

3rd APASL Single Topic Conference: HCC in 3D

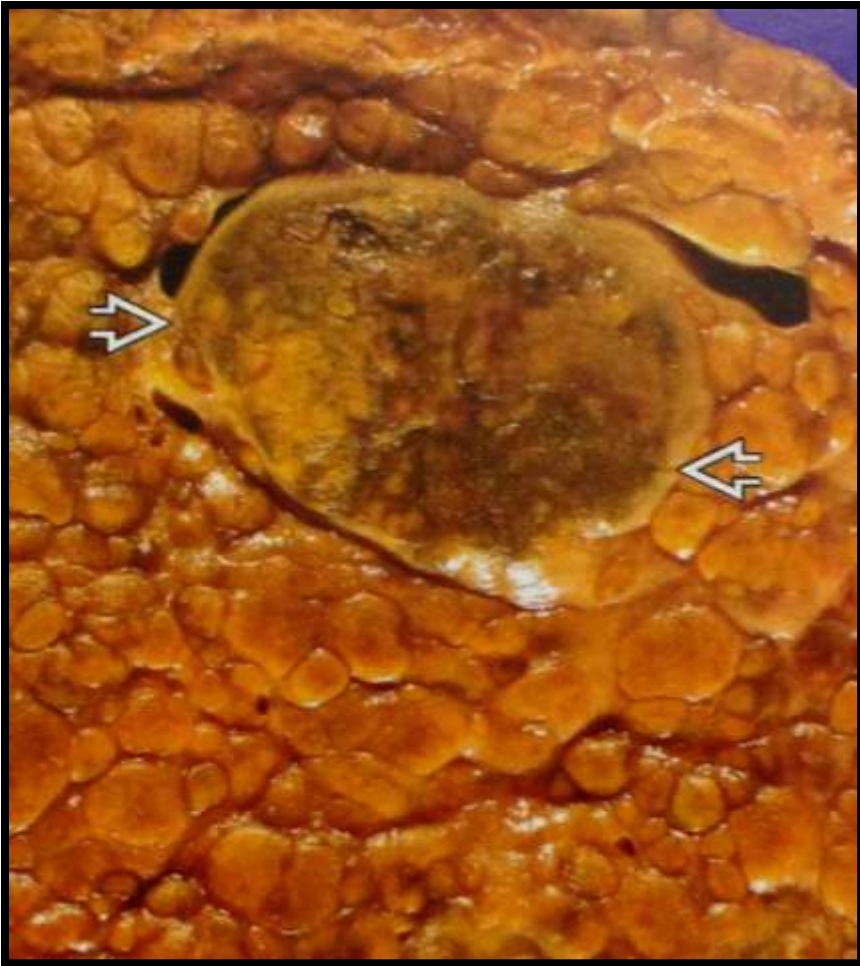
Pathological Classification of Hepatocellular Carcinoma

Glenda Lyn Y. Pua, M.D.

HCC

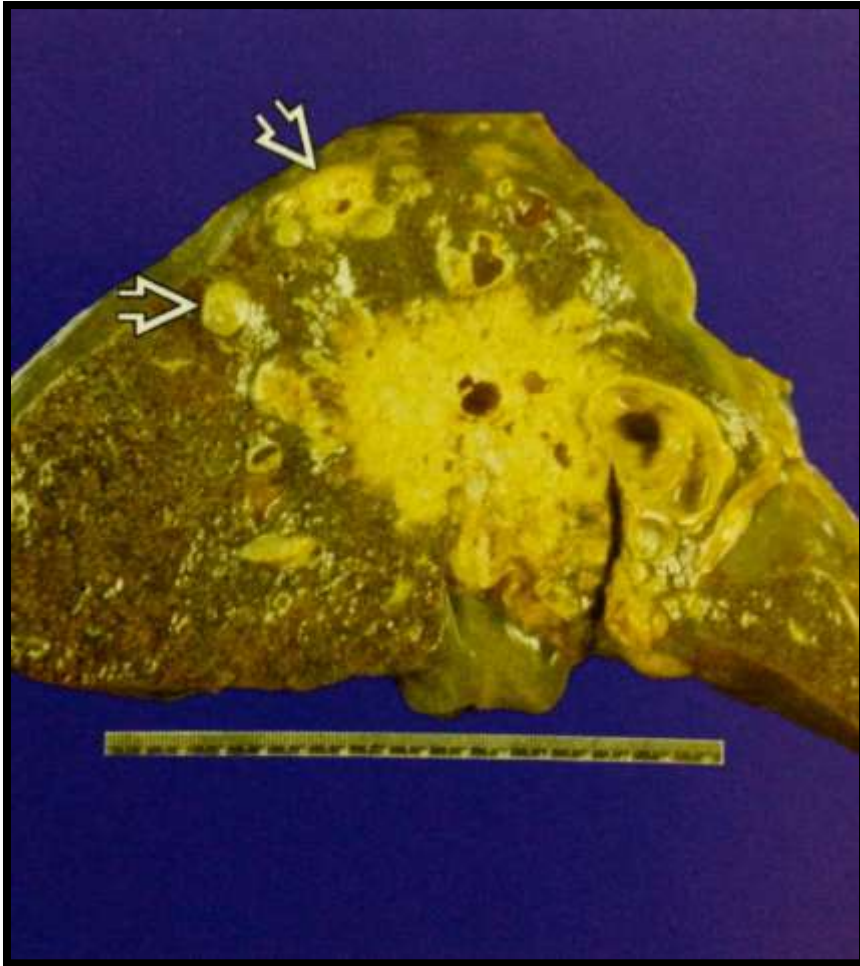
- Primary liver cancer is the 2nd most common cancer in Asia
- HCC is the most common histological type of primary liver cancer
- Prognosis depends on early detection and management
- Diagnosis can be challenging, especially with scant biopsy specimens and unusual morphology

Gross Features of HCC



- Large, well-circumscribed, bile-stained tumor in a background of cirrhosis

Gross Features of HCC



- Large central mass with small satellite nodules, in a background of cirrhosis

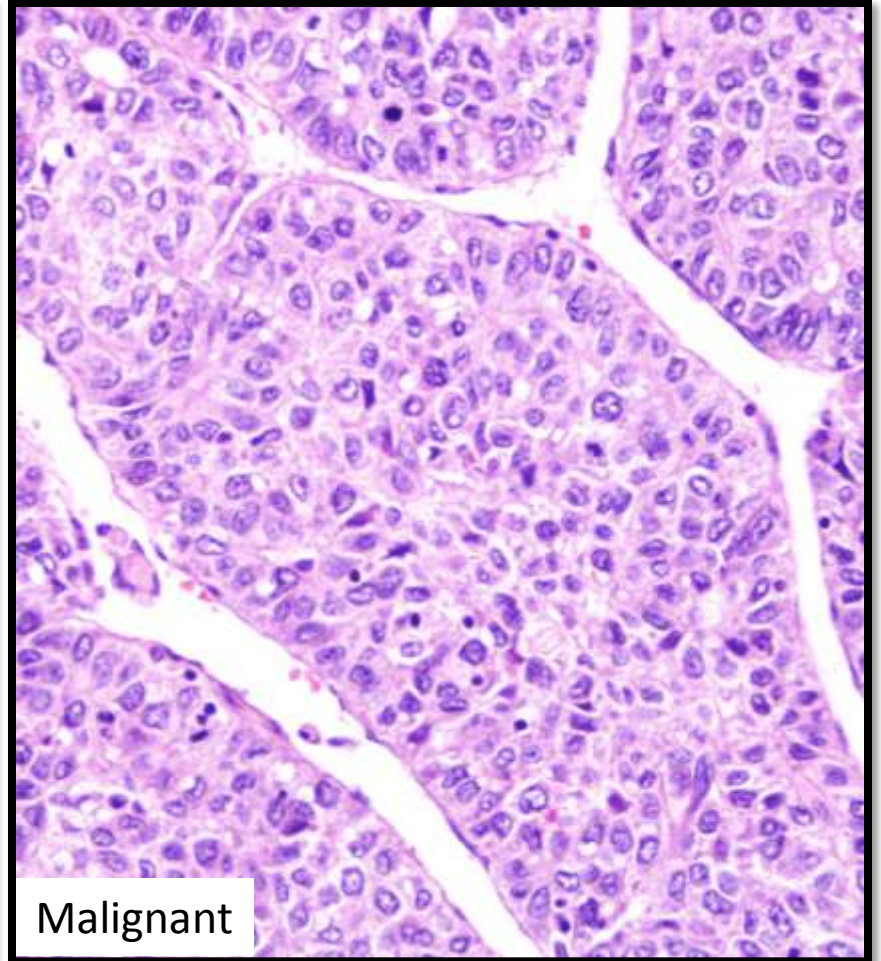
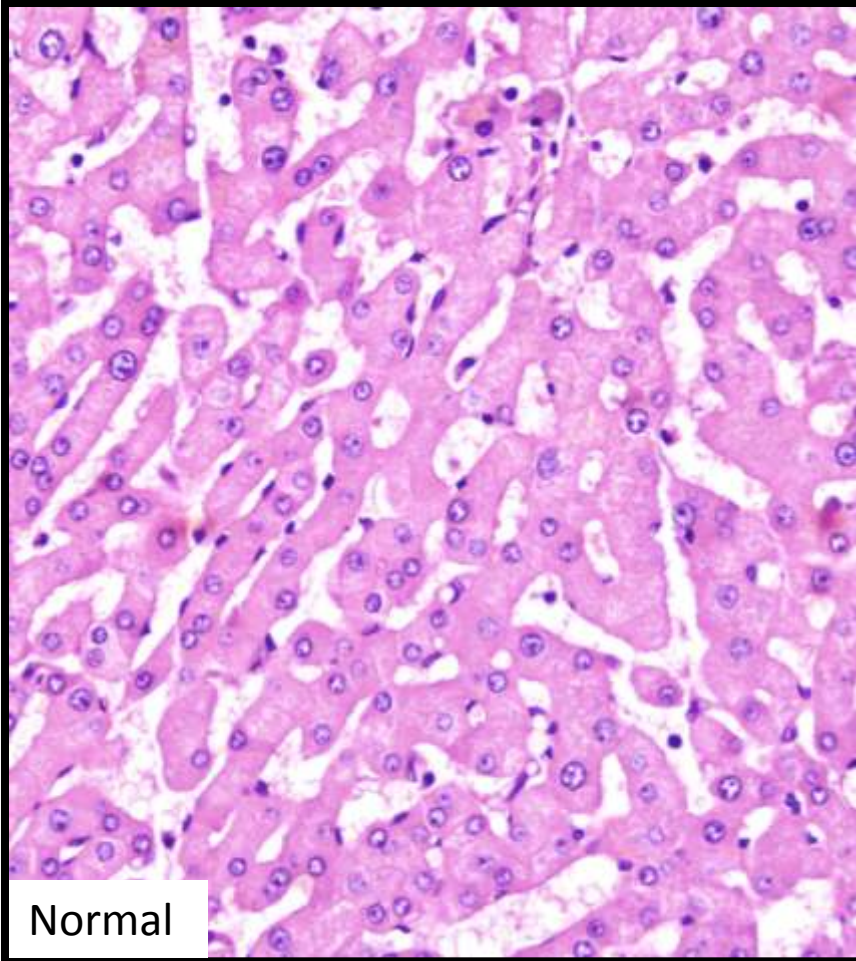
Histopathology of HCC

