PEDIATRIC LIVER TRANSPLANT
REVIEW & UPDATE

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Disclosure

Naveen Mittal, MD, has no relationships with commercial companies to disclose.

Learning Objectives

At the end of this presentation the participant will be able to:

1. To learn about the current indications as well as the medical concepts which currently shape the care of pediatric hepatic transplant candidates.
2. To learn about the listing process and current clinical practices in pediatric hepatic transplantation
3. To learn about the current concepts in surgical approaches to pediatric hepatic transplantation

End Stage Liver Disease (ESLD)

Courtesy of Dr. Peter Whittington

2 Years after Liver Transplant

Courtesy of Dr. Peter Whittington

Pediatric Liver Transplant (OLT)

- Liver conditions leading to OLT
- Evaluation & Listing process of the candidates
- Surgery & Current Outcomes
First Successful Liver Transplants

- Denver - 1967
- Hepatoblastoma

Pediatric Liver Transplant (OLT)

Liver conditions leading to OLT

- Progressive liver disease → ESLD
- Acute liver failure
- Benign & malignant liver tumors
- Metabolic disease

Biliary Atresia - ESLD

Definition: A destructive inflammatory process that affects variable lengths of the biliary tract

- Progressive fibrosis
- Obstruction of extrahepatic biliary tree

Incidence

- 1:8,000 – 18,000 live births
- Female > Male
- No family history correlation (rare for 2 in 1 family)
- Higher incidence in Asian and African American population

Etiology

Perinatal or postnatal form
- Isolated defect in a healthy term newborn
- Wide speculations
  - Rhesus – rotavirus mouse animal model

Prenatal or embryonic form
- 10-25% have associated anomalies (BASM)
- Laterality genes implicated in animal model
**Diagnosis**

- **Blood tests**
  - Evaluate for cholestasis, liver involvement, and impaired function
- **Ultrasound**
- **HIDA scan**
- **Liver Biopsy**
- **Intraoperative cholangiogram**

**Surgical Treatment**

- **Hepatoportoenterostomy**
  - Option if diagnosed in the first 3 months of life
  - Re-establishment of bile flow 30-80%
- **Liver transplant**
  - Even with successful HPE, 70-80% of patients

**Kasai Procedure (KP) or Portoenterostomy**

- [Graph showing percentage of jaundiced-free patients by age at surgery (weeks)]

**ESLD - Clinical picture**

- Jaundice
- Malabsorption of lipids and lipid soluble vitamins → Failure to thrive
- Portal HTN → GI bleeding
- Pruritus
- Hepatosplenomegaly → Hypersplenism
- Ascites, Pleural effusion
- Xanthomas – rare in infancy
- Other organs- Hepatopulmonary Syndrome, Hepatorenal syndrome, Hepatic Encephalopathy....

**ESLD - Biochemical picture**

- High Conjugated bilirubin
- High serum levels of bile salts
- High Alkaline phosphatase & GGT, AST, ALT
- Low or normal GGT – PFIC
  - Bile acid synthesis defects
- Coagulation defect, low albumin
- Electrolyte, minerals, vitamins problems
- Low cell counts
ESLD Management
Supportive therapy:
• Increase bile flow - URSO, Rifampicin
• Elemental MCT rich feeding formulas
• Lipid soluble Vitamins (A,D,E,K) supplements
• Control of pruritus

Pediatric Liver Transplant (OLT)
Liver conditions leading to OLT
• Progressive liver disease → ESLD
• Acute liver failure
  • Benign & malignant liver tumors
  • Metabolic disease

Acute liver failure
◊ Acute onset of coagulopathy, encephalopathy
◊ Indeterminate cause common, infections.....
◊ Hepatic encephalopathy, coagulopathy
◊ Fluid overload, HRS….CVVH/D, plasma exchange

Acute Liver Failure
Acetaminophen Toxicity
• Single dose of 100-150 mg /kg is the risk factor.
• Multiple small doses of therapeutic dosing as a second hit?

Pediatric Liver Transplant (OLT)
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Hepatoblastoma Staging
Liver Transplant for Liver Tumors

- Hepatoblastoma
- Other malignant tumors
- Benign tumors

Pediatric Liver Transplant (OLT)

Liver conditions leading to OLT

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Metabolic Liver Disease

Who has Alpha-1 AT Deficiency?

#1. Alpha-1 AT deficiency is the most common cause of liver transplant in children with metabolic diseases.

#2. Second most common in public after Cystic Fibrosis.

#3. No medical cure yet available.

