Surgical Management of HCC

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Case Presentation

• 63M with pmhx of PVD, Hepatitis C and alcohol induced cirrhosis

• Pugh - Child’s Class A cirrhosis, MELD 6

• Social Hx – recent cessation of ETOH use (<2 months)
Case Presentation

- Meds - none
- Recent EGD negative for evidence of portal HTN
- Negative Dobutamine stress test
Physical Exam

• Vitals are WNL
• ECOG 0-1
• HEENT and neck exam are WNL
• Lungs – CTA b/l
• Heart – nml S1, S2
• Abd – soft, NT/ND, no ascities
• Extremities – w/w/p
• Neuro – grossly intact
Pre-op laboratory Data

- CBC – 4.7/14.9/43.5/149
- BMP – 139/4.5/106/27/13/0.8/120
- LFT –
  - TP – 8.0/ Alb – 4.0/ AST-72/ALT-98/Alk Phos – 78/ TB -1.6
- Coags – PT - 12.5/PTT - 25/ INR - 1.09
- AFP –
  - 4/10 – 63.7
  - 10/10 – 117.8
Abdominal CAT Scan
Abdominal MRI
Intraoperative Details

• Taken to OR for a hepatic resection
  – Bilateral subcostal incision

  – Inspection of the liver revealed macronodular cirrhosis and a large tumor mass in segment IV

  – Ligamentous attachments of the entire liver were divided
Intraoperative Details (cont’d)

• Taken to OR for a hepatic resection
  – Suprahepatic IVC was isolated and a red rubber catheter was placed around the vein for vascular control if needed
  – All HV were isolated and controlled
  – Gastrohepatic omentum was opened and a red rubber catheter was placed around the porta hepatis for inflow control if needed
Intraoperative Details (cont’d)

• Taken to OR for a hepatic resection
  – Intraoperative ultrasound again confirmed the location of our HCC to be in segment IV and no other lesion in the parenchyma. The HCC was abutting the MHV.
  – The MHV was clamped temporarily
  – Used argon beam to mark our margin of resection
  – Used the Habib RFA probe to coagulate the parenchyma around our margin of resection
Intraoperative Details (cont’d)

• Taken to OR for a hepatic resection
  – Used a combination of the CUSA EXcel™ Ultrasonic Surgical Aspirator and Weck clips to resect the liver mass
  – FloSeal was applied to our resection site
  – 10 mm JP drain was left at the resection site
  – Extubated and transferred to MICU
Intraoperative Details (cont’d)

• Taken to OR for a hepatic resection
  – Total OR time – 4.5 hours (including anesthesia time)
  – Intake – 2500ml of crystalloid, 2 units of FFP
  – EBL - 250ml
  – Urine Output – 275ml
  – CVP kept below 2-3 mmHg
• Moderately differentiated hepatocellular carcinoma
  – The specimen consists of a 40g segment of liver which is soft brown measuring 7.5 x 6.5 cm
  – pT2, pN X, pM -not applicable
Post-Operative Course

• POD #1
  – Without complaints
  – Good urine output
  – Vitals are WNL

  – Lab values
    • ALT - 104, AST - 96, ALK PHOS - 62, TB - 2.9
    • PT - 15.4, PTT-33.2, INR - 1.3

  – Clear liquid diet
• POD #2
  – Pt. is hypertensive (SBP – 140-160) and tachycardic (sinus tachycardia to 110)
  – HGB/HCT stable, Chem are WNL
  – PT - 17.4, INR – 1.5
  – JP drain – 50ml serosangious fluid
• POD #3
  – Pt. became moderately agitated and hypoxic
    • PE protocol CAT scan
  – Pt. has SVT to 240 bpm
    • Refractory to adenosine boluses
    • Started on diltiazem and esmolol drips
    • Cardiology recommended DC electrical cardioversion
      – Failed x 3
    • Amiodarone Drip and unfractionated heparin infusion was started
• POD #3
  – Coags remain elevated but unchanged
  
  – LFTs increased (Alb – 3.6, TP- 6.6, AST -283, ALT – 528, Tb - 11 )
  
  – Abdominal Ultrasound was normal
• POD #4 - 5
  – Pt. continues to be tachycardic
  – Now appears somnolent and drowsy
    • Lactulose started for high ammonia level
  – Later that day the patient was emergently intubated
    • complicated by aspiration
POD #4 – 5

- Overnight the patient was noted to be hypotensive, febrile, with a low MAP, and no urine output

- Broad spectrum antibiotics were started and the patient was pan-cultured
  - Blood cultures grew staphylococcus aureus
- Aggressive fluid resuscitation with crystalloid, albumin, and FFP was started

- Vasopressor support was started

Post-Operative Course (cont’d)

• POD #6
  – Pt. underwent full ACLS protocol for cardiac arrest event
    • Patient expired.
Post-Mortem Details

