NEOPLASMS AND TUMOR-LIKE CONDITIONS OF LIVER
Focal nodular hyperplasia

- Focal nodular hyperplasia is a localized hyperplasic overgrowth of hepatocytes around a vascular anomaly, particularly an arterial malformation.
- Coexists with hepatic cavernous hemangiomas in approximately 20% of cases.
- FNH is found mainly in women of reproductive age (80% to 95%).
- Oral contraceptive use is implicated in promotion of FNH growth but is generally not considered a causative factor.
Clinical Presentation

• Usually an incidental finding; nonspecific abdominal pain is the most common complaint in symptomatic patients.
• Serum alpha fetoprotein (AFP) level is normal.
• Suggested when computed tomography or magnetic resonance imaging shows a mass with a central scar.
GROSS FINDING

Focal nodular hyperplasia is well circumscribed and contains a central stellate scar with radiating fibrous bands.
Histopathology

FNH is composed of nodules of **bland hepatocytes** surrounded by **fibrous septa** that contain **artery branches**, **bile ductules** (a variable but **key feature**), a variable **chronic** or **acute** inflammatory infiltrate, and **decreased** or **absent** interlobular bile ducts and portal vein branches.
focal nodular hyperplasia showing nodular liver parenchyma separated by fibrous bands containing bile ductules in the absence of normal portal tract
Part of a central scar with abnormal arterioles has been sampled. Radiating fibrous septa show small bile-duct-like structures at their edges.
OUT COME and THERAPY

- Not progressive lesions
- Not undergo malignant degeneration.
- Deaths are primarily related to operative complications.
- Resection is considered.
hepatic adenoma

- It is a benign hepatocellular neoplasm arising in a noncirrhotic liver.
- Most cases (95%) develop in women in their childbearing years.
- Long-term oral contraceptive steroid use is a common risk factor.
- In men, HA is seen in the context of the use of anabolic or androgenic steroid.
Clinical Presentation

- Patients with HA often present with acute abdominal pain secondary to hemorrhage within the tumor.
- Intraperitoneal rupture produces hemoperitoneum and may lead to shock.
- Serum AFP levels are normal.
Hepatic adenoma is often paler than the surrounding liver because of accumulation of glycogen or fat within the tumor. Intra tumoral hemorrhage is common.
Histopathology

- most HAs resemble normal liver microscopically, being composed of virtually normal hepatocytes in cords that are one to two cells thick and separated by sinusoids lined by inconspicuous Kupffer cells
- no normal portal tracts are present
- lack of biliary epithelium is notable
- haphazardly distributed arteries and thin-walled veins
Hepatocellular adenoma. Liver cells appear normal or contain fat vacuoles.
The hepatocytes are bland and resemble are scattered haphazardly within the tumor, which lacks biliary structures normal hepatocytes. Thick vascular channels.
Prognosis and Therapy

• Rupture with subsequent massive bleeding into the peritoneal cavity is the most common cause of death related to HA....therefore
• completely excised when technically possible
• Liver transplantation is occasionally performed for very large or multiple lesions
hepatocellular carcinoma

- HCC, the single most common histologic type of primary epithelial liver tumor, is a malignant neoplasm of the liver showing differentiation along hepato cellular lines.
- responsible for 20% to 40% of cancer-related deaths in regions of high incidence
- is a tumor of elderly men
- In areas of higher incidence, HCC occurs at earlier ages (20s to 30s)
• The most common predisposing condition is **cirrhosis of any origin**, with hepatitis **B**, hepatitis **C**, and **alcoholic** liver disease

The **most common causes**;

• Obesity-related liver disease is increasingly recognized as a risk factor for HCC

• others
Clinical Presentation

• Patients may present with abdominal pain
• HCC rarely manifests with metastases
• The most useful serum marker is AFP, which may be highly elevated in patients with large tumors
Molecular classification of hepatocellular carcinoma

- G1 tumors show low HBV copy number and overexpression of genes expressed in fetal liver and controlled by parental imprinting.
- G2 tumors have high HBV copy number, and mutations of PIK3CA and TP53.
- G3 tumors are TP53 mutated, lack HBV infection, and show frequent P16 methylation as well as overexpression of genes controlling the cell cycle.
G4 tumors are heterogeneous, including *TCF1* mutated adenomas and carcinomas.

G5 tumors show *CTNNB1* (β-catenin) mutations leading to Wnt pathway activation.