- Classical HCC
- Special types of HCC
 - Fibrolamellar carcinoma
 - Scirrhous HCC
 - Undifferentiated HCC
 - Lymphoepithelioma-like carcinoma
 - Sarcomatoid HCC

Classical HCC

- Tumor cells resemble normal hepatocytes to a variable extent
- The stroma is composed of sinusoid-like blood spaces lined by endothelial cells
- “Unpaired arteries” or “nontriadal arteries”
- No portal tracts

Comparison



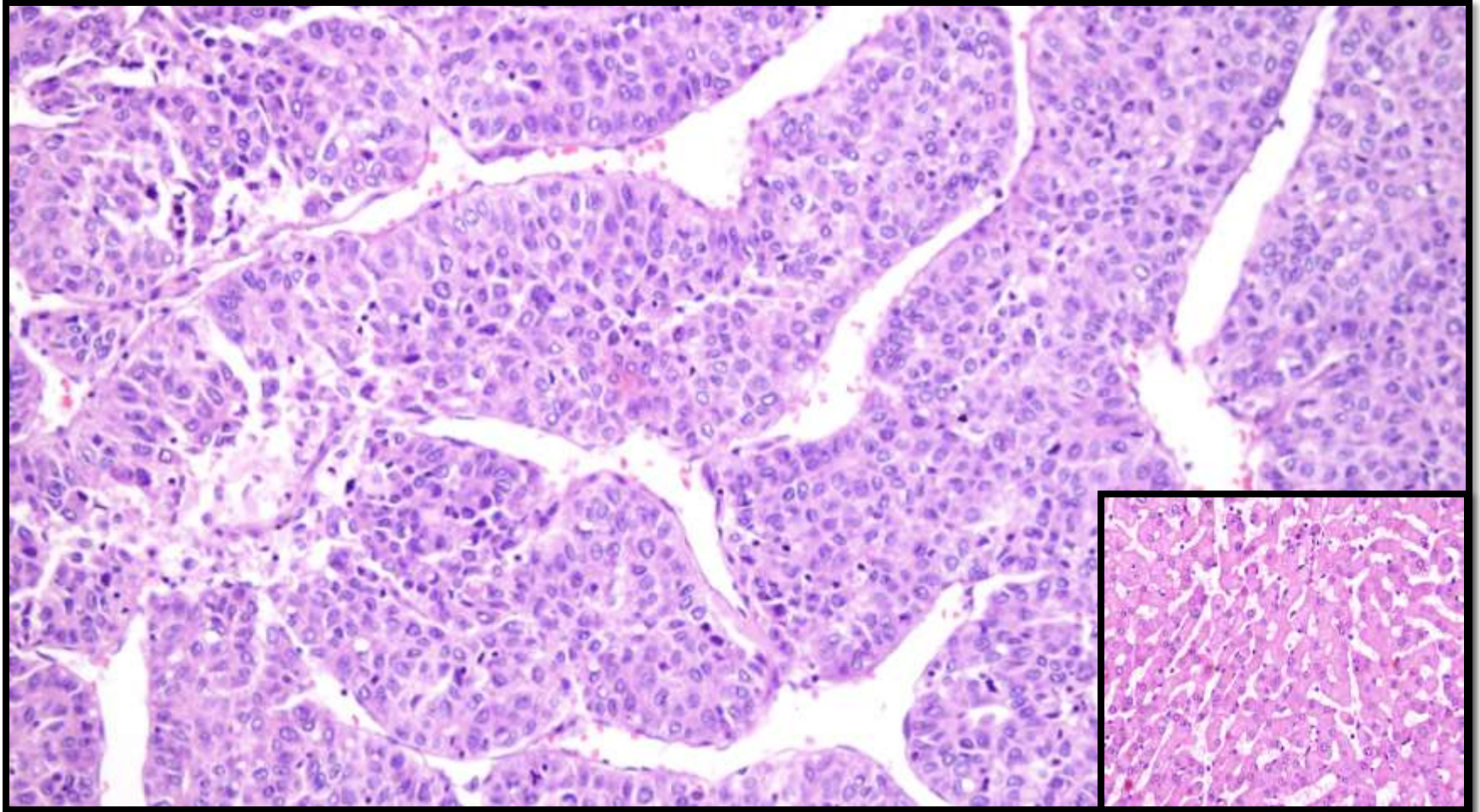
Classical HCC

- Vary architecturally and cytologically
 - Architectural patterns (trabecular, pseudoglandular or acinar and compact)
 - Cytological variants (pleomorphic cells, clear cells, spindle cells, fatty change, bile production, hyaline bodies, pale bodies, ground glass inclusions)
- The different architectural patterns and cytological variants frequently occur in combination

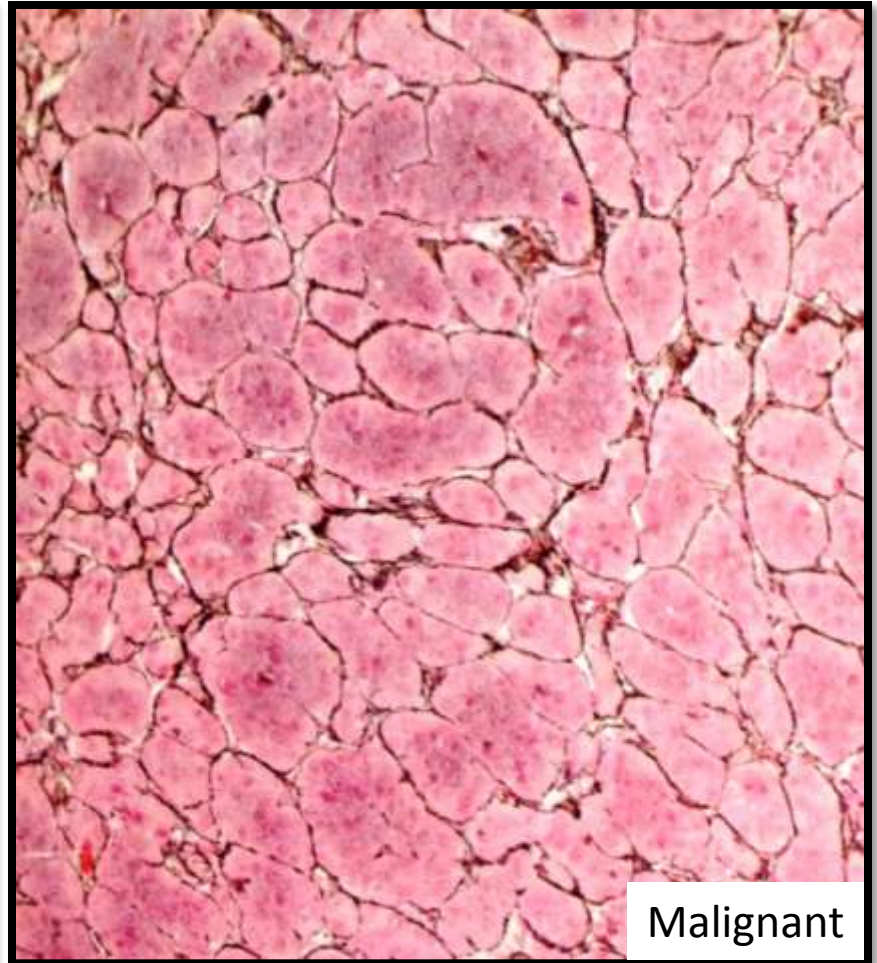
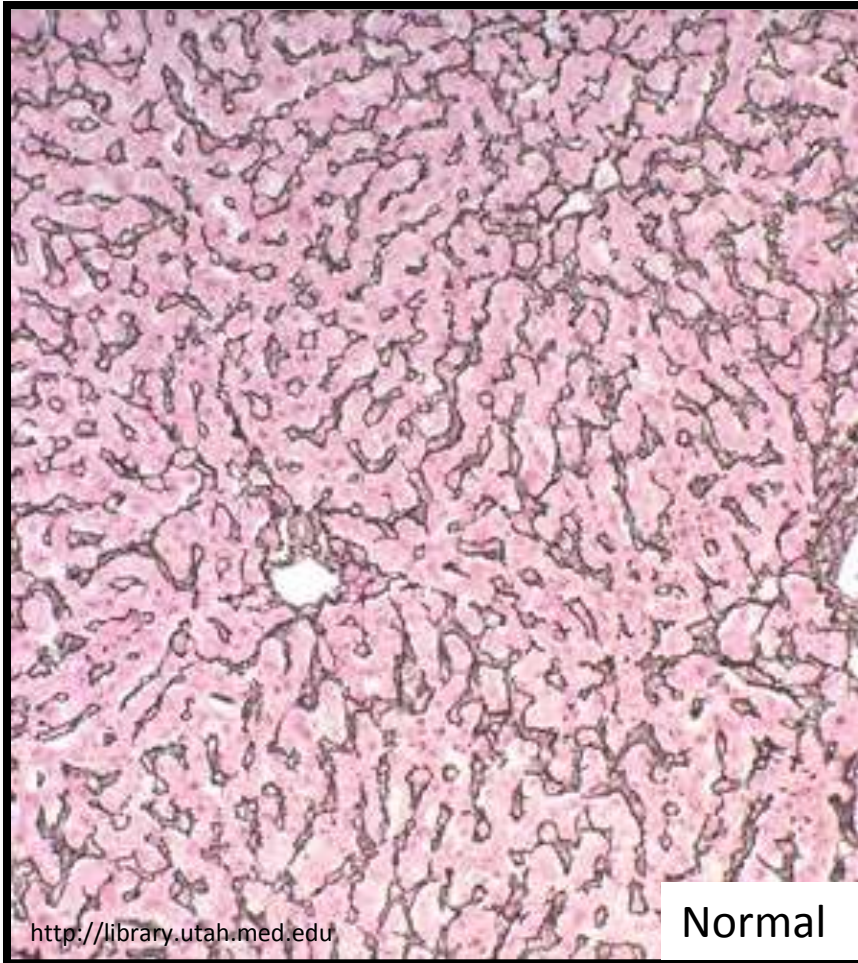
Classical HCC Patterns

