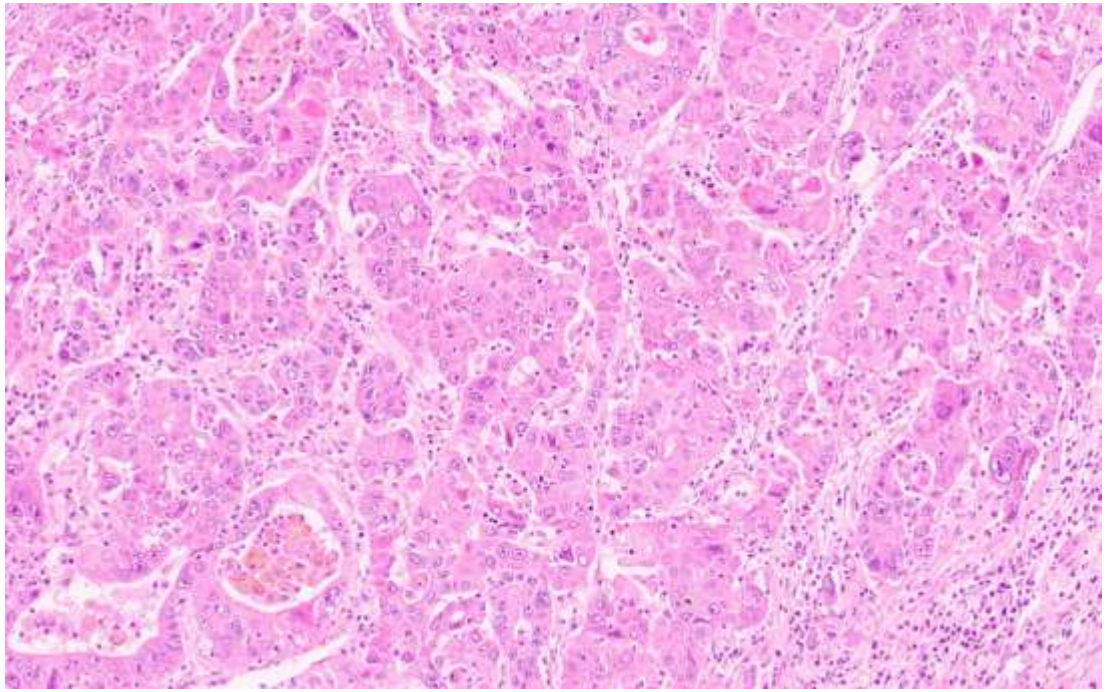


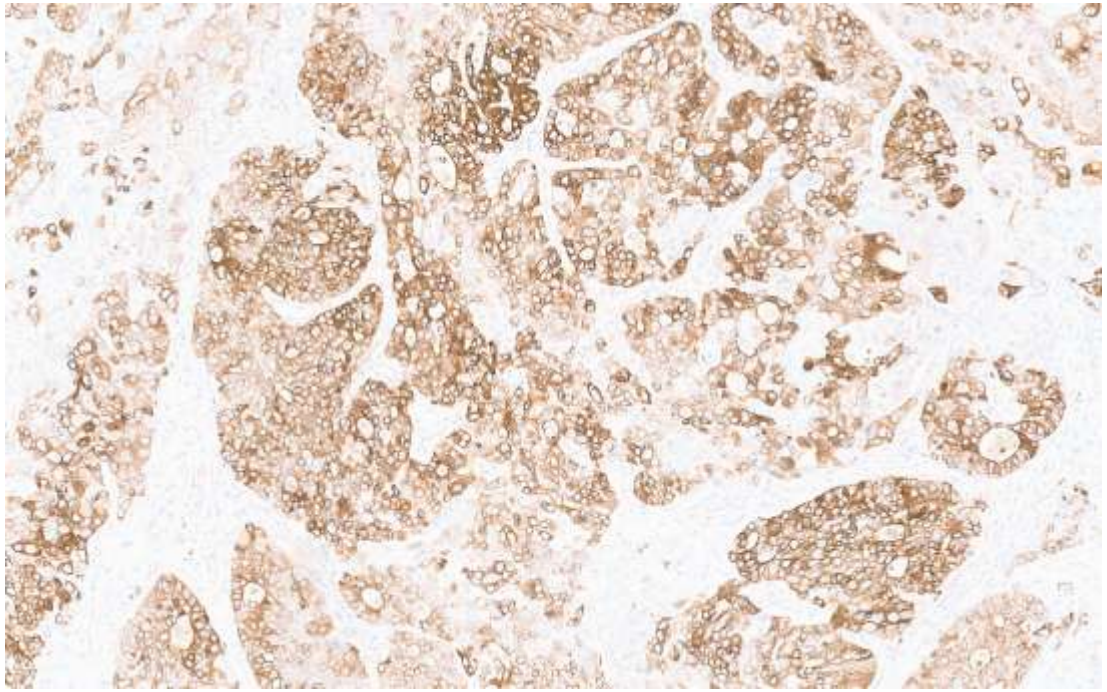
- Well to moderately differentiated
- Upregulation of interleukin-6
- C-reactive protein

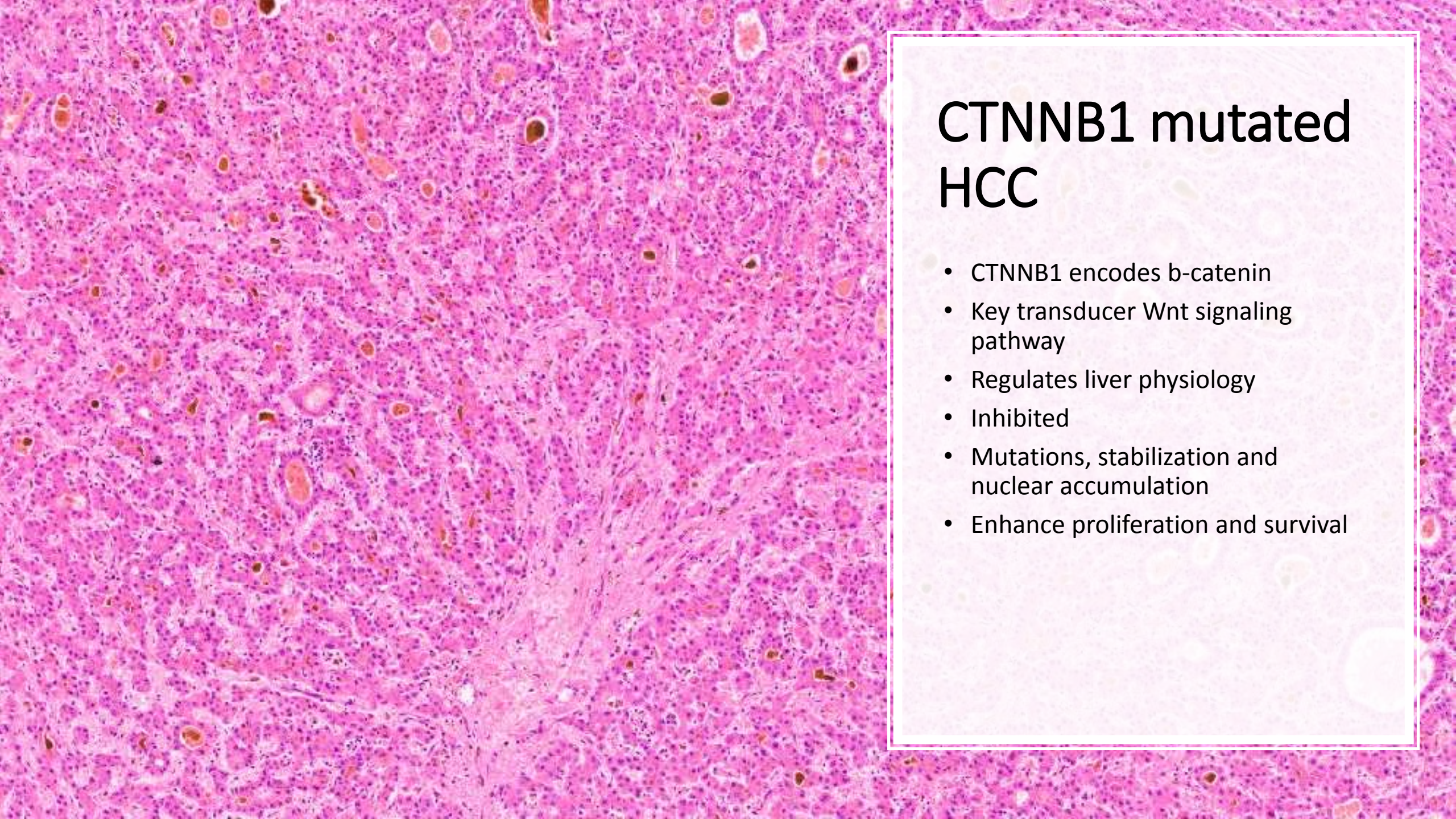


Steatohepatitic HCC

CK19 Positive HCC (Proginator subtype)

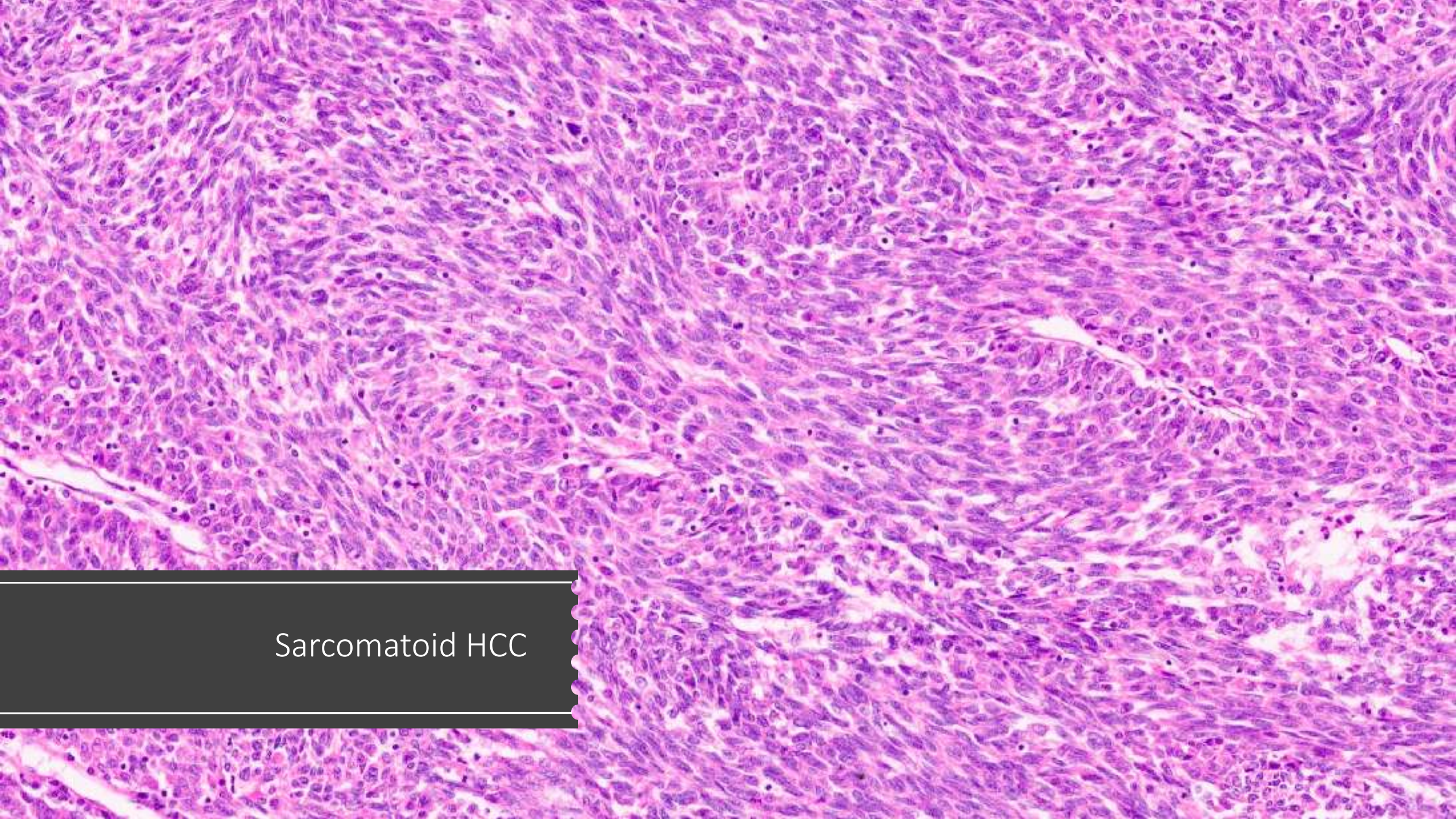




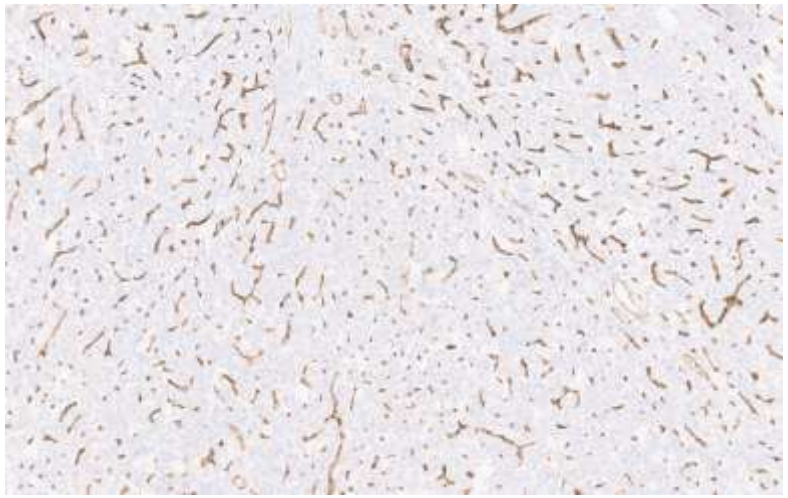


CTNNB1 mutated HCC

- CTNNB1 encodes b-catenin
- Key transducer Wnt signaling pathway
- Regulates liver physiology
- Inhibited
- Mutations, stabilization and nuclear accumulation
- Enhance proliferation and survival


Sarcomatoid HCC

CD34 (VETC)



Multicenter Study > Hepatology. 2020 Jan;71(1):183-195. doi: 10.1002/hep.30814. Epub 2019 Aug 9.

Vessels Encapsulating Tumor Clusters (VETC) Is a Powerful Predictor of Aggressive Hepatocellular Carcinoma

Salvatore Lorenzo Renne [1], Ha Young Woo [2], Sarah Allegra [1], Noemi Rudini [1], Hirohisa Yano [3], Matteo Donadon [4,5], Luca Viganò [4,5], Jun Akiba [6], Hye Sun Lee [7], Hyungjin Rhee [8], Young Nyun Park [2], Massimo Roncalli [1,5], Luca Di Tommaso [1,5]

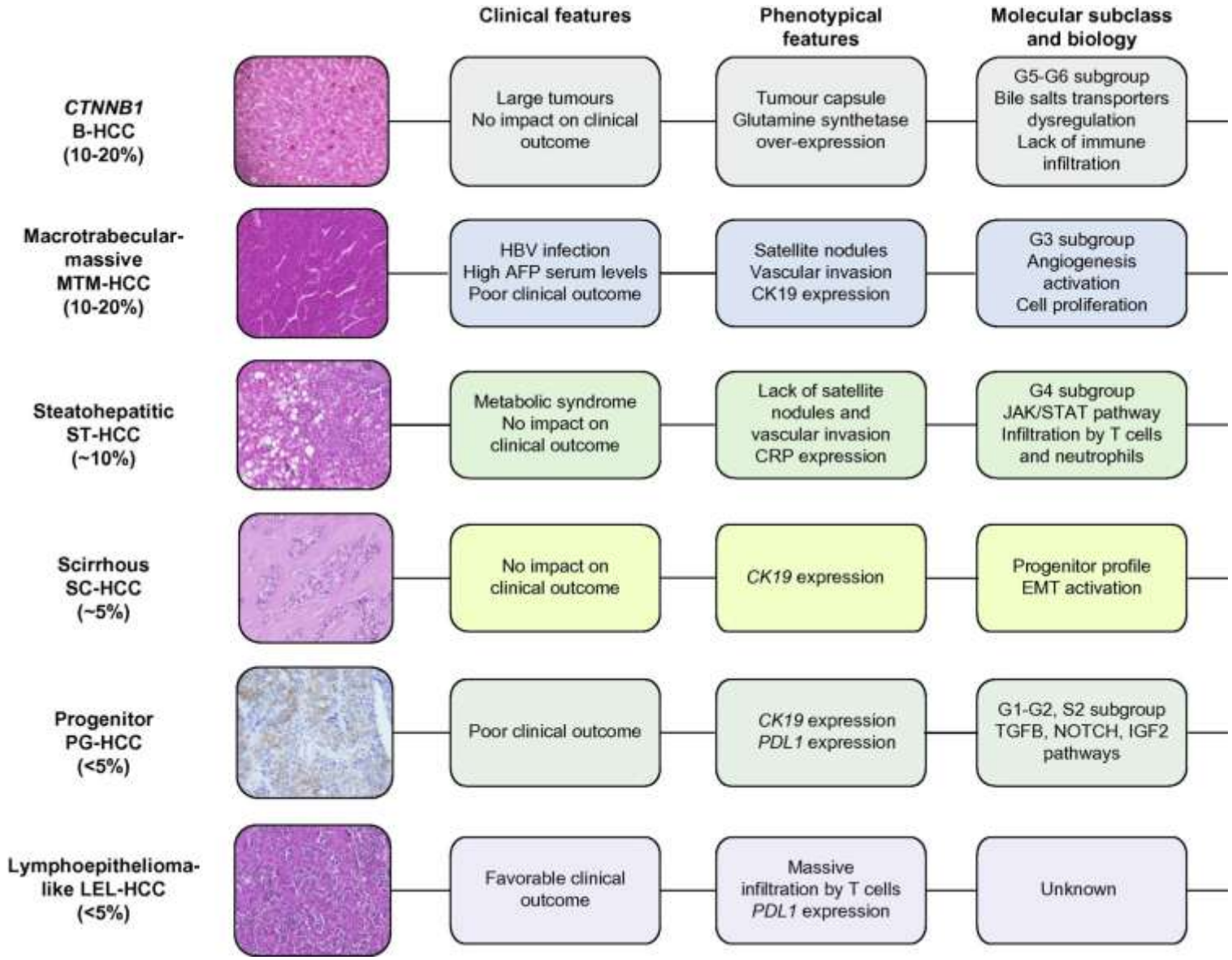
Multicenter Study > Hepatology. 2019 Sep;70(3):824-839. doi: 10.1002/hep.30366. Epub 2019 Mar 15.

Vessels That Encapsulate Tumor Clusters (VETC) Pattern Is a Predictor of Sorafenib Benefit in Patients with Hepatocellular Carcinoma

Jian-Hong Fang [1], Li Xu [2], Li-Ru Shang [1], Chu-Zhi Pan [3], Jin Ding [4], Yun-Qiang Tang [3], Hui Liu [4], Chu-Xing Liu [1], Jia-Lin Zheng [3], Yao-Jun Zhang [2], Zhong-Guo Zhou [2], Jing Xu [2], Limin Zheng [1], Min-Shan Chen [2], Shi-Mei Zhuang [1,2,3]

Clinical, biological, pathological and molecular features of main HCC subtypes

Most frequent alterations: TERT promoter, CTNNB1 and TP53 mutations

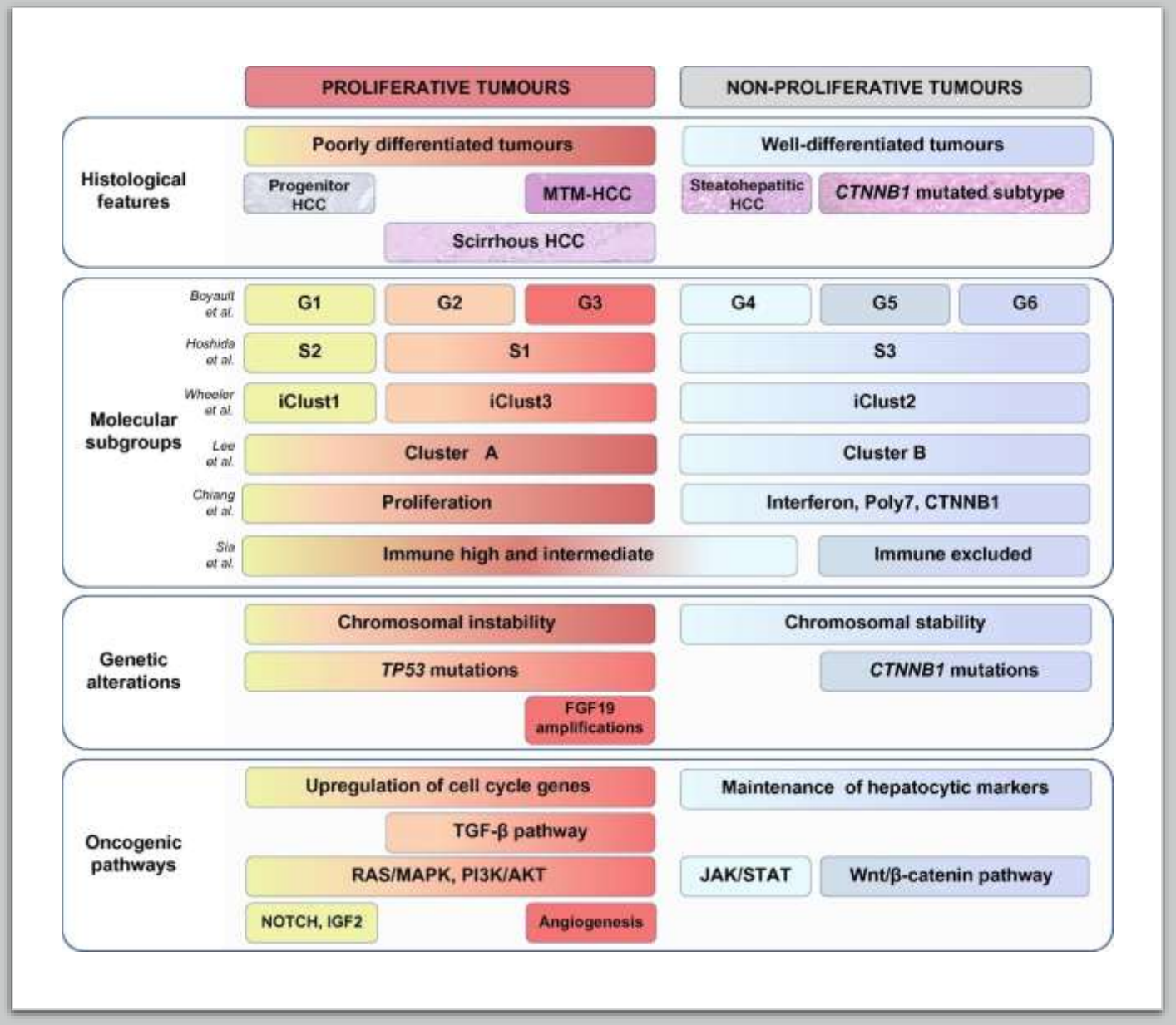


Review > J Hepatol. 2019 Sep;71(3):616-630. doi: 10.1016/j.jhep.2019.06.001. Epub 2019 Jun 10.

Molecular and histological correlations in liver cancer

Julien Calderaro [1], Marianne Ziol [2], Valérie Paradis [3], Jessica Zucman-Rossi [4]

Molecular subclasses and oncogenic pathways of hepatocellular carcinoma (HCC) with clinicopathological correlates



Review > J Hepatol. 2019 Sep;71(3):616-630. doi: 10.1016/j.jhep.2019.06.001. Epub 2019 Jun 10.

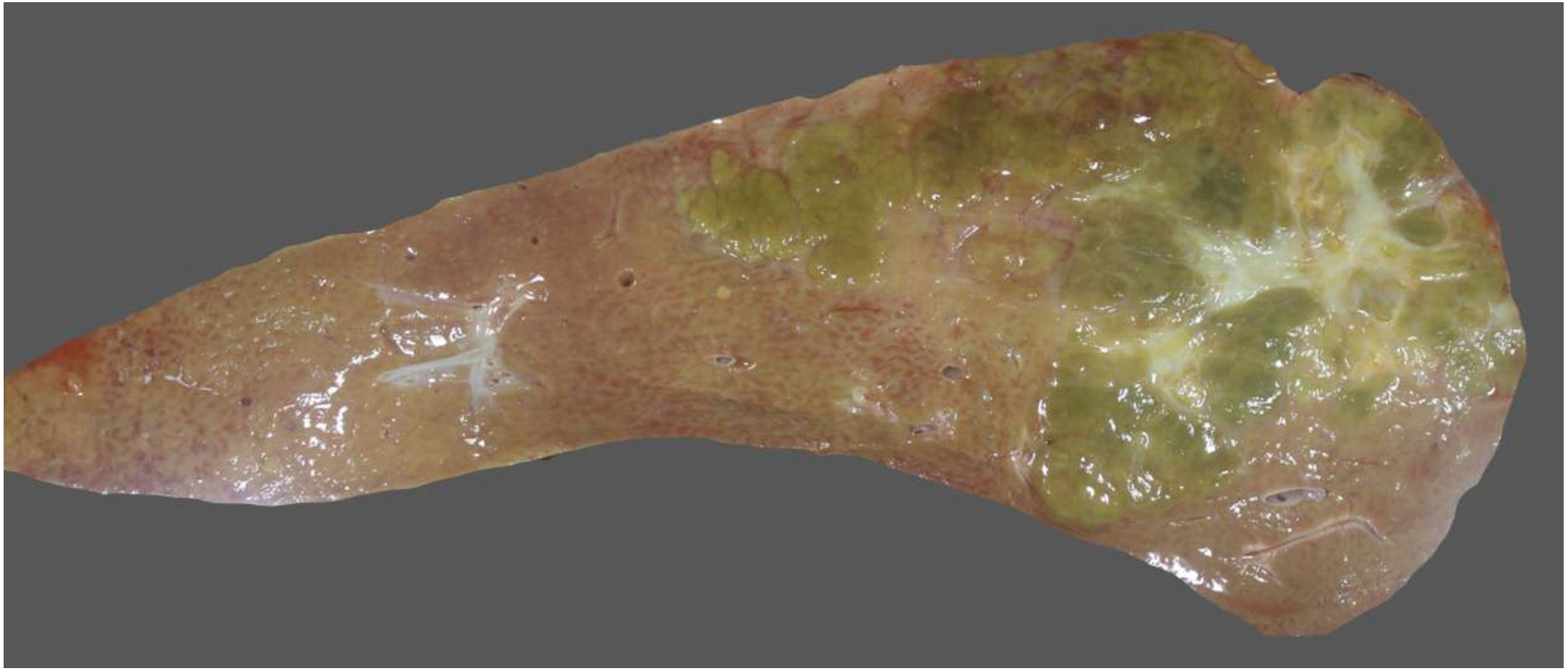
Molecular and histological correlations in liver cancer

Julien Calderaro [1], Marianne Ziol [2], Valérie Paradis [3], Jessica Zucman-Rossi [4]

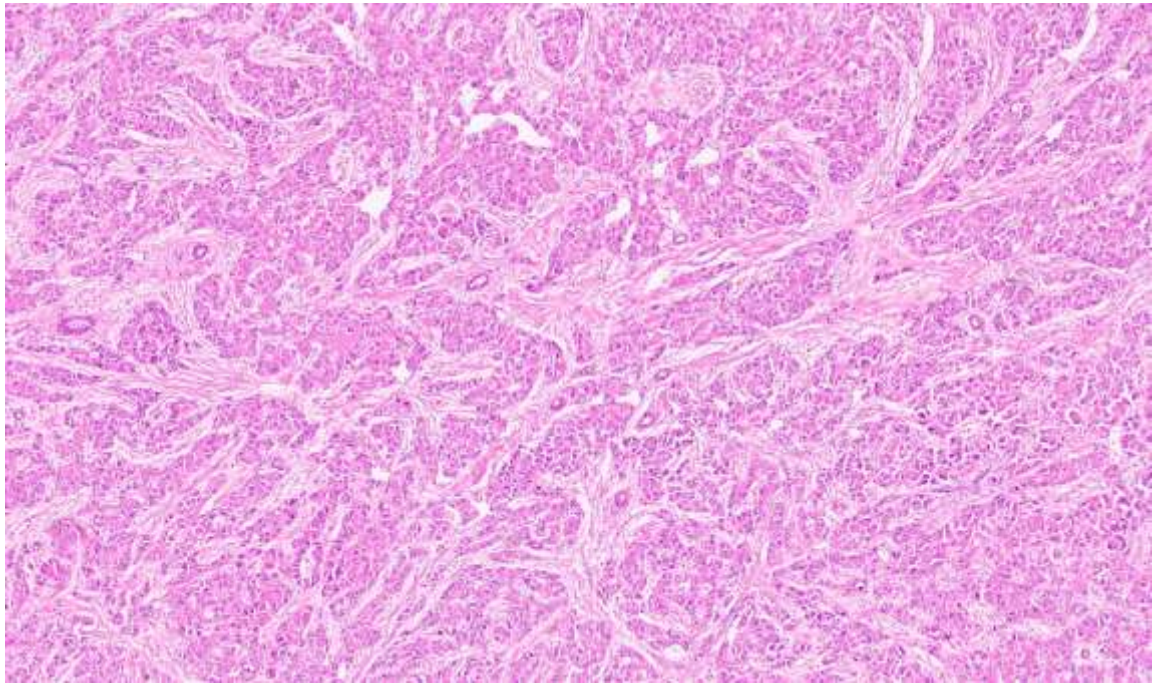
Fibrolamellar HCC (FL-HCC)