G6 tumors show *CTNNB1* (β-catenin) mutations leading to Wnt pathway activation, as well as satellite nodules, higher activation of the Wnt pathway and E-cadherin.
Macroscopy

Single mass in a cirrhotic liver. Note the poorly circumscribed border and heterogeneous appearance with focal bile staining.
VARIANTS

- Clear cell
- Sclerosing
- Small cell
- Sarcomatoid
- Lymphoepithelioma like
- Mixed hepatocellular carcinoma–cholangiocarcinoma
- Fibrolamellar carcinoma
dilated sinusoids result in sharply outlined tumor islands which are very typical
Histopathology

The tumor cells grow in trabeculae lined by endothelial cells and have a moderate amount of eosinophilic
macrotrabecular
Hepatocellular carcinoma with pseudoglandular
Hepatocellular carcinoma. Adenoid pattern
Hepatocellular carcinoma with macrovesicular steatosis
small hepatocellular carcinoma Mallory hyaline and globular cytoplasmic proteinaceous accumulations
Hepatocellular carcinoma with clear cell features
Hepatocellular carcinoma with bile in dilated bile canaliculi
Large polygonal cells separated by parallel bands of hyaline fibrous tissue in fibrolamellar carcinoma
fibrolamellar type. Groups of large, eosinophilic tumour cells are surrounded by fibrous septa in parallel arrays.
Fine-needle aspiration specimen, demonstrating clusters and trabeculae of HCC cells surrounded by an attenuated rim of endothelial cells
IMMUNOHISTOCHEMISTRY

- Hep Par 1 (hepatocyte)
- GPC-3
- Moc 31
- Arginase 1
- AFP
- CEA, CD10 (CANALICULAR)
- TTF1 (CYTOPLASMIC)

Staining for biliary canalicular structures............
CEA, canalicular staining pattern
The tumor cells express hepatocyte (HepPar-1) in a granular cytoplasmic pattern.
Prognosis and Therapy

- HCC generally carries a very poor prognosis, with survival after diagnosis measured in months,
- Nonoperative palliative therapies include percutaneous ethanol injection,
- At autopsy, metastases, most commonly to lung and porta hepatis, lymph nodes, are found in up to 75% of patients
- Bone, adrenal gland, and virtually any site in the body can be involved by metastatic disease
PROGNOSTIC FACTORS

• **Stage.** This constitutes the most important prognostic determinant.

• **Size.** In most series, patients with ‘small’ tumors (from 2 to 5 cm in diameter) had a significantly better prognosis. Some authors, however, have not found size per se to be an important prognostic determinant.

• **Encapsulat**
• Number of tumors
• Portal vein involvement
• Microscopic type
• Presence of cirrhosis
• Serum AFP levels
• Use of progesteron
• Sex and age
• CMYC amplification
hepatoblastoma

• most common primary hepatic tumor in children, accounts for approximately 50% of all primary pediatric hepatic malignancies
• Most cases occur by 2 years of age
• some cases occur in the setting of inherited disorders such as familial adenomatous polyposis
• an association with low birth weight is recognized
Clinical Presentation

- Patients generally present with an **abdominal mass** noticed by the parent, **but some patients present with precociouspuberty** related to human chorionic gonadotropin production by the tumor.
- The serum AFP level is **elevated**, often to very high levels, in **90% of cases**.
GROSSLY

single, fleshy variegated tumor nodule in the right lobe.
HISTOPATHOLOGY

Hepatoblastoma is subclassified histologically into six histologic patterns:

- Fetal pattern (31%). The tumor consists of sheets of small and uniform cells, which are slightly smaller than the cells of the non neoplastic liver. The tumor displays an architecture of thin trabeculae (one to three cells thick), which are lined by endothelial and Kupffer cells.
- Macrotrabecular pattern (3%). Presence of trabeculae more than 10 cells in thickness. The cells of the tumor may be fetal epithelial.
- Small-cell undifferentiated pattern (3%), this pattern is composed of sheets of small, discohesive cells with scant cytoplasm, oval, irregular, hyper chromatic nuclei, and frequent mitoses.
- Mixed epithelial and mesenchymal pattern (44%).
The embryonal pattern is characterized by cells that have a higher nuclear-to-cytoplasmic ratio with greater nuclear pleomorphism.
The fetal pattern, most resembling normal hepatocytes, often demonstrates “light” and “dark” foci related to the conspicuous presence or relative absence of glycogen and fat, respectively.
Small-cell undifferentiated pattern
IMMUNOHISTOCHEMISTRY

✓ The epithelial components of HB test positive for HepPar-1
✓ AFP
✓ chromogranin may be noted in embryonal, fetal, and osteoid components
✓ Keratin8,18,7
✓ B.catinin
✓ Basement membrane for extracellular material
Prognosis