- Trabecular (plate-like pattern)
 - Most common in well and moderately differentiated tumors
 - Tumor cells grow in cords of >3 cell plates thick that are separated by sinusoid-like blood spaces
 - Reticulin or CD34 stain helps highlight this pattern

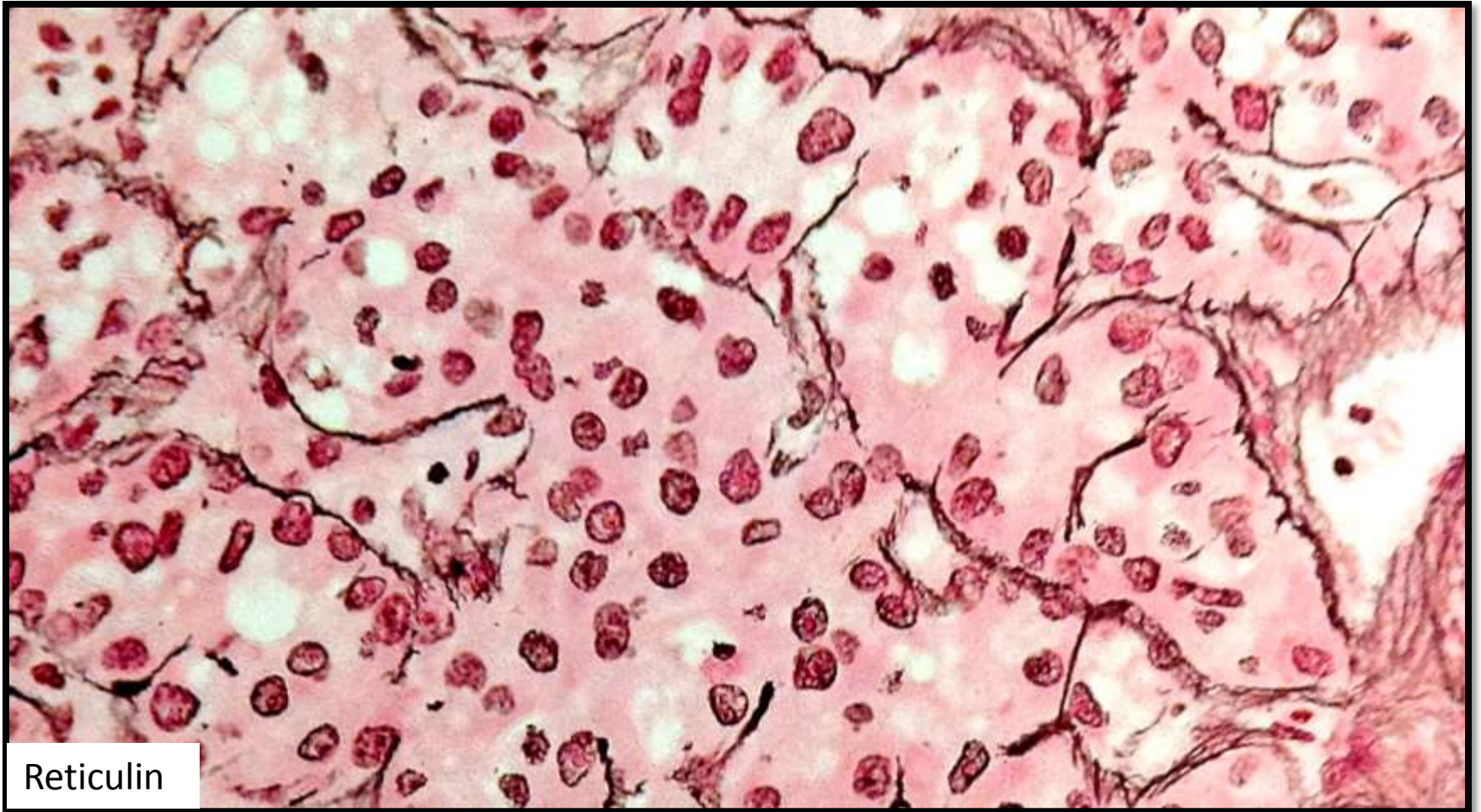
Classical HCC Patterns



Reticulin Stain



Classical HCC Patterns

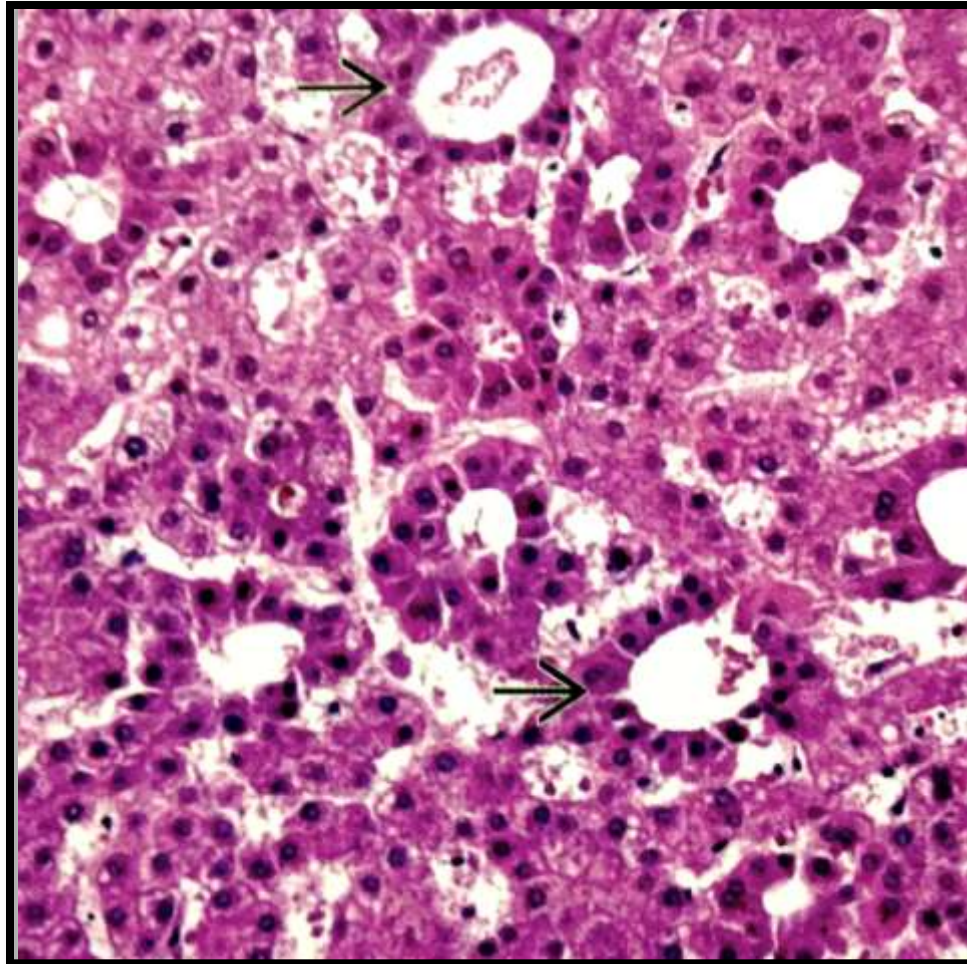


Reticulin

Classical HCC Patterns

- Pseudoglandular or acinar pattern
 - Presence of gland-like spaces or acini lined by hepatocytic tumor cells
 - Modified abnormal bile canaliculi formed between tumor cells
 - Pseudoglands frequently contains bile or proteinaceous material
 - Could lead to a misdiagnosis of adenocarcinoma
 - Frequently admixed, as a minor component, with the trabecular pattern

