Case Report: Unsuspecting Liver Lesion

Maryam Kashi, D.O.
Medical Director, Endoscopy
Florida Hospital
Central Florida Hepatology & Gastroenterology
Case Report: Unsuspecting Liver Lesion

- 59 yo Asian Female presented to PCP with Right-sided rib pain x 1 month.
- s/p MVA 5 wk prior -- 45 miles/hour and she was hit from behind. There was some car damage. Immediately after, she had a lot of back pain as well as anterior lower chest pains.
- s/p chiropractor: back pain has improved, but pain in the front still bothering her
- Constant dull pressure underneath her breasts. Location: RUQ/Lower border of sternum/ ribs. +worse with heavy lifting and eating
- Exam: Pinpoint tenderness RUQ/ lower ribs.
- PMH: Glaucoma, Osteopenia
- ROS: No pleuritic CP/ SOB. No heartburn, N/V, diarrhea, constipation, blood in stool. Decreased appetite, lost 7 lbs in 7 mo
- PSX: Right ankle surgery in 4/2014

- Dx: Pain in Right rib. Suspect injury from seat belt due to location. Less likely GI source of pain.
- Plan:
  - XR ribs obtained. Await radiology read.
  - Advised heat, NSAID and muscle relaxant
  - If not improving, will consider imaging such as MRI.
Case Report: PCP Eval

• Rib X-ray: No acute Abnormality

• Back to PCP: Complaint is now RUQ, bloating after eating. Increased burping.
• Denies: Heart burn N/V, Constipation, no blood in stool, no melena.
• She is concerned persistent weight loss: from 109 down to 100 lbs in the last year. She has been under some stress with an ankle fracture as well as a recent MVA and is likely eating less. Last CSP 3-5 years ago - repeat in 5 years per pt.
• Dx: Abdominal pain, RUQ.
• Plan:
  • Obtain RUQ U/S
  • Trial of protonix
  • Try Boost/Ensure once a day
  • Recheck CMP
  • Referral to GI
Case Report:

- 2/25/14: LFT’s: 0.3/ 84/ H 36/ 25
- 10/3/14: LFT’s: 0.4/ 94/ H 78/ H 47

- 10/3/14 US: LIVER: Measures 14 cm in size. Heterogeneous echotexture with a large heterogeneous mass with central hypoechoic areas replacing majority of the left lobe measuring 10.7 x 10.7 x 10 cm. There are 2 additional right hepatic cysts measuring 3.4 x 2.2 x 3.3 cm and 1.3 x 1.4 x 1.4 cm. No intrahepatic ductal enlargement.

- GALLBLADDER: No gallstones. Gallbladder wall thickness 2 mm in size. No pericholecystic fluid. No sonographic Murphy sign.

- COMMON BILE DUCT: 2 mm in size.

IMPRESSSION:

- 1. 11 cm heterogeneous mass replacing most of the left lobe of liver. Recommend MR with contrast for further evaluation.
- 2. Right hepatic cysts
Solid Liver Lesions

• Asymptomatic
• Normal physical examination
• Normal laboratory

• Some patients will have findings related to the lesion
  • Pain
  • Palpable mass
  • Predisposing conditions (e.g., an extrahepatic malignancy)
Size of the Liver Lesion

- >1 cm: Most can be dx by Imaging, Histology
- <1cm:
  - Commonly benign (as long as no risk factors for HCC)
  - Incidental
  - Most represent small cysts, hemangiomas, or biliary hamartomas
  - Frequently difficult to definitively characterize by imaging methods due to their small size
  - Difficult to biopsy
  - Often clinical follow-up is recommended
- AASLD Guidelines:
  - US in 3 months
  - Then repeat Annual US
  - If lesion is stable after 3 radiographic examinations, stop radiographic surveillance.
Solid Liver Lesions

• Benign-ish Liver Lesions:
  • Hepatic Hemangioma
  • Focal Nodular Hyperplasia
  • Hepatic Adenoma
  • Idiopathic Non-cirrhotic Portal HTN (Nodular Regenerative Hyperplasia)
  • Regenerative Nodules

