Last Updated: 5/17/2020

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Hepatocellular Lesions

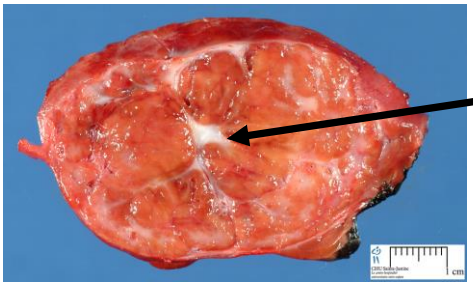
Note: <u>All</u> of these lesions stain with Hepatocellular stains (Hepar-1 and Arginase)!
Also, canalicular staining with CD10 and pCEA. Cytoplasmic TTF-1. Negative MOC-31.

Macroregenerative Nodule

An unusually large regenerative nodule (often >1 cm) that develops in the setting of **<u>cirrhosis</u>**.

Hyperplastic liver parenchyma. Plates may be slightly thickened (usu. 1-2 cells thick, maybe focally 3). Have **<u>normal constituents</u>** (bile ducts, arteries, veins, etc…). **No atypia** (Unless dysplastic).

Focal Nodular Hyperplasia (FNH)

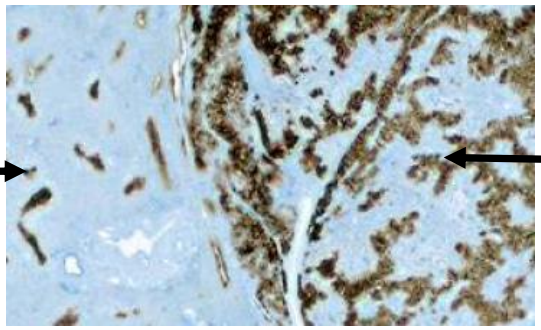


<u>Not a true neoplasm</u>; "<u>Focal Cirrhosis</u>"
Regenerative hyperplastic response of hepatocytes <u>secondary to vascular abnormalities</u>
Very common

Well-circumscribed with **<u>central stellate scar</u>** with fibrous septae with entrapped vessels, bile ducts, and inflammatory cells
Normal plate thickness. No true portal tracts.
"<u>Map-like" staining with glutamine-synthetase</u>

<u>Glutamine Synthetase IHC:</u>

Normal, pericentral staining



Strong "Map-like" staining

Note: In cirrhosis it shows weak, patchy periseptal staining.

Hepatocellular Adenoma

<u>Benign</u> liver neoplasm.
Assoc. with oral contraceptives/steroids.
Risk of transformation to HCC and/or bleeding/rupture

Benign-appearing hepatocytes, No significant atypia.
Normal plate thickness (1-2 cells thick)
<u>Unpaired arteries, absent bile ducts</u>
No mitoses

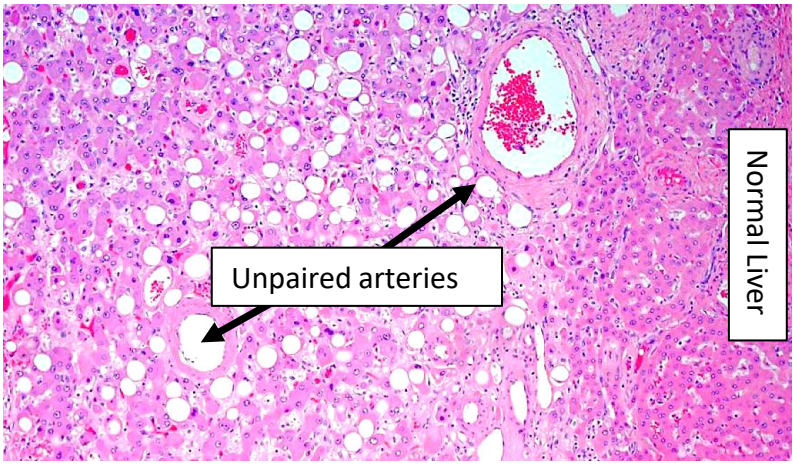
<u>Subtypes:</u>

Inflammatory/Telangiectatic *(~45%)* → Stain with serum amyloid A and CRP; associated inflammatory infiltrate, peliosis, and bile ductular reaction in fibrous septae. Transformation to HCC occurs.

