Learning Objectives

• Review the diagnostic approach to common FLL
• Review the imaging characteristics of common FLL
• Identify common pitfalls in the clinical evaluation of FLL
Background

• FLL, especially cysts and hepatic hemangiomas are common in the general population
  HH ~ 7%, Cysts ~ 4%
• Majority of FLL incidental findings; symptomatic lesions significantly less common

Karhunen PJ. J Clin Path 1986

Three Categories of FLL

• Benign lesions usually requiring no further intervention
• Benign lesions requiring further investigation and therapy
• Malignant lesions requiring appropriate management
Benign FLL
Usually requiring no further intervention

- Hepatic hemangioma
- Simple cyst
- Focal fatty change/sparing
- Focal nodular hyperplasia (?)

Benign Lesions
Typically requiring further management

- Adenoma
- Liver abscess (pyogenic, amebic)
- Atypical/complex cysts
  - Cystadenoma
  - Echinococcal cyst
  - Focal nodular hyperplasia (?)
Malignant Lesions

- Metastases
- Primary liver neoplasms
  - Hepatocellular carcinoma
  - Cholangiocarcinoma
  - Other rare tumors
    - (cystadenocarcinoma, angiosarcoma)
- Lymphoma

Clinical Approach to FLL

- Symptoms: RUQ pain common, usually not due to FLL; subcapsular FLL and those > 5 cm more likely to cause symptoms than central or smaller lesions
- History of malignancy, cirrhosis, or liver mass
- Exam: lymph nodes, stigmata of cirrhosis
- Laboratory studies: CBC, liver panel, selected use of tumor markers
- Imaging characteristics
### LIVER IMAGING MODALITIES

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>CT</th>
<th>MRI</th>
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<tbody>
<tr>
<td>Least expensive</td>
<td>Less expensive than MR</td>
<td>Most expensive</td>
</tr>
<tr>
<td>Widely available but operator dependent</td>
<td>Full body evaluation</td>
<td>Multiple contrast agents</td>
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<tr>
<td>Portable</td>
<td>Limitations:</td>
<td>Limitations</td>
</tr>
<tr>
<td>No need for IV access</td>
<td>ionizing radiation</td>
<td>IV contrast</td>
</tr>
<tr>
<td>Good characterization</td>
<td>IV contrast</td>
<td>allergy, renal function</td>
</tr>
<tr>
<td>cystic structure</td>
<td></td>
<td>less tissue contrast than MR</td>
</tr>
<tr>
<td>hemangioma</td>
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<tr>
<td>Biopsy</td>
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**Imaging Characteristics**

- Solid lesions usually require dynamic contrast for optimum imaging
  - BOTH arterial and portal venous phases
  - Cross-sectional imaging studies with IV contrast (when indication is abdominal pain) frequently only include venous phase images
- Deciding CT vs MRI depends on availability, local expertise and clinical suspicion; overall MRI preferred
Hepatic Hemangioma
HEPATIC HEMANGIOMA

US: hyperechoic, avascular mass
HEPATIC HEMANGIOMA
Clinical Features

- Prevalence: very common; 5% of all patients undergoing CT scan; multicentric in up to 30%
- Presentation: nearly always asymptomatic
- No malignant potential
- Although vascular, safe to biopsy (rarely required; imaging alone is usually characteristic)
FOCAL NODULAR HYPERPLASIA
Mass similar in density to normal liver, central scar.

Enhancement during arterial phase, central scar.

Becomes isodense during late portal venous phase.

Focal nodular hyperplasia: MR showing mass and central “scar”.
FOCAL NODULAR HYPERPLASIA
Histologic Features

- Irregular pattern of thin fibrous septa – “focal cirrhosis”
- Arteries and proliferating bile ductules in the fibrous septa
- Central scar with large myxomatous vessel

Sodium Gadoxetate MRI for Distinguishing FNH from Adenoma

Brightly enhancing in arterial phase
Isointense in portal venous phase
Retained intensity in the hepatobiliary phase supports the diagnosis of FNH
FOCAL NODULAR HYPERPLASIA
Clinical Features

- Benign reaction to congenital or acquired focal area of increased hepatic arterial flow
- Occasionally multiple, may coexist with HH or hepatocellular adenoma (HA)
- Females > males
- Central scar by CT or MRI:
  - May be mimicked by inflammatory HA and fibrolamellar HCC
  - Only present in larger lesions
- No malignant potential

Focal Nodular Hyperplasia
Management

- If images “diagnostic” for FNH, nothing further required; if images “suggestive,” short interval (6-12 m) repeat imaging or biopsy advised
- Management: no treatment unless symptomatic (unusual); no role for stopping oral contraceptives
- ACG guideline suggests annual imaging x 2-3 years in patients continuing oral contraceptives

Marrero, et al; ACG guideline FLL 2014
40 yo woman presents with abdominal pain and syncope. Exam is notable for hypotension and a distended abdomen. Labs are notable for hemoglobin of 5. Paracentesis demonstrates fresh blood. The patient is resuscitated and states that two years ago she was told of a benign liver mass. She is on oral contraceptives. **This liver mass is most likely:**

