Hepatocellular Carcinoma: A Guide to Screening and Diagnosis

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Agenda

• Hepatocellular carcinoma (HCC) introduction
• Index patient: clinical presentation
• Surveillance for HCC
• Index patient: screening ultrasound
• Anatomy review
• Index patient: Differential Diagnosis
• Diagnostic imaging for HCC
• Index patient: Diagnostic imaging
• Treatment and Outcome
• Summary
HCC: Epidemiology

• 20,000 new cases each year in the US
  – 5\textsuperscript{th} most common cancer in men
  – 7\textsuperscript{th} most common cancer in women
• Cirrhosis is present in 80-90\% of patients diagnosed with HCC.
• Any condition leading to cirrhosis is considered an important risk factor
  – HBV or HCV
  – Alcoholic cirrhosis
  – NAFLD

NEJM. 2011;365:1118-27.
HCC: A Global Disease

- Burden of disease is greatest in developing countries, specifically those where HBV is endemic.

- Worldwide, half a million cases of HCC are diagnosed each year.

The incidence of HCC in the United States has tripled in the last 30 years.

We have reviewed facts about risk factors and incidence of HCC. We will now discuss our index patient.
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Index Patient: Clinical Presentation I

• 56-year-old male with a history of alcohol-induced cirrhosis with multiple complications of ESLD
  – Diuretic resistant ascites now improved status post TIPS placement (2007).
  – Spontaneous bacterial peritonitis (SBP) now on Bactrim prophylaxis
  – Hepatic encephalopathy (on lactulose and rifaximin).
  – Grade II hemorrhoids
  – Grade I varices
Index Patient: Clinical Presentation II

- Past medical history (continued)
  - Non-insulin dependent Diabetes mellitus
  - Hypothyroidism
  - Anemia
  - Ventral hernia repair
- He has ultrasound surveillance every three months to evaluate his TIPS shunt and to screen for HCC.
- Previous ultrasounds have shown no focal lesions and AFP has been within normal limits.
Before continuing with our index patient, we will pause to review indications for liver ultrasound screening and concerning findings on screening exams.
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HCC Surveillance

We will discuss the following concepts.

• Who should be screened?
• What radiologic and non-radiologic studies should be used to screen?
• What results warrant additional testing?
HCC Surveillance: Screening population

- The American Association of Liver Diseases (AASLD) suggests screening in
  - All patients with cirrhosis (annual incidence of HCC of 3-8%)
  - Some patients with HBV (those whose annual incidence surpasses 0.2%)
    - Asian men over 40
    - Asian women over 50
    - Africans and North African blacks
    - Patients with a family history of HCC
HCC Surveillance: Evidence

- Evidence for screening is limited.
- One study randomized 18,816 people, aged 35–59 years with HBV infection or chronic hepatitis in urban Shanghai to every 6 month screening with US and AFP or no screening.
- Demonstrated a 37% decrease in HCC-related mortality with screening over five years.

HCC Surveillance: Imaging Modality

• Ultrasound sensitivity varies widely depending on the study (55%-89%) but is equivalent to CT in most studies and is much more cost-effective.
Now that we know the evidence behind ultrasound surveillance, we will examine some examples of screening ultrasound. The images include examples of cirrhotic livers and various presentations of HCC.
Companion Patient 1: Cirrhotic liver on US

Findings:
1. Nodular liver surface
2. Ascites

Companion Patient 2: Nodular liver on US

Transverse US

Findings:
1. Extremely nodular liver with heterogeneous appearance.

A nodular appearance decreases the sensitivity of ultrasound for identifying HCC.

Companion Patient 3: HCC

Transverse US

HCC can present with
1. single mass
2. multiple masses
3. diffuse disease

Classically HCC lesions are hypoechoic.
Companion Patient 4: HCC

HCC can present with:
1. single mass
2. multiple masses
3. diffuse disease

Classically HCC lesions are hypoechoic.

Companion Patient 5: HCC

HCC can present with
1. single mass
2. multiple masses
3. diffuse disease

Classically HCC lesions are hypoechoic.

Companion Patient 6: HCC

Transverse US

However HCC can present with varying echogenicity.

