Hepatocellular Carcinoma

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Our Patient

**HISTORY**

- 52 year old man; h/o IV drug abuse with needle sharing during the Vietnam War
- Hepatitis C diagnosed in 1996
- Child’s A (compensated) cirrhosis of the liver diagnosed in 1997
- S/p Interferon/Ribavirin therapy x 2
- S/p U/S x 2 (6, 12 mos. prior to presentation); Alpha-fetoprotein level normal
- Asymptomatic, in for routine screening
Our Patient
SCREENING ULTRASOUND FINDINGS

• Ultrasonography of the liver reveals a new 2x2 cm hypoechogenic lesion with discrete margins within the right posterior lobe of the liver.

(courtesy of BIDMC)
Our Patient

**CT FINDINGS**

- CT scan reveals a low attenuation mass with discrete margins in the right posterior lobe of the liver, which displays enhancement during the arterial phase of imaging.

![CT Scan Images](image_url)

- Noncontrast Scan
- Contrast Enhanced Scan

Enhancing lesion

Low attenuation mass seen on liver window

(courtesy of BIDMC)
DDx for Focal Low Attenuation Mass on Noncontrast CT Showing Enhancement After IV Contrast

- Hepatocellular Carcinoma
- Cholangiocarcinoma
- Focal Nodular Hyperplasia
- Abcess
- Adenoma
- Lymphoma
- Cavernous Hemangioma
- Metastasis
Our Patient

DIAGNOSIS

- CT guided biopsy was performed to provide a definitive diagnosis
- Pathology revealed atypical hepatocytes indicative of hepatocellular carcinoma

Livraghi T, Makuuchi M, Buscarini L: Diagnosis and Treatment of Hepatocellular Carcinoma, 1st ed. Greenwich Medical Media, 1997
Hepatocellular Carcinoma (HCC): General

• Malignant liver neoplasms usually represent metastases

• Hepatocellular Carcinoma (HCC) accounts for greater than 80% of primary malignant hepatic neoplasms

• HCC results in 250,000-1 million deaths globally per year; 7th and 9th most frequent cause of cancer related deaths in men and women, respectively
Epidemiology and Risk

- Wide regional variation in incidence (>15/100K in China, Sub-Saharan Africa; <3/100K in N. America); variation reflects differences in exposure to risk factors (HBV, HCV, aflatoxin, and cirrhosis)
  - HBV carriers had 223 x RR in one study
  - Found in 1-2%/yr of those with HCV and cirrhosis; increased risk w/ HCV genotype Ib
  - Aflatoxin (thought to mutate p53) confers increased risk
  - Cirrhosis from all causes (3-4% annual incidence w/ compensated cirrhosis)
Clinical Presentation

- Symptoms typically relate to chronic liver disease; clinical presentation is usually late because of the liver’s functional reserve and a lack of findings pathognomonic for HCC
- Consider HCC with a decompensation (ascites, varices, encephalopathy) of previously stable cirrhosis
- Some patients present with abdominal pain, weight loss, or even a palpable mass—these are usually advanced HCC
- Rarely, HCC presents with jaundice, intraperitoneal bleeding, symptoms from metastases, or paraneoplastic syndromes (diarrhea, hypoglycemia, erythrocytosis, hypercalcemia, and cutaneous lesions)
Diagnosis

- Diagnosis usually rests upon use of serum AFP, radiologic imaging, and biopsy
  - Alpha-fetoprotein is often elevated in HCC and levels above 500 ug/dl (nl 10-20) are usually diagnostic. However, AFP lacks sensitivity (concentrations are nl in up to 40% of small HCCs) and may be elevated by other causes
  - U/S, CT, and MRI are used for detection and diagnosis
  - Core biopsy is obtained under U/S or CT guidance when diagnosis by imaging is uncertain; confers risk of spread to chest wall (~2% in one study)
  - Standard LFTs are not useful in diagnosis
Menu of Imaging Options

• **Ultrasound**: typically used (with AFP) as a screen for HCC in patients with cirrhosis because of its availability, low cost, and lack of ionizing radiation.

• **Computed Tomography**: often used to evaluate abnormalities found on ultrasound; helical CT with contrast has high sensitivity—especially with lipiodol injection (93-97%).