• Autopsy
  – Congestive splenomegaly
  – Pulmonary congestion with bilateral atelectasis and effusions, no air in the alveoli
  – Tracheobronchial mucus plugging
  – Moderate serosanguinous ascites
  – Cardiomegaly with coronary sclerosis, but without occlusion or stenosis
Overview

- Epidemiology
- Review of Liver Anatomy
- Prognostic Indicators in Cirrhotic Patients
- Surveillance of HCC
- Diagnosis of HCC
- Staging systems
- Treatment
Epidemiology

- 6th most common cancer worldwide
  - (626,000 or 5.7% of new cancer cases)
- Third most common cause of cancer mortality
  - Deaths = 598,000
- Survival rates 3% - 5% for the US and developing countries
- Fastest growing cause of cancer-related death in men in the US
  - 19,160 cases and 16,780 deaths
Evaluation of the cirrhotic patient

- **Child-Pugh classification**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 Point</th>
<th>2 Points</th>
<th>3 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/dl)</td>
<td>&gt;3.5</td>
<td>2.8–3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>&lt;2</td>
<td>2–3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.7–2.3</td>
<td>&gt;2.3</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Slight</td>
<td>Moderate</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>1–2</td>
<td>3–4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Points</th>
<th>Op. Mortality</th>
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</thead>
<tbody>
<tr>
<td>5-6</td>
<td>5%</td>
</tr>
<tr>
<td>7-9</td>
<td>10-15%</td>
</tr>
<tr>
<td>10-15</td>
<td>&gt;25%</td>
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</table>
Evaluation of the cirrhotic patient

- **MELD score** (Model for End Stage Liver Disease)
  - \[ \text{MELD} = 3.78 \times \ln(\text{serum bilirubin (mg/dL)}) + 11.2 \times \ln(\text{INR}) + 9.57 \times \ln(\text{serum creatinine (mg/dL)}) + 6.43 \]

- In interpreting the MELD Score, 3 month mortality is:
  - <9 — 1.9% mortality
  - 10–19 — 6.0% mortality
  - 20–29 — 19.6% mortality
  - 30–39 — 52.6% mortality
  - 40 or more — 71.3% mortality

- MELD score was the only statistically significant predictor of 30-day mortality
• AASLD guidelines
  – Patients in the high risk group should undergo an abdominal ultrasound and AFP level every 6 months

• UNOS and Liver Transplant Centers
  – MRI or CT scan every 3 months
**Table 3. Surveillance Is Recommended for the Follow Groups of Patients (Level III)**

<table>
<thead>
<tr>
<th>Hepatitis B carriers</th>
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<tbody>
<tr>
<td>Asian males $\geq 40$ years</td>
</tr>
<tr>
<td>Asian females $\geq 50$ years</td>
</tr>
<tr>
<td>All cirrhotic hepatitis B carriers</td>
</tr>
<tr>
<td>Family history of HCC</td>
</tr>
<tr>
<td>Africans over age 20</td>
</tr>
</tbody>
</table>

For non-cirrhotic hepatitis B carriers not listed above the risk of HCC varies depending on the severity of the underlying liver disease, and current and past hepatic inflammatory activity. Patients with high HBV DNA concentrations and those with ongoing hepatic inflammatory activity remain at risk for HCC.

**Non-hepatitis B cirrhosis**

| Hepatitis C |
| Alcoholic cirrhosis |
| Genetic hemochromatosis |
| Primary biliary cirrhosis |

Although the following groups have an increased risk of HCC no recommendations for or against surveillance can be made because a lack of data precludes an assessment of whether surveillance would be beneficial.

| Alpha1-antitrypsin deficiency |
| Non-alcoholic steatohepatitis |
| Autoimmune hepatitis |
HEPATOCELLULAR CARCINOMA (HCC) SURVEILLANCE

Patients at risk for HCC:
- Cirrhosis
  - Hepatitis B, C
  - Alcohol
  - Genetic hemochromatosis
  - Autoimmune hepatitis
  - Non-alcoholic steatohepatitis
  - Primary biliary cirrhosis
  - Alpha-1-antitrypsin deficiency
- Without cirrhosis
  - Hepatitis B carriers

Liver mass nodule (See HCC-2)
- Alfa-fetoprotein (AFP)/Ultrasound (US) every 6-12 mo
  - Mass confirmed
    - Follow pathway for HCC, (See HCC-3)
  - Rising AFP
    - Liver imaging studies
      - No mass
        - Follow every 3 mo with AFP, liver imaging
      - Mass confirmed
        - Follow pathway for HCC, (See HCC-3)


Additional risk factors include patients with active viral replication, high HBV DNA levels, family history of HCC, Asian males ≥ 40 y, Asian females ≥ 50 y, Africans ≥ 20 y.

If ultrasound negative, CT/MRI should be performed.

MRI/CT scan to define extent and number of primary lesions, vascular anatomy, involvement with tumor, and extrahepatic disease; triphasic helical CT or MRI to include early arterial phase enhancement.

