Work up of the focal liver lesion

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World’s Most Accurate Pie Chart

- Pie I have eaten
- Pie I have not yet eaten
• Incidental findings are common with increasing use of abdominal imaging
• The goal of this lecture is to describe how to evaluate focal liver lesions and identify those lesions requiring further intervention
Focal Liver Lesions: Basic Concepts

- All solid liver lesions require investigation.
- Contrast enhanced, multiphase, cross sectional imaging is always required in the initial diagnostic work up.
- Histologic confirmation with a core or fine needle biopsy is usually not necessary and can be harmful.
<table>
<thead>
<tr>
<th></th>
<th>Hepatocellular carcinoma</th>
<th>Metastatic carcinoma</th>
<th>Hepatocellular adenoma</th>
<th>Focal nodular hyperplasia</th>
<th>Cavernous hemangioma</th>
<th>Simple cyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence / 100,000*</td>
<td>1-4000*</td>
<td>0-50</td>
<td>16-40</td>
<td>3-4</td>
<td>400-7500</td>
<td>170</td>
</tr>
<tr>
<td>Solitary</td>
<td>20-40 percent</td>
<td>5-10 percent</td>
<td>90 percent</td>
<td>90 percent</td>
<td>90 percent</td>
<td>70</td>
</tr>
<tr>
<td>Coexisting liver disease</td>
<td>HBV, HCV, cirrhosis, hemochromatosis</td>
<td>Uncommon in cirrhosis</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>HBV, HCV, alcohol, lymphatic or direct spread</td>
<td>Hemorrhagic, lymphatic, or carcinomatous</td>
<td>Estrogens, anabolic steroids</td>
<td>Congenital, estrogen</td>
<td>Congenital, estrogen</td>
<td>Congenital</td>
</tr>
<tr>
<td>Imaging§</td>
<td>US, CT</td>
<td>US, CT, CTAP</td>
<td>US, CT, 99mTc</td>
<td>US, CT, MRI, 99mTc</td>
<td>Dynamic bolus CT, 99mTc SPECT scan, MRI</td>
<td>US, CT</td>
</tr>
<tr>
<td>Alpha-fetoprotein</td>
<td>&gt;300-500 ng/mL</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Characteristic gross features</td>
<td>Hemorrhage, necrosis, invasion/ obstruction</td>
<td>Hemorrhage, necrosis, umbilicated</td>
<td>Hemorrhage, necrosis</td>
<td>Central scar</td>
<td>Blood filled cyst*</td>
<td>Thin walled cyst with clear fluid</td>
</tr>
<tr>
<td>Characteristic microscopic features</td>
<td>&quot;Thick&quot; (&gt;3-4 cells) trabeculae</td>
<td>Replacement of hepatocytes, by malignant cells no portal structures</td>
<td>&quot;Neohepatocytes&quot;, normal cord structure, no portal structures</td>
<td>&quot;Focal cirrhosis&quot; with pseudocysts</td>
<td>Blood filled spaces lined by single layer of flat epithelium</td>
<td>Simple cuboidal endothelium</td>
</tr>
<tr>
<td>Diagnosis§</td>
<td>FNAB or core biopsy</td>
<td>FNAB or core biopsy</td>
<td>Imaging, biopsy</td>
<td>Imaging, biopsy</td>
<td>Imaging</td>
<td>Imaging</td>
</tr>
<tr>
<td>Treatment</td>
<td>&quot;Curative resection&quot; or arterial injection if solitary; ≤3.0 cm; ≤3.0 cm; 7 transplantations; chemotherapy</td>
<td>&quot;Curative resection&quot; if &lt;3.0 cm and 3 or fewer nodules especially if large; otherwise, percutaneous biopsy, malignant potential</td>
<td>Discontinue estrogens/ androgens, resect if possible, especially if large; otherwise, hormonal therapy, malignant potential</td>
<td>Discontinue estrogens; periodic imaging</td>
<td>Surgical resection only if symptomatic or &gt;10.0 cm; discontinue estrogens; periodic imaging</td>
<td>Usually no surgery, instead hormonotherapy or symptomatic</td>
</tr>
</tbody>
</table>