• **Magnetic Resonance Imaging**: has similar sensitivity to helical CT, but is less favored because of its cost; uniquely able to discriminate between mass lesions (dysplastic nodules, vascular lesions); useful in patients with contrast allergy.

• **Angiography**: invasive, so less used except for controlling rupture and for chemoembolization procedures; when combined with CT, provides the most precise imaging for diagnosing hepatic masses.

• **Scintigraphy**: provides functional imaging, but less diagnostic use because of its poor resolution relative to CT and MRI.
Anatomy

• Knowledge of segmental liver anatomy is important in determining the location of focal lesions and in planning for hepatic resections or embolizations. The right and left lobes are divided into segments by the hepatic veins.


KEY:
LLS=left lateral segment
LMS=left medial segment
RAS=right anterior segment
RPS=right posterior segment
CL=caudate lobe
LHV=left hepatic vein
MHV=middle hepatic vein
RHV=right hepatic vein
PV=portal vein
IVC=inferior vena cava
Morphology of HCC (I)

- Grossly, HCC may present in several forms:
  - As a single mass (most common)
  - As multiple masses of varying size
  - As a diffusely infiltrating tumor (least common)

(courtesy of BIDMC)

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Morphology of HCC (II)

- HCC may be encapsulated (15% in US, 58% in Asia)

- Encapsulated HCC typically represents less aggressive tumor and is less likely to invade the portal vein (and thus has a better prognosis, as we shall see later)

Ultrasonography of HCC

- Small HCC (<3 cm) tend to be hypoechoic, because of a homogeneous cellular structure.
- Larger HCC are often hyperechoic or of heterogeneous echogenicity due to necrosis, hemorrhage, fibrosis, or fatty change.

Livraghi T, Makuuchi M, Buscarini L: *Diagnosis and Treatment of Hepatocellular Carcinoma*, 1st ed. Greenwich Medical Media, 1997
Computed Tomography of HCC (I)

- **On Unenhanced CT scans:** HCC appears hypodense, or low attenuation, compared to normal liver. HCC tends to appear hyperdense to fatty liver.

![Large HCC showing low attenuation on unenhanced CT scan](courtesy of BIDMC)
Dynamic CT is preferred for evaluating HCC: First, a bolus of iodinated IV contrast is administered. Early scans demonstrate arterial opacification, while later scans show portal/venous systems, and finally, interstitial tissues (equilibrium phase). HCC, with a predominately arterial supply, enhances early; the liver, perfused mostly by the portal vein (80%), appears higher attenuation than HCC on later scans.
Dynamic CT: Arterial Phase

• *During the arterial phase*, HCC enhances (and becomes high attenuation) because of the extensive hepatic artery supply to the tumor.
Dynamic CT: Portal Venous Phase

• *During the portal venous phase*, HCC becomes hypodense to the liver parenchyma. Because of its hypervascularity, HCC is sometimes isodense to normal liver during this phase.
Dynamic CT: Equilibrium Phase

- *During the equilibrium phase*, often referred to as the delayed scan, the normally hypodense capsule of HCC enhances.
Magnetic Resonance Imaging of HCC

- HCC tends to appear hypointense on T1 weighted images and hyperintense on T2 weighted images.
- Fatty change, hemorrhage, or necrosis may cause increased signal intensity of HCC on T1 weighted images.
- Multiphase gadolinium enhanced MRI is similar to dual phase CT, but may be superior in accuracy.
Distinguishing Features of Focal Liver Lesions

- Cholangiocarcinoma- assoc dilated biliary ducts; increased bilirubin levels
- Focal Nodular Hyperplasia- young women w/o liver dz; typically contains central low attenuation scar w/ radiating arteries
- Abcess- assoc symptoms; usually encapsulated w/ low attenuation center
- Hepatic cysts- low attenuation before contrast; don’t enhance with contrast
- Adenoma- young women using OCPs
- Lymphoma- usually other areas of involvement (liver rarely primary); difficult to exclude
- Cavernous Hemangioma- contrast enhancement of periphery first w/ centripetal filling and prolonged enhancement seen on delayed scan
- Metastasis- often multiple, look for primary; difficult to exclude
Complications

- HCC causes several clinical complications, including:
  - Vascular occlusion
  - Metastatic spread
  - Hemorrhage
Portal Vein/IVC Thrombosis

• Vascular invasion is common with the infiltrating form of HCC (PV thrombosis 44%, IVC thrombosis ~ 5%)