Classical HCC Patterns

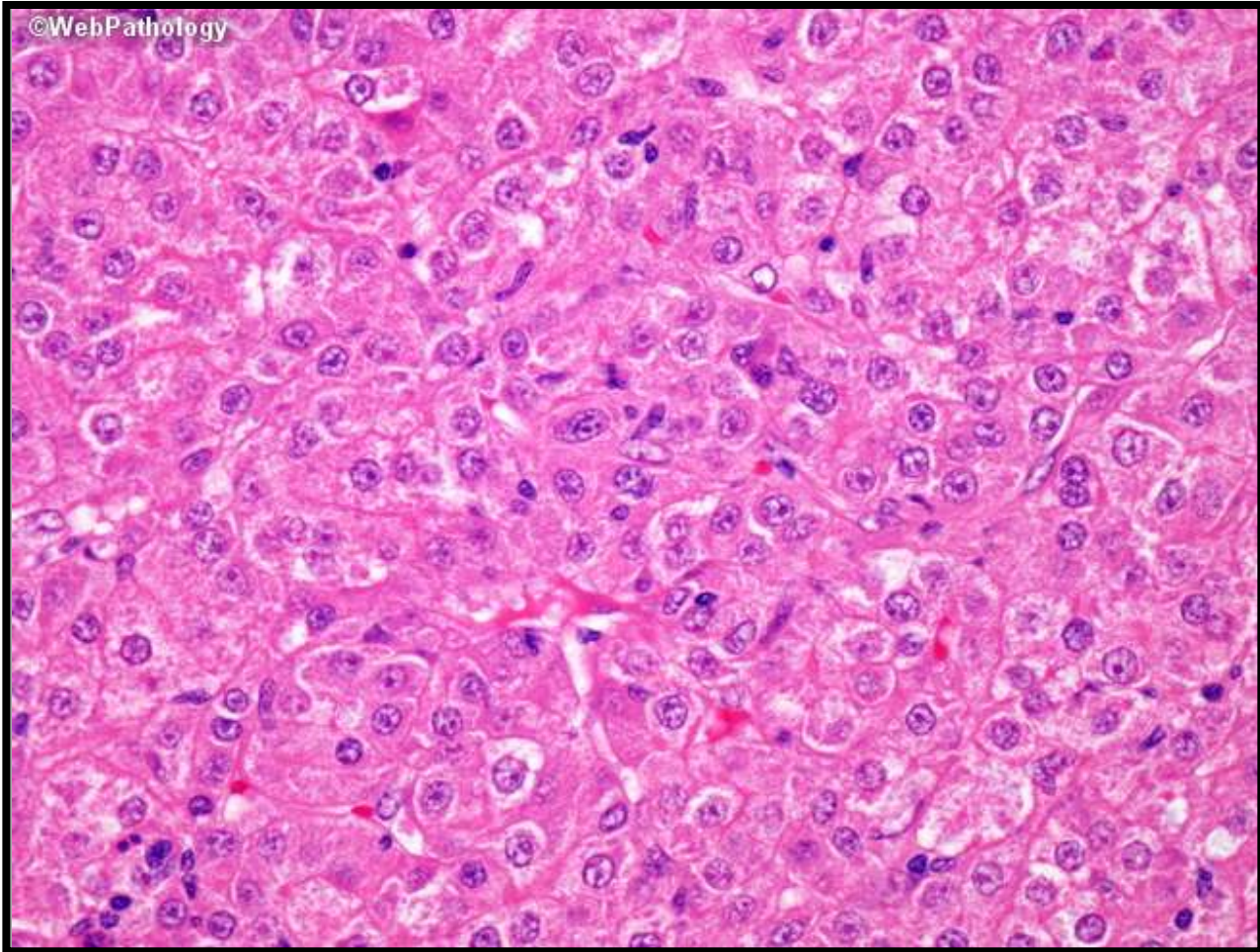


	HCC	Adenocarcinoma
Desmoplastic stroma	Rare	Yes
Trabecular growth	Yes	No
Glandular growth	No	Yes
Bile	50%	No
Bile canaliculi	Usually	No
Mucin	No	Usually
pCEA	Canalicular	Diffuse
AFP	50%	Rare
HepPar-1	90%	Rare
Pankeratin	Weak	Strong
MOC-31	10–20%	90%
Other antibodies		
CD10	Canalicular	Negative
RCC antibody	Negative	Negative
PAX8	Negative	Unknown
S-100	Negative	Negative
HMB-45	Negative	Negative
Chromogranin	Negative	Negative
Synaptophysin	Negative	Negative

Classical HCC Patterns

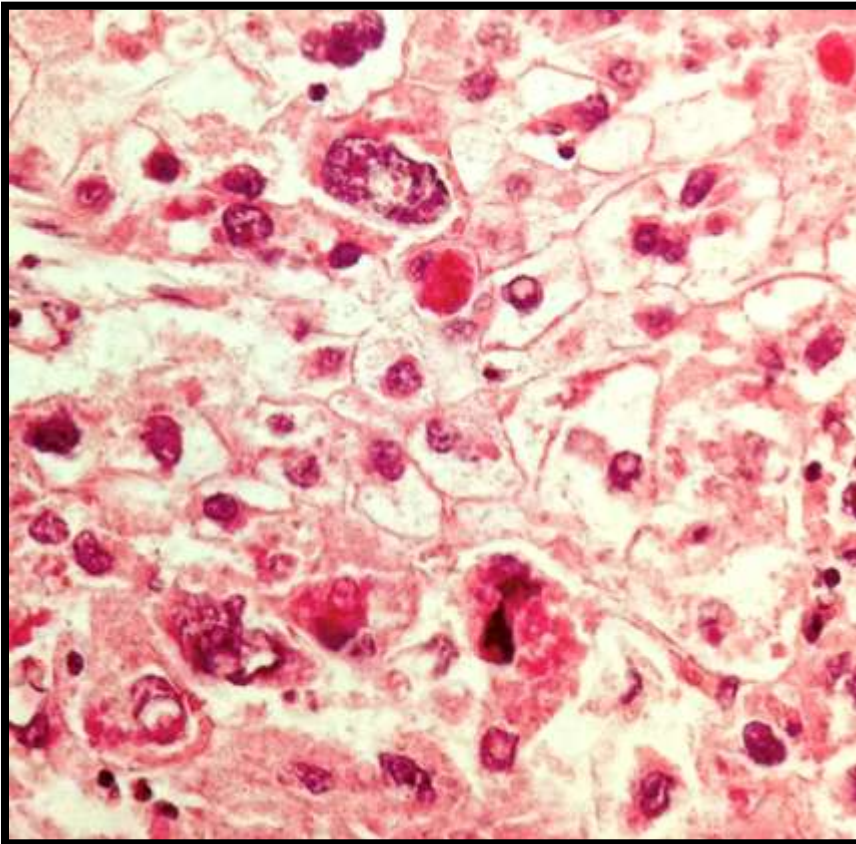
- Compact (Solid) pattern
 - Dense aggregates of tumor cells
 - Compressed or slit-like sinusoid-like blood spaces
 - Common in poorly differentiated tumors