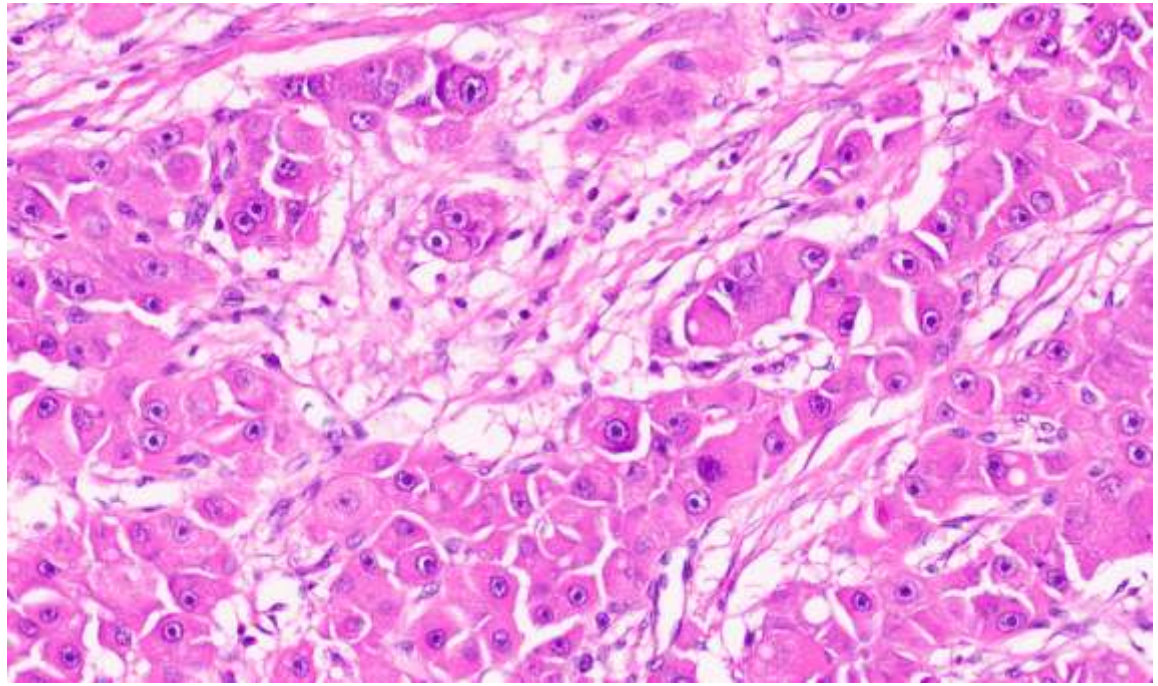
- Rare and unique histologic subtype with a predilection for adolescent and young adults
- Without underlying liver disease
- Mostly solitary, large and well circumscribed grossly, with a yellow tan to greenish coloured cut surface and areas of central scarring
- Tumour cells are large polygonal with abundant eosinophilic granular cytoplasm, centrally located nuclei with vesicular chromatin, and prominent nucleoli
- Dense bands of intratumoral fibrosis arranged in lamellar (parallel arrangement) pattern separates the trabeculae and clusters of tumour cells
- Recurrent-specific translocation PRKACA-DNAJB1
- Immunophenotyping: Positivity of CD68 and CK-7 (biliary lineage) apart from markers of hepatic differentiation (Arginase 1, Hep-par1 and albumin mRNA as detected by in situ hybridization).
- Both FISH or RT-PCR are available now to detect DNAJB1-PRKACA fusion

Fibrolamellar HCC



Fibrolamellar HCC



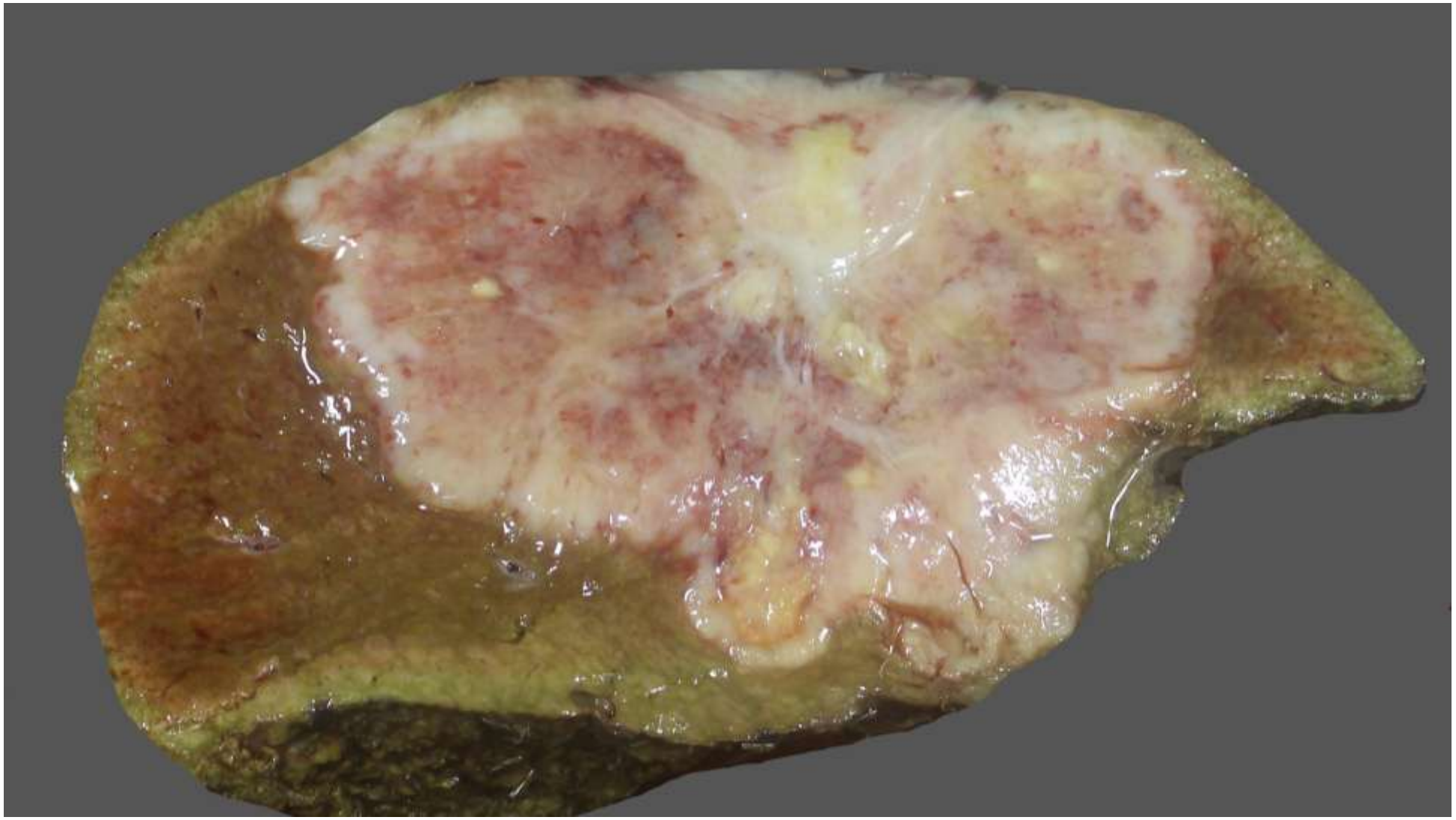


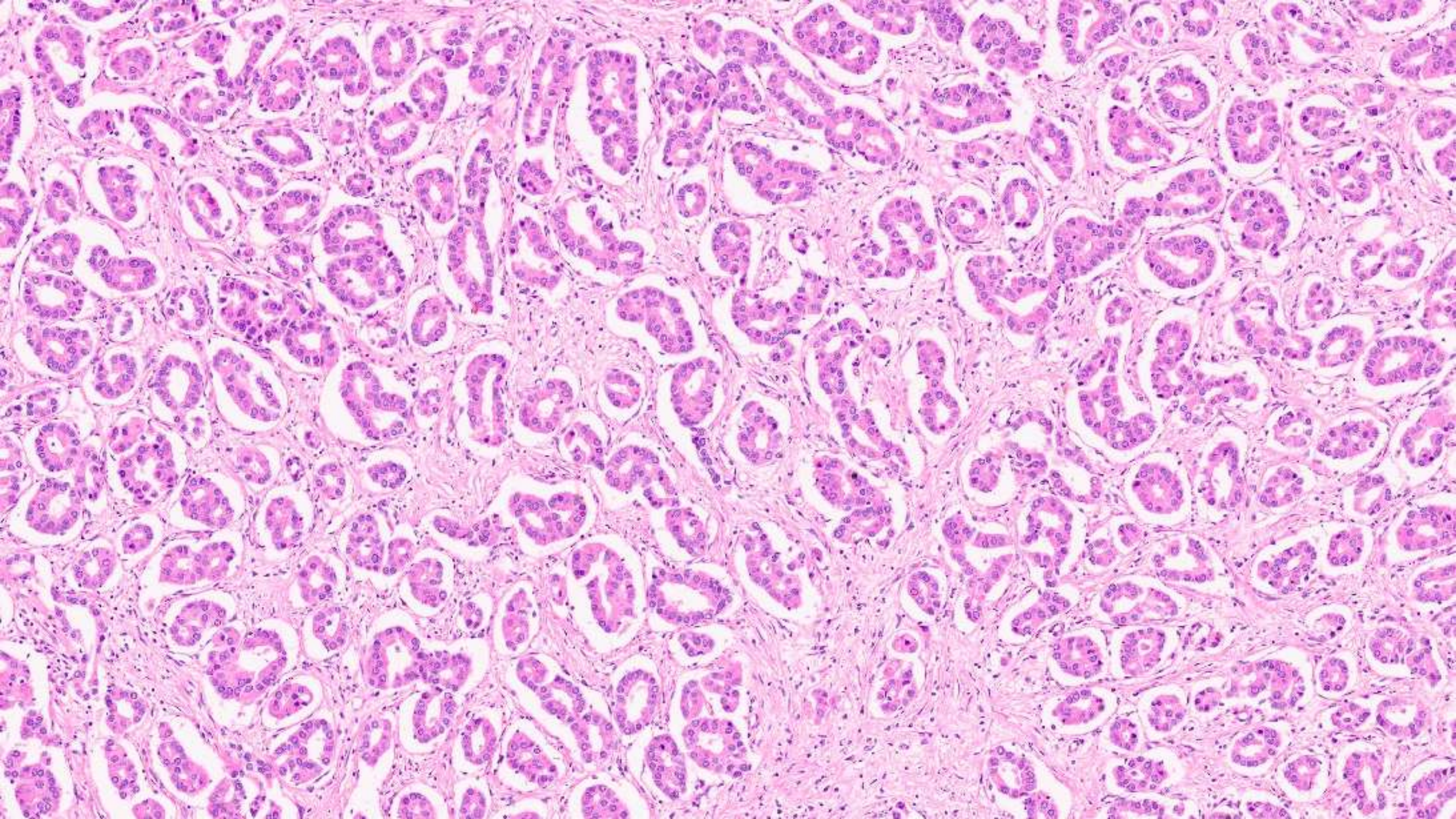
Cholangiocarcinoma

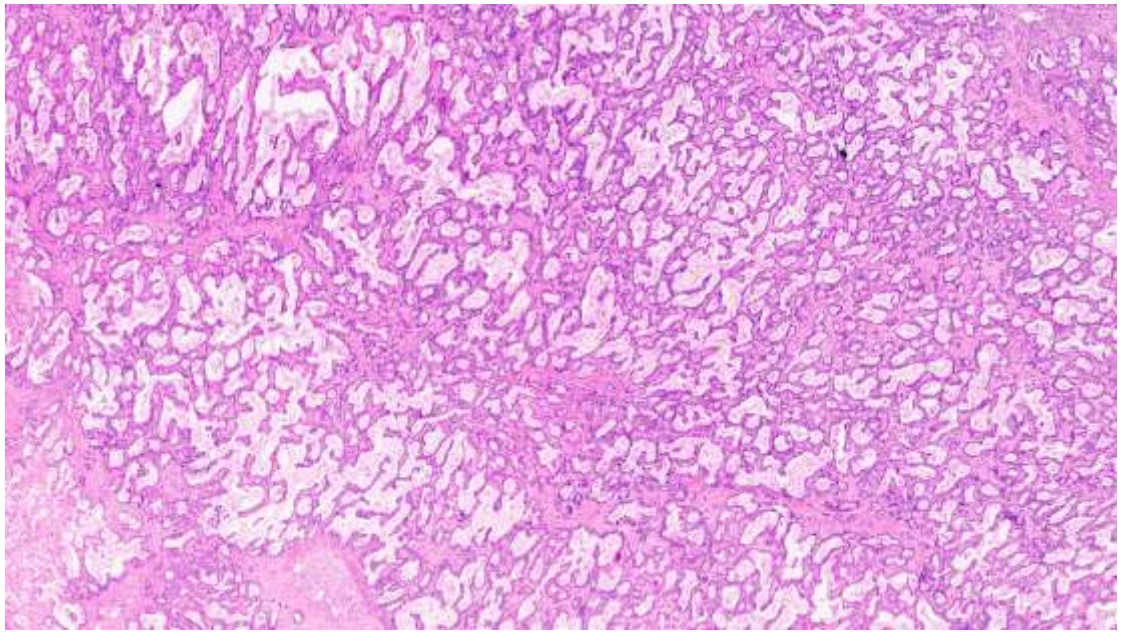
- Heterogeneous group of highly aggressive cancers
- May arise anywhere within the biliary tree
- Wide geographical variation
- Most cases (70%) are sporadic, occurring without any probable or known risk factors
- Intrahepatic, perihilar and distal based on their anatomical location
- Significant turning point in iCCA treatment: identification of *IDH* mutations and *FGFR* fusions
- Can be targeted with currently available therapies.

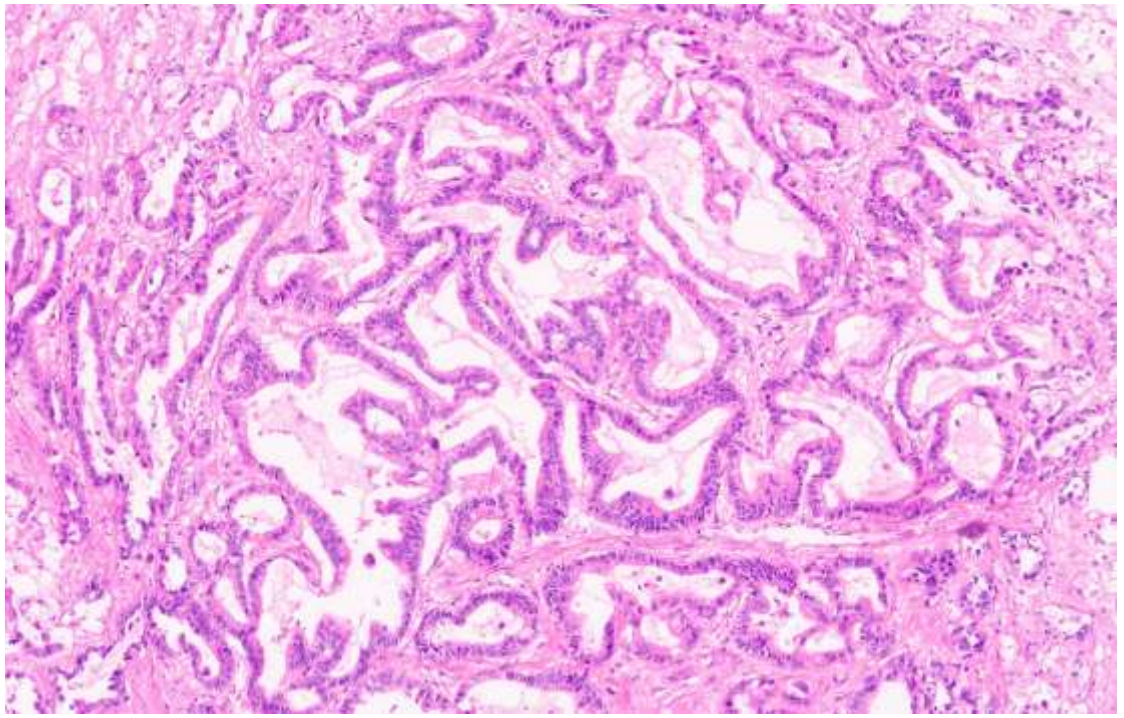
Vij M et al. Pathological, molecular, and clinical characteristics of cholangiocarcinoma: A comprehensive review. World J Gastrointest Oncol. 2022 Mar 15;14(3):607-627.

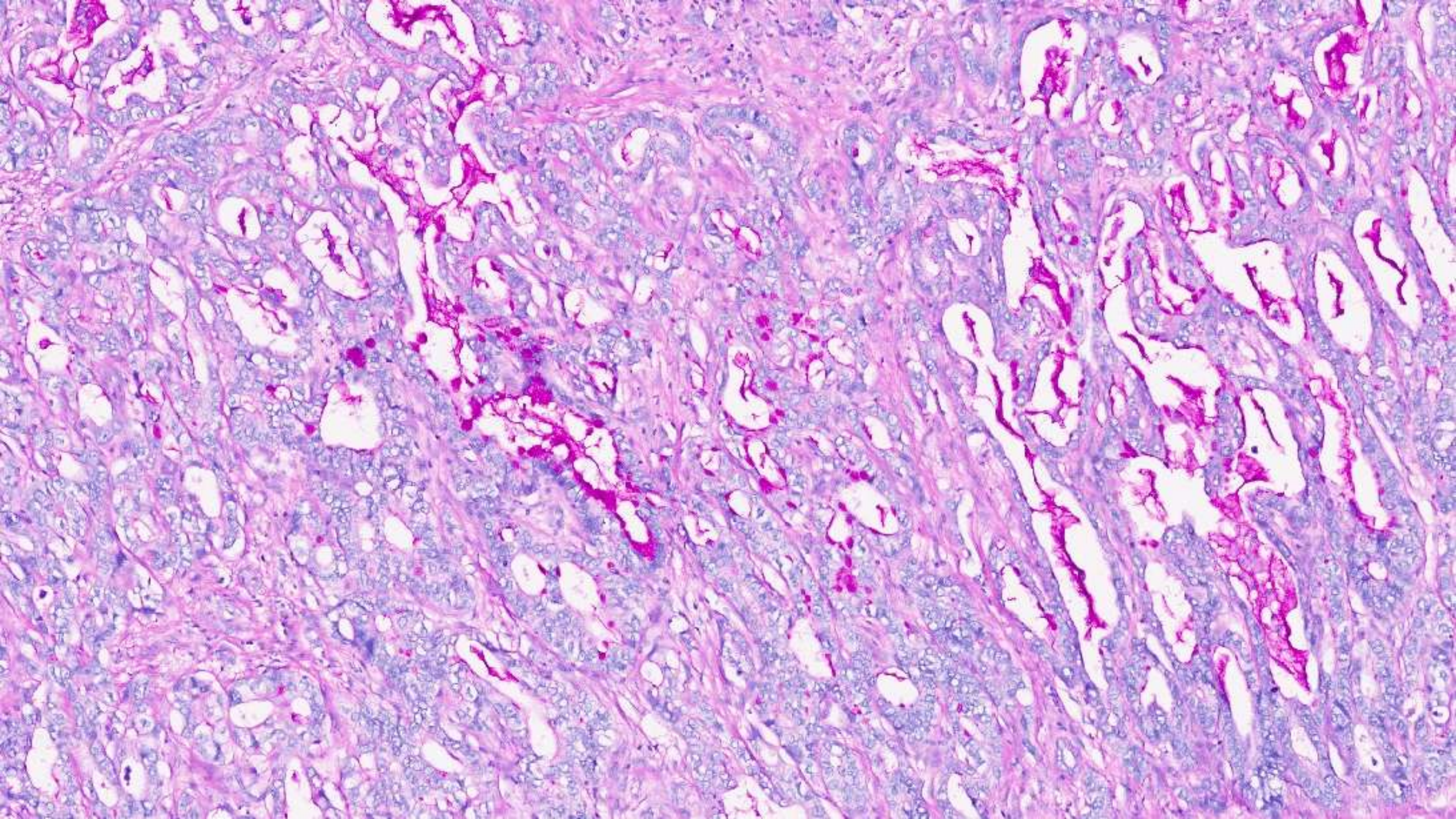
Mass forming Intrahepatic Cholangiocarcinoma









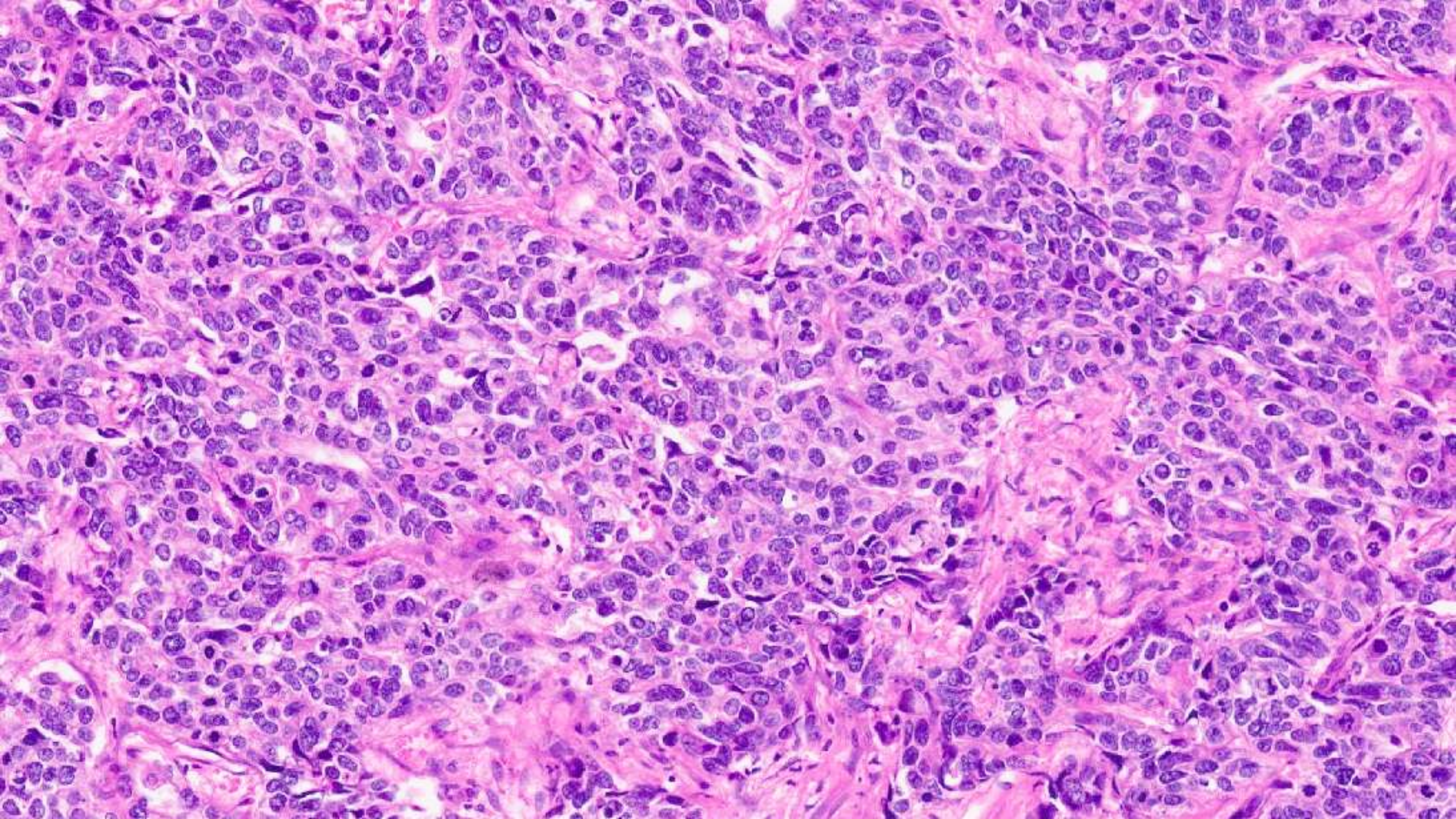


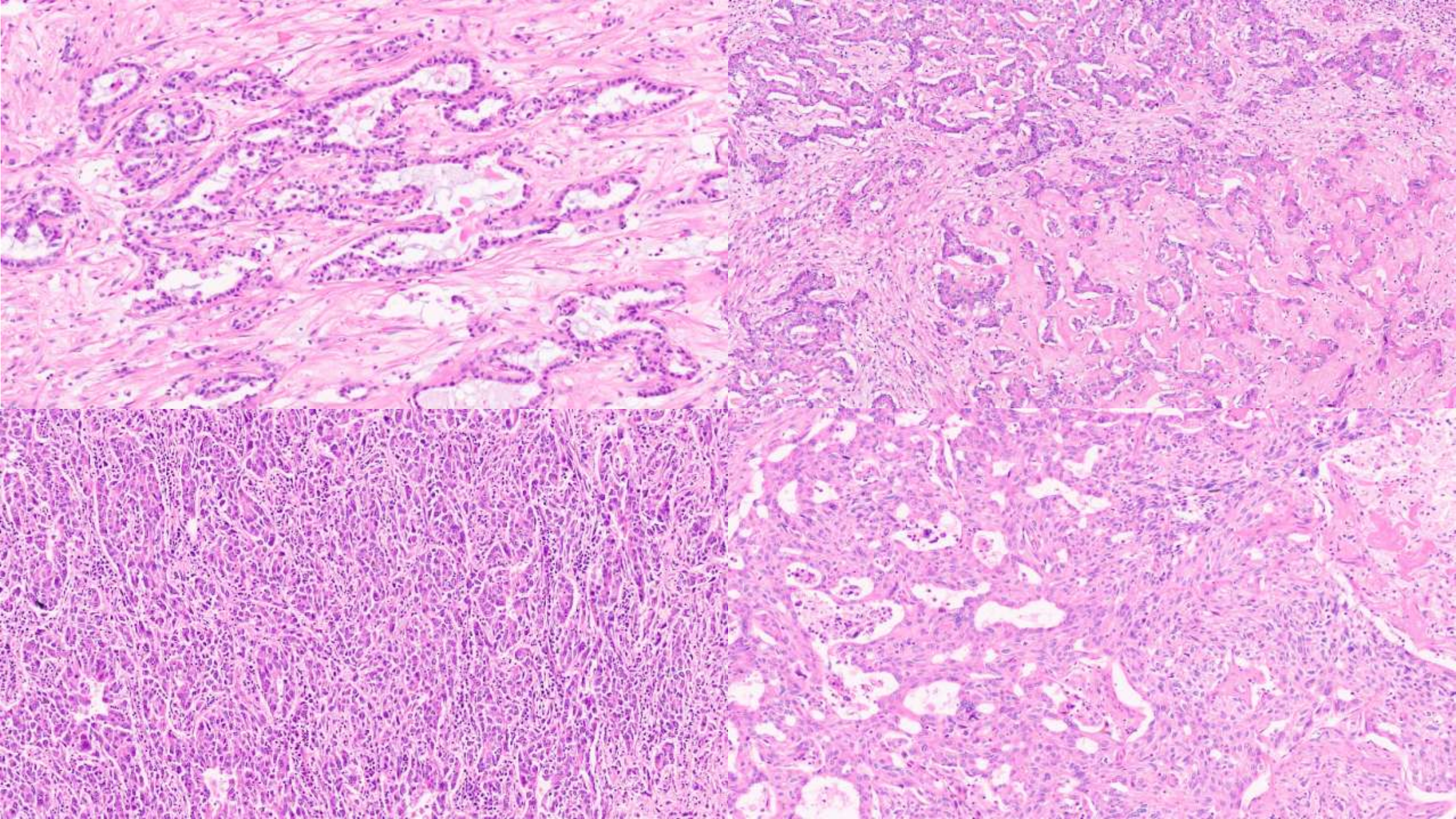
	Large duct type	Small duct type
Location	Proximal to hepatic hilum	Peripheral
Risk factors	PSC, Liver fluke infection, Hepatolithiasis	Chronic liver disease, viral hepatitis
Gross features	Periductal infiltrating, Mixed pattern	Mass forming
Precursor lesion	BilIN, IPNB, ITPN	Unknown
Pathology	Large, widely spaced glands, Columnar with mucin production, desmoplastic stroma	Small tubules, fused or anastomosing glands, cuboidal to low columnar, central scarring, minimal to no mucin
Perinerual invasion	Common	Rare
Lymphovascular invasion/lymph node metastases	Common	Rare
Tumour border	Infiltrative	Expansile or pushing, rarelyinfiltrative
Immunohistochemical features	S100P and TFF1	CD56, N-cadherin, CRP
Molecular alterations	KRAS and GNAS mutationsCOX2 upregulations	IDH1/IDH2 and BRAF mutations, FGFR2 fusion

