MALIGNANT LIVER TUMORS IN CHILDREN - OUR 10-YEAR EXPERIENCE

Chua JHY¹, Chen TA², Leong WL², Kua HX², Jacobsen AS¹, Tan AM³

¹Department of Pediatric Surgery, KK Women’s and Children’s Hospital, Singapore
²National University of Singapore, High School of Math and Science, Singapore
³Department of Pediatric Subspecialties, Hematology and Oncology Service, KK Women’s and Children’s Hospital, Singapore
Background

- Liver cancers are rare in children
- Understanding and prognosis of hepatoblastomas much improved
- Hepatocellular carcinomas in children poorly understood.
  - Prognosis dismal
Materials and Methods

- IRB approval
- Retrospective Review
- Singapore Childhood Cancer Registry
- Clinical charts of patients treated for pediatric liver cancers at
  - KK Women’s and Children’s Hospital
  - between January 1, 1997 and December 31, 2007
Results - Patients

- 27 patients treated for primary liver malignancies
- 19 treated for hepatoblastoma (HB)
- 6 treated for hepatocellular carcinoma (HCC)
- 2 excluded from analysis
  - Focal Nodular Hyperplasia at resection
  - Foreign patient with incomplete follow up
Results - Demographics

- Majority are Singaporean Chinese
  - 55% of HB
  - 83% of HCC

- Majority are boys
  - HB- Male: Female = 13: 7
  - HCC- Male : Female = 5:1
Results - Age

Age of Patients at Diagnosis

Age of patients (year)

HCC

HB
### Results – Clinical Presentation

<table>
<thead>
<tr>
<th>Presenting Symptoms</th>
<th>HB</th>
<th>HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdominal Distension</strong></td>
<td>17 (89.5%)</td>
<td>4 (66.7%)</td>
</tr>
<tr>
<td><strong>Abdominal Pain</strong></td>
<td>3 (15.8%)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td><strong>Other GI complaints</strong></td>
<td>6 (31.6%)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td><strong>Systemic Complaints</strong></td>
<td>9 (47.4%)</td>
<td>5 (83.3%)</td>
</tr>
<tr>
<td><strong>Surveillance</strong></td>
<td>0</td>
<td>1 (16.7%)</td>
</tr>
</tbody>
</table>
Results – Serum Alpha-Feto-Protein Levels

Graph of Alpha Feto Protein (AFP) Level at diagnosis

- HB
- HCC

AFP level (ug/L)
## Results – Hepatitis B Carrier Status

<table>
<thead>
<tr>
<th></th>
<th>No. HBsAg Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB (n = 19)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>HCC (n = 6)</td>
<td>2 (33.3)</td>
</tr>
</tbody>
</table>
Results – Imaging Studies

- All patients had CT Abdomen done at diagnosis
  - 54% of HBs considered primarily resectable
  - Only 1 HCC was deemed resectable
- Disease further staged with CXR and / or CT Thorax in all patients
Results – CT Scans of Liver

Hepatoblastoma
- Rt hepatic lobe tumor

Hepatocellular Carcinoma
- multi-focal disease
Results – Stage at Diagnosis

Stage of Disease at Diagnosis

No. of Patients

<table>
<thead>
<tr>
<th></th>
<th>Stages 1 &amp; 2</th>
<th>Stages 3 &amp; 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>HCC</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>
# Results – Treatment Outcomes of HBs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Patients</th>
<th>No. (%) Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Resection alone</td>
<td>3</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Primary Resection + Adjuvant Chemotherapy</td>
<td>7</td>
<td>6 (85.7)</td>
</tr>
<tr>
<td>Neoadjuvant Chemotherapy → Resection → Chemotherapy</td>
<td>8</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Others*</td>
<td>1</td>
<td>1 (100)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>19</strong></td>
<td><strong>16 (84.2)</strong></td>
</tr>
</tbody>
</table>

