Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.
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LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2021 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2022 for this activity.

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If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.
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Week 11, 2021
Managing Complications of GI Endoscopy
Shivangi T. Kothari, MD, FACP
March 18, 2021 at Noon Eastern

Visit gi.org/ACGVR to Register

Disclosures:

Speaker:
Catherine T. Frenette, MD
Dr. Frenette has no conflicts of interest related to this talk.

Moderator:
Anjana A. Pillai, MD
Speaker: Simply Speaking Hepatitis (CME);
Medical Advisory Board: Genentech, Eisai Inc, Exelixis
Evaluation of Liver Masses

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Scripps Center for Organ and Cell Transplantation
Director, Liver and Hepatocellular Cancer Program
Scripps MD Anderson Cancer Center
La Jolla, CA

What is the next step?
Forward to the Beginning

Liver Mass

Benign

History

Physical Exam

Labs

Radiographic Studies

Biopsy

Malignant

metastasis

primary

Work Up

• History
  – Age
  – Symptoms
  – Family History
  – Surgical History
  – Travel History
  – Social History
  – Medications
Work Up

- Physical Exam
  - Jaundice
  - Weight loss
  - Ascites
  - Abdominal Tenderness
- Labs
  - Liver panel, CBC
  - Viral serologies
  - Tumor Markers (AFP, CA19-9, CEA)

Approach to Focal Liver Lesions

Marrero J et al, Am J Gastro 2017
Benign lesions usually requiring no further intervention

- Cavernous hemangioma
- Focal nodular hyperplasia
- Simple cyst
- Focal fatty change or sparing

Benign lesions requiring further investigation and therapy

- Hepatic adenoma and adenomatosis
- Biliary cystadenoma
- Hepatic abscess – pyogenic or amebic
- Echinococcal cyst
- Granulomatous inflammation
- Inflammatory pseudotumor
Malignant lesions requiring appropriate management

- Metastasis from other primary sites
- Hepatocellular carcinoma
- Cholangiocarcinoma
- Biliary cystadenocarcinoma
- Lymphoma
- Hepatic angiosarcoma
- Epithelioid hemangioendothelioma

Hemangioma

- The most common benign mesenchymal tumor
- Often solitary, may be multiple in up to 40%
- Larger than 5 cm are “giant”
- Epidemiology from 1-20% depending on the study
- 60-80% diagnosed in patients age 30-50
- More frequent in woman 3:1
Hemangioma

- Considered to be vascular malformations or hamartomas of congenital origin
- Can enlarge during pregnancy and estrogen therapy
- Micro: cavernous vascular spaces of varying sized lined by a single layer of flat epithelium and filled with blood

Hemangioma

- Most often asymptomatic
- Symptoms can occur:
  - Larger than 4 cm
  - Can have pain: acute thrombosis or bleeding
- Rupture is rare
  - Occurs in large, peripherally located hemangiomas
  - Traumatic rupture following blunt trauma
  - Iatrogenic rupture after biopsy or FNA
Hemangioma: Rare things

- Giant: can cause high output cardiac failure
  - In children this is associated with hypothyroidism
  - Presence of high levels of 3 iodothyronin deiodinase activity
- Kasabach-Merritt syndrome: in children, a consumptive coagulopathy can occur
- Hepatic Hemangiomatosis: rare in adult patients, associated with hereditary hemorrhagic telangiectasia and use of metoclopramide (Reglan)

Hemangiomas: Radiology

- US: well demarcated homogenous hypoechoic mass
  - blood flow seen with doppler in 10-50%
- CT: peripheral nodular enhancement on early phase, followed by centripetal pattern or “filling in” during late phase
- Technetium-99 red blood cell study: initial hypoperfusion during arterial flow, followed by gradual tracer peaking 30-50 min after injection
Hemangiomas: Radiology

Hemangioma Management

- If typical on US, and no liver dz or extrahepatic malignancy, just repeat US in 3-6 months to document stability
- If anything else, proceed with CT or MRI
- NEVER biopsy: risk of fatal bleeding
- If asymptomatic and >1.5 cm, reassure
- If symptoms, growth, >5 cm and subcapsular: may consider resection
- Non-surgical options: arterial embolization, radiotherapy
- Stop OCPs
- Monitor closely during pregnancy, and if large, may need resection prior to pregnancy