Classical HCC Patterns

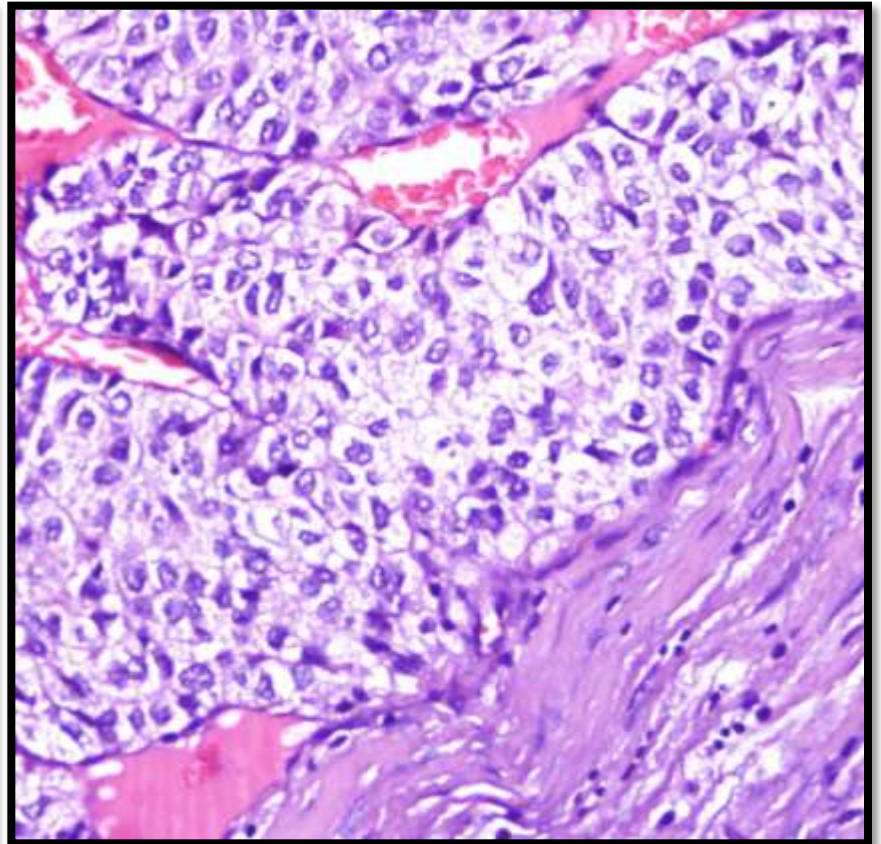


Classical HCC Cytological Variants

Pleomorphic cells

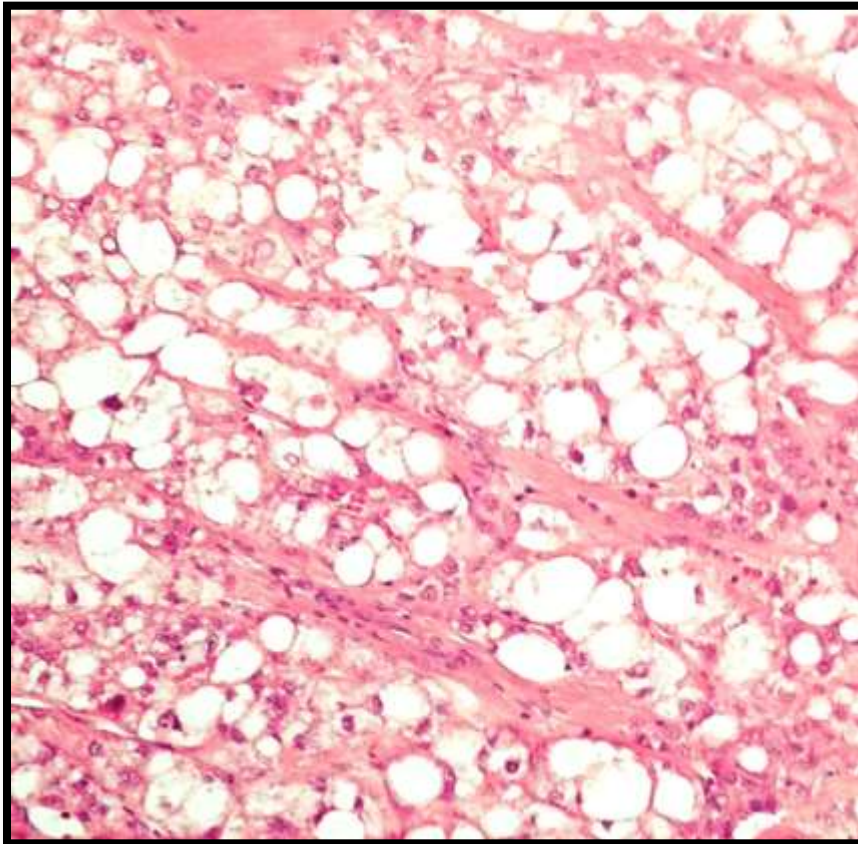


Clear cells

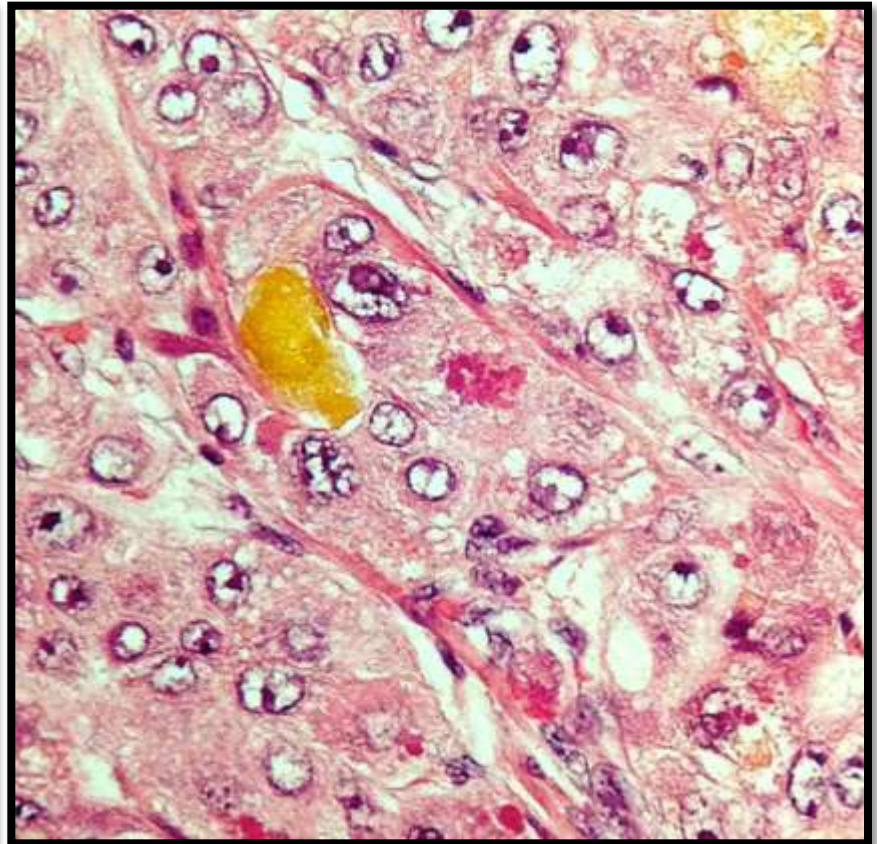


Classical HCC Cytological Variants

Fatty Change

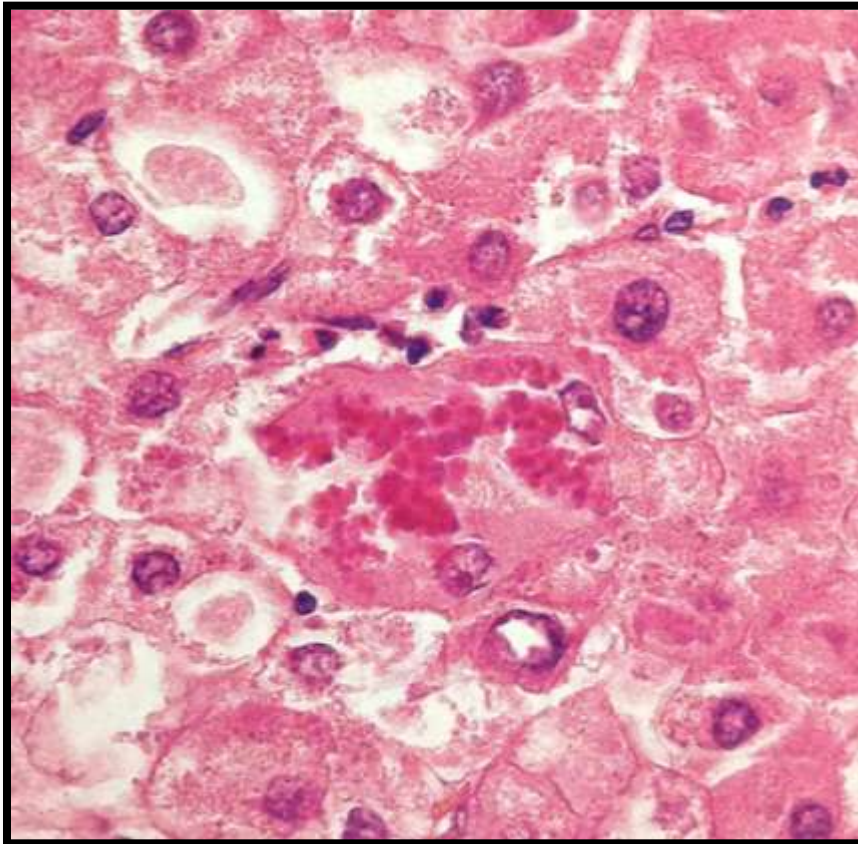


Bile production

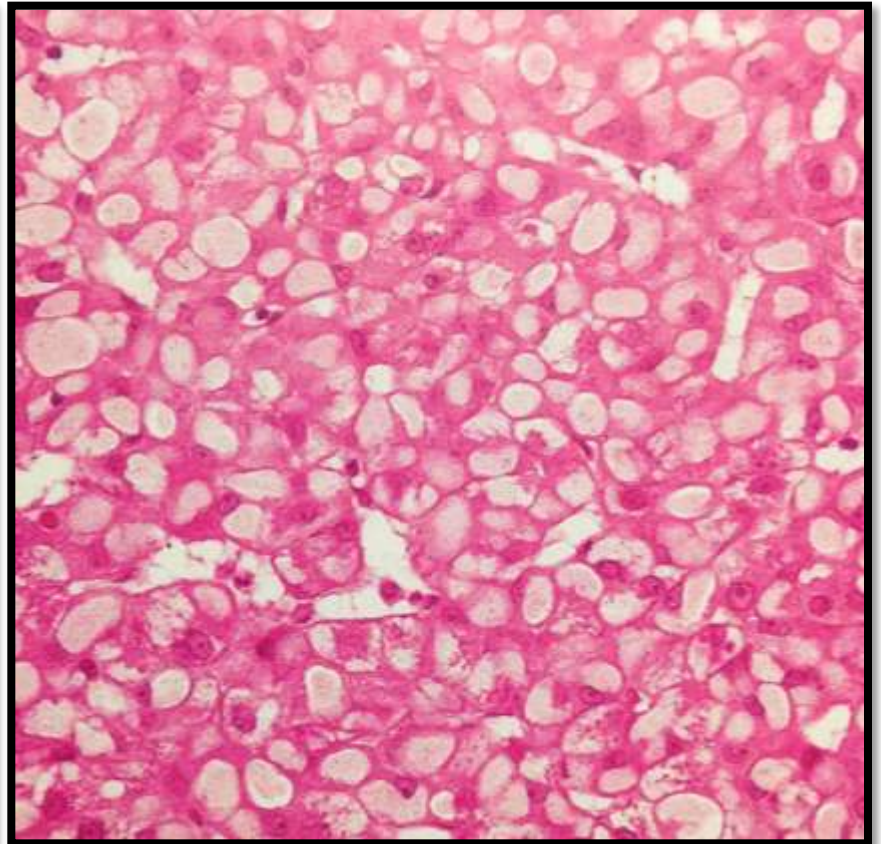


Classical HCC Cytological Variants

Mallory bodies



Pale bodies



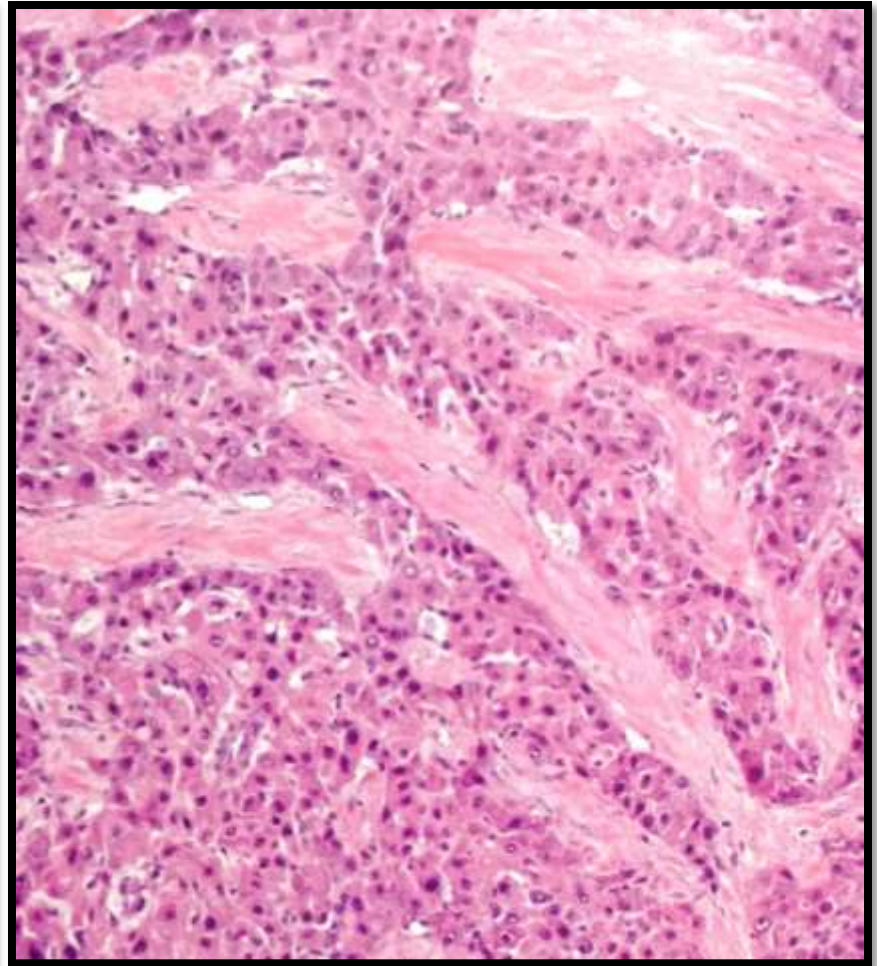
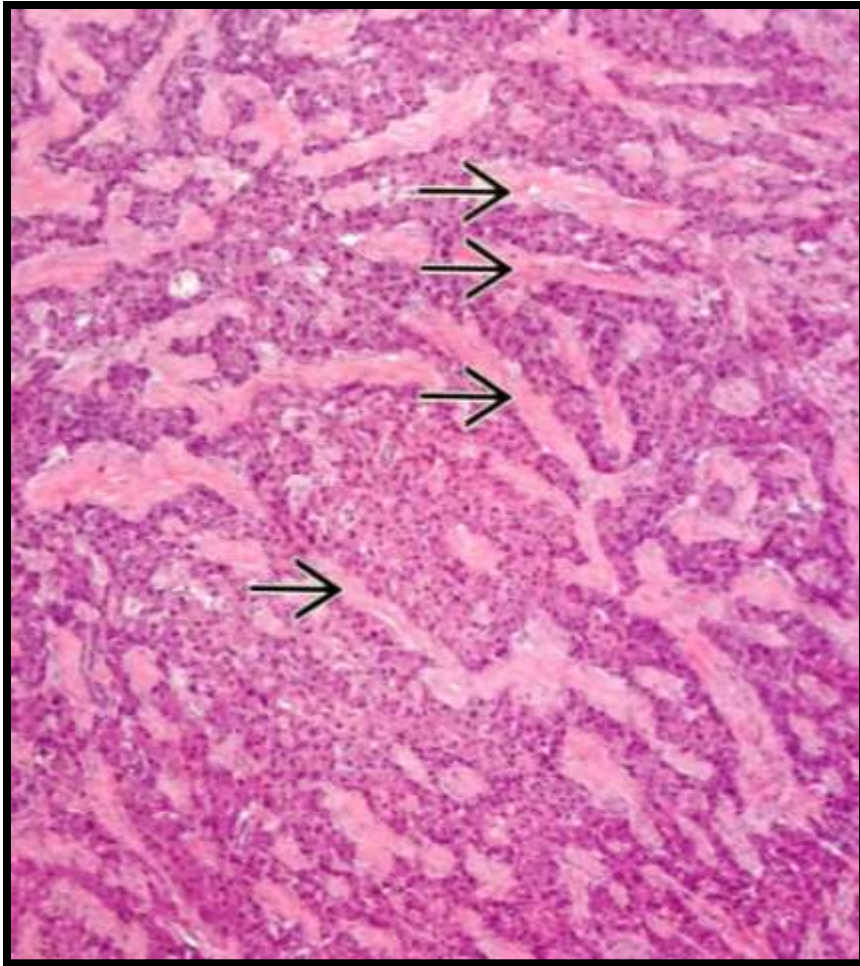
Fibrolamellar HCC