US: ultrasound; CT: computed axial tomography; dynamic bolus CT: rapid sequential CT images taken at plane of the mass, with delay for images up to 20 minutes; CTAP: computed axial tomography arteriography; MRI: fast spin echo magnetic resonance imaging; 99mTc: 99mTc-cerelium labelled sulfur colloid scan; SPECT: 99mTc-thulium tagged red blood cell study utilizing single photon emission computerized tomography; FNAB: fine needle aspiration biopsy for cytology.

* From autopsy series.
† Varies with geographic origins.
§ Overall population.
+ Females on oral contraceptive pills.
$ Most useful imaging technique with which to obtain a diagnosis.
||| Definitive test required for confident diagnosis.

Adapted from: LaRocque, L. G., and A. Management of Liver Neoplasms in Medical Management of Liver Disease, 5th Ed, Marcel Dekker, Inc. 1999, p.316.
Focal liver lesions Basic Concepts

- Diagnostic evaluation utilizing a combination of history, physical, basic lab findings, and imaging has an accuracy of >99%, which exceeds the accuracy of either core biopsy or FNA.

Torzilli et al, Hepatology 1999
Focal Liver Lesions Basic Concepts

• Solid liver lesions in older patients are more likely to be malignant, with metastases more common than primary liver cancer in the absence of liver disease.

• Solid liver lesions in patients with chronic liver disease (cirrhosis or active Hepatitis B) are more likely to represent primary liver cancer rather than metastases or benign tumors.

• In non-cirrhotic patients, the most common solid liver tumor is hemangioma.
Basic questions

• Is the lesion cystic or solid?
• Does the patient have risk factors for malignancy (age, prior malignancy?)
• Does the patient have known liver disease or risk factors for liver disease?
50 year old man comes to the ED with vague abdominal pain, has a CT with contrast which shows hypertrophy of the caudate lobe, slight nodularity of the spleen.

Normal bilirubin, normal Alk Phosph, AST/ALT are moderately abnormal
WBC normal, Platelets 100K
GI Evaluation

- HCV antibody positive
- Active virus confirmed by PCR
- AFP 100
CT with liver protocol (multiphase contrast imaging)
AASLD Practice Guidelines For HCC Diagnosis of Lesions found on Screening in At Risk Groups

- Suspicious lesions less than 1cm: surveillance imaging only
- Typical lesions over 1cm can be diagnosed radiologically, without biopsy:
  - Multiphase imaging with two modalities increases the positive predictive value
  - If lesions are not typical in enhancement pattern on imaging, then biopsy is indicated, or document growth with serial imaging
Therapeutic Options In HCC

Hepatocellular carcinoma

Stage 0
PST 0, Child-Pugh class A
- Very early stage (0)
  - Single tumour < 2 cm
  - Carcinoma in situ
- Single
- Portal pressure and bilirubin
  - Normal
  - Increased
- Resection
- Liver transplantation
- Percutaneous ethanol injection or radiofrequency ablation
- Curative treatments (30%)
  - 5 year survival 40-70%

Stage A-C
PST 0-2, Child-Pugh class A-B
- Early stage (A)
  - Single tumour or 3 nodules ≤ 3 cm, PST 0
- 3 nodules ≤ 3 cm
- Associated diseases
  - No
  - Yes
- Transarterial chemoembolisation
- Randomised controlled trials (50%)
  - Median survival 11-20 months

Stage D
PST > 2, Child-Pugh class C
- Intermediate stage (B)
  - Multinodular, PST 0
- Advanced stage (C)
  - Portal invasion, N1, M1, PST 1-2
- Sorafenib
- Symptomatic treatment (20%)
  - Mean survival 3 months