American College of Gastroenterology
Adenoma

- Young women, 20-44 years old
- Most common in right lobe
- 80% solitary
- Multiple adenomas
  - Think of prolonged OCPs
  - Glycogen storage disease
    - Particularly Type I and III, usually <20 yrs, males, multiple
    - Can resolve after dietary therapy
  - Hepatic adenomatosis

Adenoma

- Strongly associated with use of
  - OCPs
  - Anabolic steroids
  - Pregnancy: increased risk of rupture with 59% maternal and 62% fetal mortality
  - Diabetes?
- Incidence increasing
- Highest risk in women >30 yrs on OCPs for >25 months, particularly OCPs with high estrogen component
- Regression has been seen after d/c of OCPs with recurrence during readministration or pregnancy
Adenoma: Microscopic

- Large plates of adenoma cells, which are larger than normal hepatocytes and contain glycogen and lipid
- No normal hepatic architecture
- No septa, portal tracts, bile ductules
- Minimal Kupffer cells
- Prominent “naked” arteries

Adenoma

- Mostly asymptomatic
- Can have abdominal pain in epigastrium/RUQ
- Risk of bleeding reported to be as high as 25-41%
  - Higher with pain, long OCP use, subcapsular location, larger size
- Risk of malignant transformation: 8-13%, mainly in >5 cm size lesions
Adenomatosis

- More than 10 adenomas
- Lack of correlation with steroids/OCPs
- Lack of resolution with steroid withdrawal
- Lack of association with GSD
- Both men/women
- Increases in alk phos/GGT
- Hemorrhage is common
- May need to consider OLT

Adenomas: Diagnosis

- Biopsy rarely indicated: increased risk of bleeding, difficult to make the diagnosis
- US: well-demarcated and hyperechoic, may be heterogenous
- CT: peripheral enhancement during arterial phase with subsequent centripetal flow during portal venous phase, then iso- or hypo-dense
- MRI: most helpful with sodium gadoxetate (Eovist): has hepatobiliary excretion, which adenomas cannot take up and excrete, so dark spot
## Classifications of Hepatocellular adenomas

<table>
<thead>
<tr>
<th>Adenoma Classification</th>
<th>Prevalence</th>
<th>Clinical Features</th>
<th>Pathway</th>
<th>Imaging: MRI is preferred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory Hepatocellular Adenoma</td>
<td>Most common (40-55%)</td>
<td>young women with OCP history, obese patients 30%</td>
<td>JAK-STAT</td>
<td>T1-weighted images: iso-hyperintense</td>
</tr>
<tr>
<td>(includes telangiectatic hepatocellular</td>
<td>10% can be β-Catenin-</td>
<td></td>
<td></td>
<td>T2-images: diffusely hyperintense along periphery</td>
</tr>
<tr>
<td>adenoma/focal nodular hyperplasia)</td>
<td>mutated</td>
<td></td>
<td></td>
<td>T1-weighted images: extracellular contrast show persistent enhancement on delayed phase</td>
</tr>
<tr>
<td>HNF-1α-mutated Hepatocellular Adenoma</td>
<td>Second most common (30-40%)</td>
<td>Females &gt;90% OCP use Adenomatosis more common, least aggressive</td>
<td></td>
<td>Diffuse and homogenous signal dropout on opposed-phase T1 images reflecting steatosis</td>
</tr>
<tr>
<td>β-Catenin-mutated Hepatocellular Adenoma</td>
<td>Least common 10-20%</td>
<td>Highest risk of malignant transformation, androgen use, males</td>
<td></td>
<td>MRI No diagnostic findings</td>
</tr>
<tr>
<td>Unclassified</td>
<td>10%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Beta-catenin exon 3 mutated adenomas have higher risk of malignancy

- Management of Hepatic Adenoma
  - Follow up 6 months, q1 yr x5 yrs, then q2 yrs
  - High risk: resect
    - Lesions ≥5 cm (or increasing in size)
    - Hemorrhage
    - Male gender (increased malignant risk)
    - Beta-catenin mutated adenomas
    - Older females with no history of OCP use
  - Low risk: stop OCPs, lose weight
    - Young females, lesions <5 cm on OCP
    - Follow with US q6-12 weeks during pregnancy
  - Alternatives to resection: RFA, embolization
Focal Nodular Hyperplasia

- The most common non-malignant hepatic tumor not of vascular origin
- Women:men 8-9:1
- Age 20-50
- Symptoms infrequent
- Thought to be a regenerative response to hyperperfusion by the characteristic anomalous arteries found to feed them
- Associated with hereditary hemorrhagic telangiectasia and hemangioma

