Liver Transplantation for Cholangiocarcinoma

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Objectives

- Cholangiocarcinoma—brief review
- Historical treatment and prognosis
- Indications for Liver Transplantation
  -- patient selection
  -- neoadjuvant therapy
  -- literature review
- Conclusions
Cholangiocarcinoma

- Incidence 1-2/100,000
- 2% of all cancer diagnoses in US
- 15% of all liver cancers
  - intrahepatic  2,600 cases/yr
  - extrahepatic  3,000 cases/yr
Risk Factors

- Chronic Biliary Inflammation
  - PSC, choledochal cysts
- Hepatitis B and C
- Cirrhosis
- ETOH
- Liver flukes
- Toxic exposure: thorium dioxide (Thorotrast)
Clinical Presentation

- **Symptoms**: pruritus, abdominal pain, weight loss
- **Signs**: jaundice, hepatomegaly
- **Laboratory**:
  - elevated bilirubin
  - elevated alkaline phosphatase
  - elevated CEA and CA 19-9
Classification of biliary tract cancers
Treatment

- **Non-Surgical**
  - Palliative: 5-8 months

- **Surgical**
  - Resection: 5-20% 5-yr survival
  - Negative surgical margins: 33-46% 5-yr survival
Transplantation: Historical Data

Retrospective analysis: 249 patients

Resection (n=125) overall 5-yr 27% (stage I/II 42%)
Transplant (n=25) overall 5-yr 17% (stage I/II 38%)
Ex-lap (n=99)

→ Prognostic significance:
   1. tumor stage
   2. tumor-free margins

*Pichlmayr et al, Ann Surg, 1996*
Transplantation: Historical Data

1984 - 1992:

- 795 liver transplants $\rightarrow$ **17** for cholangiocarcinoma
  - 3 patients excluded for early post-op mortality
  - 11/14 patients experienced recurrence
  - 7 patients died secondary to their recurrence

$\rightarrow$ **1yr survival rate 53%**

*Goldstein et al., Baylor, Am J Surg, 1993*
Transplantation: Historical Data

- Cincinnati Tumor Transplant Registry

207 patients received OLT for nonresectable CCA

Survival rates:
1yr → 72%
2yr → 48%
5yr → 23%

51% had recurrence of their tumors
Survival after recurrence was rarely more than 1 yr

Meyer et al, Cincinnati, Trans, 2000
Transplantation: Historical Data

72 patients between 1981-96

resection: 34 patients  transplant: 38 patients

TNM Staging

- **Primary Tumor (T)**
  - **T1** Solitary tumor without vascular invasion
  - **T2** Solitary tumor with vascular invasion or mult. tumors < 5 cm
    - T 3 Mult. tumors > 5 cm or tumor involving the portal or hepatic vein(s)
    - T4 Tumors with direct invasion of adjacent organs

- **Regional lymph nodes (N)**
  - N0 NO
  - N1 YES

- **Distant metastasis (M)**
  - M0 NO
  - M1 YES

**Stage I** T1N0M0

**Stage II** T2N0M0
  - Stage IIIA T3N0M0
  - Stage IIIB T4N0M0
  - Stage IIIC Any TN1M0
  - Stage IV Any T Any NM1
Neoadjuvant Therapy

- biliary brachytherapy
- external beam radiation
- radiation sensitization with 5-FU
Neoadjuvant Therapy

17 patients with nonresectable CCA

- underlying PSC (n=9) and cirrhosis (n=3)
- brachytherapy and chemotherapy
- staging laparotomy

11 → transplanted
5 → tumor progression
1 → death (sepsis)

Sudan et al., U of Nebraska, Am J Trans, 2002
Results

5/11 disease-free survival
- no evidence of recurrence (median 7.5 yrs)

6/11 deaths
- 2 tumor recurrences (10 and 18 months)
- 3 deaths fungal peritonitis and sepsis
- 1 retransplanted, then hepatic artery thrombosis

Sudan et al., U of Nebraska, Am J Trans, 2002
Mayo Clinic Protocol

1. nonresectable CCA by brush cytology or biopsy
2. mass lesion <3cm on imaging
3. clinical staging (CT scan, U/S, bone scan)
4. suitable for neoadjuvant therapy
   → EBRT, 5-FU, brachytherapy
5. staging laparotomy
6. liver transplant

Heimbach et al, Mayo, Liver Trans, 2004
Mayo Clinic Protocol

Awaiting OLT:
6 patients

Enrollment
56 patients

Staging Lap
48 patients

OLT
28 patients

Survival
22 patients

Dz spread/death
during radiation:
8 patients

Metastatic Dz
precluding OLT:
14 patients

Death after OLT:
6 patients

Heimbach et al, Mayo, Liver Trans, 2004
Mayo Clinic Protocol

Results:

88% 1-yr survival

82% 5-yr survival

3/22 perioperative deaths

4/22 tumor recurrences
OLT vs. Resection

- 1993-2004 Mayo Clinic
- 71 patients entered protocol → 38 received OLT
- 54 patients explored for resection → 26 resected

Rea et al, Mayo Clinic, Ann Surg, 2005
OLT vs. Resection

OLT advantages:

- Neoadjuvant Tx
- Younger age
- More stringent medical selection
- Wider excision

Rea et al, Mayo Clinic, Ann Surg, 2005
Our Experience

1996-2006 at University of Colorado

- 10 transplants for cholangiocarcinoma
  - PSC (n=7)  
  - HCV/cirrhosis (n=3)

- 8/10 alive (median 4 years)
Areas for Further Study

Living donor transplants
Appealed MELD scoring
Neoadjuvant delivery systems
Trisegmentectomies with adjuvant tx
Conclusions

- Stringent patient selection
  - Stage I & II only
- Neoadjuvant therapy
- Integrated surgical and medical treatment teams