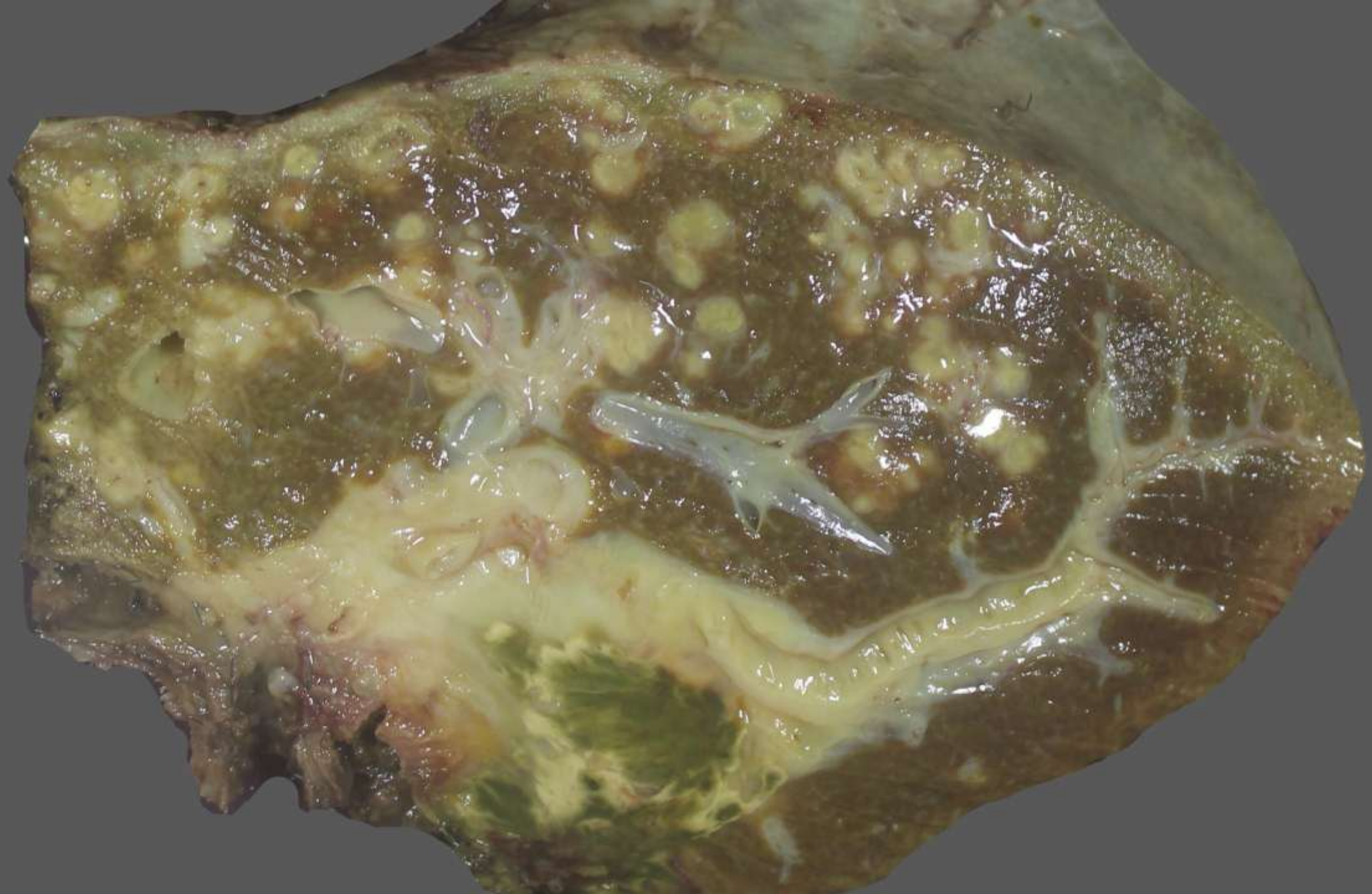
BilIN: Biliary intraepithelial neoplasia; CRP: C-reactive protein; IPNB: Intraductal papillary neoplasm of the bile duct; ITPN: Intraductal tubulopapillary neoplasms; PS

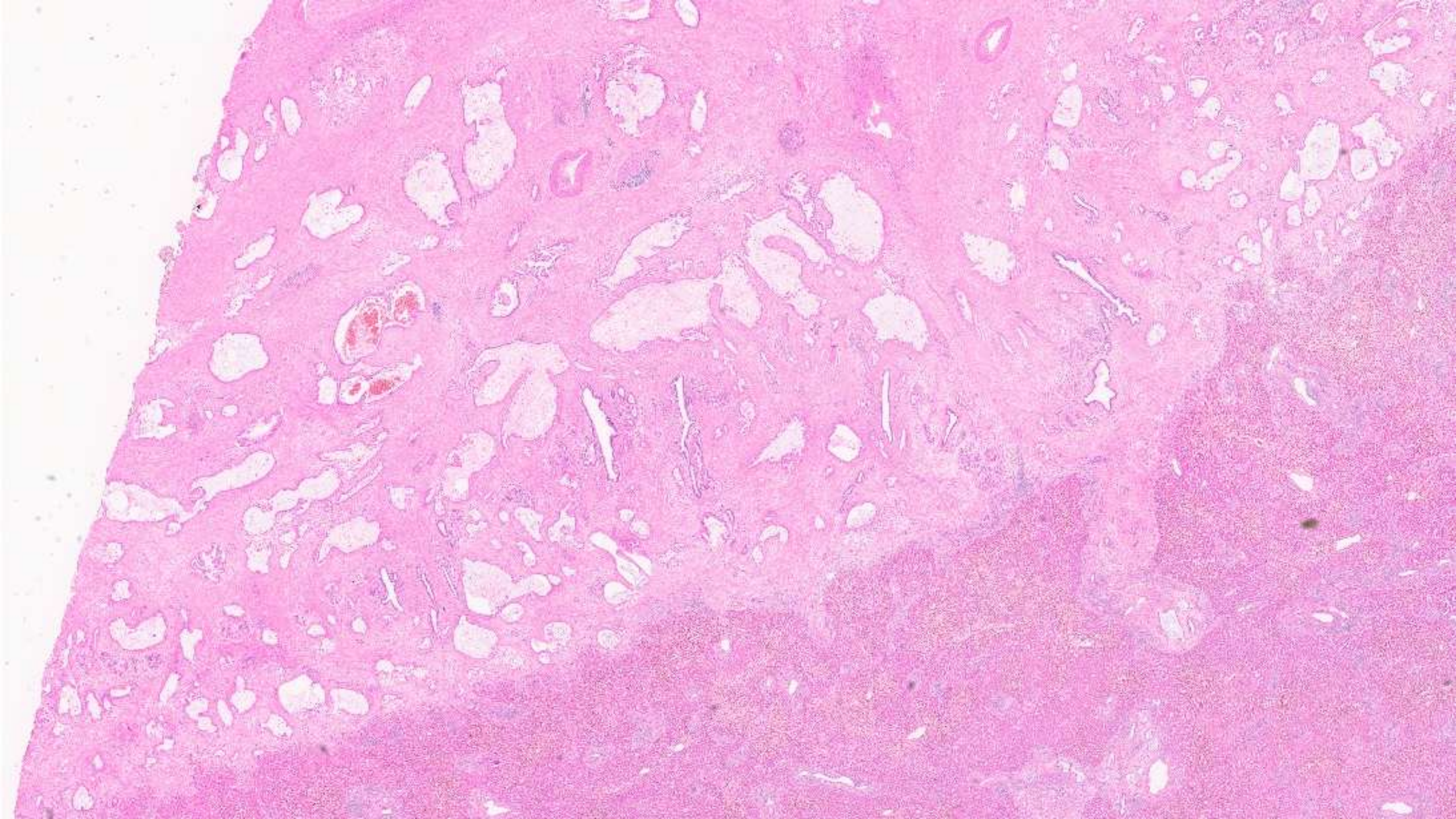
Ivosidenib, an *IDH1* inhibitor
Infigratinib, an *FGFR2* inhibitor

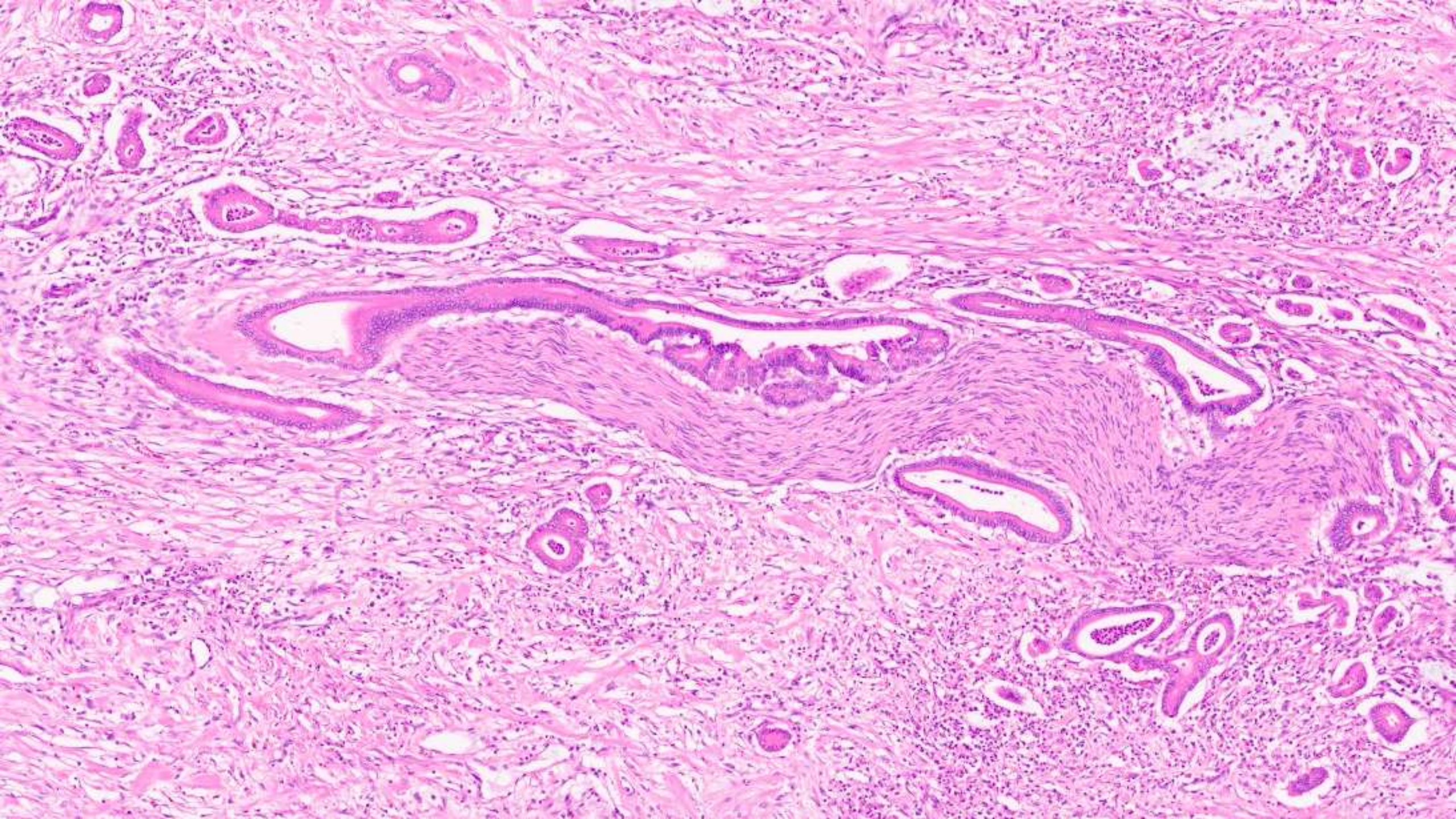
Vij M et al. Pathological, molecular, and clinical characteristics of cholangiocarcinoma: A comprehensive review. World J Gastrointest Oncol. 2022 Mar 15;14(3):607-627.

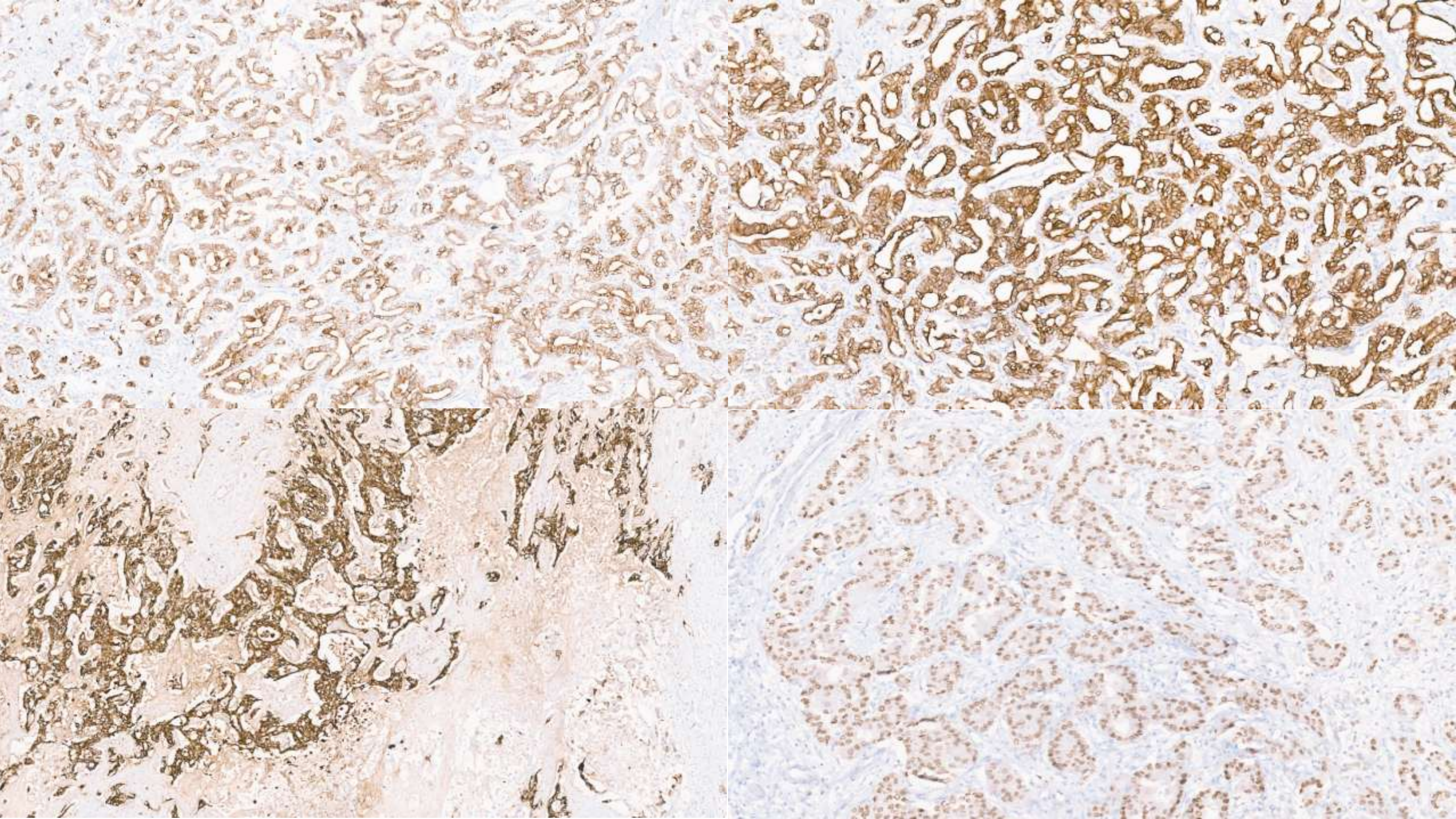




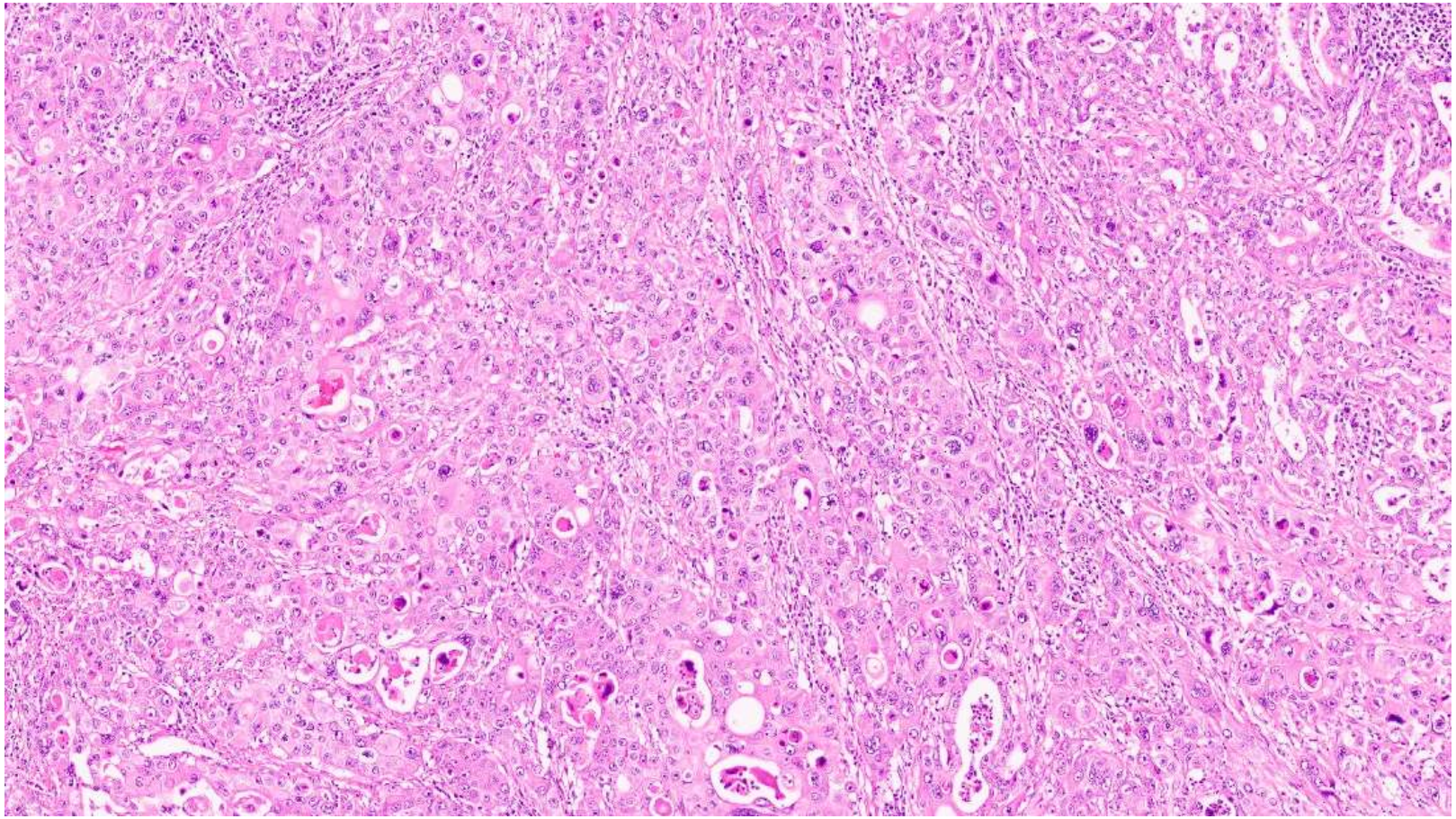








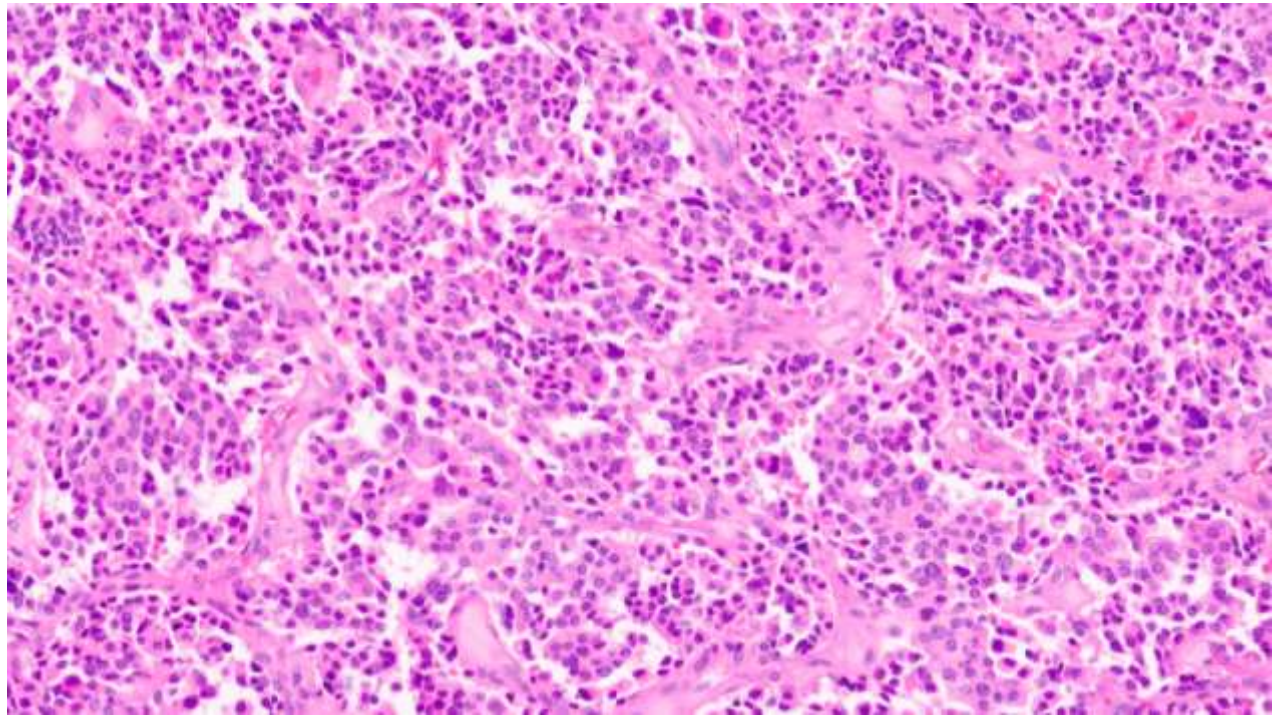
Adenosquamous carcinoma



Cancer Manag Res. 2018 Mar 7;10:439-446.

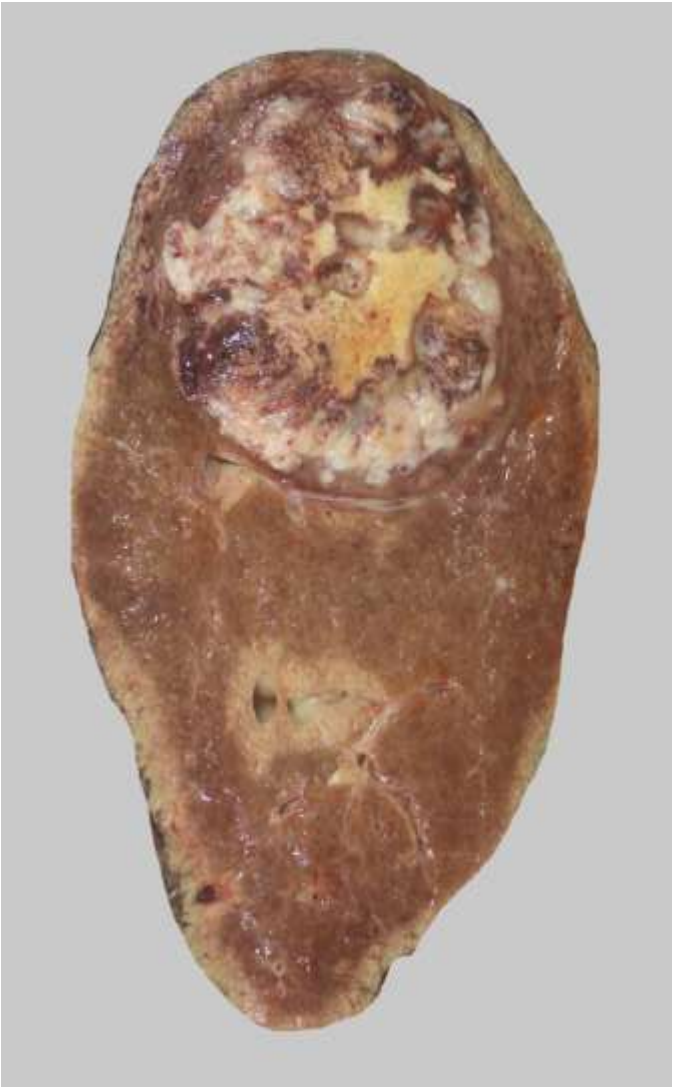
Neuroendocrine tumours

- Extremely rare
- 0.01%
- Small (generally < 2 cm)
- Greyish-white or yellow submucosal nodules
- Prognositic data is highly limited because of the rarity of these tumours;
- Prognosis seems to be similar to that of NETs in the GI tract