• The outcome **depends on** the resectability of the tumor

• **Most** patients are **treated with** neoadjuvant multiagent chemotherapy

• More than **70%** of patients have **long term** survival

• The **most** frequent metastatic sites are **regional lymph nodes** and lung

• Liver **transplantation** may be considered in some cases
Biliary Tumors

Bile duct hamartoma

- small, incidental, clinically asymptomatic lesions, reported in up to 27% of all autopsies
- may be related to autosomal dominant polycystic kidney disease, polycystic liver disease, congenital hepatic fibrosis, or other genetic disorders
- BDHs appear as single or multiple subcapsular, gray-white or occasionally green nodules less than 0.5 cm in diameter.
• These lesions are most commonly encountered in frozen section and should not be confused with metastatic adenocarcinoma,

• Rarely, malignant transformation has been reported.
MICROSCOPY

• consist of ectatic, branched bile ducts lined by a single layer of bland, low columnar to cuboidal biliary epithelium. The lumens may contain granular eosinophilic material or bile.
• The stroma is dense and hyalinized, with minimal inflammation.
Bile duct hamartoma consists of dilated biliary channels
bile duct hamartoma, angulated bile ducts, containing intra luminal bile, embedded in a fibrotic stroma
Bile duct adenoma

- benign proliferation of bile ducts
- usually an incidental finding at autopsy or in the resected liver
- some larger BDAs may carry a potential for malignant transformation
- solitary, well-circumscribed firm, gray-white or tan, subcapsular nodules. Most measure 5 mm or less.
Histologically

• consist of a compact proliferation of simple tubular ducts embedded in a variable amount of fibrous stroma. The tubules have small lumens, unlike the dilated channels of BDH, and do not contain intra luminal secretions or bile.
tightly packed biliary channels embedded in a scant fibrous stroma
Biliary cystadenoma and cystadenocarcinoma

- *Biliary cystadenomas and cystadenocarcinomas are cystic mucinous neoplasms similar to those arising in the pancreas*
- Approximately 95% of cases develop in women, with a mean age at diagnosis of 45 years
- Patients may present with abdominal pain or an abdominal mass
- Biliary cystadenocarcinomas are rare hepatic malignant tumors. Some arise in a preexisting cyst adenoma
• unlike cystadenomas, cystadenocarcinomas show no female predominance and usually occur in older patients
• cystadenomas are encapsulated and solitary multicystic lesions ranging from 2.5 to 28 cm in diameter
• The cyst fluid is usually clear and mucinous.
• biliary cystadenocarcinoma exhibits consistent reactivity for keratin, CEA, and CA19-9
Histopathology

• The cysts of biliary cystadenomas are lined by tall columnar mucinous epithelium and resemble ovarian mucinous cystadenomas.

• Intestinal metaplasia is found in a minority of cases, and neuroendocrine cells can occasionally be identified.
Biliary cystadenoma is lined by columnar biliary-type mucin producing epithelium
Biliary cystadenocarcinoma
Biliary cystadenocarcinoma is characterized by cytologic and architectural features of malignancy and stromal invasion.
TREATMENT & OUTCOME

- Complete excision of a cystadenoma is the treatment of choice and is curative.
- Incomplete resection or cyst fenestration usually results in persistent disease. Approximately 50% of patients with cystadenocarcinoma survive up to 4 years. The prognosis may be worse for men.
Cholangiocarcinoma

• primary carcinomas of the liver arising from the biliary tree and usually showing differentiation along biliary lines.
• subdivided into peripheral (intrahepatic) or hilar types.
• incidence of intrahepatic cholangiocarcinoma appears to be increasing
• these tumors are associated with chronic inflammatory lesions of the bile ducts
Conditions associated with bile stasis, including primary sclerosing cholangitis (PSC), parasitic infections with liver flukes such as Clonorchis and Opisthorchis, and recurrent bacterial cholangitis with hepatolithiasis.
Clinically

• Generally occurs in older adults; most patients are between **50 and 70** years of age
• Often clinically **silent** until late in the course
• Patients typically **complain of** fever, weight loss, anorexia, and vague abdominal pain
• Rarely present with jaundice
• Elevated serum CA 19-9 levels, if greatly raised, may be of utility
• Serum CEA is **elevated** in approximately **40%** of patients with PSC and with cholangiocarcinoma, but this marker is less sensitive and specific than CA 19-9
Cholangiocarcinoma grows as a poorly circumscribed firm mass, often with satellite nodules.
A large, tan, homogeneous, firm mass with infiltrative borders typical of peripheral cholangiocarcinoma
Histopathology

Cholangiocarcinoma is characterized by formation of glands and small tubules in a densely fibrotic stroma.
Dense sclerosis is characteristic of cholangiocarcinoma
Immunohistochemistry

• Cholangiocarcinoma tests **positive** for CK 7 and **positively variable** for CK 20,50,51 and it shows cytoplasmic reactivity for CEA.