B-catenin activated *(~15%)* → Nuclear B-catenin (focal), Diffuse, strong glutamine synthetase. Highest risk of malignant transformation

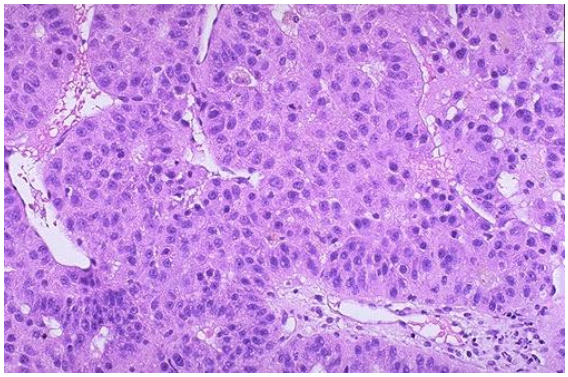
HNF1α-inactivated *(~30%)* → Loss of LFABP staining. Associated with adenomatosis (>10 adenomas). Very low risk of transformation.

Unclassified (~10%) → None of the above (~10%)



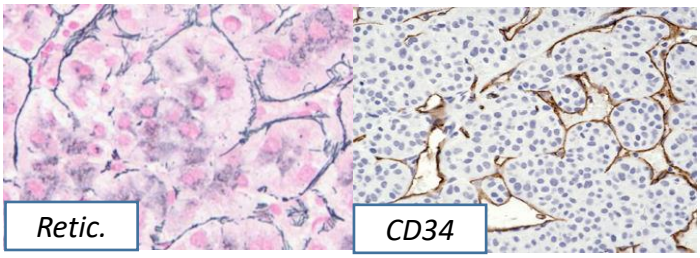
Hepatocellular Lesions

Hepatocellular Carcinoma



Malignant tumor with hepatocellular differentiation
Often occurs in setting of **cirrhosis** (associated with chronic liver damage such as viral hepatitis, EtOH, and NASH)
Dx often made *clinically* (Radiology + ↑ AFP = HCC)
Treat often with embolization, resection, or transplant

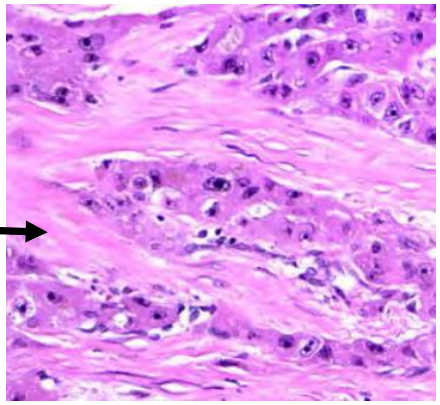
Widening of hepatic plates (>2 cells thick)
Absent portal tracts, often unpaired arteries.
Architecture and cytologic atypia varies and includes pseudoacini/pseudogland formation and wide trabeculae.
Often bile production by tumor cells.



Staining:
Reticulin→ Widening of hepatic plates
CD34→ Diffuse sinusoidal ("capillarization")
Glypican-3→ +/- (but negative in benign liver, Positive staining supports malignancy)

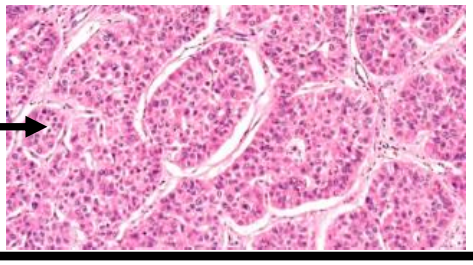
Variants:

Fibrolamellar HCC → Often young, non-cirrhotic patients. Normal AFP. Often large, solitary. Large oncocytic tumor cells with bands of lamellar fibrosis. Cytoplasmic pale bodies. Recurrent DNAJB1-PRKACA translocation. Stain with CD68 and CK7.
Classically thought to be better prognosis, but this is likely mostly due to demographics (younger, non-cirrhotic patients)



Steatohepatitic HCC → Assoc with Hep C with NASH.
Macrovesicular steatosis, ballooning degeneration, M-D bodies.
Can be hard to recognize on biopsy (esp. if background NASH)!

Macrotrabecular-Massive HCC → Thick trabeculae coated by endothelial cells and surrounded by vascular space. Aggressive subtype with high AFP and TP53 mutations or FGF19 amplification.