FNH

- 80-95% solitary
- Usually <5 cm in size
- Presence of a central stellate scar
  - Composed of abnormally large portal tracts including large feeding arteries, portal veins, and bile ducts
- The lesions have bile ductules, sinusoids, and Kupffer cells (different than adenomas)
FNH: Pathology

“Mini-Cirrhosis”

FNH: Radiology

Arterial phase with feeding vessel
Arterial phase showing central scar
Portal venous phase isointense
FNH: Management

- Role of OCPs is unclear
- If cannot stop, probably ok but reimage in 6-12 months
- Resect only if symptomatic or highly suspicious
- If >8 cm and patient wants to become pregnant, may also consider resection due to very tiny risk of enlargement during pregnancy

Sodium Gadoxetate (Eovist) MRI for distinguishing FNH from Adenoma

- Brightly enhancing in arterial phase
- Homogenous enhancement with central scar
- Isointense in portal venous phase
- Retained intensity in the hepatobiliary phase supports the diagnosis of FNH
Which one is FNH and which is adenoma?

Fibrolamellar HCC

- 5-25 years old
- No male predominance: affects both sexes equally
- No association with underlying liver disease
- 2/3 involve left lobe
- Aggressive surgery recommended
Metastatic Disease

- Most often multiple lesions
- Most tumors appear hypodense compared to surrounding liver
- Hypervascular lesions are one of these tumors: neuroendocrine, renal cell, breast, melanoma, thyroid
- Confirm metastatic disease with biopsy
- MRI with sodium gadoxetate is also helpful for metastatic disease, since it is a biliary specific imaging
  - Mets appear dark on biliary phase compared to liver

Epithelioid Hemangioendothelioma

- Low-grade malignant vascular neoplasm: somewhere between hemangioma and angiosarcoma
- Middle age
- 2/3 women
- Single or multiple masses that are avascular or calcified and may involved entire liver
- 75% can present with regional and distant metastasis
- Can undergo liver transplant for extensive hepatic disease even in the setting of metastatic disease
Epithelioid Hemangioendothelioma

Neuroendocrine tumor metastasis

- 40-80% of patients present with liver metastasis at time of diagnosis
- 20-50% primary tumor is elusive
- Liver > bone > lung
Treatment Options

- Surgery: Resection, liver transplant
- Non-surgical liver directed therapies: TACE, Y90, RFA
- Medical therapy:
  - Octreotide
  - Chemo

Liver Transplant Criteria

- Inclusion:
  - Well- or moderately-differentiated
    - Mitotic rate <20 per 10 HPF, <20% Ki67 positive markers
    - Primary tumor drained by the portal system
    - Resection of primary malignancy and extrahepatic disease without recurrence >6 months
    - <50% involvement of the liver
    - Age <60?
- Exclusion
  - No previous attempts at major liver resection
  - No previous upper abdominal exenteration
Liver Transplantation

**FIGURE 2.** Overall survival of 106 patients according to the number of adverse prognostic factors: hepatomegaly, resection in addition to LT, and age more than 43 years. Top: 5-year survival rates: 77%, 79%, 39%, and 33% for 0, 1, 2, or 3 factors, respectively. Bottom: after gathering in 2 groups: 0-1 factor (n = 38) and 2-3 factors (n = 48). F = 0.0001.

Cystic Liver Lesions
Classification of Hepatic Cysts

- Simple (solitary) cyst
- Polycystic liver disease
- Parasitic
  - Hydatid (echinococcal)
- Neoplastic
  - Primary
    - Cystadenoma, cystadenocarcinoma, squamous cell carcinoma
  - Secondary
    - Ovarian, pancreatic, colon, kidney, neuroendocrine
- Neoplastic
  - Primary
    - Cystadenoma, cystadenocarcinoma, squamous cell carcinoma
  - Secondary
    - Ovarian, pancreatic, colon, kidney, neuroendocrine
- Duct related
  - Caroli’s disease
  - Bile duct duplication
- False cysts
  - Traumatic intrahepatic hemorrhage
  - Infarction
  - Biloma
- Ciliated foregut cyst

More than a simple cyst?