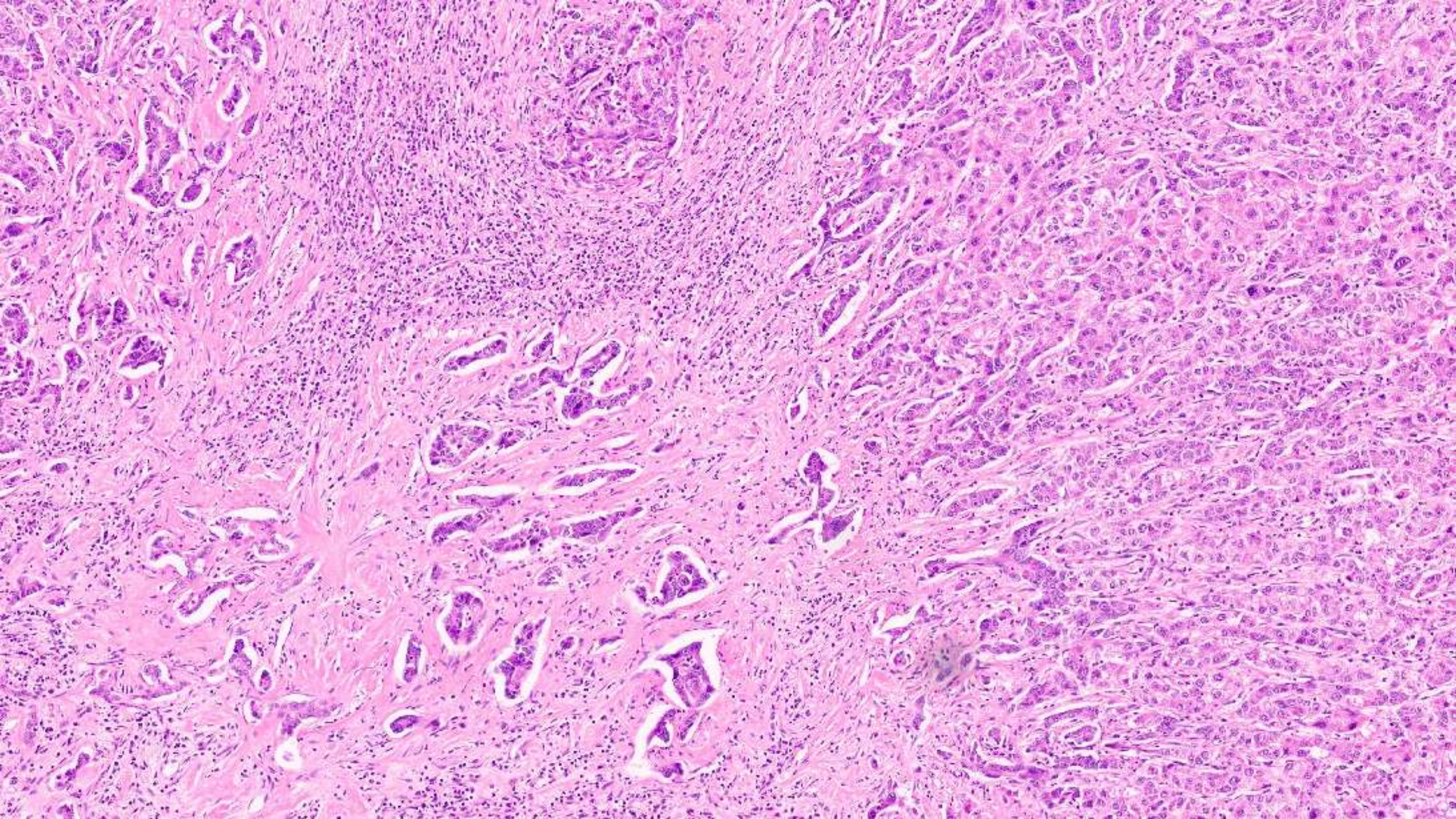


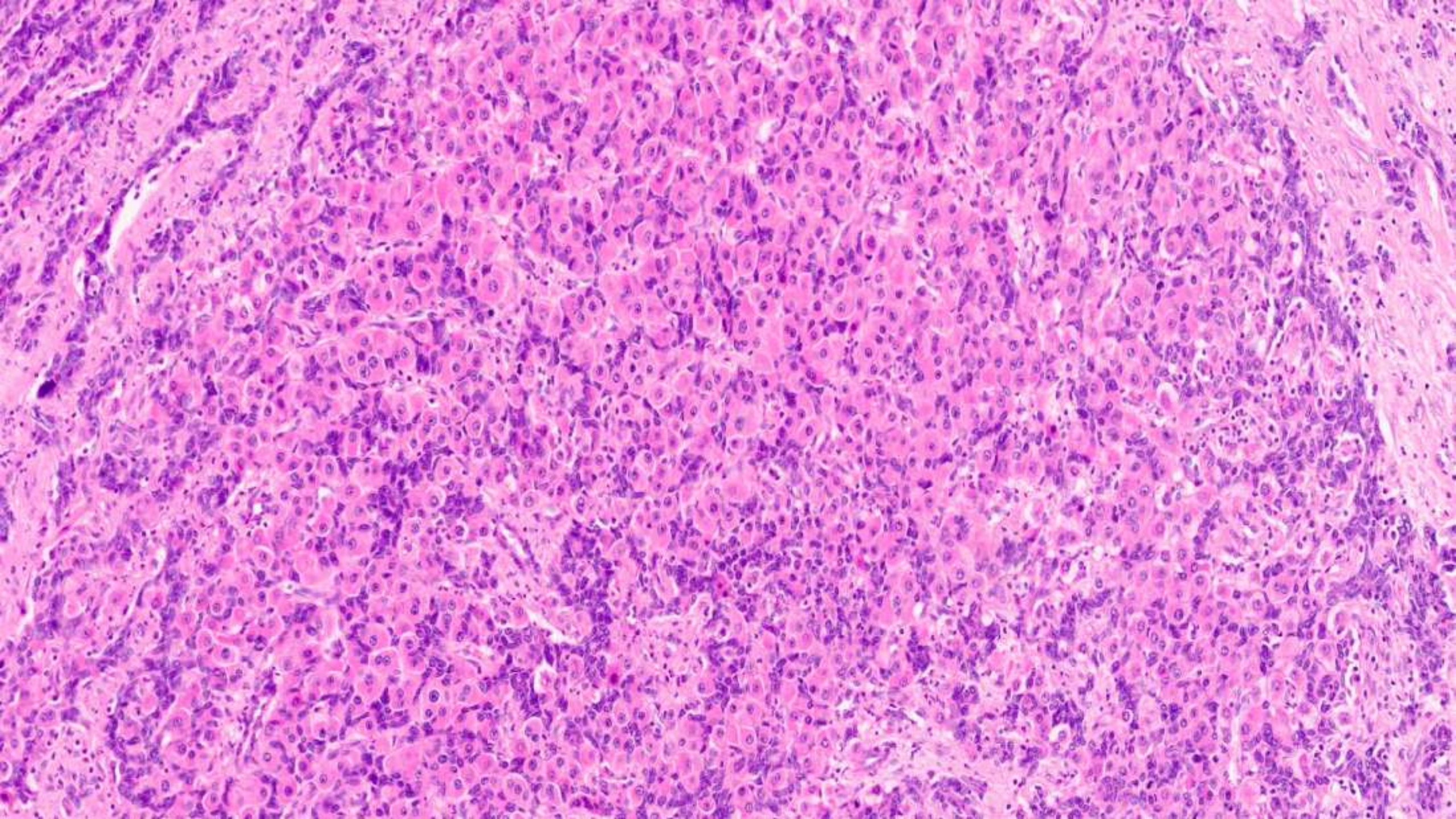
Combined hepatocholangiocarcinoma

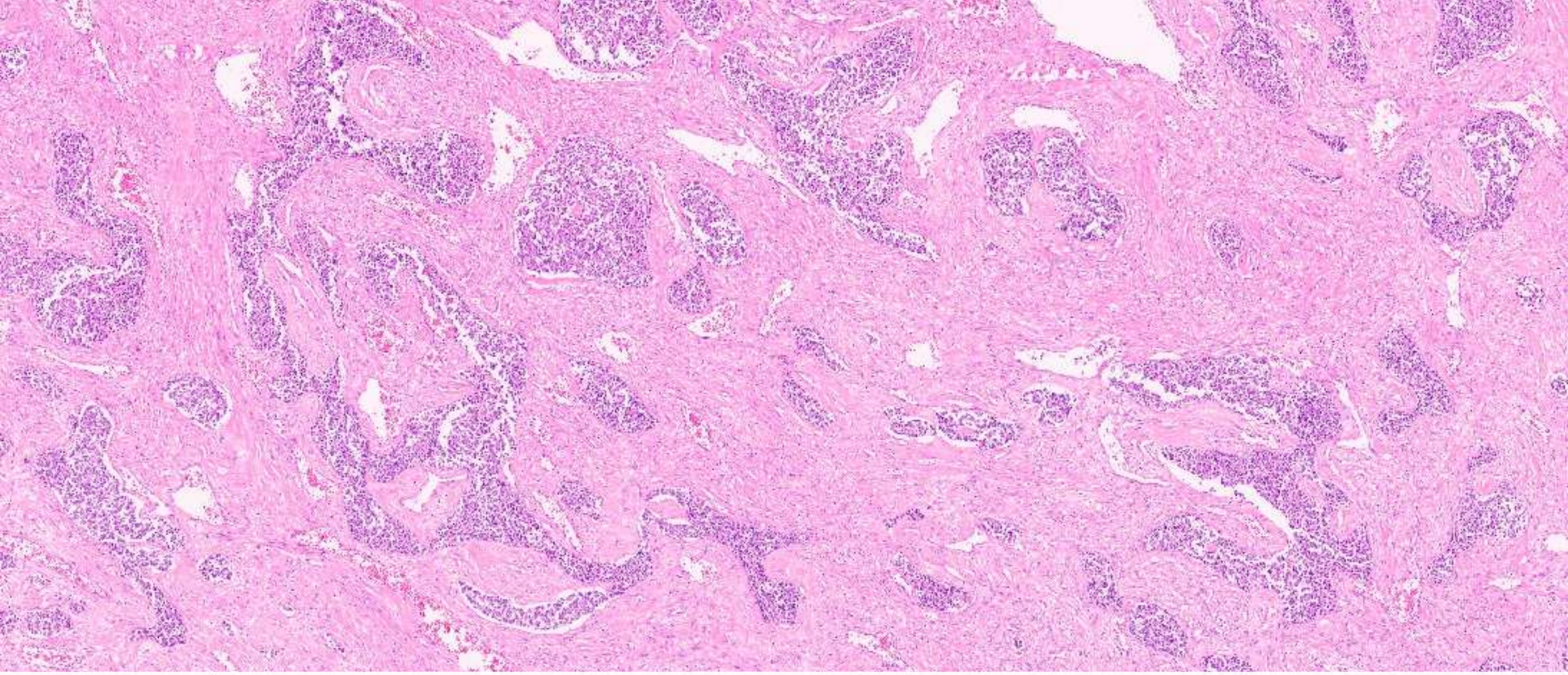
- Both hepatocytic and biliary differentiation.
- Pathological definition has evolved over time.
- Primarily based on morphology using routine staining
- Molecular evidence supports clonal nature of cHCC-CCA
- Genetic alterations observed in HCC and/or iCCA.
- Morphological diagnosis of cHCC-CCA is challenging
- cHCC-CCA's cell of origin remains an area of active research
- Prognosis is generally worse than HCC, and similar to that of iCCA.
- Resection with lymph node dissection is unfortunately the only curative option for patients with cHCC-CCA



Hepatology. 2018 Jul;68(1):113-126.



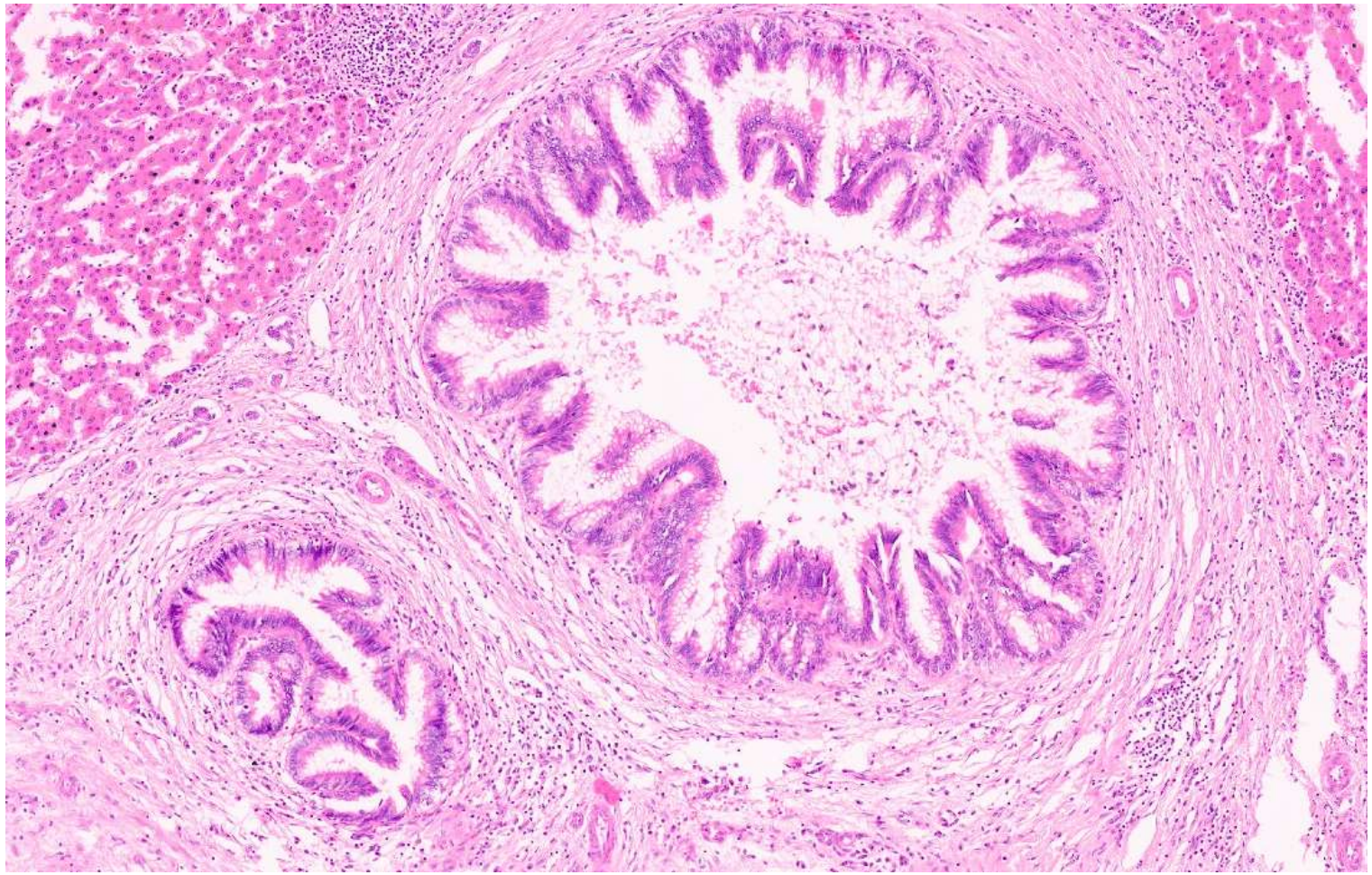




Intermediate cell carcinoma

PRECURSORS LESIONS OF CHOLANGIOCARCINOMA

Biliary epithelial neoplasia

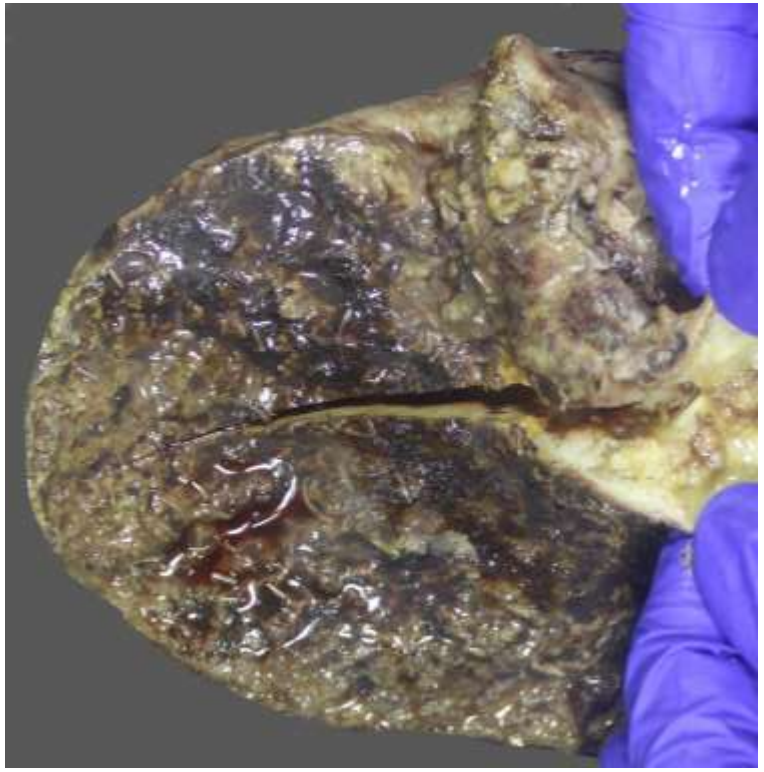


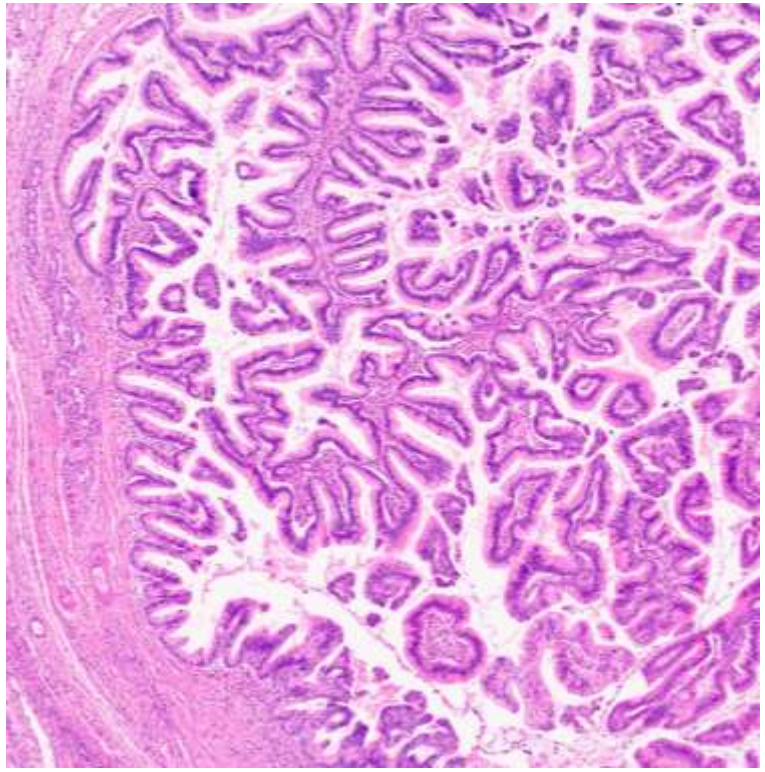
Intraductal papillary neoplasms of the bile duct

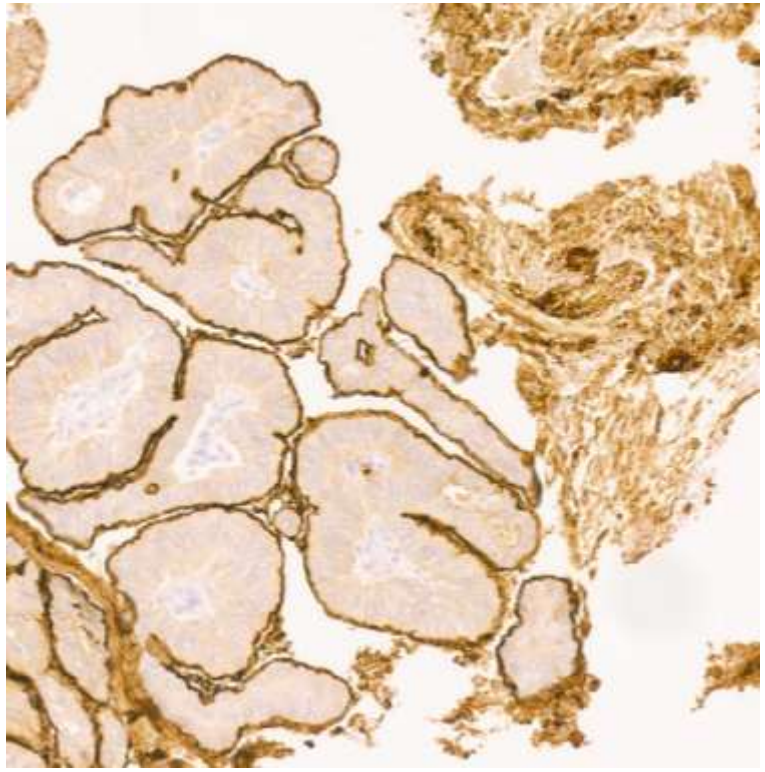
- Uncommon tumours
- Incidence of IPNB ranges widely by geographic locationsingular or multiple
- Polypoid, exophytic masses arising in dilated bile ducts
- IPNBs can be classified into subtypes based on the nature of the neoplastic epithelium: pancreatobiliary-type, intestinal-type, gastric-type, and oncocytic-type
- High risk of malignancy, with studies reporting an invasive component in up to 80% of cases
- Type 1, or pancreatic type
- Type 2, or nonpancreatic type

Hum Pathol. 2021 Jun;112:70-83

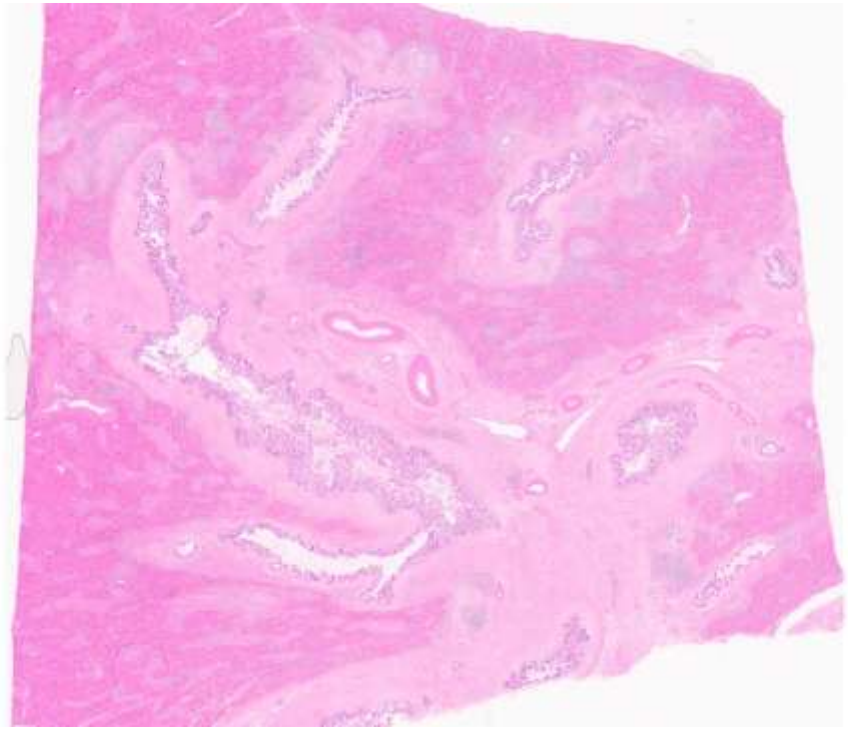
Intraductal papillary neoplasms of the bile duct