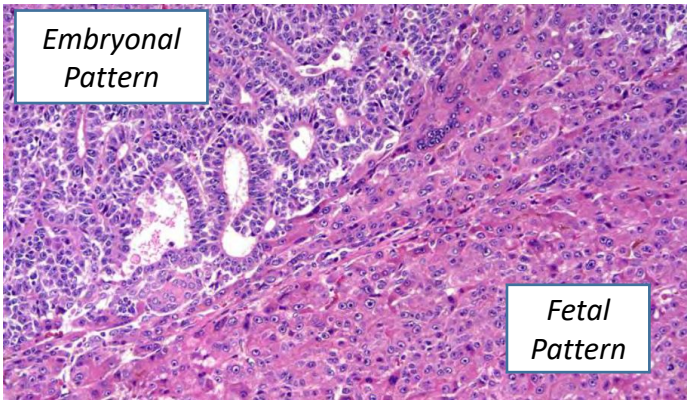


Hepatoblastoma

Most common liver tumor in Children.
Malignant. Assoc. w/ Beckwith-Wiedmann

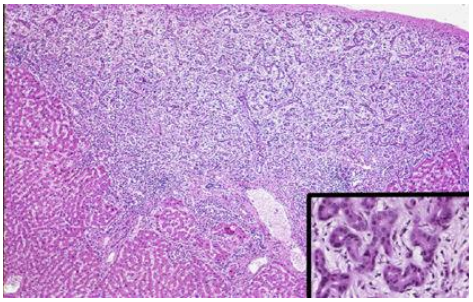
Shows a variety of epithelial (e.g., fetal and embryonal) and mesenchymal cell types ("teratoid") recapitulating hepatic ontogenesis.

Frequent ß-Catenin mutations
Nuclear localization by IHC→ worse prognosis



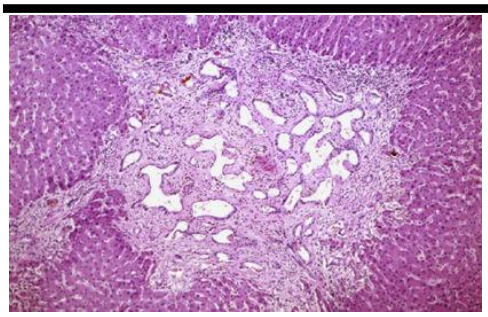
Biliary Lesions

Note: The epithelium in all of these lesions stain with CK7, CK19, and MOC31 (among other stains). These lesions are negative for hepatocellular stains (Hepar-1, Arginase, and Glypican-3).



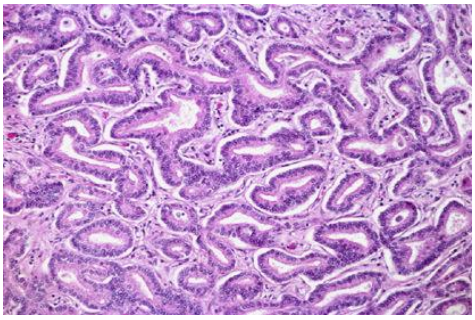
Bile Duct Adenoma

Benign bile duct proliferation
Usu. <1 cm, subcapsular, and well-circumscribed.
Small, uniform, small ducts with cuboidal cells and regular nuclei.
Biliary adenofibroma→ more complex epithelial growth with abundant fibroblastic stromal components
Clinically, may mistake intraoperatively for a metastasis



Bile Duct Hamartoma
aka Von Meyenburg Complex

Benign, may be multiple.
Usu. small (several mm)
Irregular to round bile **dilated bile ducts**
Associated with **fibrous/hyalinized stroma**
Lumens **contain bile** and proteinaceous material

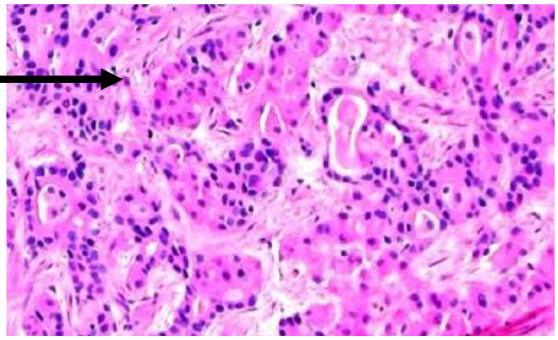


Cholangiocarcinoma

Adenocarcinoma arising from intrahepatic bile ducts

Inflammatory disorders can predispose (e.g., PSC or liver fluke infection). Must **clinically distinguish from metastasis as overlap.**
Usu. tubular pattern. Sometimes large ducts. Often sclerotic center.
Non-specific IHC profile, but (+) Albumin ISH supports intrahepatic

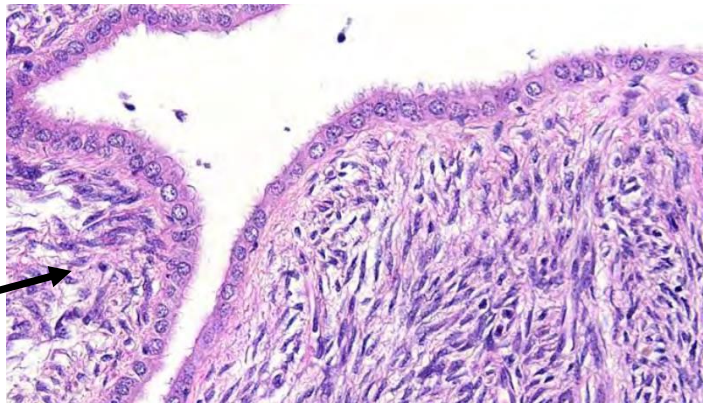
Combined Hepatocellular - Cholangiocarcinoma
A single tumor with morphologically distinct areas of HCC (Arginase and Hepar +) and Cholangiocarcinoma (CK7+).
Treated and prognosis similar to cholangiocarcinoma (Worse than HCC, No transplantation).