• Malignant Liver Lesions:
  • Hepatocellular Carcinoma
  • Cholangiocarcinoma
  • Mets

• Rare Lesions:
  • Sarcomas (i.e. Epithelioid Hemangioendothelioma), Fibrolamellar carcinoma, Non-Hodgkin Lymphoma
Diagnostic Approach to Liver Lesions

- Identification of risk factors for specific lesions
- Hx or Exam: Alcohol hx, Family hx, etc.
  - Clinical findings: Palmar Erythema/ Spider Telangiectasia of Cirrhosis
- Imaging:
  - 3-Phase CT
  - MRI with Gadolinium
- Labs: AFP, HBsAg
- Possible FNA or Sx
• Study of 160 consecutive Pt’s with focal liver lesions
• Detailed evaluation: labs (including tumor markers), imaging
• All subsequently underwent Sx excision
• 98% had correct Pre-op Dx
Hepatic Hemangioma
(Aka Cavernous Hemangioma)

- Most Common Benign Hepatic Tumors
- Usually found Incidentally
- More common in women-- ratio of 3:1
- Symptomatic if >4 cm

- Non-contrast CT scan: Well-demarcated hypo or hyper- dense mass
  - 10% have Calcifications
A: Well-demarcated hypodense lesion on non-contrast scan in the posterior right lobe of the liver

B: Peripheral Nodular Enhancement on Early phase with gradual "filling in" of the lesion. The center of the lesion remains hypodense.

C: Isodense lesion on Post contrast delayed image
Focal Nodular Hyperplasia

• Hyperplastic response to an anomalous artery
• Most commonly in women in their 30s and 40s
• Usually diagnosed incidentally during
A: Pre-gadolinium shows a hypointense lesion in the left lobe of the liver.

B: Immediately after Gad infusion, the arterial phase reveals a hyperintense mass with a hypodense central scar, characteristic of FNH.

C: After 2 min, mass appears nearly isodense with the normal liver, & central scar is difficult to distinguish.

D: After 3 min, central scar is hyperdense due to delayed accumulation of gadolinium.
T2-weighted MRI:
hyperintense lesion in the left lobe of the liver with a striking hyperintensive central scar
Hepatic Adenoma

• Benign epithelial liver tumor
• Most commonly seen in premenopausal women older than 30
• Most are assoc with oral contraceptives x >2 yr
• May cause pain, esp. if assoc with rupture and bleeding
• Also noted in patients with Type 1 Glycogen storage diseases

*Small risk of neoplastic transformation
- Well-demarcated
- Isodense on noncontrast CT
- CT w/contrast: peripheral enhancement during the early phase
- Subsequent centripetal flow during the portal venous phase
- Late Phase: isodense and then hypodense

Adenomas often have areas of hemorrhage, necrosis, or fibrosis, giving them a heterogeneous appearance. The presence of fresh blood within the adenoma gives the appearance of a high-attenuating lesion.

CT w/contrast: Large complex enhancing mass (X) in the left lobe of the liver displacing vessels (arrowheads).
-A smaller, low attenuation mass is also noted in the right lobe of the right lobe of the liver
Idiopathic Non-cirrhotic Portal HTN
(includes Nodular Regenerative Hyperplasia)

• Multiple foci of proliferating hepatocytes form nodules throughout the liver
• Frequently associated with a Systemic Autoimmune Disease
• More common in older adults

• CT is of limited dx value since the nodules are generally nonspecifically hypodense
Regenerative Nodules

- Regenerating hepatic tissue in response to hepatic injury
- Typically seen in cirrhosis
Hepatocellular Carcinoma (HCC)

- Primary liver malignancy
- Most commonly occurs in the setting of chronic liver disease
  - Cirrhosis
  - Chronic hepatitis B
- May cause decompensation in a patient with previously compensated cirrhosis
- May be symptomatic: Abdominal pain, wt loss, early satiety
CT w/contrast: ill-defined mass in dome of liver representing the region of the hepatoma (long arrow). A filling defect in the contrast filled inferior vena cava (IVC; arrowhead) reflects tumor thrombus extending from the primary tumor into the IVC.