Montefiore

• 30 year old woman who is a student in an ultrasound technologist school underwent an abdominal ultrasound as part of a simulation session, was found to have a 5cm solid right lobe liver lesion
History

• She has no symptoms
• Currently on oral contraception
• No prior liver disease
• Lesion is solid on US
Differential Diagnosis of Solid Liver Lesions in Young Patients without Liver Disease

• Focal Nodular Hyperplasia
• Adenoma
• Hemangioma
• Less likely:
  – Well differentiated hepatocellular carcinoma
  – Hypervascular metastasis (renal cell, neuroendocrine tumor)
• Best **single** next test is a multiphase MRI with gadolinium (Magnevist)
  – FNH and adenoma: rapidly enhancing and washes out quickly
    • FNH’s have central scars
    • FNH v Adenoma can be further if necessary using specialized MRI contrast agents (Eovist-gadoxetic acid)
  – Hemangioma: centripetal enhancement pattern and delayed wash out
Diagnosis of Solid Liver Lesions in Young Patients

- **Adenoma**
  - Hypervascular
  - Purely a hepatocyte tumor, cold on nuclear sulfur colloid scan
  - May cause pain and can bleed
  - Malignant degeneration

- **Focal Nodular Hyperplasia**
  - Hypervascular
  - Contains all the liver ultrastructure including RES and bile ductules (isointense on sulfur colloid scan)
  - May cause pain
  - Central scar
  - No malignant risk
  - Minimal bleeding risk
Hepatic Adenoma Demographics

- Most are solitary fat containing lesions
- Incidence is increasing
- Often found incidentally on imaging
- Usually in the right lobe
- Most common in young women
- Symptoms (pain, bleeding) are size related
- Multiple adenomas (adenomatosis) is a rare condition associated with Glycogen Storage Diseases
Hepatic adenomas

This gadolinum enhanced magnetic resonance image of the liver acquired during the early bolus phase of contrast administration demonstrates two enhancing masses in the liver, one in the left lateral segment, the second immediately anterior to the right portal vein (arrows). The enhancement characteristics are non-specific and are seen with any vascular tumor of the liver. 

*Courtesy of Jonathan Kruskal, MD.*
Hepatic Adenoma Association with Oral Contraception and Androgenic Steroids

- Association is well documented, but there are no large epidemiologic studies to quantify risk.
- Mechanism of hepatocyte transformation is poorly understood, but there are identifiable oncogene mutations within adenomas that confer malignant risk.
- Risk of adenomas appears related to the duration of OC use (> 2 years) and estrogen component, but adenomas have been described with even 6 months of OC use.
- Regression can occur after discontinuation.
Hepatic Adenoma Symptoms are Size and Location Related

- Pain related to capsular distention/compression
- Pain related to necrosis
- Pain related to intrallesional bleeding
- Life threatening hemorrhage
  - Risk increased with size, symptomatic lesions, subcapsular location, long duration OC use.
Hepatic Adenoma Management

• Small asymptomatic adenomas in women on OC: Resect or conservative management?
  – Risk of malignant degeneration and need for lifelong surveillance imaging and AFP screening
  – Major hepatic resection (lobectomy) is associated with 20-30% morbidity, which may not be reasonable in young women with asymptomatic benign tumors
Montefiore Approach

- Resection of large (>5cm) or symptomatic adenomas
- Discontinuation of OC in asymptomatic smaller adenomas and counselling regarding options, including future pregnancy
- Patients with subcapsular lesions and those planning future pregnancy may be better served with resection
Minimally Invasive Hepatic Resection
Ruptured adenoma management

- Monitored setting of care, resuscitation and pain control
- Urgent embolization
- Elective resection after resolution of acute hematoma may permit more limited resection
- Urgent resection if ongoing bleeding
Focal Nodular Hyperplasia

- Thought to be a congenital vascular anomaly; associated with Osler-Weber-Rendu and liver hemangiomas (in up to 20%)
- Lesions classically (though not always) have a central scar containing an unusually large artery, with radiating branches to the periphery (Hub and spoke pattern)
- Lesion is a hyperplastic response to abnormal arterial flow
- Sinusoids, bile ductules, and Kupffer cells are present on histology
Focal nodular hyperplasia of the liver

Surgical specimen showing a mass lesion within a noncirrhotic liver. Note the central stellate scar.