- Differ from classical HCC in many aspects
 - Occurs mainly in young adults (less than 35 years of age) without cirrhosis
 - No definitive risk factors have been identified
 - No strong gender predilection
 - Serum AFP levels are usually normal
 - 2/3 of cases involve the left lobe
 - Prognosis is better than classical HCC that arises in cirrhotic livers, but similar to classical HCC that arises in non-cirrhotic livers

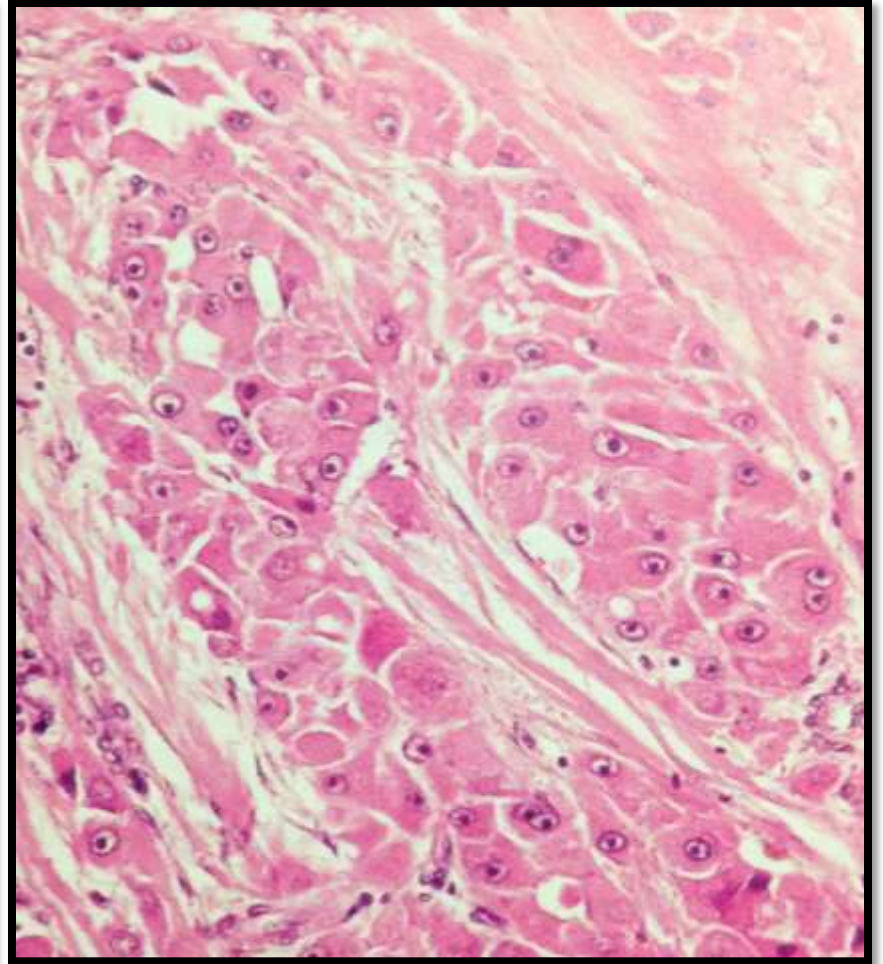
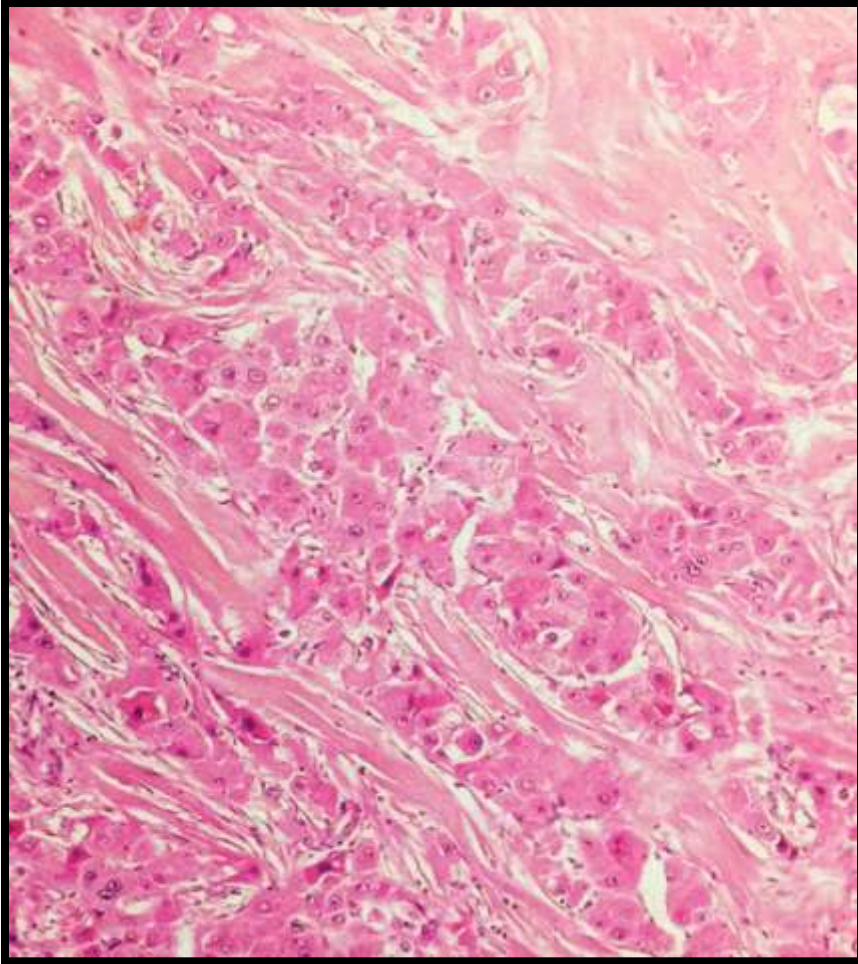
Fibrolamellar HCC