• Arterial waveform detected by Duplex and color Doppler sonography differentiate tumor from bland thrombus; a basket pattern of flow is typical for HCC

• PV thrombosis is the worst prognostic factor in predicting recurrence of HCC after surgical resection

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Metastases

- Metastases found in about 14% of patients

Osteolytic bone mets in head and neck of a femur with a pathologic fracture

- 2/3 of metastases are to bones and the lungs
- Abdominal lymph nodes are also frequently involved

Hemorrhage

• Intraperitoneal hemorrhage is a rare complication of large, hypervascular tumors; it is a clinical emergency that is treated with emergency embolization

(courtesy of BIDMC)

Intra-lesion Hemorrhage on T2 weighted MRI, axial section

Intraperitoneal Hemorrhage on Arteriography

• Livraghi T, Makuuchi M, Buscarini L: Diagnosis and Treatment of Hepatocellular Carcinoma, 1st ed. Greenwich Medical Media, 1997
Staging HCC

• HCC is commonly staged by the Okuda system, which takes into account tumor characteristics and underlying liver disease, rather than a traditional TNM system.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Size</td>
<td>&gt; 50%</td>
<td>&lt; 50%</td>
</tr>
<tr>
<td>Ascites</td>
<td>Clinically Detectable</td>
<td>Clinically Absent</td>
</tr>
<tr>
<td>Albumin</td>
<td>&lt; 3 mg/dL</td>
<td>&gt; 3 mg/dL</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>&gt; 3 mg/dL</td>
<td>&lt; 3 mg/dL</td>
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• Stage I = no positives, Stage II = 1-2 positives, Stage III = 3-4 positives
Treating HCC

- Therapeutic options are typically determined by the tumor stage and hepatic reserve:
  - **PARTIAL HEPATECTOMY**: with a solitary nodule (<5 cm) that doesn’t invade hepatic vasculature and preserved hepatic function; ~30% of patients eligible; Intraarterial lipiodol, interferon-beta, and other therapies are used as adjuvants; 30% 5 yr survival
  - **PERCUTANEOUS ETHANOL INJECTION**: 51% 5 yr survival for Child’s A
  - **SYSTEMIC CHEMOTHERAPY**: HCC relatively refractive to chemotherapy
  - **TRANSARTERIAL CHEMOEMBOLIZATION**
  - **RADIOFREQUENCY ABLATION**
Arterial Chemoembolization

• Involves occlusion of the hepatic artery via catheter to induce necrosis with simultaneous administration of chemotherapeutic agents

• Generally reserved for those with advanced disease and significant symptoms; survival benefit not yet proven
Radiofrequency (RF) Ablation

- Involves the local application of RF to the tumor to cause necrosis
- May be suitable for those with medium and large lesions (complete necrosis- 48%, nearly complete necrosis- 32%)
- Studies are pending on long term survival
Prognosis

- Median post-diagnostic survival is 6-20 mo.
- Okuda’s staging system correlates well with length of survival
- Lack of encapsulation, vascular invasion, and nodal metastases are also associated with higher mortality
Our Patient
TREATMENT AND COURSE

• Our patient underwent RF ablation without complications. He continued to have no pain or other symptoms, and good energy.

• Imaging 1 month ago revealed persistent tumor adjacent to the site of RF ablation, but no other lesions. Repeat RFA was recently performed.

• The patient has one brother with the same blood type and is considering living donor transplant.
Summary

• Patients with cirrhosis, especially of HCV and HBV origin, are at a markedly increased risk for developing HCC
• HCC has various radiologic presentations, and thus must always be part of the differential for liver masses in a cirrhotic liver
• Helical CT with dual phase contrast is preferred for evaluating hepatic lesions suspicious for HCC; HCC is typically a low attenuation mass with enhancement during the arterial phase of imaging
• Earlier stage HCC has a better prognosis; screening with U/S and serum AFP may be warranted among patients with cirrhosis
References

• Livraghi T, Makuuchi M, Buscarini L: *Diagnosis and Treatment of Hepatocellular Carcinoma*, 1st ed. Greenwich Medical Media, 1997

• Up To Date – “Clinical Features and Diagnosis of Primary Hepatocellular Carcinoma”: [http://www.utdol.com](http://www.utdol.com)
Acknowledgements

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