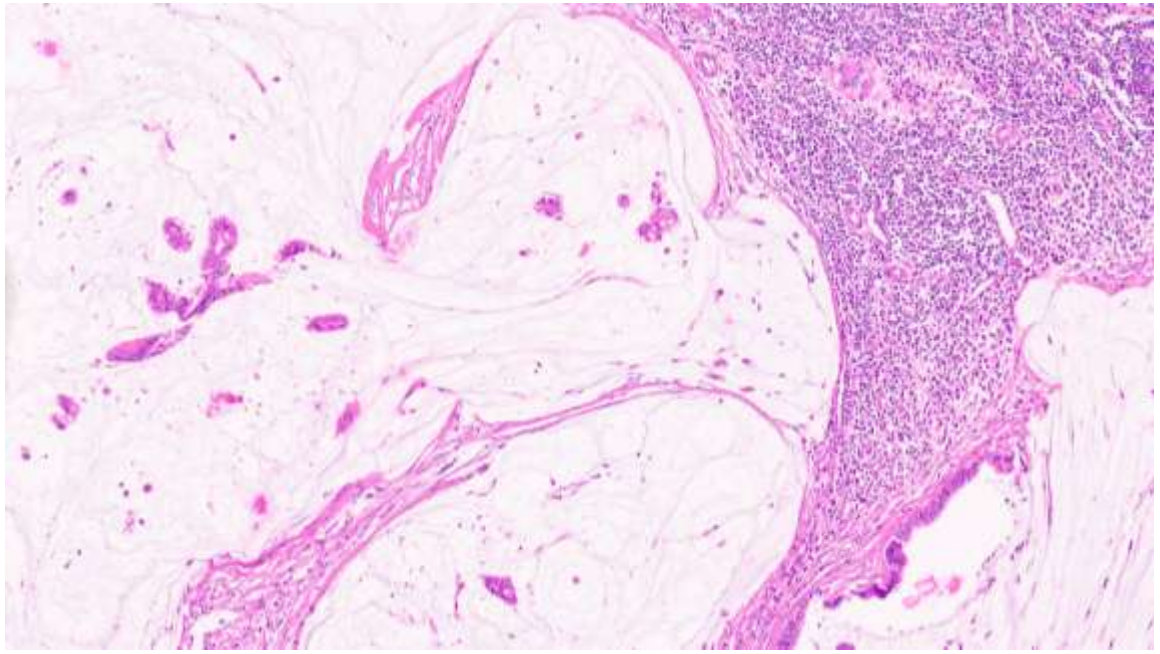


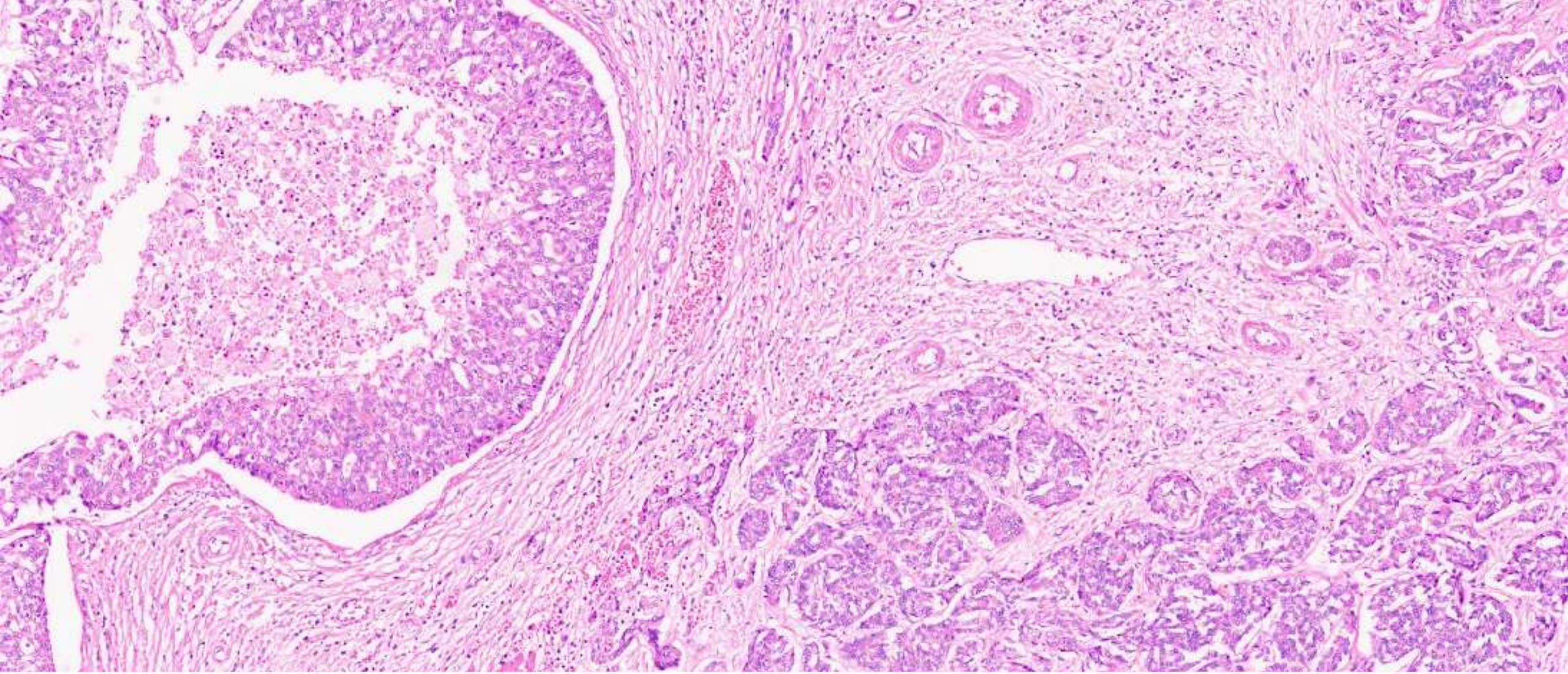




- IPNB-associated cholangiocarcinoma with mucinous (colloid) morphology

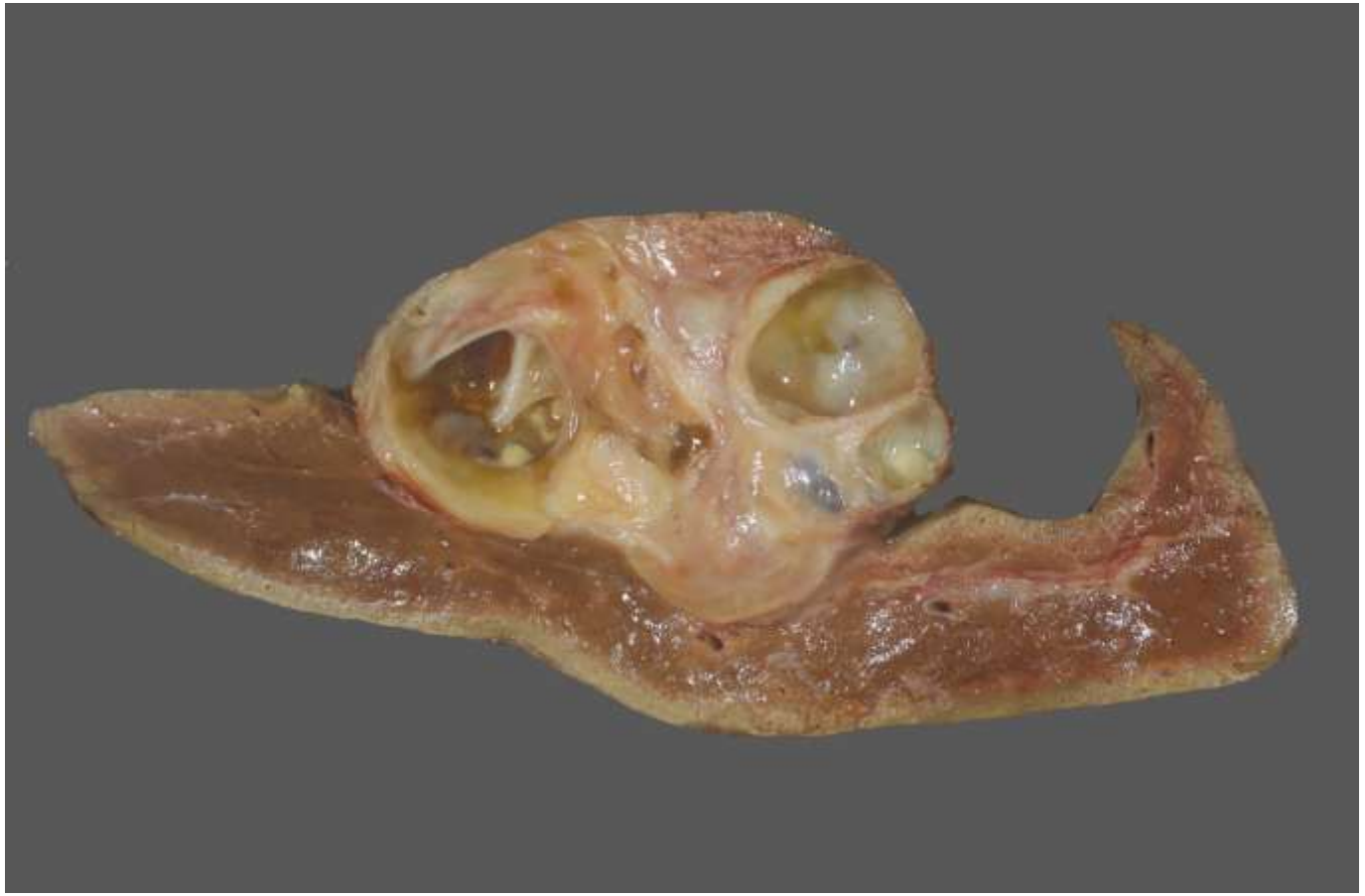


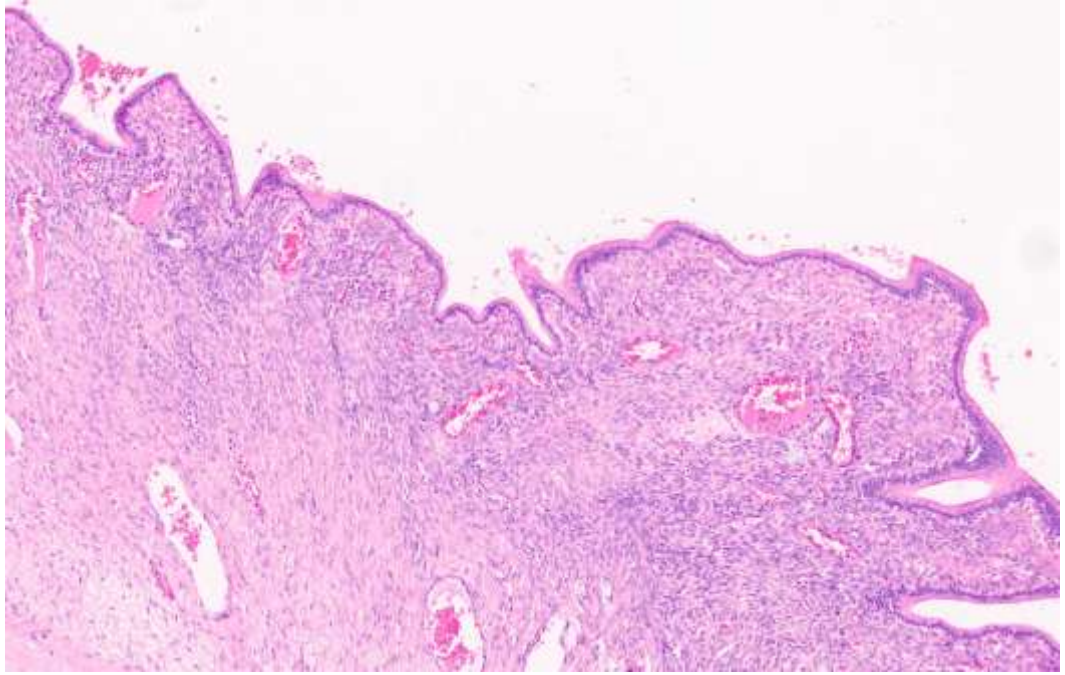


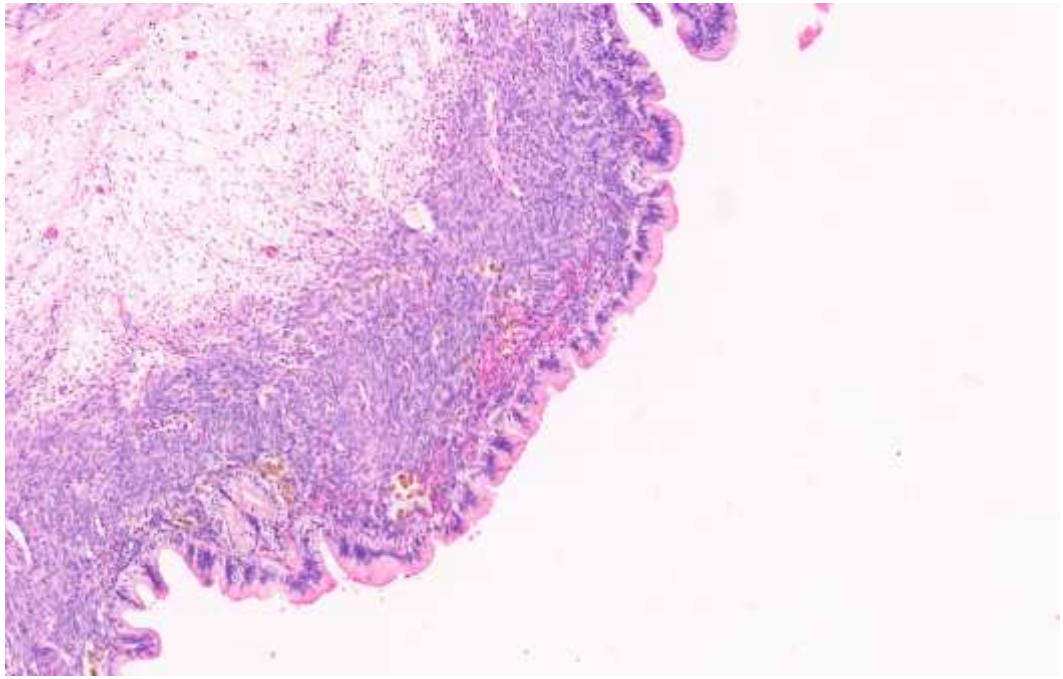


Intraductal tubulopapillary neoplasms of the bile duct

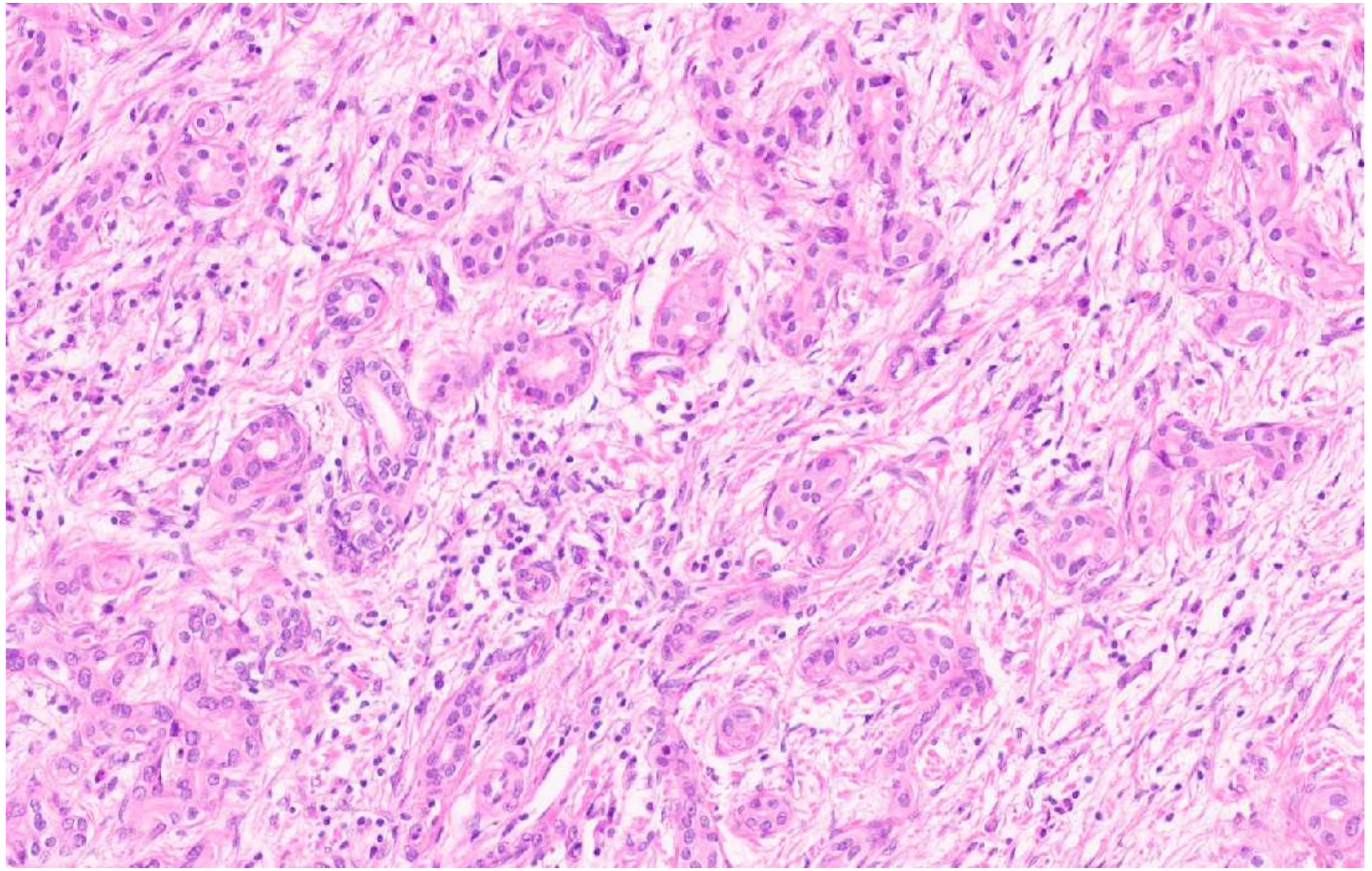
Mucinous cystic neoplasm







Bile duct adenoma

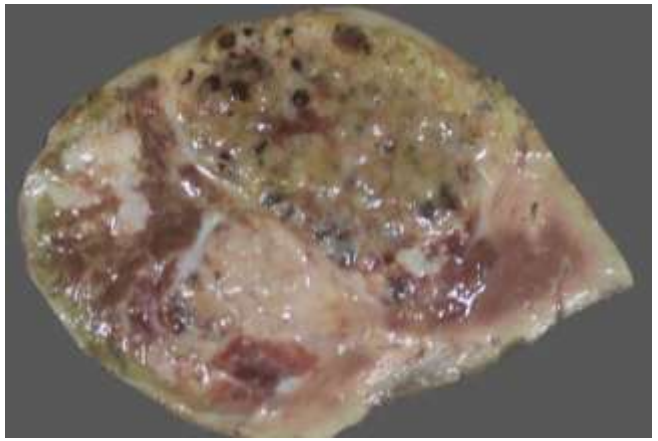


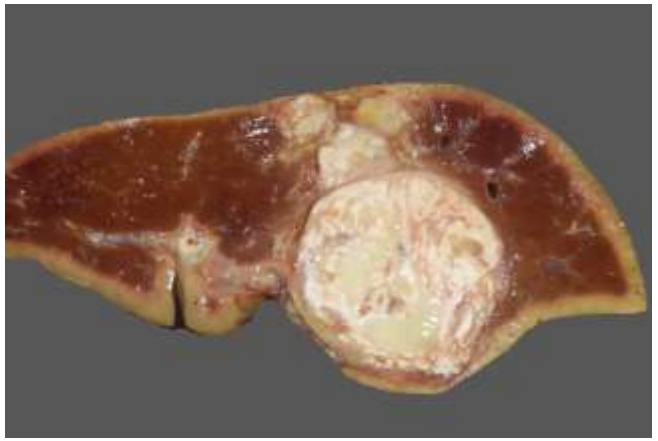
Paediatric Malignant Liver Tumours

- Extremely rare accounting for only 1% of all pediatric malignancies
- >60% are hepatoblastomas (HBs), remaining HCCs and the very rare embryonal sarcomas of liver
- Recent increase in the incidence of HBs, probably in relation with the increased survivors of premature birth
- Predisposition to develop HB with birth weight lower than 1500 g
- HB are typical of the first 3 years of life and can be congenital.
- Most are sporadic
- Subset of HB occurs in the context of familial syndromes, such as Beckwith–Weidemann syndrome, Simpson–Golabi–Behmel syndrome, Sotos syndrome, familial APC, and trisomy 18

Hepatoblastoma (HB)

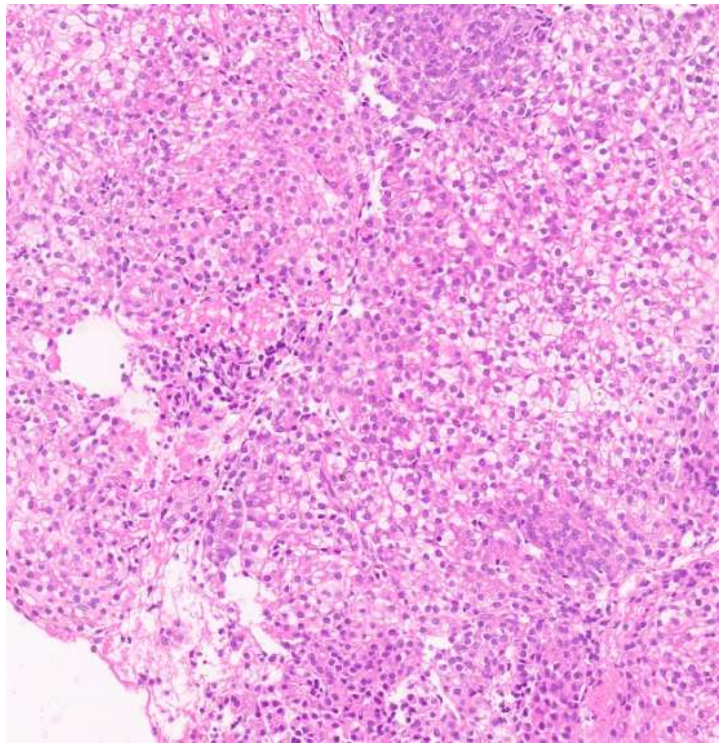
- Primary hepatoblast or undifferentiated multipotent progenitor cells
- Wnt/beta catenin signaling pathway
- Two subclasses identified in gene expression profiling
- Genetically stable and unstable
- Single (80%) or multiple nodules
- Cut surface appearance depends on tumor character (Tan, soft, gritty)
- Epithelial and mixed epithelial and mesenchymal components
- Hemorrhage, necrosis
- HB mimics the developing fetal or embryonal liver histologically

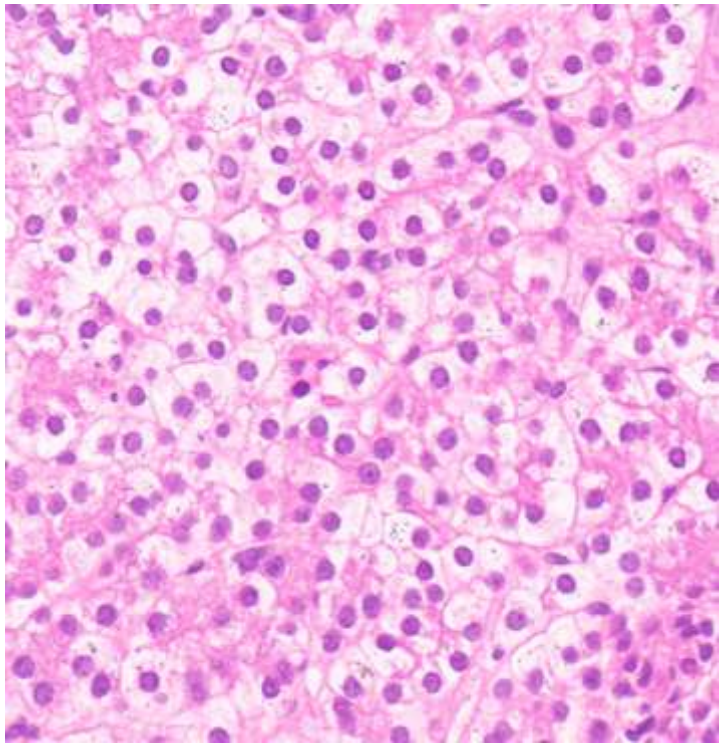


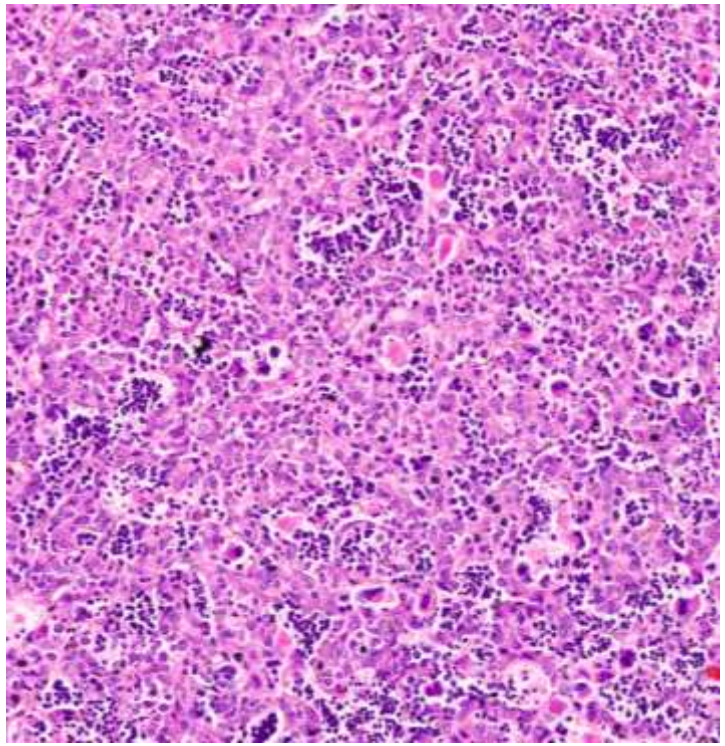


Pediatr Dev Pathol. 2020 Mar- Apr;23(2):79-95.

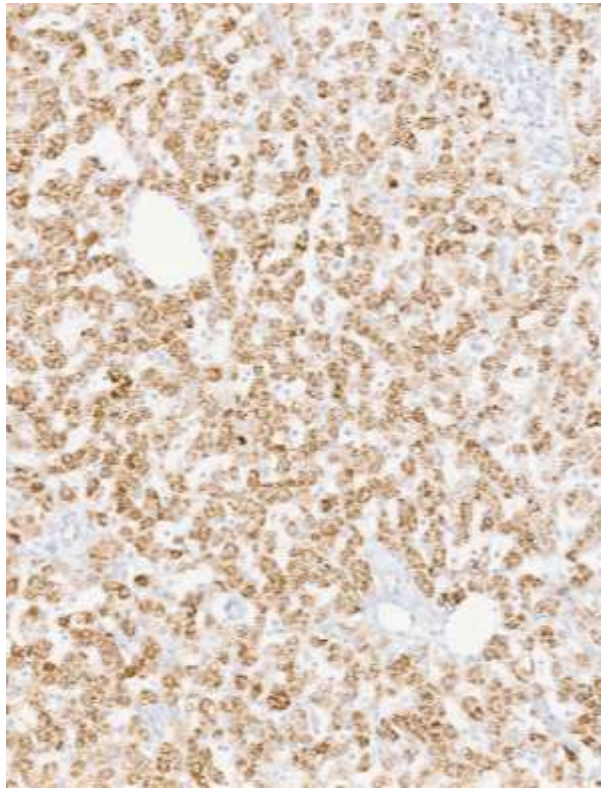
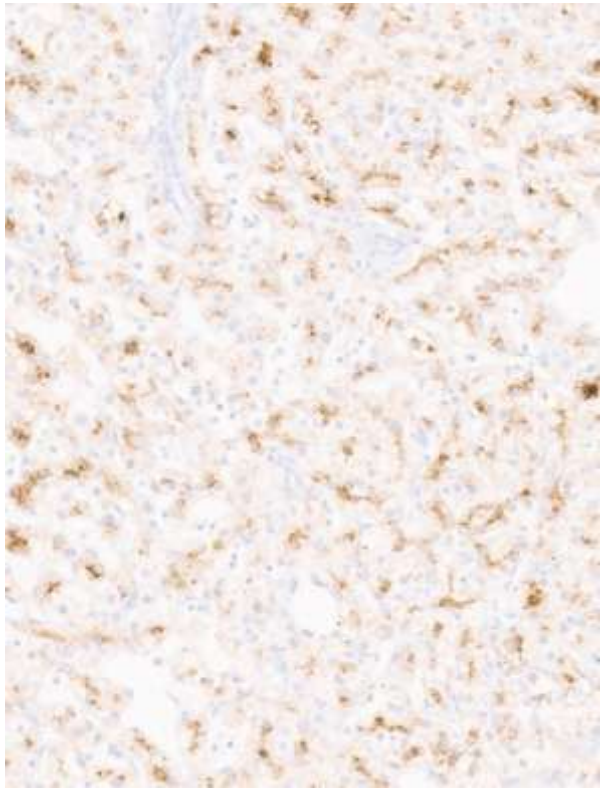
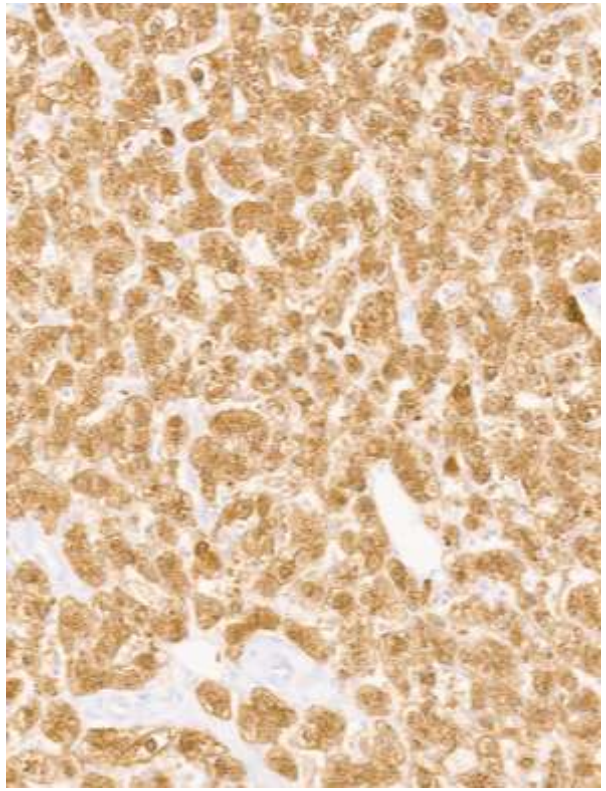
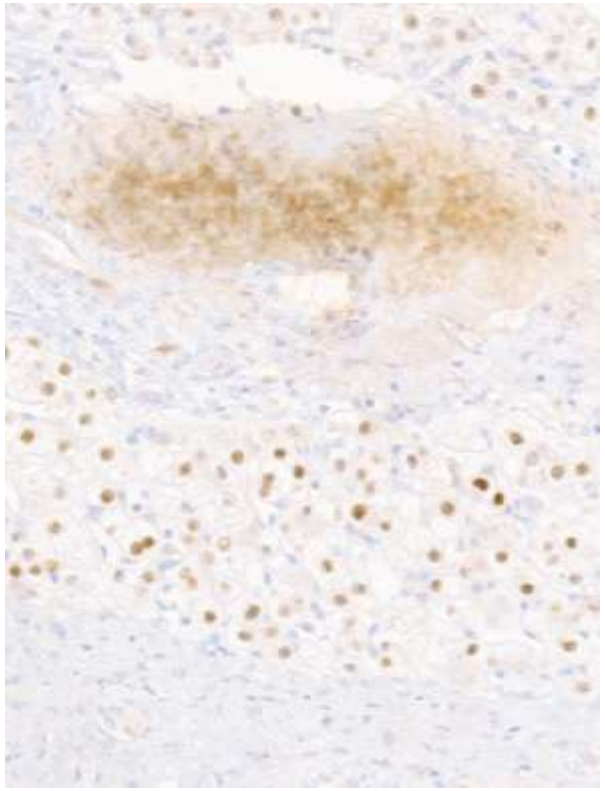
Fetal Epithelial pattern

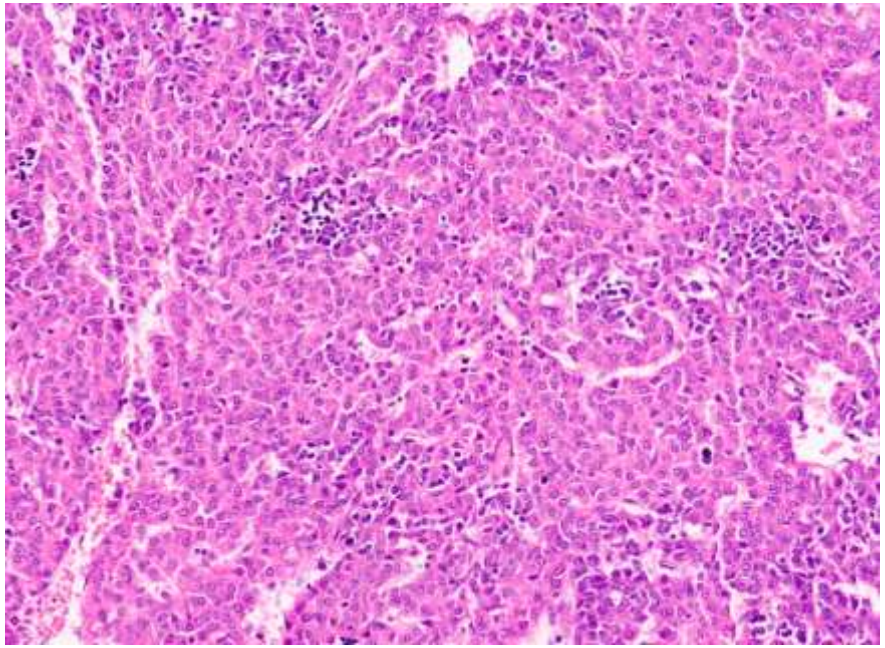


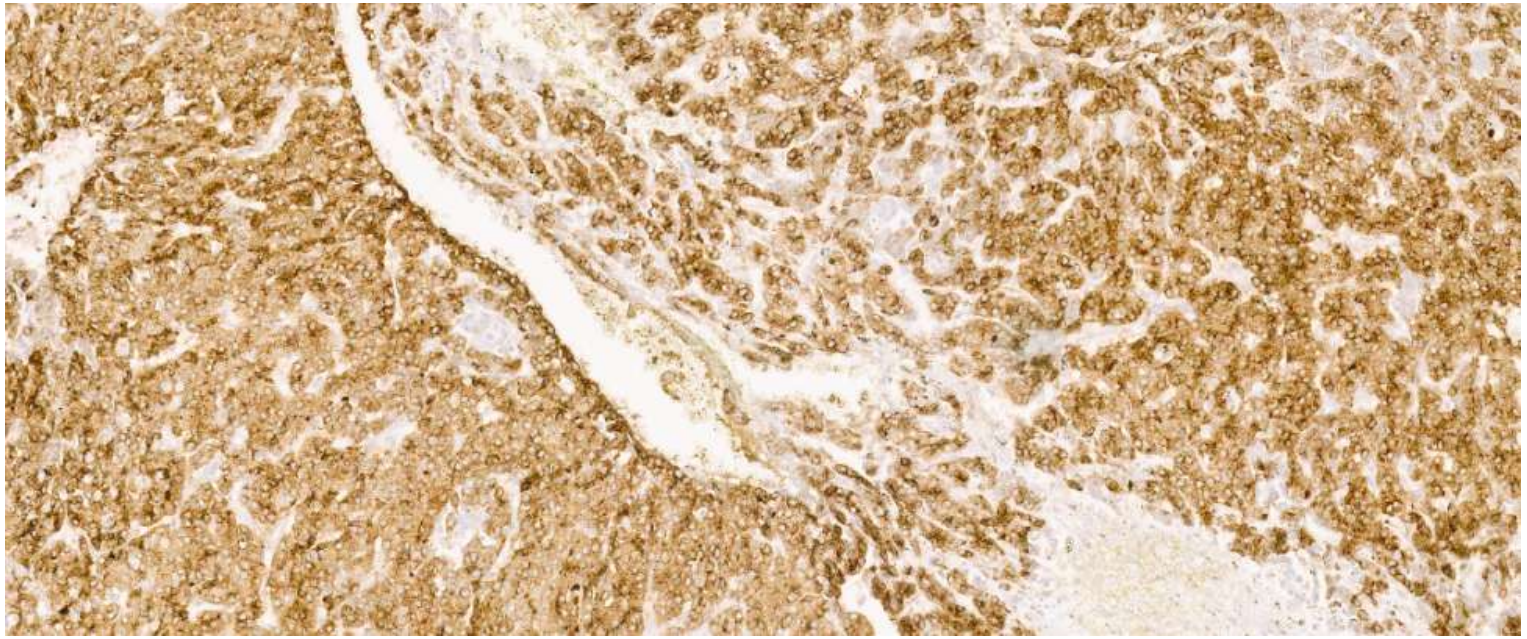


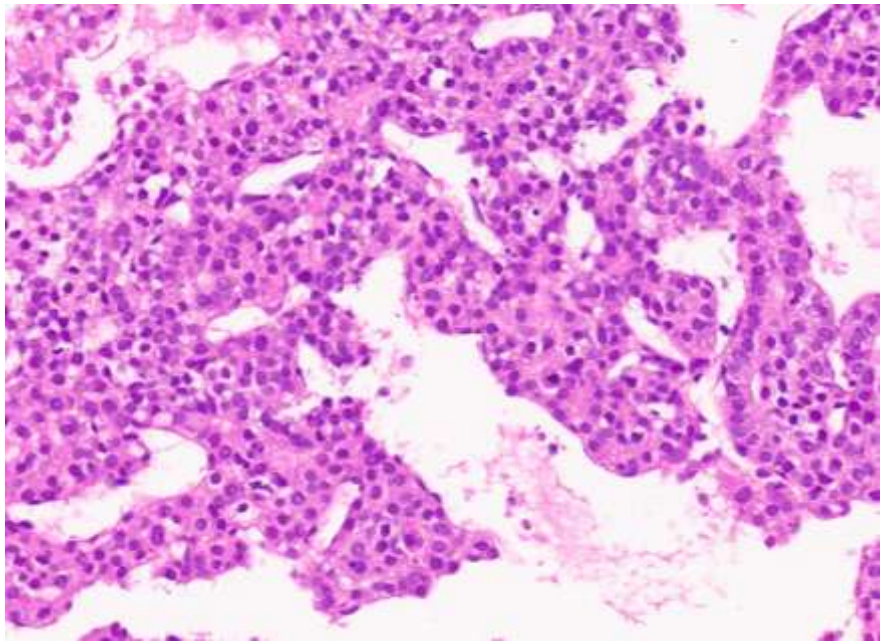


Hep-par1 & Glypican 3, Glutamine synthetase, Cyclin D1



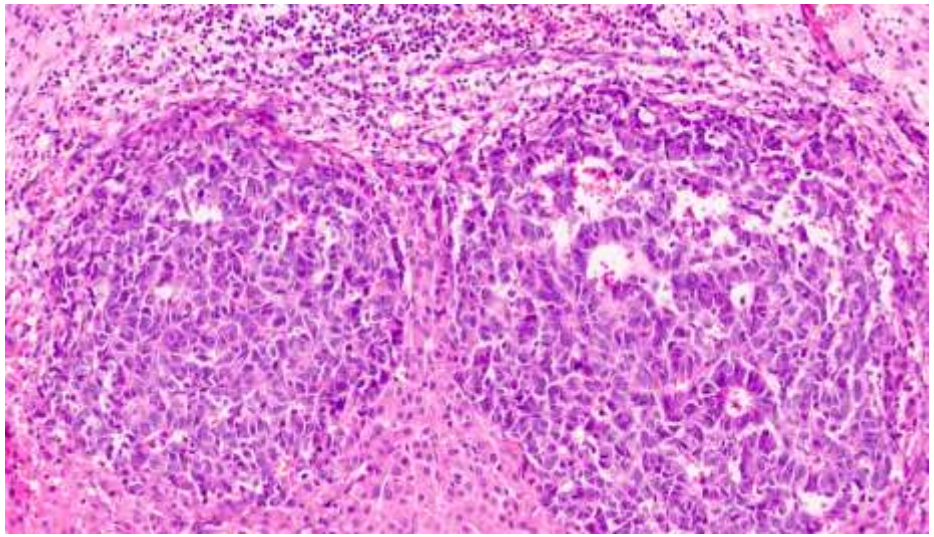


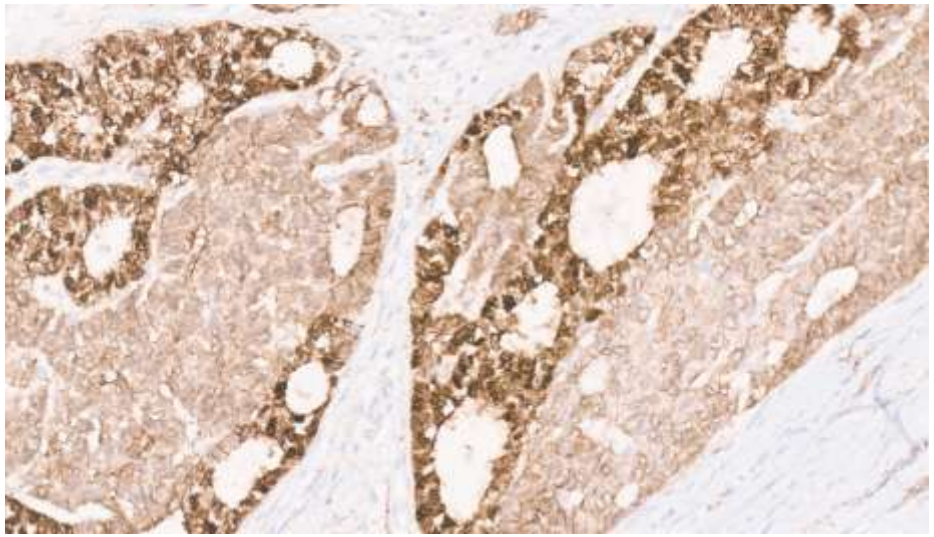


Crowded fetal (CF) HB (mitotically active fetal)