CT w/contrast: Cirrhotic liver w/ multifocal hypervascular masses (arrows) and a mass in the portal vein (arrowhead).
--The spleen is enlarged due to portal hypertension secondary to cirrhosis.
Cholangiocarcinoma

• Bile Duct malignancy
• May involve the Intrahepatic ducts and/or Extrahepatic ducts

• Risk factors:
  • Primary sclerosing cholangitis
  • Choledochal cysts
Anatomic Classification of Bile Duct Cancers
Bismuth-Corlette classification of biliary tract cancers

Type I
Tumor below the confluence of the left and right hepatic ducts.

Type II
Tumor reaching the confluence.

Type IIIa
Tumor occluding the common hepatic and right hepatic ducts.

Type IIIb
Tumor occluding the common hepatic and left hepatic ducts.

Type IV
Tumor that involves the confluence and both the right or left hepatic ducts.

Type IV
Tumors that are multicentric.
Metastatic Dz

• Most common malignant hepatic neoplasms
• Usually Not Solitary
Case Report: MRI Abd w/wo Contrast:

- Large, somewhat lobulated mass occupying the left lobe of liver. The exact nature of this is uncertain. It does appear to demonstrate some mixed contrast enhancement with enhancement signal similar to that seen with the main portion portion of the liver. This mass is somewhat ill defined due to motion unsharpness. The morphology is lobulated and hyperintense on T2 weighted images and hypointense on T1 weighted images. Hepatocellular carcinoma cannot be excluded in this case and clinical correlation is recommended. This mass measures 12.1 x 5.7 cm in axial dimensions.

- The right lobe of the liver appears to be generally benign. There does appear to be multilocular hepatic cyst at the inferior and post aspect of the right lobe of the liver.
GI wu: LIVER LAB work-up

- Pt denies any hx of liver dz. No FH liver dz or liver cancer.
- CBC: 6.8/13.7/40.8/332
- INR-1.1, PT-11.1, Alb-4.9
- AFP: 33,712
- HAV Ab+, HBcAb+, HBsAg-Neg, HBsAb—Pos, HCV Ab—Neg
- Alpha-1 AT-160 (normal), Ceruloplasmin-32, Ferritin-183, %Sat-13
- +ASMA (1:40), ANA/Anti-LKM, SLA- Neg
- IgG- 1253, IgA- 143, IgM-81
- HBV DNA <20
- Stool Parasites: Neg
Case Report: GI Eval

- Hepatocellular Carcinoma
- **10/14 US** - 11cm heterogenous mass, replacing most of the left liver lobe. Also hepatic cysts on right side.
- **10/14 MRI** - 12.1 cm Non-specific lesion, concerning for HCC.
- AFP>33,000, likely HCC in this setting

- will refer to Liver Transplant Sx for possible surgical options. Lesion is too large for RFA and likely too large for chemoembolization
Liver Lesions:  FNA & Sx

• FNA
  • Commonly Non-Dx in some types of liver lesions: Hepatic Adenomas and FNH
  • Assoc with some degree of risk: Bleeding, Seeding of Neoplastic cells

• Silva, et al: Meta-analysis of 8 studies of needle biopsy for suspected HCC estimated that the risk of needle tract seeding was 2.7 percent overall

• Surgical Resection
  • Recommended for lesions that are Symptomatic or if HCC cannot be excluded
  • Considered Curative for Hepatic adenoma and FNH
Case Report: PATHOLOGY

• MODERATELY DIFFERENTIATED HEPATOCELLULAR CARCINOMA MEASURING 12.0 CM IN GREATEST DIMENSION. THE MARGINS ARE NEGATIVE. GB-NORMAL

• The non-neoplastic liver was evaluated. The non-neoplastic liver demonstrates no significant steatosis, inflammation or fibrosis. The hepatic architecture appears to be generally intact. The sinusoidal compartment demonstrates no significant abnormality. No granulomas are identified. Intralobular bile ducts show no significant abnormality.

