Management of Cholangiocarcinoma

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PGY-5
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Case Presentation

- 37 year old male from Yemen presented with 2 week history of epigastric pain, anorexia, jaundice and puritis.
- PMH: seizures
- PSH: none
- Meds: none
- NKDA
- Social: tobacco – 10 pk/yr, no EtOH, no drugs
Physical Exam and Labs

- T 98.8 BP 100/64 HR 90 R 14
- AOx3
- Skin: jaundiced
- Abdomen: soft, nondistended, nontender, no palpable masses

- CBC 8.5/11/36/441
- BMP 132/3.7/97/22/15/0.89/120
- Albumin 3.8
- AST/ALT 74/153
- AlkP 274
- Tbil 9.2
- PT/PTT 10/29
- CEA 1.23
- Ca 19-9 81
CT Scan
MRI
ERCP

- Right hepatic duct stent placement
Transhepatic cholangiography
Operation

- Abdominal exploration
- Cholecystectomy
- Extended right hepatectomy
- Excision of bile duct tumor
- Periportal lymphadenectomy
- Roux-en-y left hepatectojejunostomy with access loop
CBD Margin

**FROZEN SECTION:**
Negative for Carcinoma
Total on clamp time: 16 mins
Left hepatic duct margin

Frozen Section: Negative for carcinoma
Hospital course

- POD#2 – diet
- POD#6 – fever 102 – CT C/A/P – pneumonia
- POD#12 – discharged home
  - AST/ALT 62/63
  - AlkP 229
  - Tbil 2.6
Pathology

- Well-differentiated sclerosing cholangiocarcinoma involving right hepatic duct and extending into the bifurcation and involving the origin of left hepatic duct (0.8 x 0.7 x 0.8cm)
- No lymphovascular invasion
- Extensive perineural invasion
- Liver: biliary cirrhosis
- Gallbladder: chronic cholecystitis
- Periportal lymph node: 0/1
- Margins
  - CBD – negative for carcinoma
  - Left hepatic duct – invasive carcinoma
    - Frozen section reviewed and shows carcinoma
- pT2N0Mx
Cholangiocarcinoma

- Intrahepatic: 20-25%
- Perihilar: 50-60%
- Distal extrahepatic: 20-25%
- Multifocal: 5%

Histology

- Adenocarcinoma (95%)
  - Sclerosing – 70%
  - Nodular – 20%
  - Papillary <5%
- Extent of tumor
- Blood/lymphatic involvement
- Perineural invasion
- Regional LN
Risk Factors

- Primary sclerosing cholangitis (5-15%)
- Hepatolithiasis
- Choledochal cysts
- Caroli disease
- Liver flukes – *Opisthorchis viverrini* and *Clonorchis sinensis*

Hilar Cholangiocarcinoma (Klatskin Tumor)

- Gerald Klatskin (1910-1986)
- “Adenocarcinoma of the Hepatic Duct at Its Bifurcation within the Porta Hepatis” (1965)
The American Journal of Medicine
Bismuth-Corlette Classification

Type 1
Type 2
Type 3a
Type 3b
Type 4
#### TABLE 1. American Joint Commission for Cancer Staging System for Cancer of the Extrahepatic Bile Duct*

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0 no evidence of primary tumor</td>
<td></td>
<td></td>
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<tr>
<td>Tis carcinoma in situ</td>
<td></td>
<td></td>
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<tr>
<td>T1 tumor confined to the bile duct histologically</td>
<td></td>
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<tr>
<td>T2 tumor invades beyond the wall of the bile duct</td>
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<tr>
<td>T3 tumor invades the liver, gallbladder, pancreas, and/or ipsilateral branches of the portal vein (right or left) or hepatic artery (right or left)</td>
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<tr>
<td>T4 tumor invades any of the following: main portal vein or its branches bilaterally, common hepatic artery, or other adjacent structures, such as the colon, stomach, duodenum, or abdominal wall</td>
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<tr>
<td>Regional lymph nodes (N)</td>
<td></td>
<td></td>
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<tr>
<td>N0 no regional lymph node metastasis</td>
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<td></td>
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<tr>
<td>N1 regional lymph node metastasis</td>
<td></td>
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<tr>
<td>Distant metastasis (M)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M0 no distant metastasis</td>
<td></td>
<td></td>
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<tr>
<td>M1 distant metastasis</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Stage grouping</th>
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<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T3</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T1, T2, or T3</td>
<td>N1</td>
</tr>
<tr>
<td>Stage III</td>
<td>T4</td>
<td>Any N</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
</tr>
</tbody>
</table>