Embryonal HB

- Embryonic stage of liver (6-8 weeks) development.
- Cells have high N/C ratio, scant cytoplasm with indistinct borders, and a large, angulated to oval nucleus with a prominent nucleolus
- Cell density is also increased.
- Frequent mitoses
- Necrosis may be seen.
- Glandular, acinar or pseudorosette.
- Serpentine and microcystic pattern can be seen.
- Myxoid change may be noted in the microcystic areas.





Pediatr Dev Pathol. 2020 Mar- Apr;23(2):79-95.

Macrotrabecular (MT) HB

Pediatric Blood & Cancer

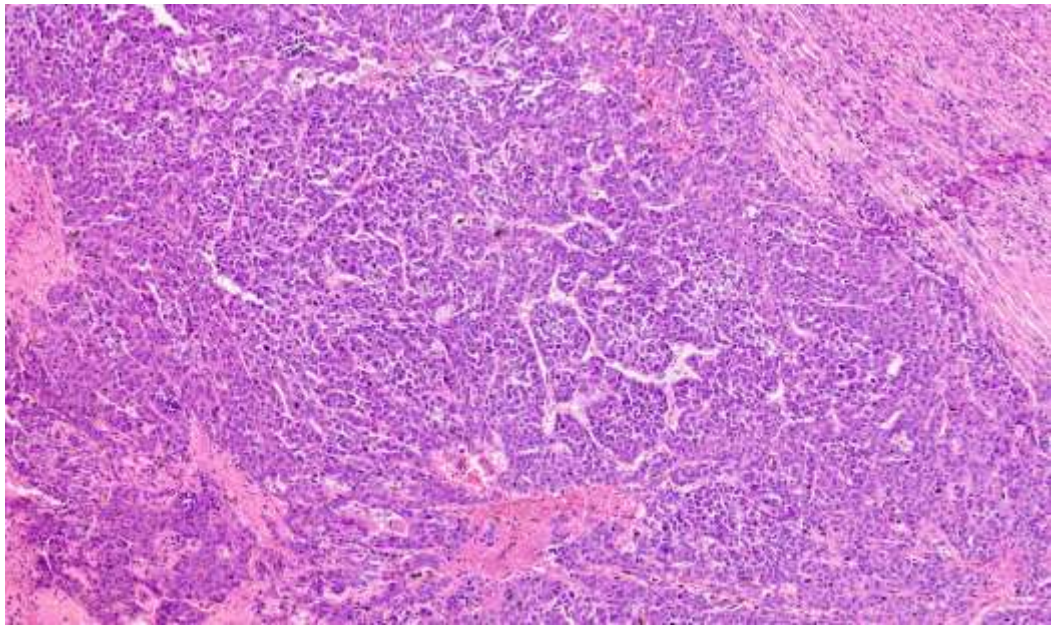
LETTER TO THE EDITOR

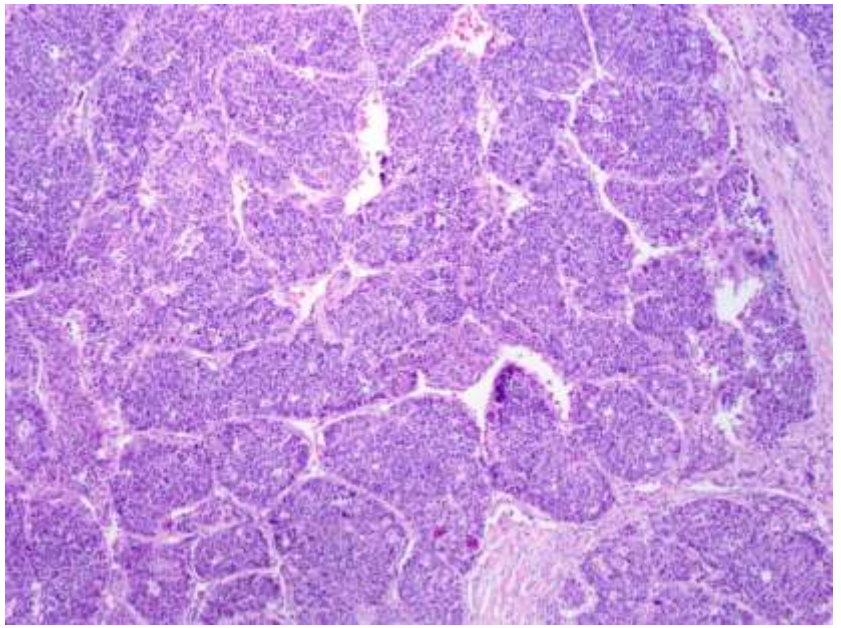
Complete remission of refractory hepatoblastoma after liver transplantation in a child with sorafenib monotherapy: A new hope?

Naresh Shanmugam, Joseph J. Valamparampil, Julius Xavier Scott, Mukul Vij, Gomathy Narasimhan, Mettu Srinivas Reddy, Mohamed Rela

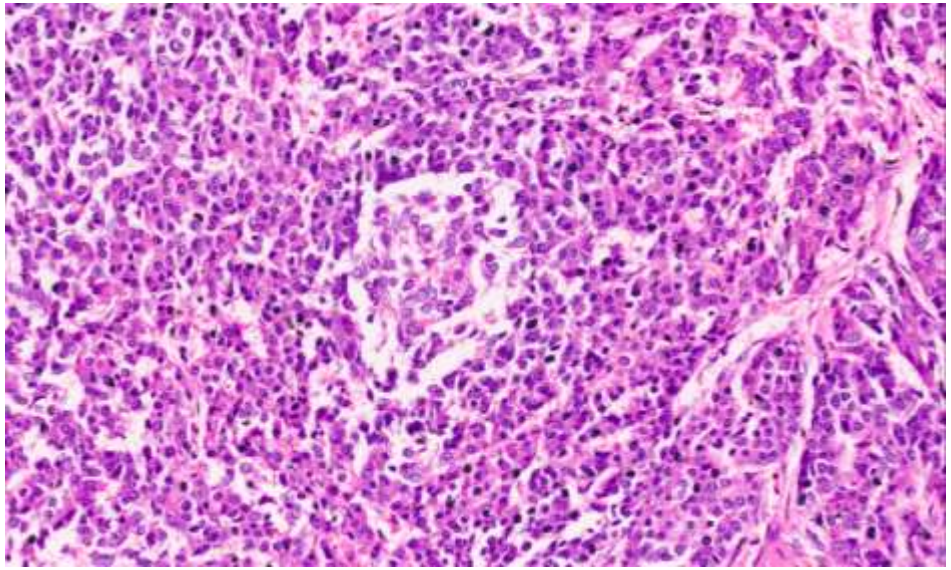
First published: 11 July 2017 | https://doi.org/10.1002/pbc.26701 | Citations: 6

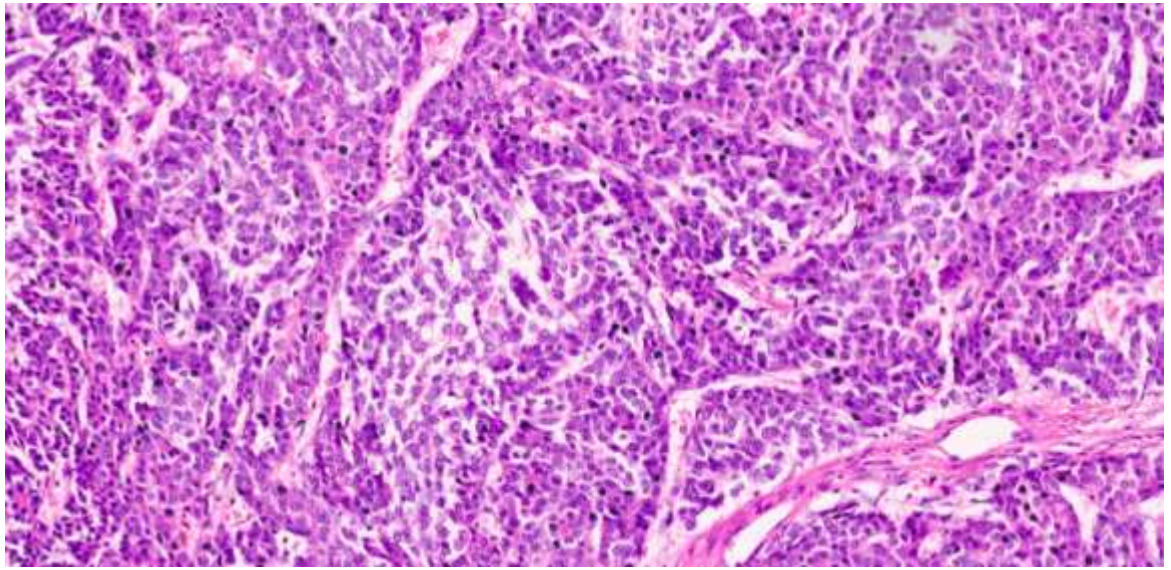
- <5%, Thick trabeculae (≧ 5-to ≧20-cell-thick –trabeculae)
- The cells can show fetal or embryonal morphology or pleomorphic cells or cells resembling HCC

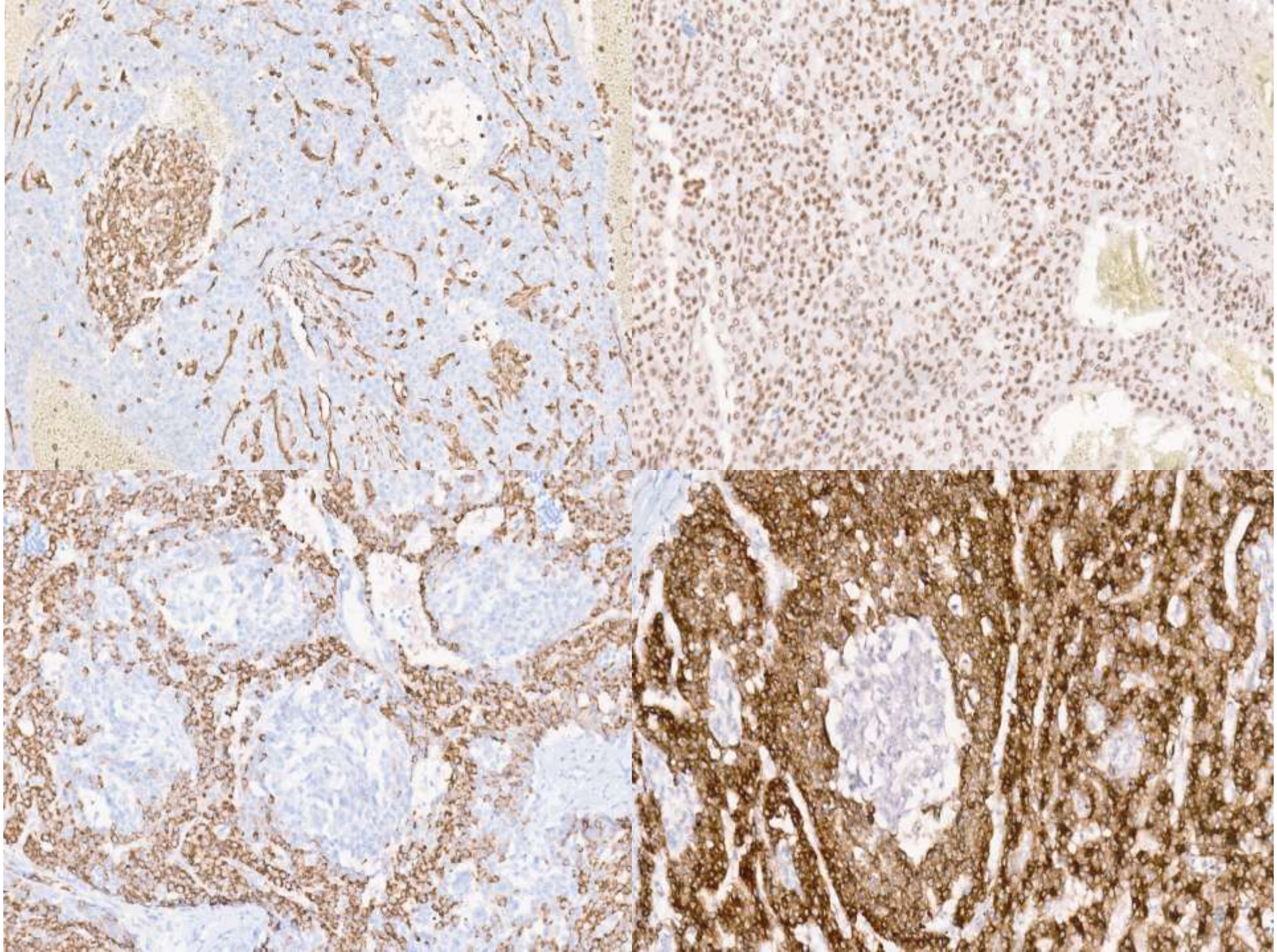




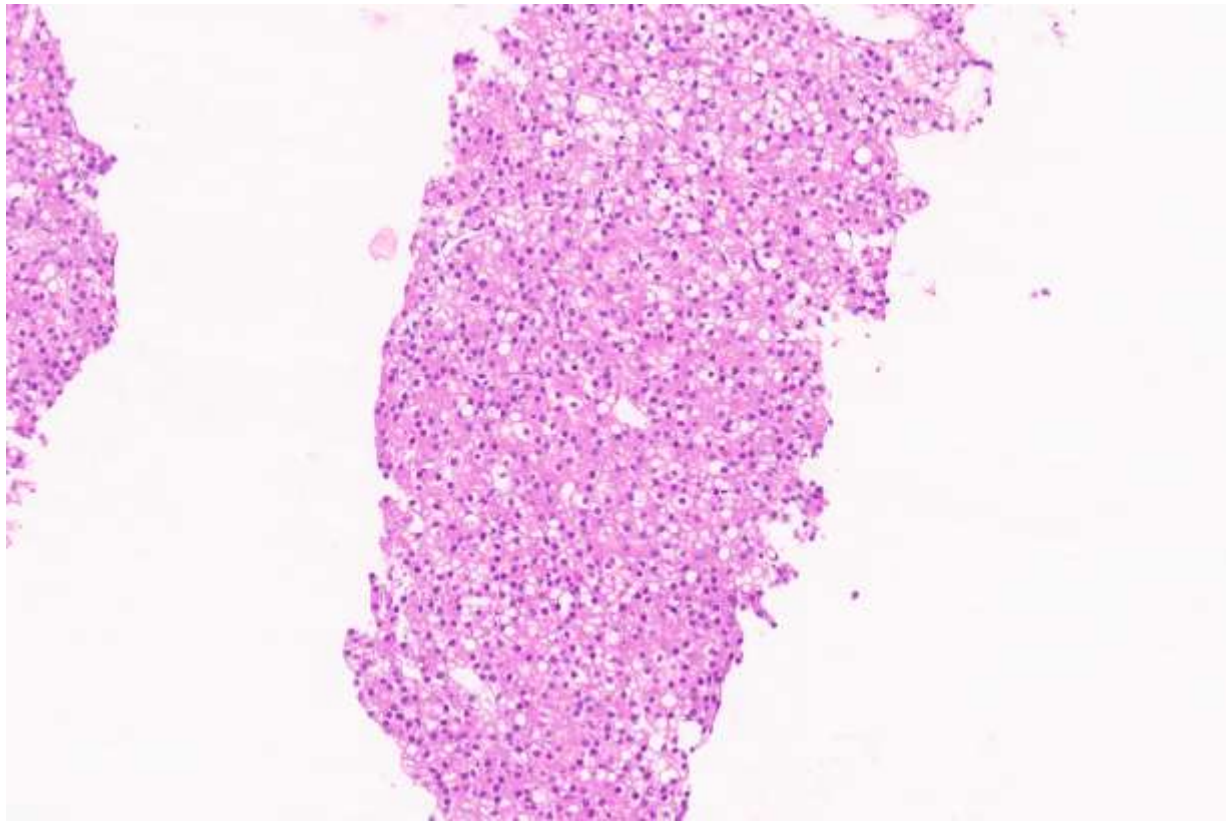
Small cell undifferentiated (SCUD)

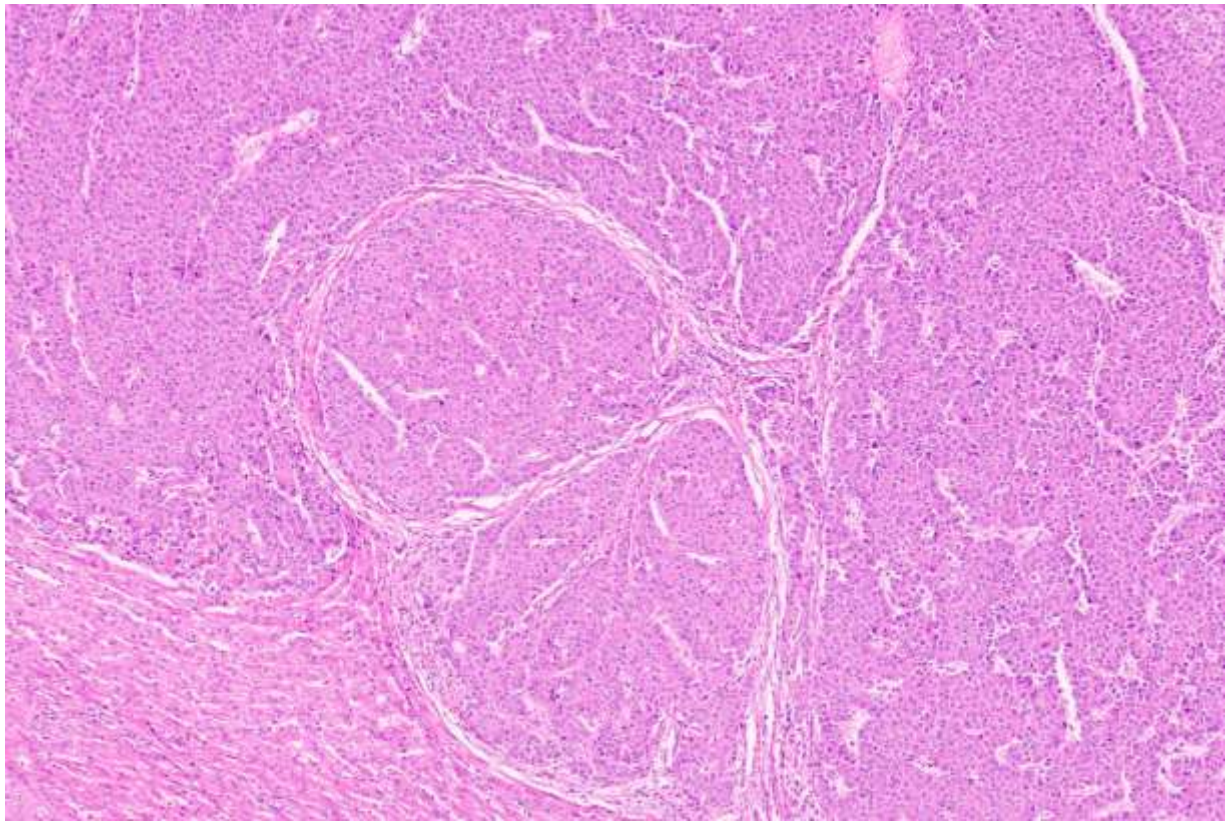


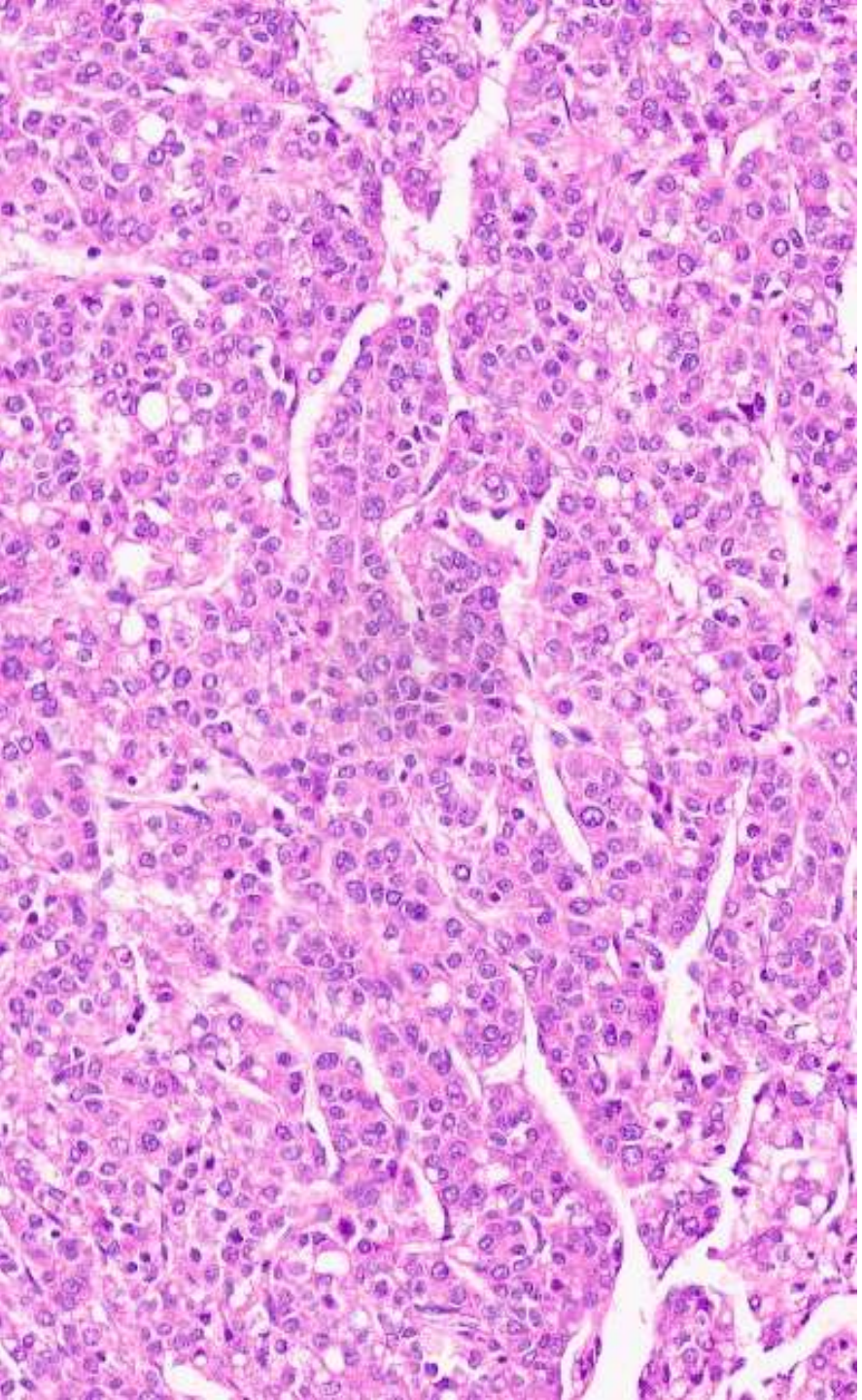




Post chemotherapy







Hepatocellular Neoplasm-NOS

- New provisional category that includes tumours previously designated as transitional cell liver tumours
- Represent lesions with intermediate or combined biology
- Histological features of both HBL and carcinoma (HCC)
- Tumour cells may also be monotonous and resemble crowded fetal cells.
- May have macrotrabecular arrangement
- HCN-NOS carry β-catenin (*CTNNB1*) mutations as well as other mutations seen in HCC, such as TERT promoter mutations,
- Poor prognosis
- More frequent in children older than 8 years
- Aggressive associated with poor outcome.
- Currently treated as Group D high-risk HBL

Pediatric HCC

~20% of all malignant pediatric liver tumors

Clinically challenging

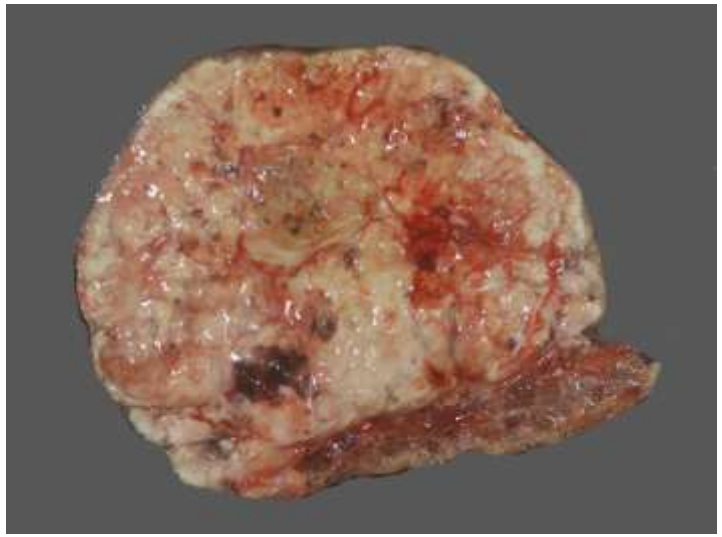
Often presenting as large, unresectable lesions, typically in older children/adolescents.