• An iron stain is negative. No definite underlying chronic liver disease is identified.

• Stains performed: PASD, trichrome, iron, DOG-1, Hepar1 and Glypican-3
Hepatocellular carcinoma: Epidemiology

- Fourth leading cause of Cancer-related death Worldwide
- U.S.: Annual incidence of HCC was at least 6 per 100,000 in 2010
- Incidence rates and Death rates: North America, Latin America, and Central Europe have increased
- From National Cancer (SEER), HCC incidence rates increased by 3.1 percent per year from 2008 to 2012

- Geographic Variation- varies widely according to racial and ethnic groups within the same country, and between regions within the same country.
  - Also varies with Hep B incidence & Environmental Factors
  - High Incidence: Sub-Saharan Africa, China, Hong Kong, Taiwan
  - Low Incidence: North/South America, most of Europe, Australia, Middle East
HCC: Risk Factors

• Cirrhosis- Any Cause

• Hepatitis B
  • Even without Cirrhosis!
  • Still, 70 to 90% of HBV Pt’s who develop HCC will have cirrhosis
  • Viral Load (>10,000 Copies/ mL)
  • HBeAg+
  • Also, Inactive Carriers (HBsAg+/ HBeAg-) and Resolved Infection (HBsAg-)!  

  • Simonetti: 1271 Alaskan natives with chronic HBV for an average of 20 years. Among patients who cleared their HBV (HBsAg negative), the incidence of HCC was lower than that of those who remained HBsAg positive (37 vs 196 per 100,000 person-years), but still higher than among the general population.

  • Yuen: Likelihood of developing HCC is greater in those who clear HBsAg when >age 50 yr
HCC in HBV: Does Genotype Matter?

- Genotype A: Northern Europe, North America, India, and Africa
- Genotypes B and C: Asia
- Genotype D: Southern Europe, the Middle East, and India.

- **Genotype C** are at higher risk for HCC than Genotype B
- **Genotype D** are at higher risk than Genotype A
HCC in HBV: Other Risk Factors

Coinfection
- HBV/ HCV Coinfection increased risk of HCC compared with infection by either virus alone
- HBV/ HDV Coinfection also appears to increase the risk of HCC

- Older age
- ETOH
- TOB
- Elevated ALT
- FH HCC

- DM
- NAFLD
- Obesity
- Hemochromatosis
- Alpha-1 AT Deficiency
  - (No Cirrhosis Needed!)
- Acute Intermittent Porphyria
HCC in HCV

• Traditionally, HCC occurs in Hep C with Cirrhosis; however, in up to 10% of Pt’s with HCV assoc HCC, only mild degrees of fibrosis were found.

• HCV tx with SVR decreases BUT does not eliminate risk of HCC
  Much of this risk seems to be in those with cirrhosis
HCC and Environmental Toxins

• Contaminated Drinking Water
  • Several studies in Rural Asia: higher HCC mortality among people who drink pond-ditch water compared with those who drink well water (100 versus fewer than 20 deaths per 100,000 population per year)
  • Blue-green algal toxin Microcystin commonly contaminates ponds and may be a strong promoter of HCC

• Betel Nut Chewing
  • Widespread in certain regions of Asia
  • May be an independent risk factor for the development of cirrhosis and HCC
  • Also implicated in development of Esophageal cancer and Squamous Cell Head & Neck cancer.
HCC and Environmental Toxins: Aflatoxin

- Mycotoxin that commonly contaminates corn, soybeans, and peanuts
- High rates of dietary aflatoxin associated with HCC, particularly in chronic carriers of HBV

- Taiwan case-control study of HBV carriers: risk of developing cirrhotic HCC or noncirrhotic HCC was higher in patients with high levels of aflatoxin B1-albumin adducts compared with those with undetectable levels

- Mutations of the p53 tumor suppressor gene have been demonstrated in patients with HCC who have chronically been exposed to aflatoxin
- Similar findings also have been demonstrated in animal models
Any Protective Factors Against HCC?

