Neurological Complications following Liver Transplantation

(How to provide them to unfollow?)

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Research Article / Araştırma Makalesi

Evaluation of Neurological Complications Following Living Donor Liver Transplantation

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A High Volume Liver Transplantation Center

- Initial tx in 2002
- Case no:1000 in April 2013
- More than 900 cases since 2008
- 303 cases in 2013
Orthotopic Liver Transplantation

- Unique definitive treatment for end-stage liver disease
  - Acute rejection
  - Ischemic reperfusion injury
  - Technical problems (vascular/biliary anastomosis)

AND

Neurological complications

- 9.7 – 46% following OLT*, **
- Most of them during early postop. period
- Increased mortality, morbidity, hospital/ICU stay, treatment costs


**Liang BC, Neurologic complications of orthotopic liver transplantation. Hospital physician, April 2000; pp43-6
Study Design

- August 2011 till August 2012
- 217 LT
- 29 (13.36%) required neurology consultation due to NEW-ONSET symptom/finding
- Patients with previous/preoperative neurological disorder history excluded
- Complications categorized into:
  - Acute confusion/Encephalopathy
  - Seizures
  - Cerebrovascular disease
## Results

### Demographics & Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group I (%)</th>
<th>Group II (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44.5</td>
<td>34.33</td>
</tr>
<tr>
<td>Male</td>
<td>19 (65.5)</td>
<td>117 (62.73)</td>
</tr>
<tr>
<td>Female</td>
<td>10 (34.5)</td>
<td>71 (37.76)</td>
</tr>
<tr>
<td>HBV</td>
<td>13 (44.8)</td>
<td>55 (29.25)</td>
</tr>
<tr>
<td>Cryptogenic Cirrhosis</td>
<td>3 (10.3)</td>
<td>33 (17.55)</td>
</tr>
<tr>
<td>HCV</td>
<td>3 (10.3)</td>
<td>12 (6.38)</td>
</tr>
</tbody>
</table>
## Results

### Neurological complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute confusion/encephalopathy</td>
<td>19</td>
<td>65.5</td>
</tr>
<tr>
<td>Seizure</td>
<td>8</td>
<td>27.6</td>
</tr>
<tr>
<td>Cerebrovascular disease (ischemic stroke)</td>
<td>2</td>
<td>6.9</td>
</tr>
</tbody>
</table>
Results
statistical analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n=29)</th>
<th>Group II (n=188)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MELD score</td>
<td>22.5</td>
<td>22.6</td>
<td>0.36</td>
</tr>
<tr>
<td>Postop hosp (days)</td>
<td>29.8</td>
<td>10.0</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Mortality</td>
<td>19.65</td>
<td>10.34</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

MELD (model for end stage liver disease)
Encephalopathy

- Most frequent, up to 84%... *
- Presence of preop. Hepatic encephalopathy increases risk
- Most patients undefined aetiology/multifactorial**
  - Central pontine myelinolysis,
  - Subarachnoid bleeding,
  - Infection,
  - Neoplasms

* Liang BC, Neurologic complications of orthotopic liver transplantation. Hospital physician, April 2000; pp43-6
central pontine myelinolysis (osmotic demyelination syndrome)

• Symmetric demyelinating focus most prominent in the central pons
• Initial study population chronic alcoholic and malnourished patients
• Rapid correction of prolonged hyponatremia
• Pathogenesis relates to osmotic injury to the endothelium
• Chronic liver disease patients prone to hyponatremia
• 1 to 8%*

- Unenhanced CT, a large central hypoattenuating focus in the central pons. Axial T1&2 weighted MRI demonstrate a mexican hat shaped signal abnormality in the basal pons with sparring of the tegmental & ventrolat. tissues. Coronal FLAIR sequence increased signal in the hippocampi.
subarachnoid hemorrhage (SAH)

- Usually within 2 months after LT, 40% mortality risk* !!!
- Coagulation disturbance
- Perioperative hypoperfusion, massive transfusion may favour injury
- Older age, hypertension, hyperchol., infections
- 50% patients experiencing haemorrhage have a mortal prognosis*.
- Frontal & parietal lobes


**Liang BC, Neurologic complications of orthotopic liver transplantation. Hospital physician, April 2000; pp43-6
SAH

- Non-enhanced CT after angiography, extensive SAH filling the right sylvian fissure, the interhemispheric fissure and the lateral and 3rd ventricles.
Infections involving CNS 5 to 10%*, **
Mostly occur in the context of cerebral haemorrhage or systemically with subsequent neurological involvement
- Enterococcus......... usually associated
- Candida................. with haemorrhage
- Aspergillus .......... usually not
- CMV...................... associated
- HBV, HCV............. with haemorrhage

**Liang BC, Neurologic complications of orthotopic liver transplantation. Hospital physician, April 2000; pp43-6
infection

- CMV encephalitis MRI T2 scan, white matter change most prominent in a ventricular distribution
infection

- Cerebral aspergillosis, MRI scan, subcortical multiple septic haemorrhagic lesions most prominent on left parietooccipital site
neoplasms

Chronic immunosuppression

Prone to develop CNS lymphoma (B-Cell)

2% of all tx. patients
neoplasms

- CNS lymphoma, MRI T2 weighted, periventricular lesion with enhancement
Seizures

- Second most frequent, 25-46%*
- 50% of cases in first week following LT
- Mostly tonic-clonic in type, may lead to an episode of status
- Usually related to a CNS lesion (CPM, stroke, CNS infection)
- Usually preceded by clinical encephalopathy**
- May result from other complicating conditions (metabolic etc.)
- Usually an indication to search CNS abnormality; encephalopathy, haemorrhage, infection..etc.

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Cerebrovascular Complications

- Ischemic stroke
- 2-6.5% patients
- Focal deficits may be obscured by diffuse encephalopathy
- 2/3 cases mortal
- Anoxia developing patients
- Anoxic ischemic events occur early postop., often preceded by transient/ varies of hypotension
- If haemorrhagic, often associated with bacteremia

Immunosuppression Neurotoxicity

- Revolutionary contribution to tx. Outcomes
- Cyclosporin, FK506 (tacrolimus), OKT3... etc. introduced side effects into clinical practice to challenge
- No assoc. found with high plasma levels of drugs.... neurotoxicity is dose-Independent
- MMF, sirolimus, everolimus...etc recently introduced, up-to-date without severe neurotoxicity
- Cyclosporin 10-30%.... Tacrolimus 32%*

Immunosuppression Neurotoxicity

- FK506: Assoc. with frequent & severe neurol. comp. as well as neprotoxic potential. 2 fold increased risk relatively to cyclosporine. Other severe metabolic toxic effects may involve neurotoxicity*

- Cyclosporine: cyc induced neurotoxicity defined with Confusion, cortical blindness, quadriplegia, seizure, coma. Also may cause a combination of termulousness, restlessness, 50% acute confusional state with psychosis, 20% seizures, 10% apraxia, action myoclonus, cortical blindness*
Thank You...