Findings:
Two hyperechoic liver masses that were found to be HCC

We have seen multiple classic examples of HCC on ultrasounds. We will now examine our patient’s screening ultrasound exam.
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Index Patient: Isoechoic lesion on US

Transverse US

Findings
1. Diffusely heterogeneous echotexture.
2. Isoechoic lesion with hypoechoic rim.
Index Patient: Focal Lesion

Transverse and Saggital US

Findings:
Isoechoic lesion with hypoechoic rim.
Index Patient: Lesion Dimensions

Transverse and Sagittal US

Findings:
Isoechoic lesion with hypoechoic rim measuring 1.2 x 2.3 x 1.2 cm.
Index Patient: Review of Findings

• Coarsened and nodular liver

• A suspicious mass in the right lobe of the liver (segment IVa) measuring 1.2 x 2.3 x 1.2 cm

• The mass is isoechoic with a hypoechoic rim.
Before discussing a differential diagnosis for our index patient’s liver findings, we will briefly review segmental liver anatomy.
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Our patient’s lesion was visualized in Section IVa.
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DDx: Focal Liver Lesion

**Benign liver masses**
1. Cysts
2. Hemangioma
3. Focal nodular hyperplasia
4. Hepatic adenoma
5. Biliary cystadenoma
6. Abscess
7. Hematoma
8. Regenerating nodules
9. Confluent hepatic fibrosis

**Malignant liver masses**
1. HCC
2. Metastases
3. Intrahepatic Cholangiocarcinoma
4. Lymphoma
5. Stromal tumors
DDx: Focal Liver Lesion

-Patient has a cirrhotic liver

Benign liver masses
1. Cysts
2. Hemangioma
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Malignant liver masses
1. HCC *
2. Metastases
3. Intrahepatic Cholangiocarcinoma
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5. Stromal tumors
**DDx: Focal Liver Lesion**

-Patient has a cirrhotic liver
-Isoechoic mass with hypoechoic rim

Benign liver masses
1. Cysts
2. Hemangioma
3. **Focal nodular hyperplasia** *
4. **Hepatic adenoma** *
5. Biliary cystadenoma
6. Abscess
7. Hematoma
8. **Regenerating nodules** *
9. **Confluent hepatic fibrosis** *

Malignant liver masses
1. **HCC** *
2. Metastases
3. Intrahepatic Cholangiocarcinoma
4. Lymphoma
5. Stromal tumors
We have prioritized our differential diagnosis for our index patient’s liver lesion based on his history and ultrasound findings. We will now discuss an evidence-based work-up.
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• **Diagnostic imaging for HCC**
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MR has greater sensitivity than CT for detecting HCC especially in cirrhotic livers and is recommended for diagnostic imaging.

### Diagnostic Imaging: ACR Guidelines

#### Clinical Condition:
Liver Lesion — Initial Characterization

#### Variant 3:
Indeterminate >1 cm lesion on initial imaging with ultrasound, CT (without or with contrast), or non-contrast-enhanced MRI. Known or suspected liver disease associated with a high risk of hepatocellular carcinoma (chronic hepatitis, cirrhosis, hemochromatosis, etc.)

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
<th>RRL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion initially identified on US</td>
<td></td>
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<tr>
<td>MRI abdomen without and with contrast</td>
<td></td>
<td>Best test in a young patient for surveillance of hepatitis B or C. See statement regarding contrast in text under “Anticipated Exceptions.”</td>
<td>O</td>
</tr>
<tr>
<td>CT abdomen without and with contrast</td>
<td></td>
<td>As an alternative to MRI when GFR precludes gadolinium.</td>
<td>☢ ☢ ☢ ☢</td>
</tr>
</tbody>
</table>
Liver imaging for both MRI and CT uses a liver protocol which includes a non-contrast study followed by 3 phase contrast-enhanced liver imaging:
- Arterial phase
- Venous phase
- Delayed phase
Diagnostic Imaging: Characteristic Findings for HCC on MRI

There are several findings that suggest that a liver lesion is HCC on MRI including:
- The lesion is hypointense on T1
- The lesion is hyperintense on T2
- The lesion shows enhancement on arterial phase with iso- or hypointensity on venous and delayed phases ("washout")

*Arterial phase enhancement with delayed phase washout is the most specific finding and is part of the radiologic diagnostic criteria for HCC.

Radiology. 2008;247:311-330
Liver tissue typically receives most of its blood supply from the portal system with a smaller portion from the hepatic artery.

In HCC, neoangiogenesis alters that basic relationship. There is a diminution of portal tracts and virtually all of the blood supply is via the hepatic artery.