1. Cavernous hemangioma
2. Focal nodular hyperplasia
3. Hepatic adenoma
4. Hepatocellular carcinoma
5. Hepatic artery aneurysm

**HEPATOCELLULAR ADENOMA**

- Large mass showing hyperdensity on non-contrast CT
Hepatocellular Adenoma
HEPATOBILIARY MR CONTRAST AGENTS FOR DISTINGUISHING FNH FROM ADENOMA

- **Multihance or Eovist**
  - gadolinium-based contrast agent
  - eliminated through both renal (95-97%) and hepatobiliary (3-5%) pathways

- **FNHs**
  - malformed but functioning biliary system
  - hyperintense in hepatobiliary phase

- **Adenomas**
  - no bile ducts
  - hypointense in hepatobiliary phase
HEPATOCELLULAR ADENOMA

• Prevalence: uncommon; much less common than cavernous hemangioma or focal nodular hyperplasia
• Presentation: Usually asymptomatic, large lesions may cause pain, lesions >5 cm at risk for rupture which may result in acute hemoperitoneum
• Predisposing factors: female, estrogen use
• Prognosis: slight potential for malignancy and/or bleeding
**GENOTYPE-PHENOTYPE CLASSIFICATION HCA**

<table>
<thead>
<tr>
<th></th>
<th>Inflammatory</th>
<th>HNF-1α mutation</th>
<th>Beta-catenin activated</th>
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<tbody>
<tr>
<td><strong>Epidemiology</strong></td>
<td>40-55% of HCA F&gt;&gt;M High BMI</td>
<td>35-50% HCA F &gt;&gt;&gt; M May have hepatic adenomatosis</td>
<td>10-15% M&gt;F Androgen use</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td>Mimic FNH</td>
<td>Often multiple</td>
<td>Mimic HCC</td>
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<tr>
<td><strong>Complications</strong></td>
<td>“Highest” risk of bleed (&gt;5 cm)</td>
<td>Least aggressive</td>
<td>Highest risk of HCC</td>
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<tr>
<td><strong>Management</strong></td>
<td>Treat if &gt; 5 cm</td>
<td>Treat if &gt;5 cm but low risk with observation</td>
<td>Treat all</td>
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Adapted from Agrawal CGH 2015

**Management of Hepatic Adenomas**

- Resection advised for high-risk lesions (defined as any of following):
  - ≥5 cm
  - Hemorrhage
  - Male gender (increased malignant risk)
  - β-Catenin IHC +
- Serial imaging (every 6 m x 2 y, annually thereafter) advised for low-risk lesions
  - d/c oral contraceptives if at all possible (up to 79% will regress)
  - pregnancy not discouraged if adenoma <5 cm
HEPATOCELLULAR CARCINOMA

Hepatocellular Carcinoma

- High index of suspicion in cirrhotic patients or non-cirrhotic chronic HBV
- Male predominance (1.4-3.3:1)
- AFP poor sensitivity and specificity
- CT/MRI: intense arterial enhancement; portal venous "washout"
- Biopsy: Often not needed; low but finite risk of tumor seeding
- Management: Resection rarely feasible; LT evaluation for early stage tumor; locoregional Rx for more advanced stage tumors

El-Serag HB, Hepatology 2014
Phasic Vascular Perfusion of HCCs

Hepatic arterial phase  Portal venous phase
LIVER NODULES IN PATIENTS WITH CIRRHOSIS

AASLD guideline; Hepatology 2010
HCC MANAGEMENT

AASLD guideline; Hepatology 2010

78 y.o. asymptomatic woman with cirrhosis
Common Pitfalls

1. Making decisions based on incomplete imaging studies; i.e. routine ED CT with only venous phase contrast images
2. Attributing non-specific symptoms to incidental liver masses; “Patients with IBS/NUD sometimes have liver cysts”
3. Attributing liver masses in patients with cirrhosis/chronic liver disease to benign etiology; requires an increased index of suspicion for HCC or intrahepatic cholangiocarcinoma

Take Home Points

- Most common benign lesions can be diagnosed non-invasively; non-invasive diagnosis relies on dedicated imaging with dynamic contrast
- Repeat imaging after an interval or biopsy when the diagnosis remains uncertain
- The commonest conundrum is the distinction between FNH and adenoma
- Liver lesions in the setting of cirrhosis are malignant until proven otherwise
METASTATIC LIVER LESIONS

- US: Approximately 20% of deaths are related to a malignancy; of those: 40% had hepatic involvement at time of death
- Multiple lesions a little more common presentation of metastasis than a single lesion
- Biopsy will show features of primary tumor
Focal Fatty Change:
65 y o Woman Referred for Evaluation of Presumed Gallbladder Carcinoma

Imaging Characteristics of Focal Fat or Fat Sparing

Ultrasound Hyperechoic

T1 Weighted In & Out of Phase

3 Month Follow-Up