CT should be with contrast. PET/CT is not adequate.

Rule out germ cell tumor if clinically indicated. MRI or triple phase CT scan may be helpful.
Diagnosis

• AASLD guidelines
  – Nodules smaller than 1cm
    • Continue ultrasound surveillance
  – Between 1-2 cm
    • Dynamic CT or MRI
      – Classic arterial enhancement and venous washout
      – If not, consider biopsy
  – Over 2cm
    • Typical appearance on imaging – proceed to treatment
    • If AFP > 200 ng/mL – proceed to treatment
      – Not elevated in 30%
Hepatocellular Carcinoma

Diagnosis of HCC

1. CLINICAL PRESENTATION
   - Imaging:
     - CT/MRI/US every 3-4 mo
     - Enlarging
       - Stable for 18 mo
       - Continue imaging every 6-12 mo
     - Progress according to nodule size
   - 1-2 cm
     - Imaging techniques: CT, US, MRI
     - 2 Classic enhancements
     - One Classic enhancement
     - Non-Classic enhancement
     - Biopsy (preferred) or FNA
   - > 2 cm
     - 1 Imaging technique: CT, US, MRI
     - Classic enhancement or AFP > 200 ng/mL

2. Additional Imaging
   - Non-Classic enhancement
   - Change in nodule size
   - Repeat imaging or followup
   - Positive
     - Repeat imaging and/or biopsy
   - Negative

Histologically confirmed HCC


CT should be with contrast. PET/CT is not adequate.

Contrast enhanced ultrasound where available.


There is no definitive evidence to support an absolute value of AFP cut-offs. AFP cut-offs among institutions may vary.
Several staging systems exist

- No clear consensus
- AASLD recommends the Barcelona Clinic Liver Cancer (BCLC) staging system
<table>
<thead>
<tr>
<th>Stage I</th>
<th>T1</th>
<th>N0</th>
<th>M0</th>
<th>55% 5 yr survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
<td>37% 5 yr survival</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>16% 5 yr survival</td>
</tr>
<tr>
<td>IIIB</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td>IIIC</td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td></td>
</tr>
</tbody>
</table>

**T definitions**
- T1 – *solitary nodule without vascular invasion*
- T2 – *solitary tumor with vascular invasion or multiple nodules all <5cm*
- T3 – *multinodular >5cm, or tumor with major vasculature invasion*
- T4 – *Tumor with invasion of adjacent organs*

Okuda staging system

criteria | positive | negative  
---|---|---
Tumor size | >50% | <50%  
Ascites | Clinically detectable | Absent  
Albumin | <3 | >3  
Bilirubin | >3 | <3  

Stage | No positive | 8.3 mos survival  
---|---|---
Stage I | 1-2 positive | 2 mos survival  
Stage II | 3-4 positive | 0.7 mos survival  
Stage III
• Surgical resection for the noncirrhotic patients with HCC is the mainstay of therapy.

• For a Child's A cirrhotic with preserved liver function
  – Transplantation and resection can both be considered.
  – BCLC and AASLD guidelines
Treatment

• Liver transplantation
  – Milan Criteria
  – LDLT or CLT
  – Combination of TACE/sorafenib (+/-) to down size the tumor mass while on waiting list

• Other treatment modalities
  – RFA and PEI
    • Bridge to transplant
    • Tumors 2-3 cm
  – TACE
  – Sorafenib
Small Hepatocellular Carcinoma in Child’s A Cirrhotic Patients: Hepatic Resection Versus Transplantation

Jean-Marc Bigourdan,*, Daniel Jaeck,*, Nicolas Meyer,† Carole Meyer,*
Elie Oussoultzoglou,* Philippe Bachellier,* Jean-Christophe Weber,* Maxime Audet,*
Michel Doffoël,‡ and Philippe Wolf*

Liver Transplantation Vol 9 2003

• Retrospective Study to compare resection versus transplantation in Child’s A cirrhotic patients

• 37 pts with tumors less than 5 cm were treated over 8 years
  – 20 pts in resection group
  – 17 pts in transplantation group

• Compared 3 and 5 year overall survival and recurrence rates
Small Hepatocellular Carcinoma in Child A Cirrhotic Patients: Hepatic Resection Versus Transplantation

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Figure 1. Intention-to-treat overall survival after LT and HR for small HCC in Child A cirrhotic patients.
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Figure 2. Intention-to-treat recurrence-free-survival after LT and HR for small HCC in Child A cirrhotic patients.
Summary

• Patient selection is important when offering surgical intervention to cirrhotic patients.

• No universal staging system exist.

• Controversy still exist over mgmt of HCC in compensated cirrhotic patients.
References


• Esnaola NF, Mirza ND, Lauwers GY: Comparison of clinicopathologic characteristics and outcomes after resection in patients with hepatocellular carcinoma treated in the United States, France, and Japan. Ann Surg 2003; 238:711. and others