Additional DX:

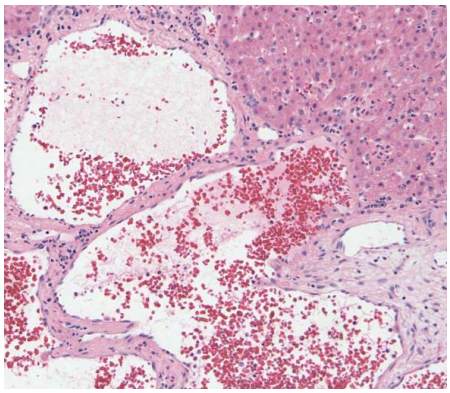
Intraductal Papillary Neoplasms → Similar to IPMNs in the Pancreatic duct. Can progress to cholangiocarcinoma.

Mucinous Cystic Neoplasms→ Just like in the pancreas! Ovarian-type stroma surrounding mucinous epithelium.



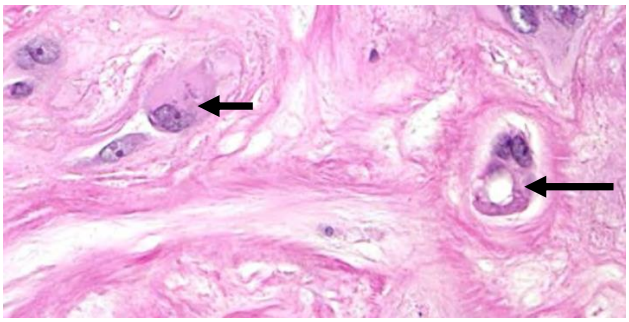
Vascular Lesions

Note: <u>All</u> of these lesions stain with endothelial markers, including CD31, ERG, and FLI-1.



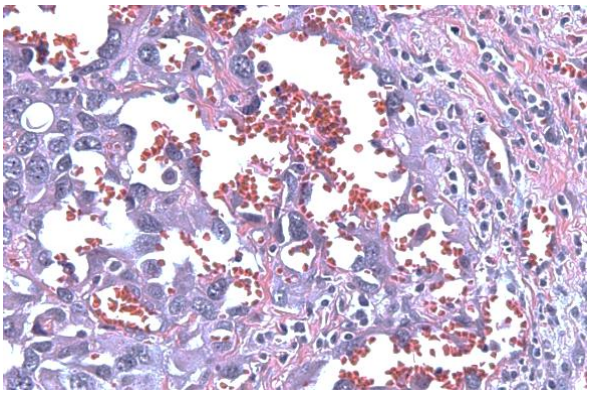
Cavernous Hemangioma

Most common benign tumor of the liver.
Thought to be malformations and non-neoplastic.
Often asymptomatic and diagnosed radiographically.
More common in females
Fibrous septae lined by single layer for flat endothelial cells.
Can thrombose and calcify.



Epithelioid Hemangioendothelioma

Endothelial tumor of **low-grade malignancy**.
Eosinophilic, slightly epithelioid cells with **signet ring-like** features representing intracytoplasmic lumina (often contain RBCs). Associated dense fibrous stroma.
Often have intravascular papillary growth and infiltrate sinusoidal spaces at edge of lesion
Translocation: **WWTR1-CAMTA1 fusion**
Sometimes focally positive for cytokeratins by IHC



Angiosarcoma

<u>Malignant</u> endothelial tumor. Most common liver sarcoma.
Spindled to epithelioid cells. Variably **atypical** endothelial cells with **multilayering and mitoses**. Anastomosing spaces.
Like to grow along pre-existing vascular spaces.
Usually **large and/or multifocal**.
Assoc. with exposure to Vinyl Chloride or Thorothrast.
Poor prognosis.

Other Tumors:

PEComa/Angiomyolipoma→ Benign tumors, just like in the kidney! Think of this if you see **fat**.
Variable admixture of fat, smooth muscle, and thick-walled blood vessels. Associated with tuberous sclerosus. Usu. Asymptomatic. <u>Stain with HMB45.</u> MelanA+/-

Embryonal Sarcoma→ Malignant tumor composed of undifferentiated mesenchymal cells. Usu. older <u>children</u>. Loose myxoid tissue with immature and giant cells. Characteristic <u>eosinophilic intracellular hyaline globules</u>. Can rupture. Previously bad prognosis, but improving.