Progressive Familial Liver Disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive Familial Intrahepatic Cholestasis (PFIC):</td>
<td></td>
</tr>
<tr>
<td>Type 1 (Byler’s disease)</td>
<td>Mutation in P-type ATPase</td>
</tr>
<tr>
<td>Type 2</td>
<td>Absence of sister of P-glycoprotein</td>
</tr>
<tr>
<td>Type 3</td>
<td>Absence of MDR3</td>
</tr>
<tr>
<td>Benign Recurrent Intrahepatic Cholestasis</td>
<td>Mutation in P-type ATPase</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>CFTR gene mutation</td>
</tr>
</tbody>
</table>

Medical Therapy for Tyrosinemia

Pediatric Liver - Heart 2006
Hypercoagulable Disorder

Mitochondrial Disease - OLT

Pediatric Liver Transplant (OLT)
- Liver conditions leading to OLT
- Evaluation & Listing process of the candidates
- Surgery & Current Outcomes

Evaluation process - OLT
- Emergency; Inpatient; Outpatient
- Multidisciplinary team members
- Confirm cause & need for OLT
- No contraindications……

Contraindications - OLT
- Active infection – Sepsis, HIV, etc.
- Progressive disease of other vital organs or systems that may result in demise – brain, heart, lungs, intestine, bone marrow, immune etc.
- Poor psycho-social support
- Severe neuro-developmental deficits unlikely to recover to achieve independent functional state
- Compliance
- Surgical contraindications

Listing process – PELD scoring
Listing process - OLT

- PELD score = (0.436[age]) – 0.687 log [albumin g/dl] + 0.480 log (total bilirubin mg/dl) + 1.857 log [INR] + 0.667 [growth failure]
- Exceptions to the rule......for non-standard patients.
- Acute liver failure – Status 1a or 1b.

Pediatric Liver Transplant (OLT)

- Liver conditions leading to OLT
- Evaluation & Listing process of the candidates
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8 Functional Segments of the Liver
Technical Variants of OLT

- Live Donation of Segments 2 & 3
- Reduced Liver Transplant
- Split Liver Transplant
- Auxiliary Liver Transplant
- Combined Organ Transplants

The New Liver is in and working!
(abg, bile, sugars)

Patient arrives to ICU...

...accompanied by the anesthesiologist and the surgeon, there must be as smooth transition to the ICU. A full report should have details that include:

- Name, age, weight, underlying condition requiring transplantation
- Surgical details type of graft, ABO, type of vascular and biliary anastomosis
- Fluids infused during the OR should be itemized
- Blood losses/urine output
- Most recent ventilatory requirements
- Most recent labs, blood gases etc
- Post operative orders should be completed by the Surgeon (a pre printed sheet) and all orders explained to the ICU fellow/attending and nurses.

Potential Targets for Immunosuppression

Infections After Liver Transplantation

<table>
<thead>
<tr>
<th>Time</th>
<th>Infection Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 mo</td>
<td>Early</td>
</tr>
<tr>
<td></td>
<td>Perforations</td>
</tr>
<tr>
<td></td>
<td>Peritonitis</td>
</tr>
<tr>
<td></td>
<td>Cholangitis</td>
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<tr>
<td></td>
<td>Liver Abscess</td>
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<tr>
<td>1-6 mo</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Viral Reactivation</td>
</tr>
<tr>
<td></td>
<td>CMV</td>
</tr>
<tr>
<td></td>
<td>EBV</td>
</tr>
<tr>
<td>&gt; 6 mo</td>
<td>Late</td>
</tr>
<tr>
<td></td>
<td>EBV-PTLD</td>
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<tr>
<td></td>
<td>Community-acquired</td>
</tr>
<tr>
<td></td>
<td>Opportunistic</td>
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</table>
CMV: Diagnosis

- CMV IgM
- CMV PCR
  - Viral load
- Viral Culture
- Histology

EBV: PTLD

- Incidence: 10%
- More common after primary infection
- Correlated with immunosuppression
- Clinical presentation
  - Mononucleosis-like
  - Disseminated lymphoproliferation
  - Extranodal lymphoma

PTLD: Management

- Reduce immunosuppression
- Antiviral therapy
  - Valganclovir or IV Ganclovir; Acyclovir
  - IgG preparations
- Monoclonal anti-CD 20
- Chemotherapy

Vaccines

Discourage Live Vaccines
- MMR
- Chicken pox
- Live Flu

Encourage Killed & Component Vaccines
- Flu vaccine
- Hepatitis A & B
- Others

Thanks