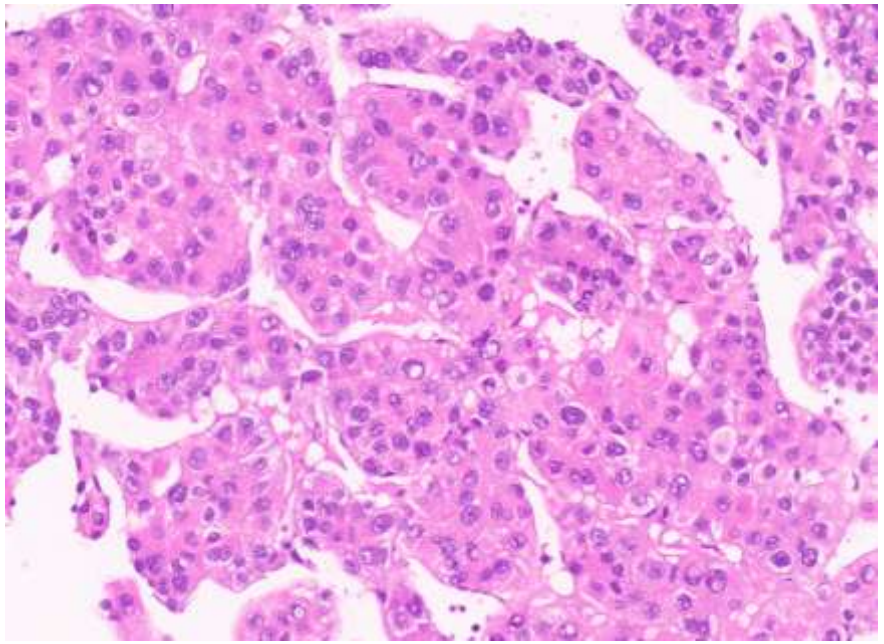
2 groups

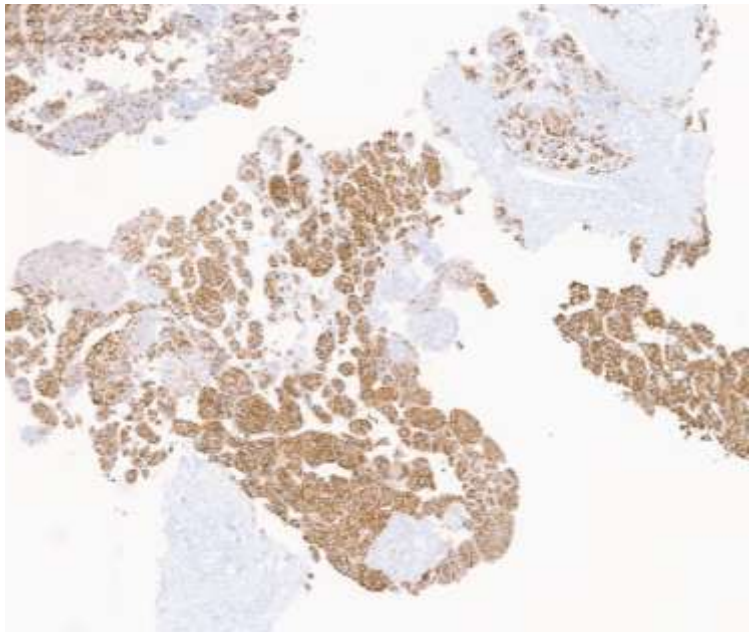
One is associated with underlying metabolic and/or genetic diseases

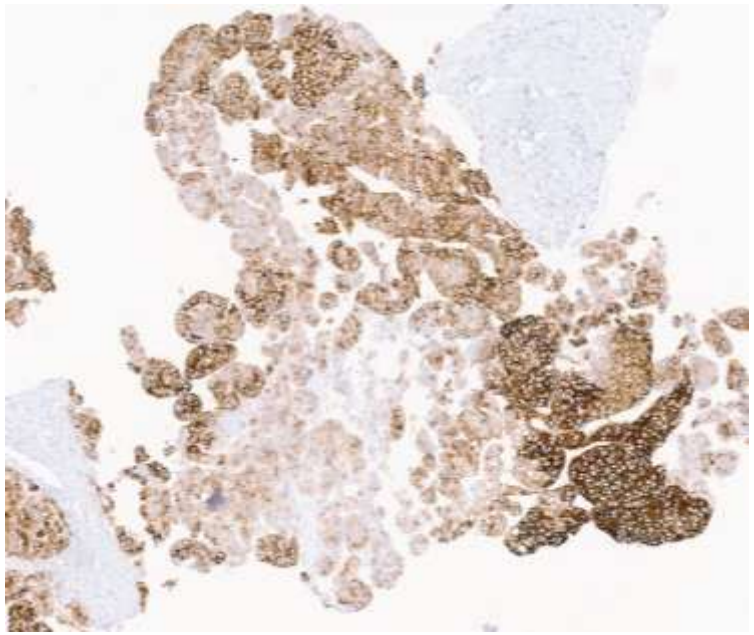
HT, BSEP, MDR 3 & TJP2 deficiency, and less often in BA and viral hepatitis.

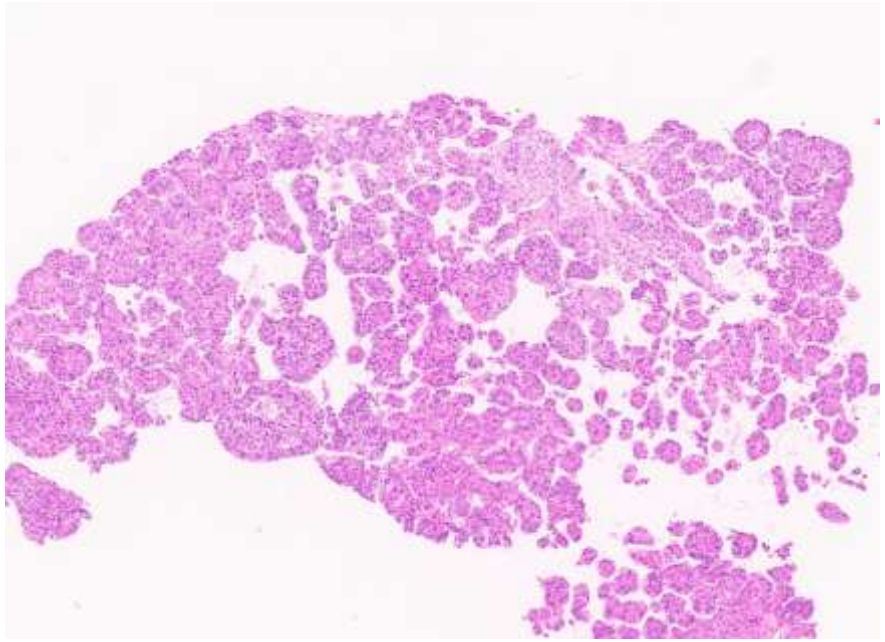
Other group with no evidence of chronic liver disease



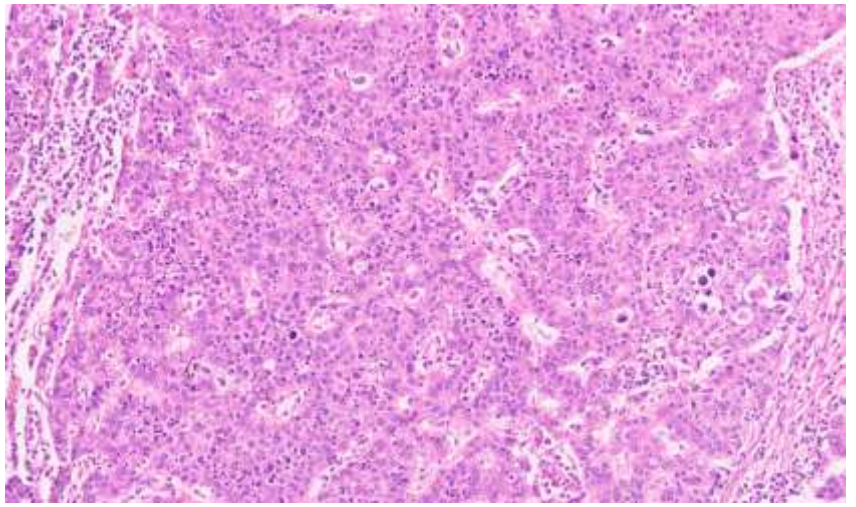


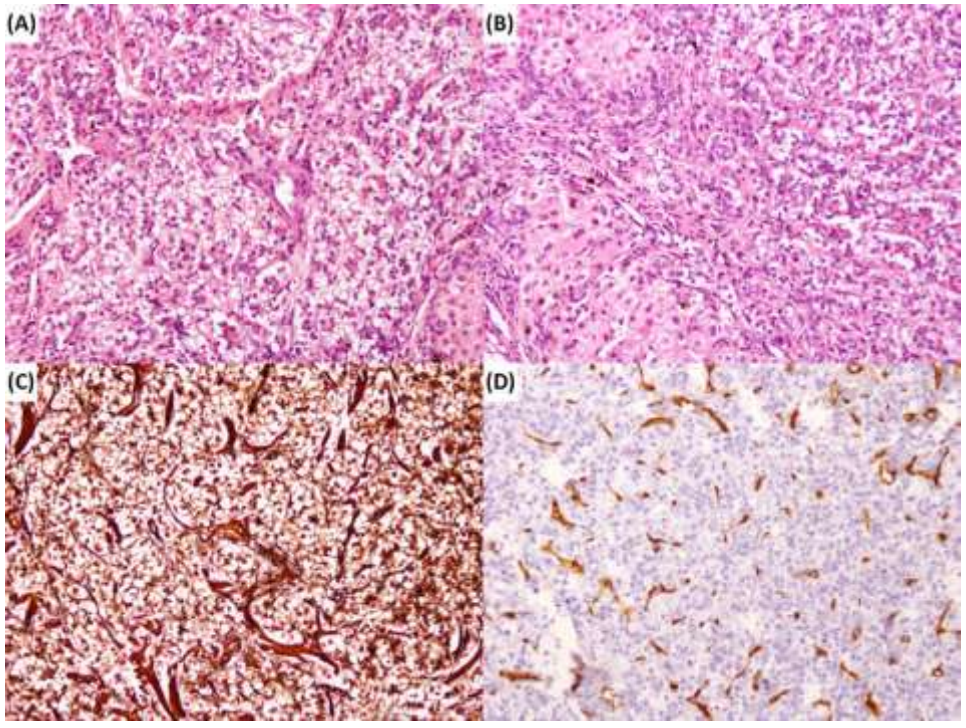






Pediatric HCC





J Gastrointest Cancer. 2020 Sep;51(3):1047-1052. doi: 10.1007/s12029-020-00391-2.

Hepatocellular Carcinoma in Paediatric Patients with Alagille Syndrome: Case Series and Review of Literature

Joseph J Valamparampil [1], Naresh Shanmugam [2], Mukul Vij [2], Mettu Srinivas Reddy [2], Mohamed Rela [2,3]

Virchows Arch
DOI 10.1007/s00428-017-2204-1

BRIEF REPORT

Paediatric hepatocellular carcinoma in tight junction protein 2 (TJP2) deficiency

Mukul Vij [1] · Naresh P. Shanmugam [2] · Mettu Srinivas Reddy [2] · Srinivas Sankaranarayanan [3] · Mohamed Rela [2,4]

CASE REPORT

WILEY

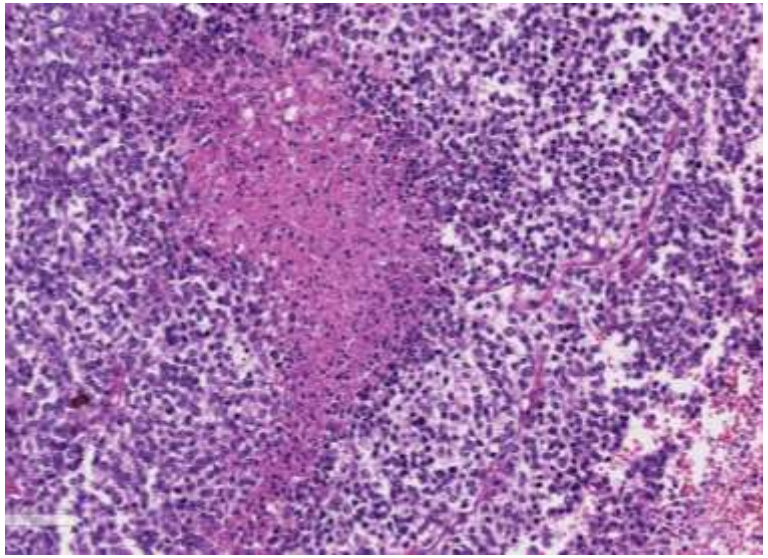
Hepatocarcinogenesis in multidrug-resistant P-glycoprotein 3 deficiency

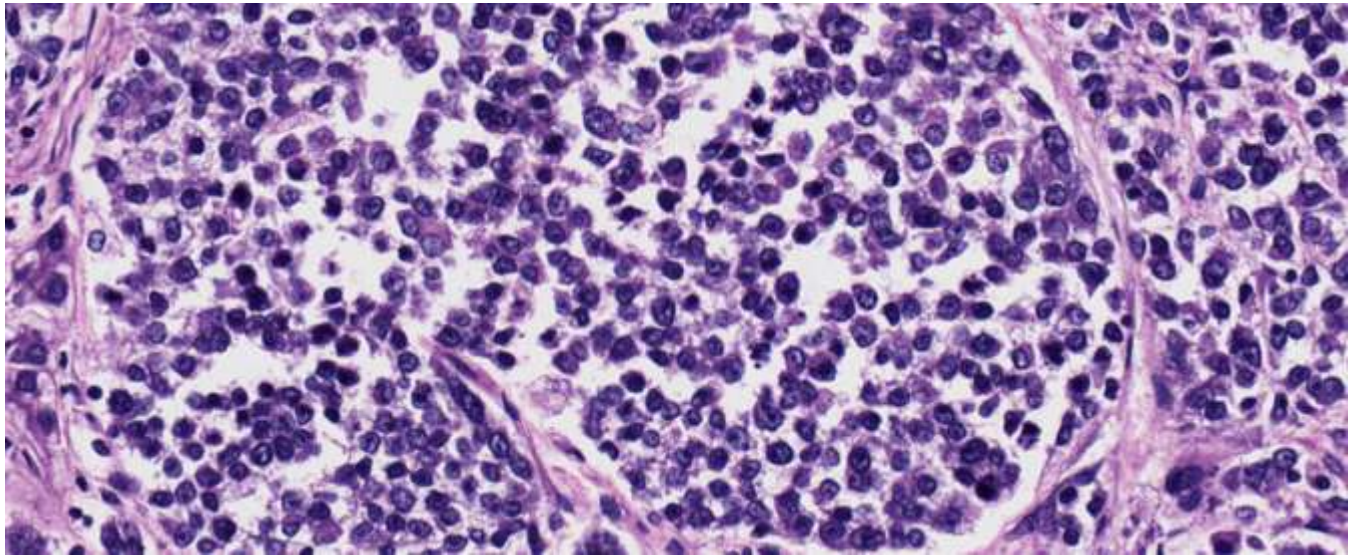
Mukul Vij[1] | Naresh P. Shanmugam[2] | Mettu Srinivas Reddy[2] | Sanjay Govil[2] | Mohamed Rela[2,3]

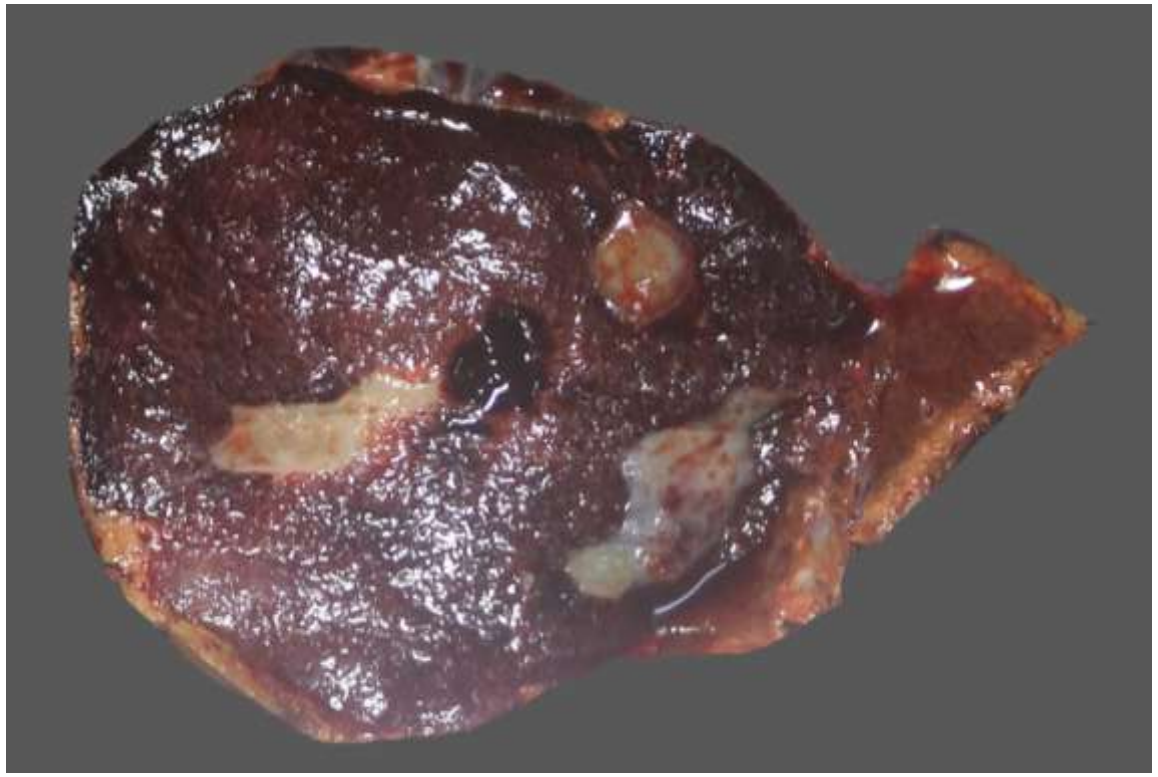
Malignant Rhabdoid tumour (MRT)

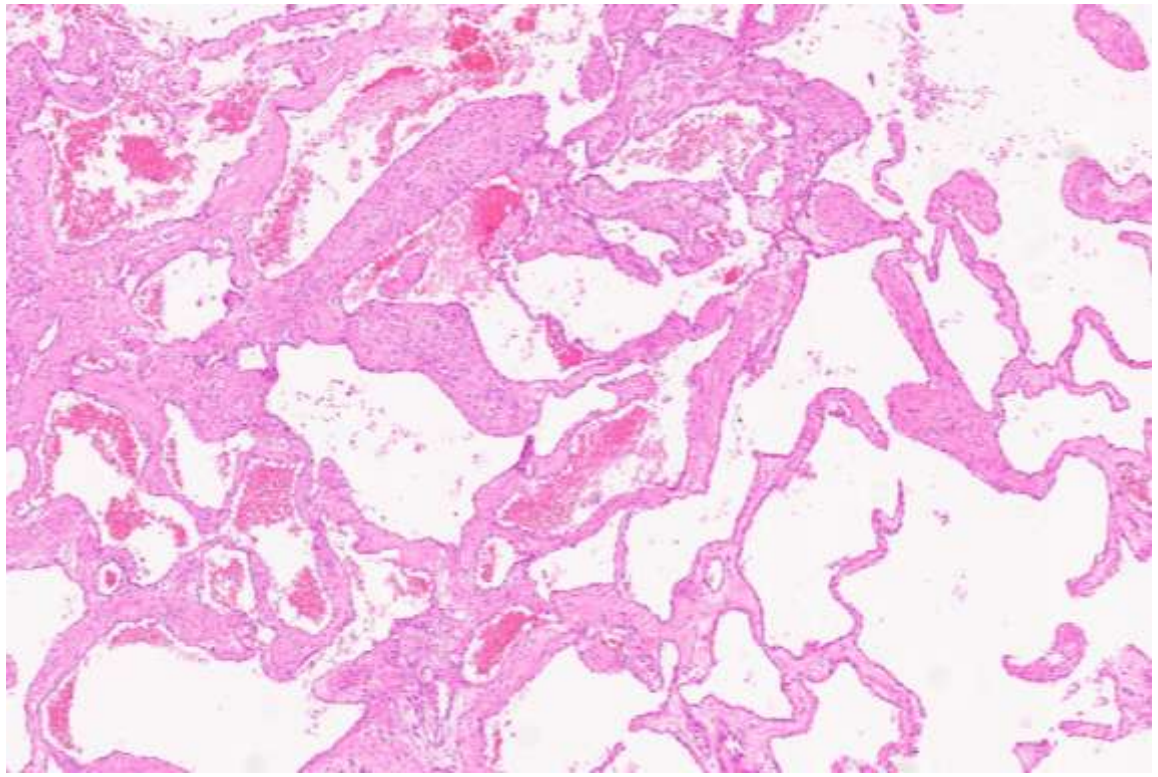
- Rare aggressive malignancies most commonly found in kidneys and central nervous system.
- MRT involving liver is extremely rare with dismal prognosis
- MRT of the liver most commonly occurs in infancy (median age 8 months)
- Characterized by mutations involving loss/deletions in SMARCB1/INI1 gene encoding the SWI/sucrose non-fermenting ATP dependent chromatin remodeling complex, involved in tumor suppression
- Varying micro architectural patterns including myxoid, myxohyaline, cord-like stranding, pseudo-alveolar, vague spindling, clear-cell and small cell undifferentiated varieties
- Kohashi et al reclassified pediatric rhabdoid tumors into conventional type, atypical teratoid/rhabdoid type, and small cell types
- Heterogenous immune profile, with the expression of neural, mesenchymal, and epithelial markers

Hepatic Rhabdoid tumour



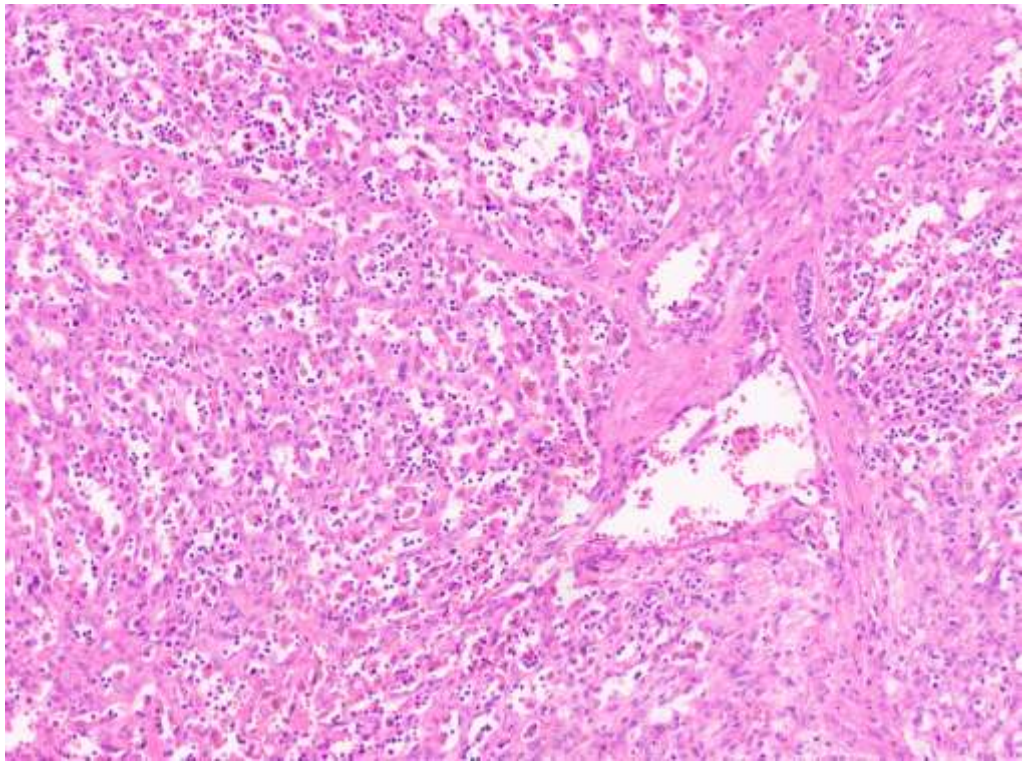






Cavernous Hemangioma

Hepatic haemangioma (HCH & HIH)

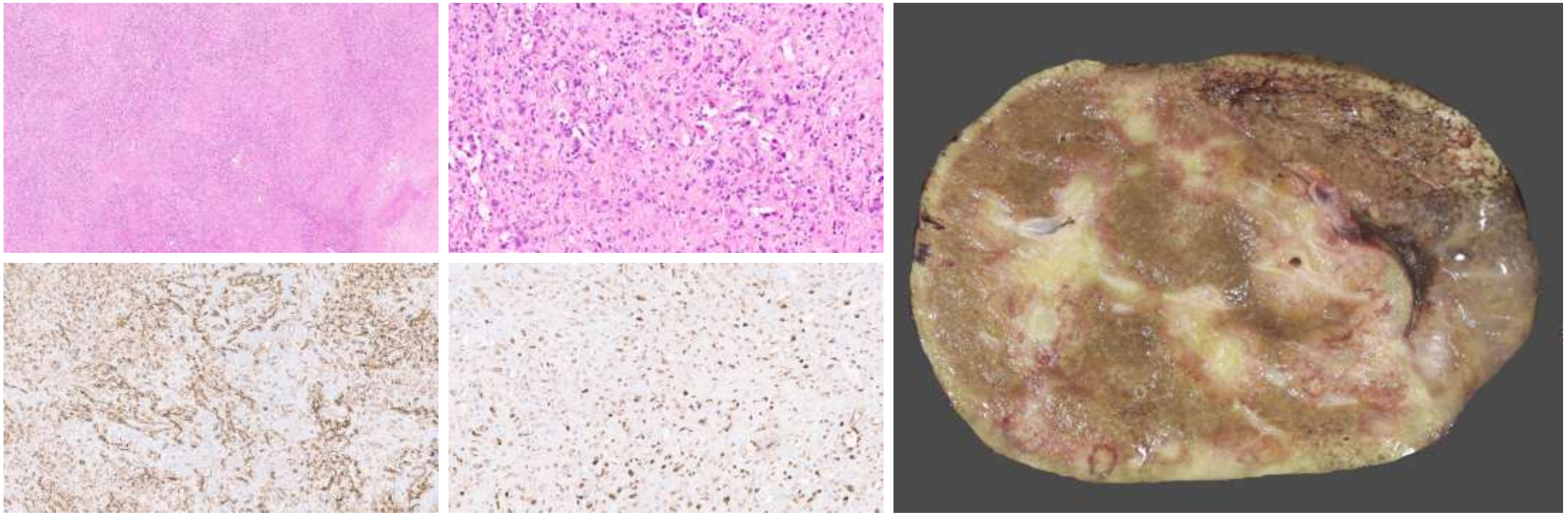


Epithelioid haemangioendothelioma

- Rare vascular tumor
- Epithelioid and histiocytoid vascular endothelial cells in myxoid or fibrotic stroma
- Can arise in multiple locations
- In liver, presents on imaging as an incidental finding of multifocal, heterogeneously enhancing nodules in both lobes
- Presents clinically with nonspecific abdominal symptoms.
- Stains positive for vascular markers, factor VIII–related antigen, CD31, and CD34
- *CAMTA1-WWTR1* fusion, most common genetic abnormality
- YAP-TFE3 fusions rare

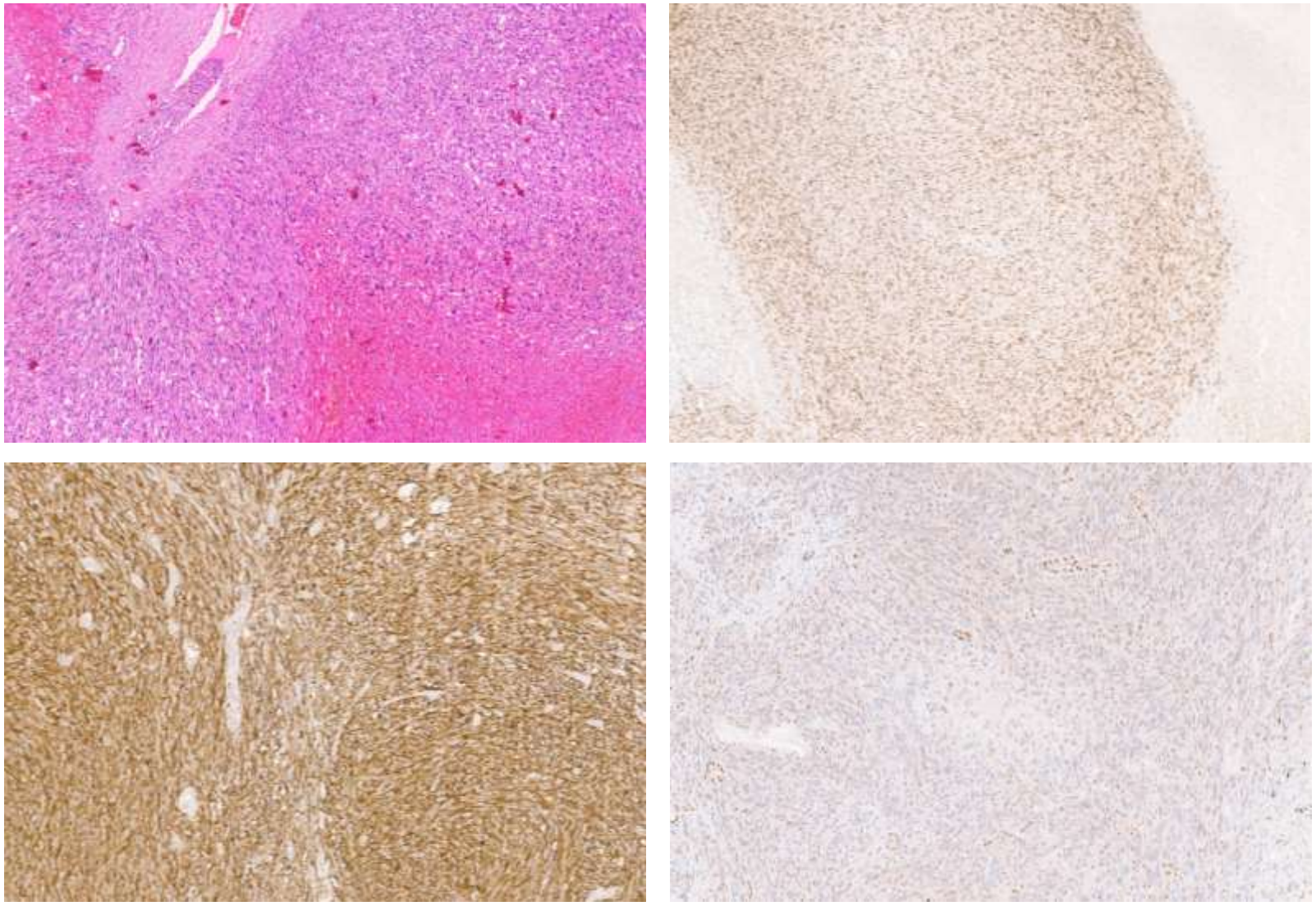
Arch Pathol Lab Med (2018) 142 (2): 263–267.