* Child presented with local and distant relapse after treatment elsewhere
## Results – Treatment Outcomes of HCCs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Patients</th>
<th>No. (%) Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Resection alone</td>
<td>1</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Neoadjuvant Chemotherapy → Resection*</td>
<td>1</td>
<td>0(0)</td>
</tr>
<tr>
<td>Chemotherapy alone</td>
<td>2</td>
<td>0(0)</td>
</tr>
<tr>
<td>Sorafenib + Chemo-Embolization (TACE)</td>
<td>1</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Palliative</td>
<td>1</td>
<td>0(0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6</strong></td>
<td><strong>1 (16.7)</strong></td>
</tr>
</tbody>
</table>

*Child initially treated for presumed HB*
Results – Resections of HBs

Rt Lobe HB with poor chemotherapy response

Good response to chemotherapy
## Results – Histology & Outcomes of HBs

<table>
<thead>
<tr>
<th>Histology Subtype</th>
<th>No. of Patients</th>
<th>No. (%) Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial - Pure Fetal</td>
<td>3</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Epithelial – Fetal + Embryonic</td>
<td>5</td>
<td>4 (80)</td>
</tr>
<tr>
<td>Epithelial - Small Cell Undifferentiated</td>
<td>1</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Epithelial + Mesenchymal</td>
<td>7</td>
<td>6 (85.7)</td>
</tr>
<tr>
<td>Hyalinized (post-chemo)</td>
<td>3</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>19</strong></td>
<td><strong>16 (84.2)</strong></td>
</tr>
</tbody>
</table>
Results – Histology of HCCs

• 1 patient underwent segmentectomy with gross total resection of tumor
• 1 patient underwent right hepatectomy following initial chemotherapy for presumed HB
• 2 had open liver biopsies
• 2 had percutaneous biopsies
• All showed features of classic HCCs
Results – Follow up & Outcomes of HBs

- Mean follow up for HB is 7.6 years
- 16 patients (84%) were alive at the conclusion of study
- 12 patients (63.1%) had survived more than 5 years from their diagnosis
Results – Follow up & Outcomes of HCCs

- Only 1 patient with HCC survived 7 years from his initial diagnosis
- Remaining 5 patients survived an average of 5.9 months from diagnosis
- Child who received no specific therapy survived 3.8 months
Results – Survival Outcomes

Survival Curve of HB and HCC patients

- Hepatoblastoma
- Hepatocellular Carcinoma

Survival Proportion

Time (in months)
Discussion

- HBs
  - malignancy in infants / toddlers
- Large asymptomatic tumors
- Marked elevation of serum AFP
- Complete surgical resection
  - cornerstone of successful therapy in non-dessiminated disease
Discussion

- Neoadjuvant chemotherapy
  - potential for cure in Stage 4 disease
  - resection with good margins, minimizes blood loss reduces surgical morbidity
Discussion

- HCCs
  - Older children
  - Advanced / multi-focal disease
- Moderate elevation of serum AFP
- **Not** always associated with Hepatitis B carrier status / liver cirrhosis
- Cure is rare
Discussion

- Surveillance in Hepatitis B carrier
- Not suitable for liver transplants.
- Sorafenib – survival benefit?
- Understanding of tumor biology → new treatment strategies → ? improved outcomes
Discussion

- Pre-treatment histological diagnosis
  - tumors in older children
  - only moderate elevation of serum AFP.

- Percutaneous biopsies
  - safe and adequate
Conclusions

- Hepatoblastoma occurs in very young children but carries an excellent prognosis.
- Hepatocellular carcinoma occurs in older children and carries a dismal prognosis.
- HCCs can occur in the absence of underlying liver disease.
Conclusions

- A better understanding of the tumor biology of pediatric HCC is required to improve the treatment outcomes.
- Pre-treatment tumor diagnosis should be confirmed in older children with liver tumors and only moderate elevation of serum AFP.
THANK YOU

KK Women’s and Children’s Hospital
SingHealth