Courtesy of Frank A Mitros, MD.
Focal nodular hyperplasia

Radiologic findings of focal nodular hyperplasia in an asymptomatic 47-year-old woman. Panel A: Contrast-enhanced CT scan shows an area of slight heterogeneity (arrow) in the right lobe of the liver, but a discrete mass is difficult to identify. Panel B: Technetium-99 sulfur colloid scan shows uptake in the mass (arrow) similar to the rest of the liver. This finding is diagnostic of focal nodular hyperplasia. Panel C: T2-weighted MR image shows the mass (arrow) as slightly increased signal intensity. Panel D: Arterial-phase dynamic gadolinium chelate-enhanced T1-weighted gradient-echo MR image shows rapid intense enhancement of the mass (arrow), typical of focal nodular hyperplasia.

Courtesy of Eric Outwater, MD.
FNH Natural History and Management

- Benign course, no malignant degeneration or bleeding
- Have been reported to increase in size during pregnancy
- May be responsive to estrogens, though discontinuation of OC is not a routine recommendation.
- No specific intervention is required, except possibly serial imaging for 6-12 months to confirm absence of changes
Hepatic hemangioma characteristics

- Peripheral nodular enhancement on MRI
- Centripetal filling in on delayed phase
- Need for Tc99 RBC scan is low in the era of MRI
- Risk of extrahepatic hemorrhage low even with large lesions
- No intervention required in asymptomatic patients—Serial imaging to evaluate growth
- Symptoms may be caused by distention/compression when they reach large size, in which case resection may be indicated
- No role for embolization
“Whenever I'm about to do something, I think, 'Would an idiot do that?' And if they would, I do not do that thing.”
Liver metastases
Suspected metastatic disease

- Multiple hypodense liver lesions on imaging or a focal liver lesion in a patient with known or suspected malignancy
  - Tumor markers
  - Evaluation for common sources of tumor
    - Colonoscopy, abdominal and chest imaging, mammography, directed nuclear scanning

- Histologic confirmation may be necessary if no primary is found (cancer of unknown primary)

- If patient has a known primary source and a liver lesion, PET can be helpful in certain tumor types that are PET avid
In conclusion…
Cystic lesions

Simple

Simple

Polycystic lesion

Hydatid

Hydatid

Pyogenic or amebic abscess

Atypical

Atypical
Simple Cyst

- Liquid collection lined by an epithelium
- No communication with biliary tree
- Solitary and uniloculated
- Most of the time asymptomatic
- Symptoms can be related to
  - Intracystic haemorrhage
  - Infection
  - Rupture (rare)
  - Compression of adjacent structures
Simple Cyst

- No follow up necessary
- If doubt, imaging in 3-6 months
- If symptomatic or uncertain diagnosis (complex cystic lesion), then consider surgical intervention
Hydatid Cyst

- Echinococcus granulosus
- Endemic regions: Eastern Europe
- Patients may present with disseminated disease, or erosion of cysts into adjacent structures and vessels (IVC)
- Clinical diagnosis based on history, appearance, and serologic testing
Hydatid Cyst

Treatment: Marsupialization or resection, albendazole
Liver Abscess

- High fever
- Leukocytosis
- Abdominal Pain
- Complex liver lesion
- History:
  - Abdominal or biliary infection
- Dental procedure
Liver Abscess

- Initial empiric broad spectrum antibiotics
- Aspiration/drainage percutaneously
- Echocardiogram
- Operation if no clinical improvement:
  - Open drainage
  - Resection
- 4 weeks antibiotic therapy with repeat imaging