Epithelioid haemangioendothelioma



Arch Pathol Lab Med (2018) 142 (2): 263–267.

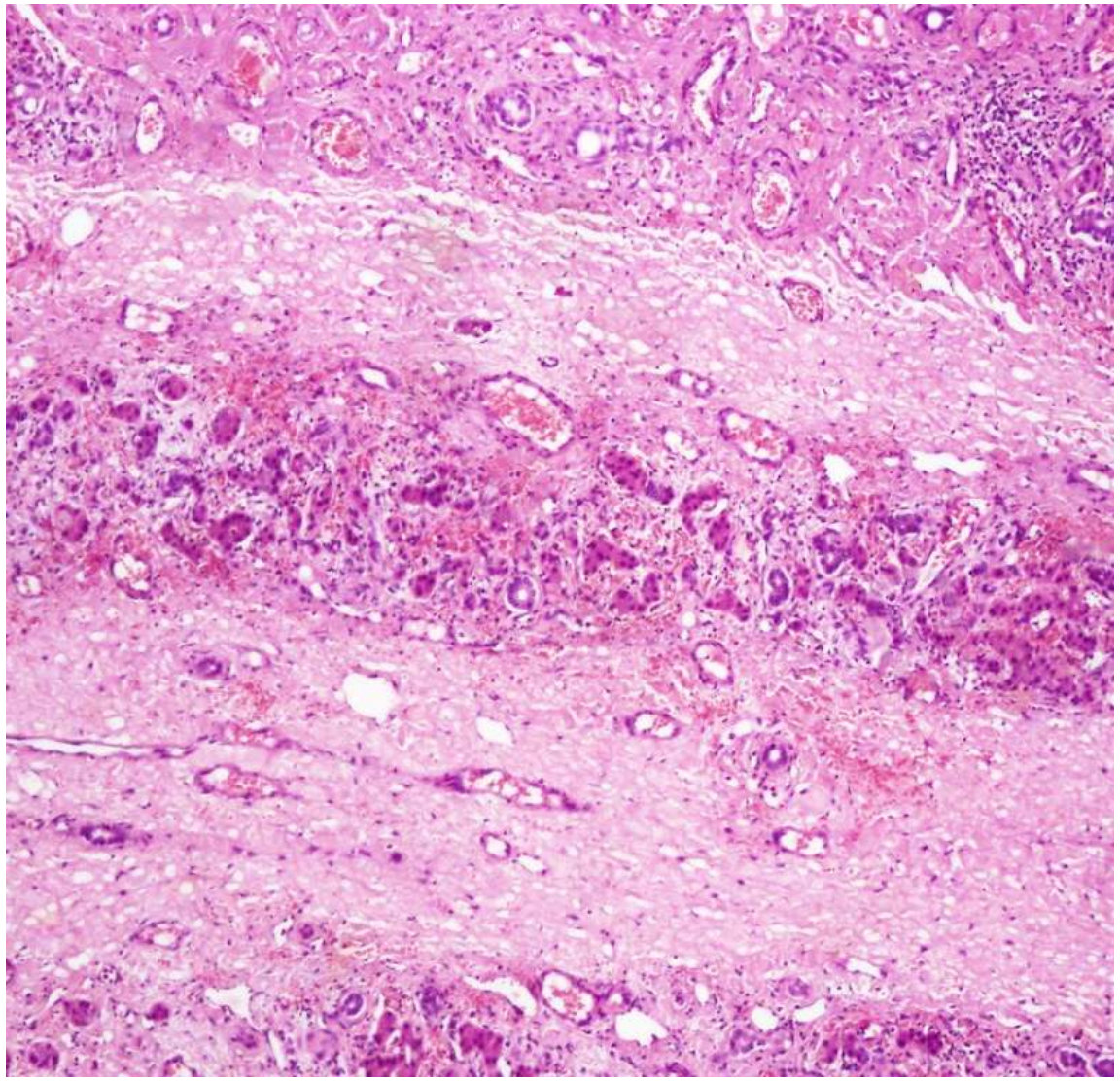
HEPATIC ANGIOSARCOMA



Am J Surg Pathol. 2019 May;43(5):581-590.

Mesenchymal hamartoma

- Benign tumour
- Well-circumscribed, multilocular or multicystic mass
- Third most common hepatic tumour in childhood
- 85% of affected children present before the age of 3 years
- Chromosomal rearrangements involving chromosome 19q13.4
- Loose connective tissue and epithelial bile ducts in varying proportions arranged in lobulated islands

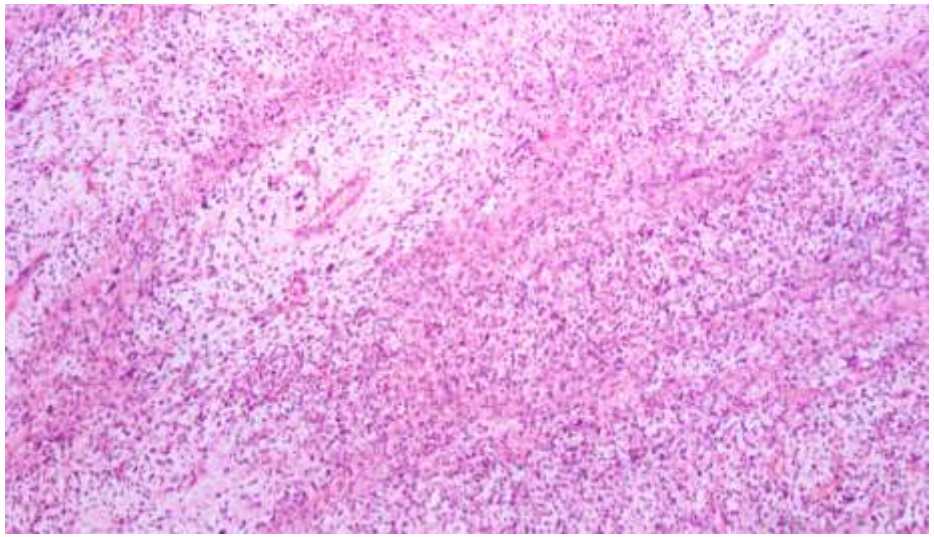


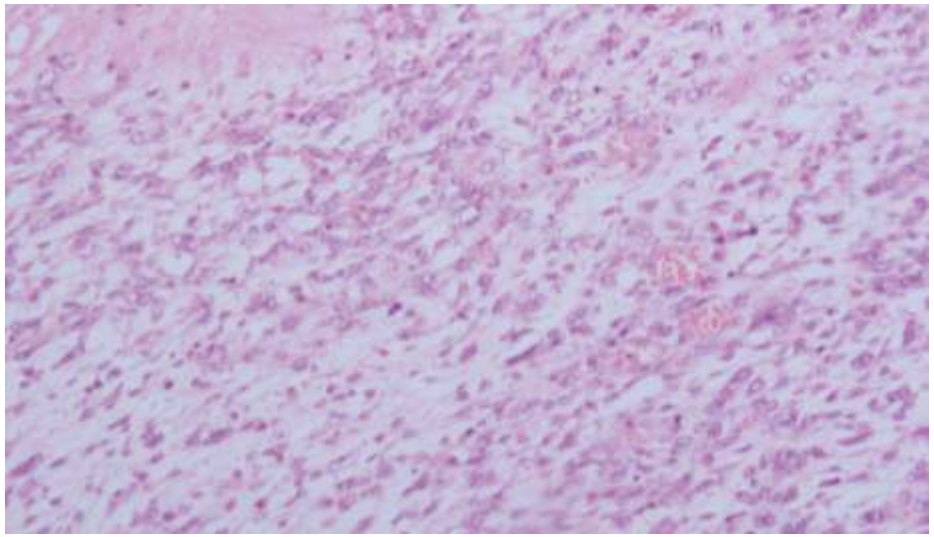
Hepat Oncol. 2020 Apr 7;7(2):HEP19.

Embryonal sarcoma

- Malignant mesenchymal tumour
- Heterogeneous morphology and no specific differentiation pattern
- Chromosome 19 microRNA cluster (C19MC), a potential oncomir
- Variable cellularity
- Medium to large spindle and stellate cells embedded in a myxoid stroma
- Bizzare cells
- t(11;19)(q13;q13.4) translocation
- *TP53* mutation

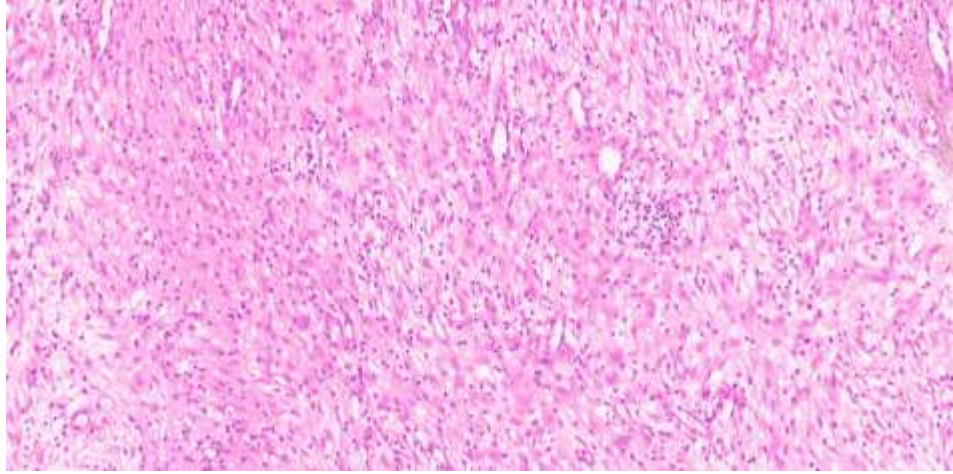
Hepat Oncol. 2020 Apr 7;7(2):HEP19.

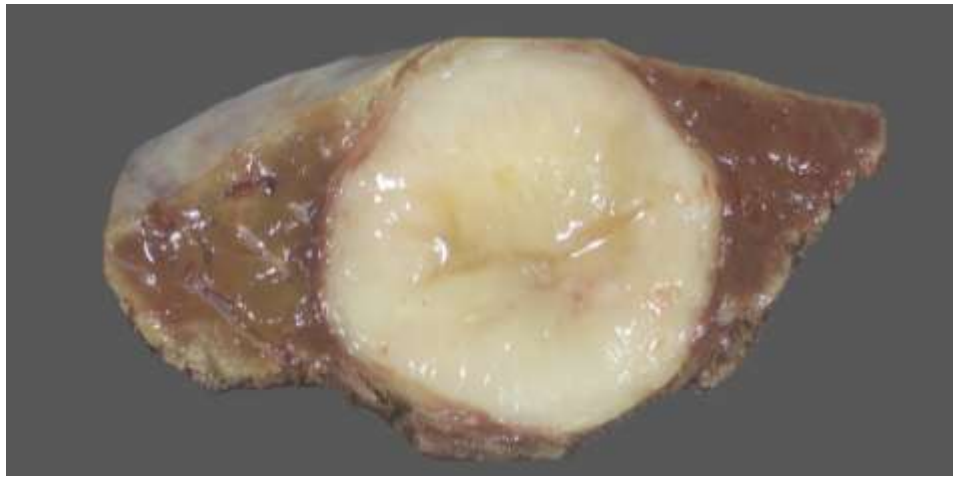


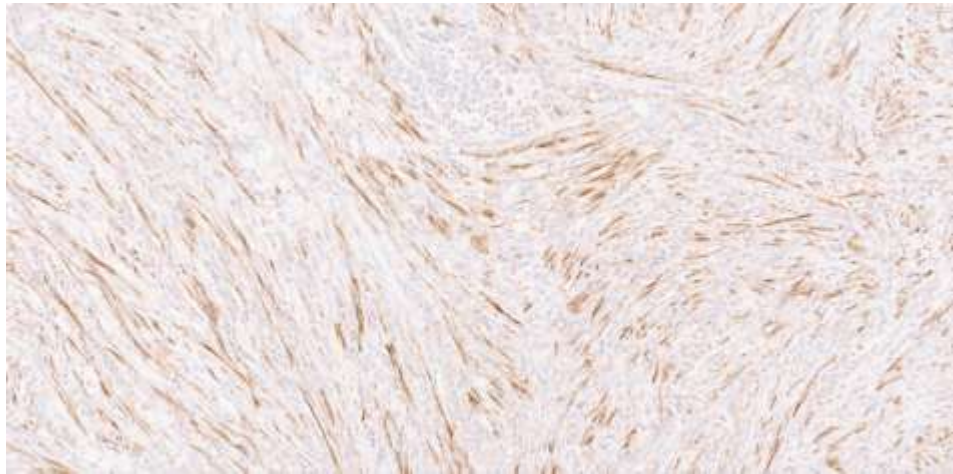


INFLAMMATORY MYOFIBROBLASTIC TUMOUR (IMFT)

- Distinctive fibroblastic/myofibroblastic neoplasm of intermediate biological potential
- Prominent inflammatory infiltrate, chiefly lymphocytes and plasma cells
- TKR gene rearrangements, most often involving the *ALK* locus at 2p23, with diverse fusion partners
- ~5% of IMFTs harbour *ROS1* gene fusions; other rare gene fusions involve *NTRK3*, *PDGFRB*, and *RET*
- ALK-negative tumours may have a higher risk of metastases

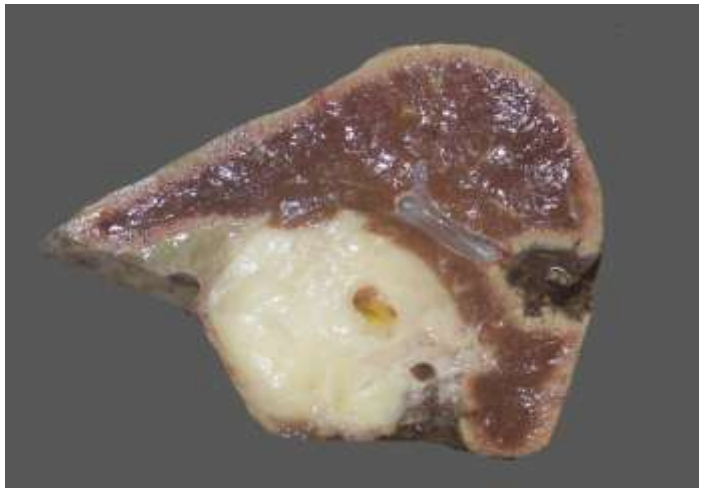


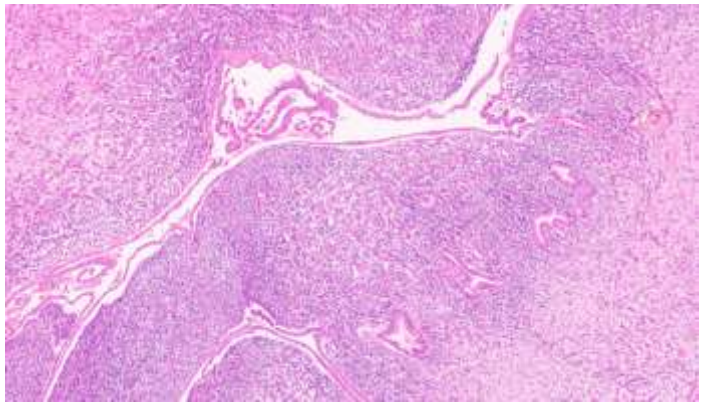




Hepatobiliary Rhabdomyosarcoma

- Rare lesion
- 0.5% of pediatric RMS and 0.04% of all pediatric malignancy
- Commonly misdiagnosed
- Most common malignant cause of obstructive jaundice in pediatric patients
- Biliary tract had been classified as “favorable site” in recent Children’s Oncology Group (COG) studies ,
- Assumed to have a better prognosis, thus requiring a less aggressive therapy

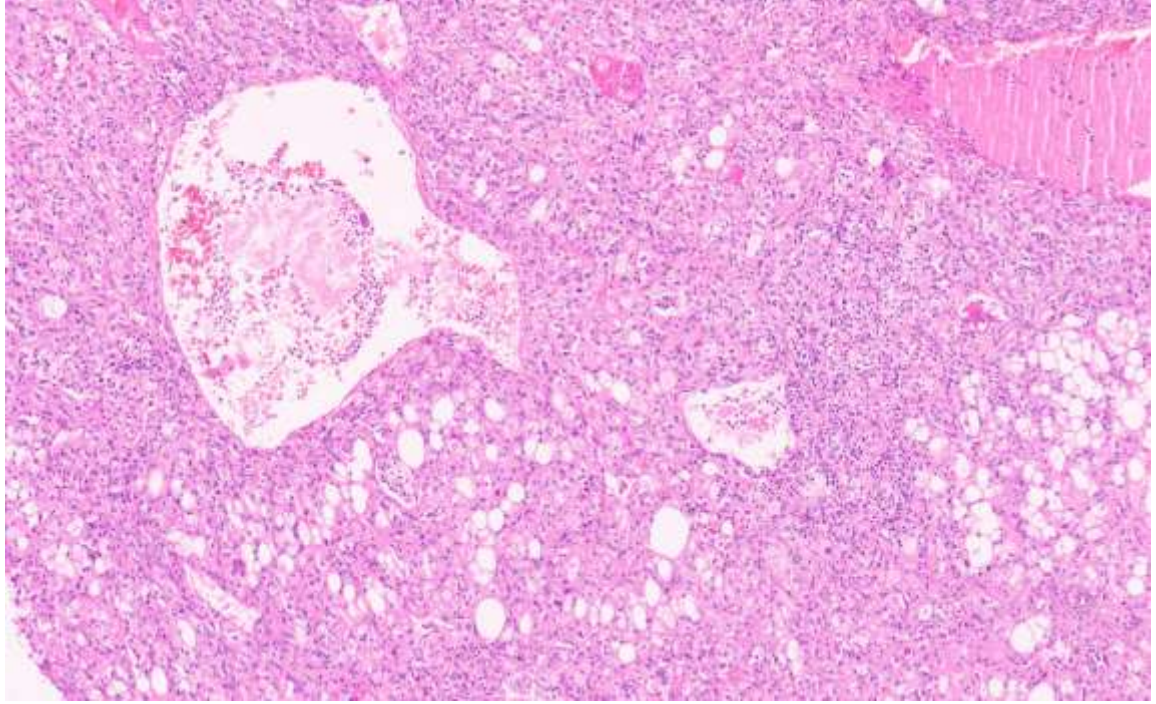


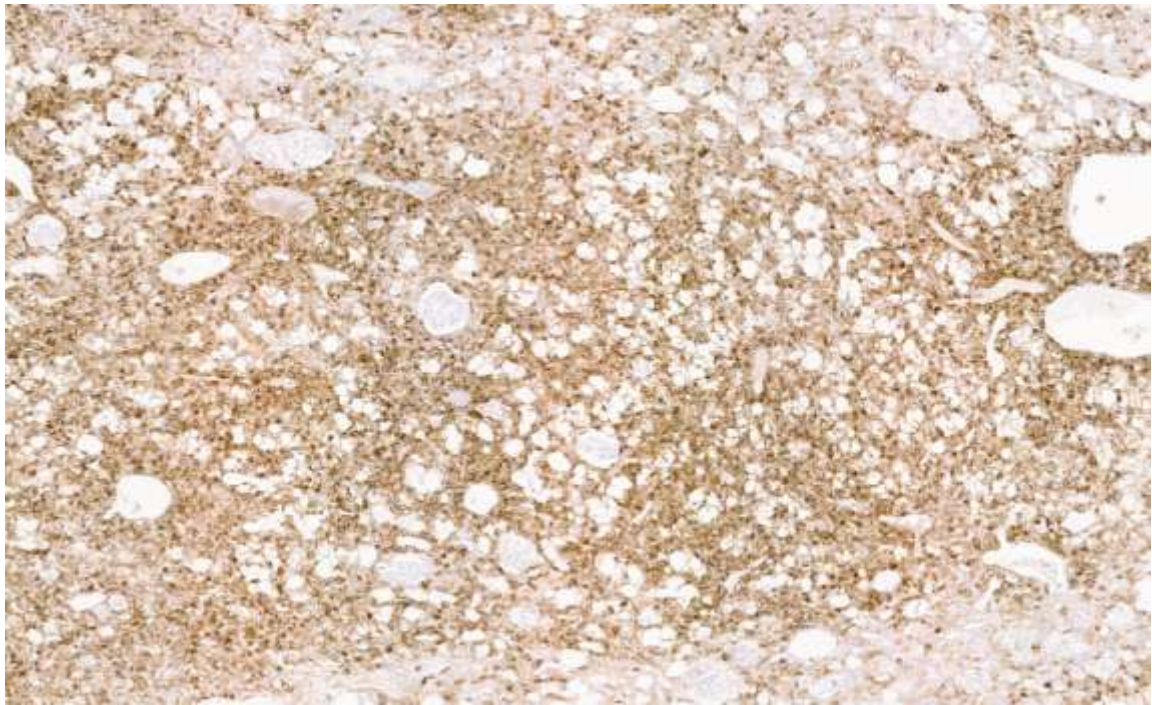


Front Oncol. 2021 Sep 30;11:701400.

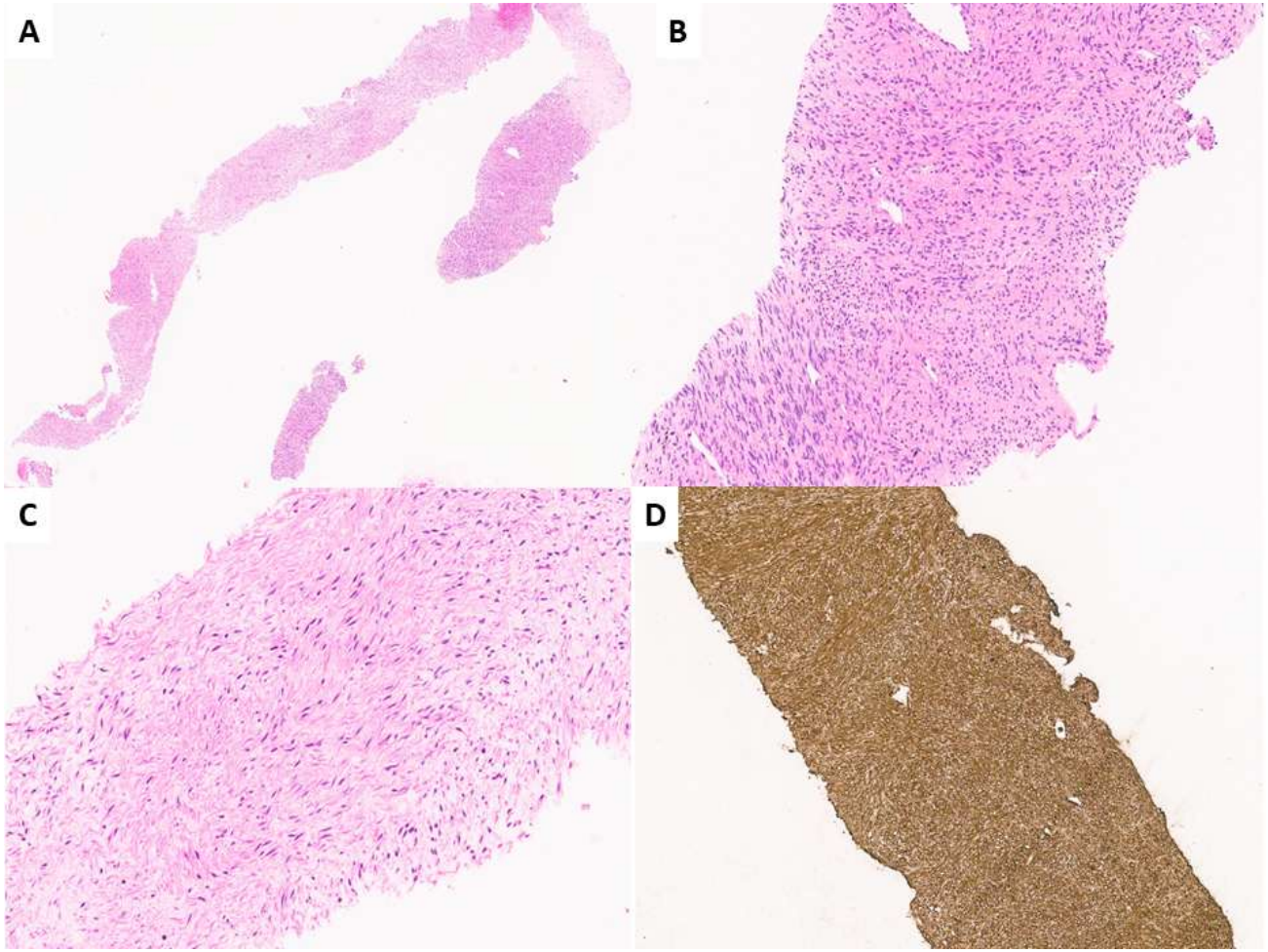
PEComa/Angiomyolipoma

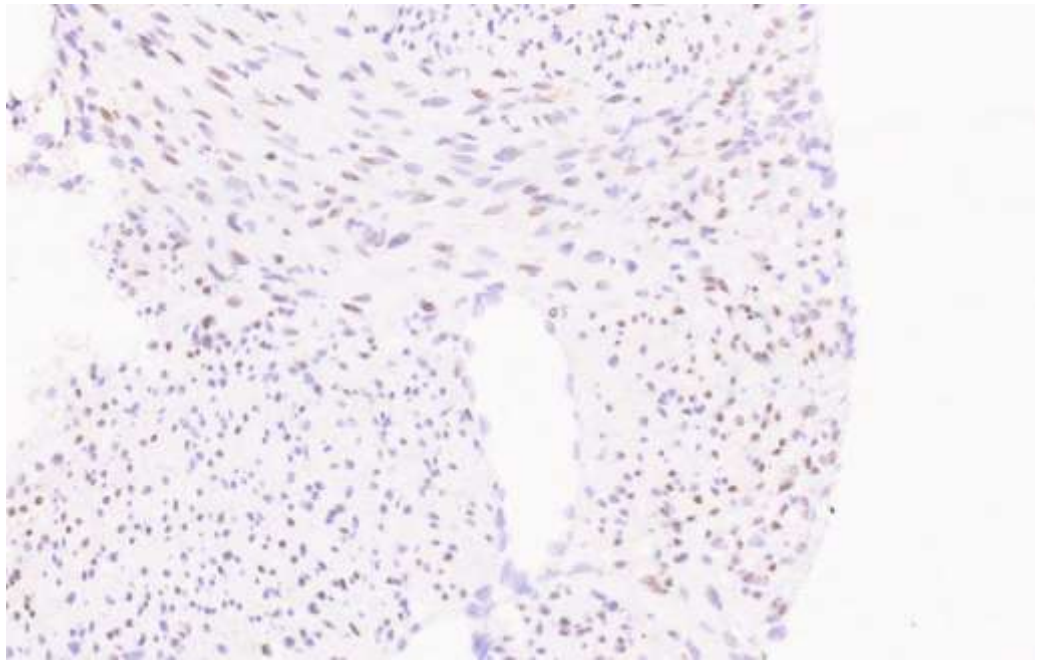
- Mesenchymal neoplasm
- Composed of distinctive, predominantly epithelioid cells
- Angiomyolipoma (PEComa subtype) that also contains adipocytes and thick-walled, tortuous blood vessels
- Variable expression of smooth muscle and melanocytic markers
- AML mostly sporadic; 5–10% with tuberous sclerosis
- *TSC2* mutations
- *TFE3* gene rearrangements





Epstein Barr Virus Associated Smooth Muscle Tumor (EBV-SMT)





Vij M et al. Fetal Pediatr Pathol. 2021 Nov 5:1-12

Thank you