- A central scar may be seen in about 75% of cases
- Typically grow with broad pushing borders
- Composed of large polygonal cells with abundant eosinophilic cytoplasm, large vesicular nuclei, and large nucleoli

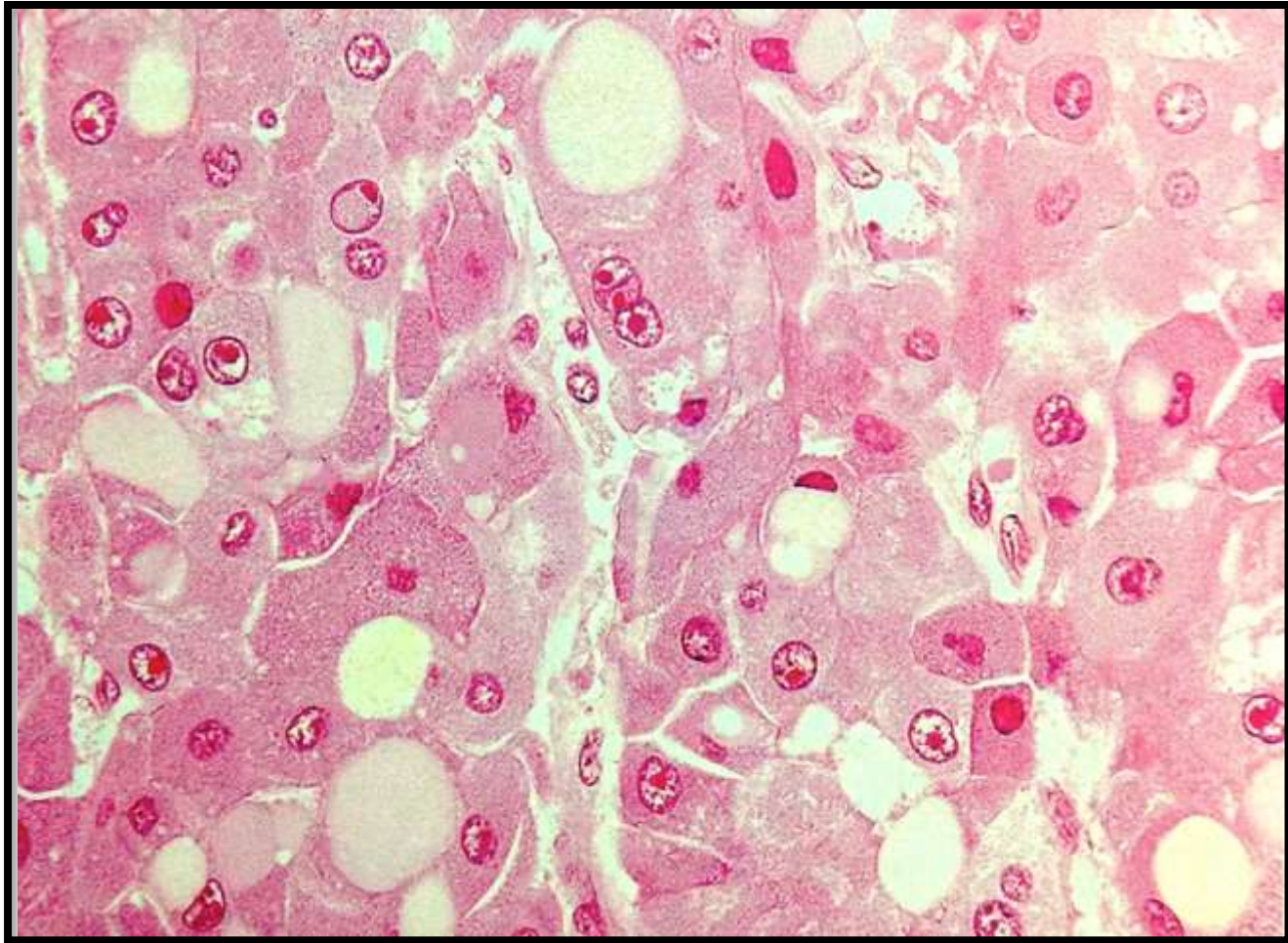
Fibrolamellar HCC



Fibrolamellar HCC



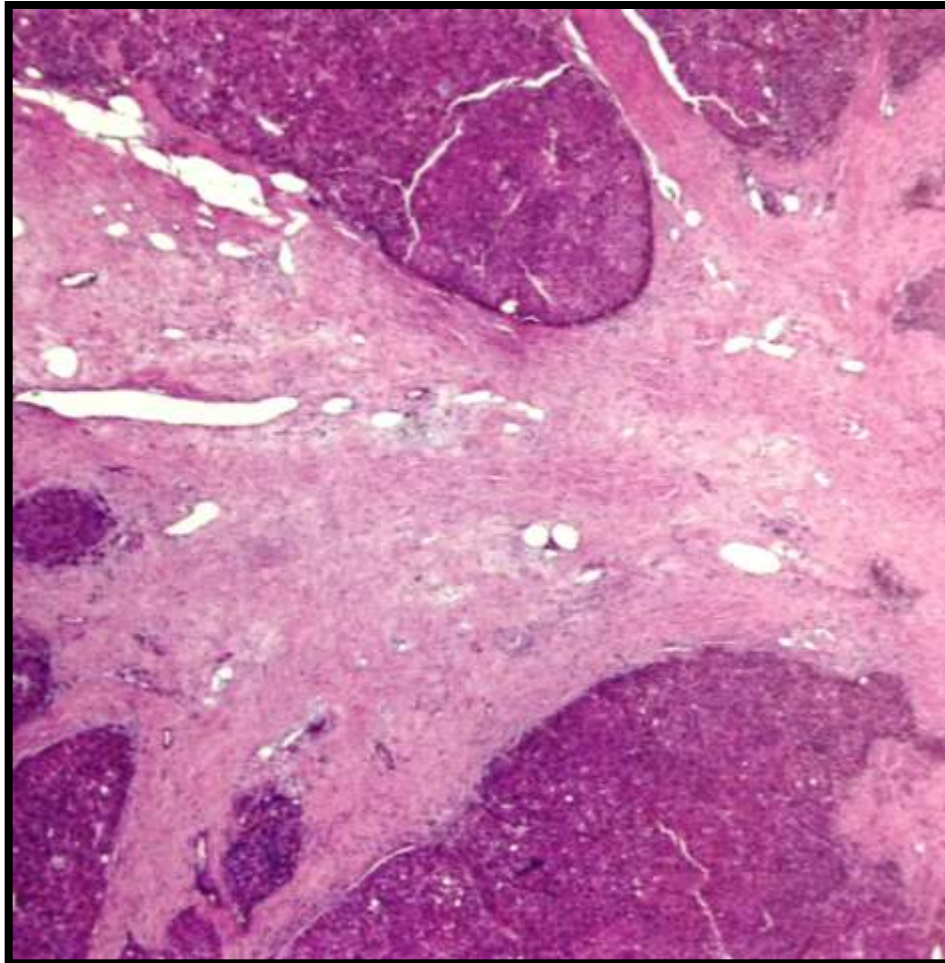
Fibrolamellar HCC



Scirrhous HCC

- Characterized by marked fibrosis along the sinusoid-like blood spaces with varying degrees of atrophy of tumor trabeculae
- Most arise immediately below the liver capsule
- A better prognosis has been reported in some, but not all studies
- Treated HCC may become scirrhous in some areas