<table>
<thead>
<tr>
<th>Finding</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive Symptoms</td>
<td>Cystadenoma, cystadenocarcinoma, metastasis</td>
</tr>
<tr>
<td>Abnormal LFTs</td>
<td>Cystadenocarcinoma, metastasis</td>
</tr>
<tr>
<td>Rapid growth</td>
<td>Cystadenoma, cystadenocarcinoma, metastasis</td>
</tr>
<tr>
<td>Calcifications or daughter cysts</td>
<td>Echinococcal cyst</td>
</tr>
<tr>
<td>Thick or irregular cyst wall</td>
<td>Cystadenoma, cystadenocarcinoma, metastasis, echinococcal cyst</td>
</tr>
<tr>
<td>Nonhomogeneous cyst content</td>
<td>Cystadenoma, cystadenocarcinoma, metastasis, echinococcal cyst, bleeding into a simple cyst</td>
</tr>
<tr>
<td>Septations or multilocular cyst space</td>
<td>Cystadenoma, cystadenocarcinoma, metastasis, echinococcal cyst, bleeding into a simple cyst</td>
</tr>
</tbody>
</table>
Simple Cyst

- Cystic formations containing clear fluid
- Usually do not communicate with the bile duct
- Benign
- Rarely large cysts can cause symptoms due to compression of adjacent structures
- Largest cyst ever reported contained 17 liters of fluid!

Simple Cyst

- Tend to occur in right lobe
- Female: male 1.5:1 in asymptomatic
  - 9:1 in symptomatic
- Huge cysts almost exclusively in women over 50
- Huge cysts can cause atrophy of the lobe with compensatory hypertrophy of the opposite lobe
Simple Cyst: Diagnosis

- US most helpful: anechoic unilocular fluid filled space with nearly imperceptible walls
  - No signal on doppler
- CT, MRI: well-demarcated water attenuation lesion without enhancement
- Hemorrhage into cyst can cause confusing picture on imaging

Simple Cyst: Treatment

- Monitor large lesions (>4 cm) with US to ensure stability at 3 months and then 6-12 months
- If stable for 2-3 yrs, nothing further
- If symptomatic or increasing in size, make sure you aren’t missing something more complex
Simple Cyst: Treatment for Large Cysts

- Aspiration alone not permanent: rapid reaccumulation in near 100%
  - Can be helpful if trying to decide if symptoms are truly from the cyst prior to proceeding with surgery
- Aspiration with subsequent injection of sclerosing agent sometimes helps

Simple Cyst: Treatment for Large Cysts

- Surgical resection
  - Unroofing of cyst
  - Drainage with cystjejunostomy
  - Resection of entire cyst
- Surgery associated with recurrence of up to 14% and morbidity up to 15%
- Potential complications
  - Wound infection
  - Bile leak
  - Subphrenic hematoma
  - Prolonged postoperative drainage
Mucinous Cystic Neoplasm

- AKA Cystadenoma and then cystadenocarcinoma
- Rare
- On imaging, septations, papillary projections, density more than water
- Thickened, irregular walls
- Fluid aspiration may show high CEA, more malignant potential

Mucinous Cystic Neoplasm

- Resect whenever possible due to high malignant potential: up to 15% have cancer in the wall of the cyst
  - Partial excision worse prognosis than complete enucleation
  - If cancer strongly suspected, then formal liver resection rather than enucleation is needed
Pyogenic liver abscess

- Rupture or leak of bile duct or bowel
- Biliary stenting, instrumentation, or chemoembolization
- Increased risk in diabetes
- Biliary: enteric gram neg and enterococci
- Other sites: mixed aerobic and anaerobic
- Treatment
  - Antibiotics
  - IR drainage, surgical

Pyogenic Liver abscess

- 50–60's
- Biliary obstruction
- Abdominal infections
- Ablative procedures
- Fevers/chills/pain
- Labs: WBC
- CT scan
- Treatment
  - Antibiotics
  - IR drainage, surgical
Hydatid Cyst

- Parasitic infection
  - Echinococcus (tapeworm)
  - Intermediate hosts
  - Migration to liver
- Cysts compress liver
  - Fluid secretion
  - Pain, fullness, rupture
- <5cm asymptomatic
- Medical treatment
  - High recurrence
- Surgical treatment
  - Risk of anaphylaxis with cyst rupture

Conclusion – Benign lesions

- Most incidental findings
- Specific treatment usually not indicated
- Radiologic examination
- Treatment
  - Symptomatic lesions
  - Cancer diagnosis uncertain
- Multi-disciplinary approach
Questions?

Speaker: Catherine T. Frenette, MD

Moderator: Anjana A. Pillai, MD

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