• Cholangiocarcinoma tests **negative** for AFP, and most cases are HepPar-1 negative.
TREATMENT AND OUTCOME

- poor prognosis, with a median survival from diagnosis of approximately 6 months
- Chemotherapy and radiation treatment have not shown great efficacy
- Surgical resection and transplantation are the only hope of a cure
- 80% of patients present with un resectable tumors
- The most frequent sites of metastasis include lymph nodes, lung, peritoneum, adrenal gland, kidney, and bone
Mesenchymal Tumors

- **Benign Mesenchymal Tumors**
  - Hemangioma
  - *Cavernous hemangioma (CH)*, the *most common primary* hepatic tumor, is usually an incidental finding at autopsy. These tumors are *more frequent in adults*; symptomatic CH is more common in women
  - most common presenting symptom is abdominal pain
The tumor is spongy with central fibrosis
MICROSCOPY

Cavernous hemangioma
dense sclerosis and scattered blood vessels
• Because most CHs are not associated with morbidity or increased mortality, asymptomatic CH is not treated.

• Symptomatic lesions larger than 10 cm are often treated by resection or enucleation.
Infantile hemangioendothelioma
the most common mesenchymal tumor of the liver in childhood, accounts for approximately 20% of all primary pediatric hepatic tumors
Most patients are less than 6 months of age at the time of diagnosis.
Girls are affected slightly more often than are boys

CLINICAL FINDING
abdominal mass and high-output cardiac failure
although many patients are asymptomatic and the lesions are discovered incidentally at autopsy
(Kasabach-Merritts syndrome)
Infantile hemangioendothelioma consists of blood-filled channels separated by a loose stroma; entrapped portal tracts may be seen within the lesion.
Infantile hemangioendothelioma. Compressed vascular spaces are lined by plump but bland endothelial cells.
Immunohistochemistry

- (factor VIII–related antigen, CD34, CD31)
- GLUT-1 help to distinguish IHEs from juvenile hemangiomas
Prognostic Factors

- 70% of patients survive at least 7 years; most deaths occur within 1 month of diagnosis. Congestive heart failure and jaundice are the factors most often associated with death.
- Multiple nodules and the absence of cavernous differentiation are also adverse prognostic features.
- Solitary lesions may be resected.
- In some cases, corticosteroids have been used. Ablative therapies may be considered, and liver transplantation has been performed. Spontaneous regression may occur.
Malignant Mesenchymal Tumors

Angiosarcoma

- It is a high-grade malignant neoplasm of endothelial cells.
- It is the most common primary malignant mesenchymal tumor of the liver in adults.
- HAS usually occurs in older men and has been associated with vinyl chloride exposure and Thorotrast administration.
- HAS resulting from environmental exposure is associated with a prolonged latency period.
MACROSCOPY

Angiosarcoma, with numerous variably sized hemorrhagic nodules and blood-filled spaces
The hemorrhagic tumor has indistinct borders and has replaced large areas of the hepatic parenchyma.
Histopathology

Angiosarcoma, well differentiated
highly atypical spindle cells forming relatively small vascular channels;
Prognosis

The prognosis of HAS is dismal. Most patients die within months of diagnosis. Available therapies are ineffective. Hepatic failure and intra-abdominal bleeding are the most common causes of death. At autopsy, most patients have metastases, most frequently to the lung.
**undifferentiated sarcoma**

- *sarcoma is a rare malignant* tumor occurring almost exclusively in the pediatric population
- Most patients are between 6 and 10 years of age, and more than 90% are 21 years old or younger.
- An abdominal mass or abdominal pain is the most common presentation
Macroscopy

The tumor is well circumscribed, largely solid, and with areas of cystic degeneration.
Histopathology

• Undifferentiated sarcomas are composed predominantly of large, highly atypical spindle to stellate cells with ill-defined cell borders embedded in abundant myxoid stroma
Undifferentiated sarcoma consists of large, bizarre highly pleomorphic tumor cells in a myxoid matrix. Some tumor cells contain large cytoplasmic globules.
Embryonal (undifferentiated) sarcoma
Prognosis

• Multiagent chemotherapy followed by complete resection has resulted in long-term disease-free survival (>10 years) in some cases

• Lung, pleura, and peritoneum are the most common sites of metastasis.
Thank you