Scirrhous HCC



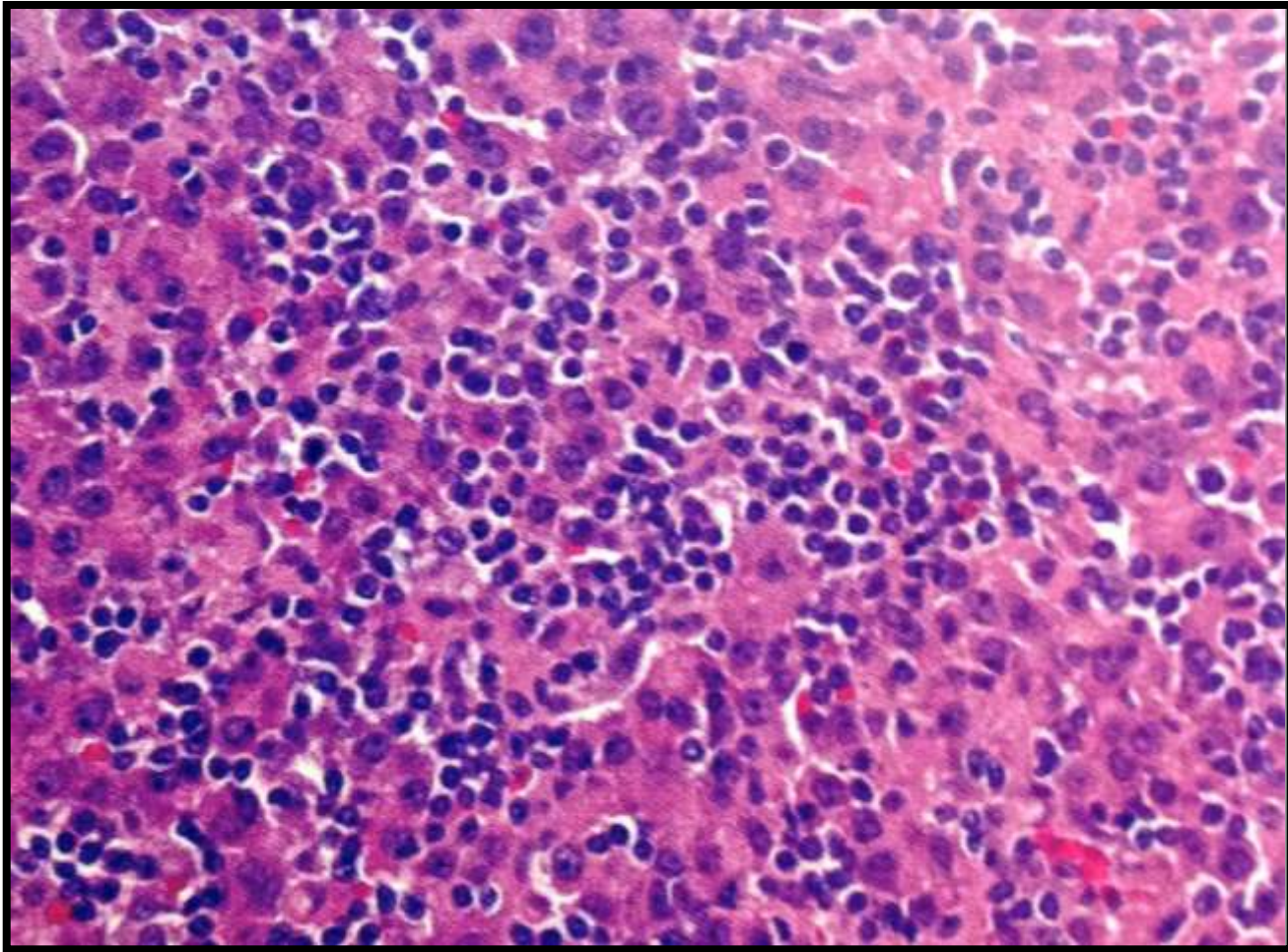
Undifferentiated HCC

- Tumors that are primary to the liver but cannot be further classified
- IHC is needed to confirm its epithelial nature
- More common in men
- Postulated to have a worse prognosis compared with classical HCC

Lymphoepithelioma-like HCC

- Pleomorphic tumor cells intermixed with numerous lymphocytes, which usually outnumber hepatocytes
- Tumor cells are small with focal syncytial growth
- EBV can be demonstrated in some, but not all, tumor cells

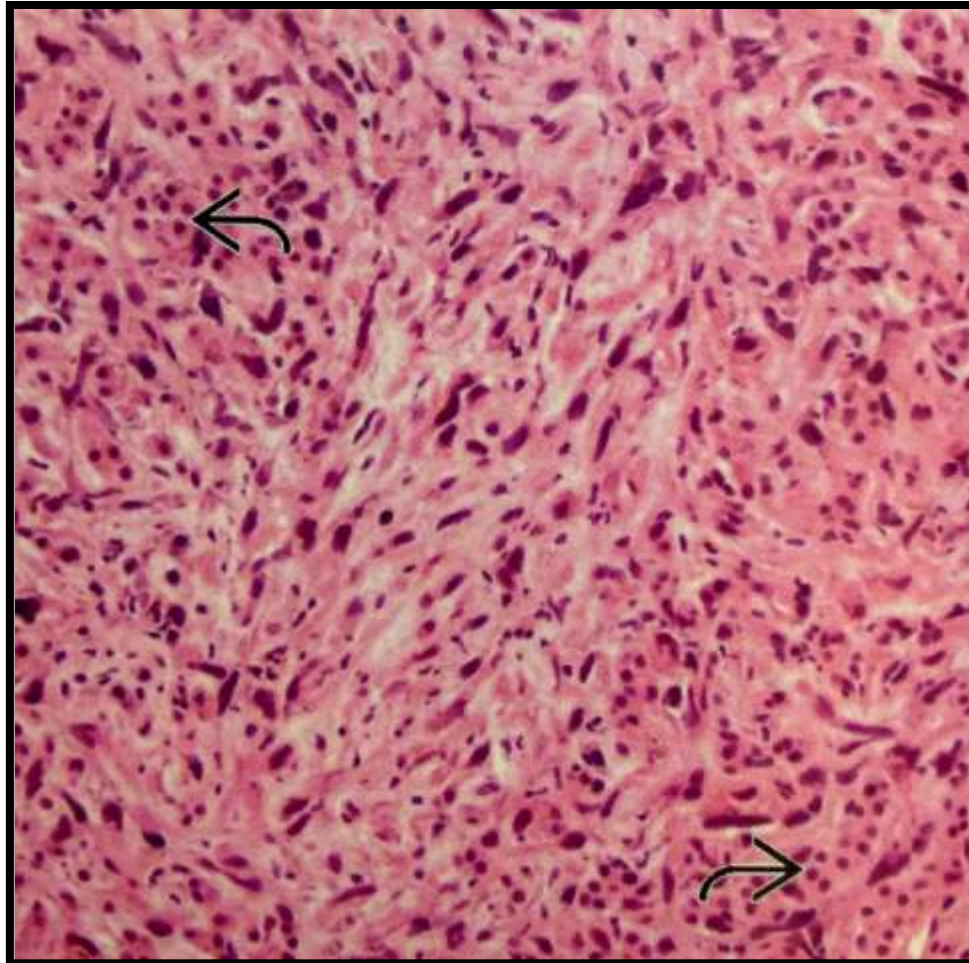
Lymphoepithelioma-like HCC



Sarcomatoid HCC

- Poorly differentiated tumor with a significant component of spindle cell differentiation, nuclear pleomorphism and high mitotic rate
- Distinguished from various sarcomas with the use of IHC
- Most sarcomatoid HCC will show areas of classical HCC in a sufficiently sampled tumor
- Sarcomatoid change is more frequent in HCC with repeated chemotherapy or transarterial chemoembolization

Sarcomatoid HCC



IHC in HCC

Immunohistochemical markers for hepatocellular carcinoma

Marker	Pattern in HCC	Pros/Cons
HepPar-1	Intracytoplasmic granules	Most specific marker for hepatocellular differentiation; not as useful in PD lesions
Polyclonal CEA	Canalicular pattern	Less useful in PD HCCs
CD34	Strongly positive in sinusoid-like vessels	Weak or negative in early (<1 cm) HCCs
Glypican-3	Cytoplasmic and/or membranous, focal/patchy to diffuse	GPC-3, HSP-70, GS and clathrin: Limited usefulness when used alone. Highly specific if combination of three or four markers. Limited sensitivity (~60%). Limited data for PD HCCs
HSP-70	Nuclear and cytoplasmic granules, patchy to diffuse	
Glutamine synthetase	Strong diffuse cytoplasmic	
Clathrin heavy chain	Diffuse cytoplasmic, variable intensity	
EZH-2	Nuclear staining	Stronger staining of early HCC compared to HG-DN; use in combination with HSP-70 and GPC-3
Arginase-1	Nuclear positivity in HCC	Cytoplasmic staining of normal liver; specific in differentiating PD HCC from adenocarcinoma

WD: well-differentiated; PD: poorly differentiated; HG-DN: high grade dysplastic nodules.

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