• Statins--- esp in East Asian Males with HBV
• Dietary Factors:
  • White Meat
  • Fish/ Omega-3 FA
  • Vegetables
  • Vitamin E
  • Coffee

• Meta-analysis: 2 or more cups Coffee/ day was associated with a 43% reduction of HCC.
• Coffee contains large amounts of antioxidants, suggesting biological plausibility for the protective effect.
HCC Tx

- Surgical resection
- Radiofrequency ablation (RFA), microwave ablation, and cryoablation
- Transarterial Chemoembolization (TACE)
- Transarterial Radiobiolates (TARE)
- Percutaneous Ethanol or Acetic Acid ablation
- Irreversible electroporation
- Radiation therapy and stereotactic radiation therapy
- Systemic chemotherapy, with cytotoxic agents and molecularly targeted therapies
- Immunotherapy
- Liver Transplantation
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Points assigned</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>&lt;2 mg/dL (&lt;34.2 micromol/L)</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt;3.5 g/dL (35 g/L)</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td></td>
</tr>
<tr>
<td>Seconds over control</td>
<td>&lt;4</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Prognostic stage groups</td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>When T is...</td>
<td>And N is...</td>
</tr>
<tr>
<td>T1a</td>
<td>N0</td>
</tr>
<tr>
<td>T1b</td>
<td>N0</td>
</tr>
<tr>
<td>T2</td>
<td>N0</td>
</tr>
<tr>
<td>T3</td>
<td>N0</td>
</tr>
<tr>
<td>T4</td>
<td>N0</td>
</tr>
<tr>
<td>Any T</td>
<td>N1</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
</tr>
</tbody>
</table>
Overview of treatment algorithm for hepatocellular carcinoma
Milan Criteria

- 1996 Mazzaferro Study: established deceased-donor liver transplantation (OLT) as a viable option for the treatment of HCC
- Showed that when transplantation was restricted to Pt’s with early HCC, a four-year survival rate of 75 percent could be achieved.
- These outcomes are similar to expected survival rates for Pt’s undergoing transplantation for cirrhosis without HCC.

• These Criteria have come to be known as the Milan Criteria
Milan Criteria

• Single lesion $\leq$ 5 cm
• Up to three separate lesions < 3 cm
• No Gross vascular invasion
• No Regional nodal
• No Distant metastases
Barcelona Clinic Liver Cancer (BCLC) staging classification and treatment algorithm

Hepatocellular carcinoma

- Very early stage (0)
  - Single ≤2 cm
  - Preserved liver function, ECOG PS 0

- Early stage (A)
  - Single or up to 3 nodules ≤3 cm
  - Preserved liver function, ECOG PS 0

- Intermediate stage (B)
  - Multinodular
  - Preserved liver function, ECOG PS 0

- Advanced stage (C)
  - Portal invasion
  - Extrahepatic spread
  - Preserved liver function, ECOG PS 1 to 2

- Terminal stage (D)
  - End-stage liver function *, ECOG PS 3 to 4

Potential candidate for liver transplantation

- Solitary
- Up to 3 nodules (≤3 cm)

No

- Portal pressure
- Bilirubin

Normal

Increased

Associated diseases

- No
- Yes

Ablation
Resection
Transplantation
Ablation

Effective treatments with impact on survival

Survival: >5 years

Chemotherapy
Systemic therapy

Effective treatments with impact on survival

Survival: >2 to 5 years

Effective treatments with impact on survival

Survival: >1 year

Best supportive care

Survival: 3 months

* ECOG PS refers to the Eastern Cooperative Oncology Group Performance Status.
Liver Transplantation

• Donor organs is given to the most severely ill patients
• In U.S., use "Model for End stage Liver Disease" (MELD) score-Adults and Children
• Statistical model based upon predicted survival in cirrhosis
• Higher point score predict worse Short-term Prognosis

• MELD Calculator:
  • INR
  • Tbili
  • Cr
  • Na
Thank you!