Signs and Symptoms

- Jaundice
- Pruritus
- Pale stool
- Dark urine
- Abdominal pain
- Weight loss
- Abnormal LFTs

Imaging

- Ultrasound
- CT scan
- MRI
- Cholangiography
  - MRCP
  - ERCP
  - PTC
- EUS
Preop Management

- Biliary Drainage
  - Malnourished patients
  - Cholangitis
  - Technical aid in difficult hilar dissection
- Portal vein embolization
- Staging laparoscopy
- Tumor markers
  - CA 19-9 – 85%
  - CEA
  - CA-125
Criteria for unresectability

- Significant medical co-morbidities
- Cirrhosis
- Hepatic duct involvement up to secondary biliary radicals bilaterally
- Encasement or occlusion of main portal vein proximal to its bifurcation
- Atrophy of one hepatic lobe with encasement/occlusion of contralateral portal vein branch
- Atrophy of one hepatic lobe with contralateral involvement of secondary biliary radicals
- Unilateral tumor extension to secondary biliary radicals with contralateral portal vein encasement or occlusion
- Distant metastases (lymph nodes outside of heptoduodenal ligament, lung, liver or peritoneal metastasis)

Surgical Management

- Local resection versus combined hepatic resection
  - Amsterdam, Netherlands
  - January 1988 to January 2003, 99 patients
  - Ro resections
    - Period 1 (1988-1993) – 13%
    - Period 2 (1993-1998) – 32%

• Memorial Sloan-Kettering Cancer Center (2001)
  ▫ Retrospective study - 225 patients
    • Ro resection
    • Hepatic Resection 84%
    • No hepatic resection 56%

• “Major Hepatectomy for Hilar Cholangiocarcinoma Type 3 and 4: Prognostic Factors and Longterm Outcomes.” (2007)
  ▫ Retrospective study – 59 pts
    • Ro resection 28%
    • R1 resection 6%
    • Unresectable 6%
Factors associated with Improved Survival

- Negative margin
- No lymph node mets
- Normalization of bilirubin
- Hepatic resection
- Well differentiated
Role of adjuvant therapy

- **Chemotherapy**
  - No evidence to support the use of postsurgical adjuvant chemotherapy outside of a clinical trial
  - Improved survival – 4 months

- **Radiotherapy**
  - No evidence to support adjuvant postoperative radiation therapy
  - No improvement in survival or quality of life
  - Possible palliative value – pain, bleeding

- **Photodynamic therapy**
Conclusion

- Cholangiocarcinoma is a rare and deadly tumor
- Survival is significantly dependent on complete surgical resection with negative margins
- Role of chemotherapy and radiotherapy is limited in the management of cholangiocarcinoma
Reference

- Jarnagin and Winston. Hilar cholangiocarcinoma: diagnosis and staging. HPB. 2005. 7:244-251
Question 1

Which is the following is a criteria for unresectability?

a. Atrophy of one hepatic lobe with ipsilateral involvement of secondary biliary radical
b. Hepatic duct involvement up to secondary biliary radicals unilaterally
c. Atrophy of one hepatic lobe with encasement of ipsilateral portal vein branch
d. Encasement or occlusion of main portal vein proximal to its bifurcation
Question 2

• Which of the following is TRUE?
  a. Papillary histology has the worst prognosis
  b. All patients should undergo biliary decompression prior to surgery
  c. Treatment with adjuvant chemoradiation improves survival significantly
  d. Lymph node metastasis is associated with a poor prognosis
Question 3

• How would you classify this tumor based on the Bismuth-Corlette classification?
  ▫ Type I
  ▫ Type II
  ▫ Type III
  ▫ Type IV