This specific findings allows for distinction from regenerating or dysplastic nodules which can otherwise closely mimic HCC on imaging.
We have discussed characteristic imaging findings for HCC. Now let’s look at some companion patients with HCC on MRI and CT.
Companion Patient 7: HCC on MRI

Axial T1 arterial phase

Axial T1 venous phase

Axial T1 delayed phase

Finding: Two liver lesions with arterial enhancement with venous and delayed phase washout.

Radiology. 2008;247:311-330
Companion Patient 3: HCC on MRI

- Axial T1 pre-contrast
- Axial T1 arterial phase
- Axial T1 venous phase
- Axial T1 delayed phase
Finding:

A 3.0 cm liver lesion near the falciform ligament is iso-intense on pre-contrast T1 imaging and shows arterial enhancement with venous and delayed phase washout on contrast imaging.
Companion Patient 3: HCC on CT

Findings:
CT shows same classic findings as MR: arterial enhancement with delayed phase washout.
We have learned classic examples of HCC on T1 multiphase MRI and on multiphase CT. Now let’s examine our index patient’s MRI exam.
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Index Patient: HCC on MRI

Axial T1 arterial phase

Axial T1 venous phase

Axial T1 delay 1 phase

Axial T1 delay 2 phase
Index Patient: MRI Findings

Findings:
- Nodular cirrhotic liver.
- 2.1 cm lesion in segment IVa.
- The lesion isointense in T1 and T2 (not shown) but shows arterial enhancement and washout pattern in venous and delayed phases (with significant motion artifact)
Index Patient: Diagnosis of HCC

Our index patient has
1. A lesion greater than 2cm AND
2. Arterial enhancement with venous and delayed phase washout.

Based on these findings, a diagnosis of HCC can be made.

What are our patient’s treatment options?
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Treatment: Surgical resection

Depends on the number, size, and location, as well as the patient's functional status.

1. **Surgical resection** –
   A. favor for lesions which are in a good location and for suitable surgical candidates.
   B. Can be curative but leaves the patient with a susceptible liver.

2. Liver transplant

3. Minimally invasive/local-regional treatment
Treatment: Transplant

Depends on the number, size, and location, as well as the patient's functional status.

1. Surgical resection

2. Liver transplant –
   A. Equivalent or better outcomes than surgical resection
   B. Patient must meet Milan criteria
      - one lesion smaller than 5cm.
      - up to 3 lesions smaller than 3 cm.
      - no extrahepatic manifestations
      - no vascular invasion

3. Minimally invasive local-regional treatment
Treatment: Local Therapy

Depends on the number, size, and location, as well as the patient's functional status.

1. Surgical resection

2. Liver transplant –

3. Minimally invasive local-regional treatment -
   1. Useful in certain patient populations (ie poor performance status, expected to receive a transplant in the future)
   2. Short-term outcomes are excellent, but long-term outcomes are inferior to above treatments.

3. Methods include:
   - Transarterial chemoembolization [TACE]
   - Percutaneous ethanol infusion (PEI)
   - Radiofrequency ablation (RFA)
   - Cryotherapy

NEJM. 2011;365:1118-27.
Index Patient: Radiofrequency Ablation

-Our patient was not a good surgical candidate and opted to undergo radiofrequency ablation.

-Under ultrasound guidance, a 20-cm long RF electrode was advanced to the site of the lesion and two 12 minute 1200 mAmp ablations were performed.
Index Patient: Post-RFA

Post-RFA Findings:
- Ablation zone measuring 25 x 41 mm surrounded by reactive hyperemia.

Axial non-contrast CT
Index Patient: Follow-up

- One month later the patient had ultrasound and CT which showed no new concerning lesions.

- He is scheduled for additional ultrasound and CT in three months and is currently clinically stable.
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Summary

- Hepatocellular carcinoma is a common cancer associated with cirrhosis and viral hepatitis. Its incidence is increasing.

- Surveillance ultrasound every 3-6 months is recommended for all patients with cirrhosis and many patients with HBV.

- Concerning lesions on screening ultrasound should be followed up with MRI which has higher sensitivity for assessing lesions than CT particularly in cirrhotic livers.
  - Arterial enhancement with venous and delayed phase washout is highly specific for HCC.

- There are numerous treatment options for HCC which are selected based on the number, size, and location of lesions, as well as the patient's functional status.
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References