Altered Mental Status

- Change in level of consciousness
- Change in the level of awareness and the ability to focus, sustain, or shift attention
- Memory difficulties, disorientation, or speech that is tangential, disorganized, or incoherent

(Francis & Young, 2014)
Altered Mental Status in Liver Patients

- Infectious
  - Bacteremia/ Fungemia
  - Sepsis
- Metabolic
  - Electrolyte
  - Glycemic
  - Nutritional
- Organ Failure
  - Kidney failure: uremia
  - Liver failure: encephalopathy
  - Respiratory failure: Hypercarbia/ Hypoxemia
- Iatrogenic
  - Medication
  - Different environment
  - Irregular sleep patterns

Hepatic Encephalopathy

<table>
<thead>
<tr>
<th>Hepatic Encephalopathy Precipitants in Patients with Cirrhosis</th>
<th>Vascular Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Hepatic vein thrombosis</td>
</tr>
<tr>
<td>Narcotics</td>
<td>Portal vein thrombosis</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
</tr>
<tr>
<td>Increased ammonia production or absorption</td>
<td>Portosystemic Shunting</td>
</tr>
<tr>
<td>GI Bleed</td>
<td>Placed shunts</td>
</tr>
<tr>
<td>Infection</td>
<td>Spontaneous shunts</td>
</tr>
<tr>
<td>Metabolic Alkalosis</td>
<td></td>
</tr>
<tr>
<td>Dehydration</td>
<td>Primary HCC</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
</tr>
</tbody>
</table>

Hepatic Encephalopathy: Diagnosis

- History
- Physical Exam:
  - Orientation
  - Asterixis
  - Hyperreflexia
- Cultures
- Labs: AMMONIA level not helpful
- Abdominal u/s with doppler
Hepatic Encephalopathy

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Neuropsychiatric Symptoms</th>
<th>Neurological Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal</td>
<td>No evidence of LOC</td>
<td>Measurable with psychometric testing</td>
<td>No physical exam findings</td>
</tr>
<tr>
<td>Grade I</td>
<td>Slight mental slowing</td>
<td>Irritability; euphoria; Decreased attention span; altered sleep pattern</td>
<td>Fine motor skill impairment</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Fatigue; apathy</td>
<td>Slight disorientation to time</td>
<td>Flapping Tremor, Slurred speech</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Somnolence; confusion</td>
<td>Marked disorientation to time and space</td>
<td>Clonus, asterixis</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Coma</td>
<td>–</td>
<td>Unresponsive to painful stimuli</td>
</tr>
</tbody>
</table>

(Vilstrup, Amodio, Bajaj, & Cordoba, 2014)

Hepatic Encephalopathy: Treatment

- Identifying the underlying cause
  - Diagnose and treat infection
  - Stop GI bleed
  - Correct electrolyte imbalance
  - Stop narcotics and sedatives
  - Identify cancer or vascular occlusion

Post Transplant

- Lower ammonia levels
  - Lactulose
    - Initial treatment, and prophylaxis after an episode has occurred
    - Rectal vs PO
    - 30 gm Q1-2 hours until 2-3 bowel movements, then titrate to 2-3 bowel movements daily
  - Rifaximin
    - Recommended for hepatic encephalopathy refractory to lactulose
    - 550 mg PO BID

(Rahimi, Singal, Cuthbert & Rockey, 2014)

- Polyethylene glycol
  - Small study of 50 patients randomized to either lactulose or polyethylene glycol demonstrated resolution of HE sx.
Altered Mental Status

- Infectious
  - Bacteremia
  - Fungemia
- Metabolic
  - Primary nonfunction
  - Small for size
- Iatrogenic
  - Medication
    - Steroids
    - Calcineurin Inhibitors

Small for Size Syndrome

**Defined**

Clinical syndrome defined by the presence of prolonged cholestasis, coagulopathy and ascites, occurring when a partial liver graft is inadequate to sustain metabolic demand in the recipient.

*Increased portal inflow leads to hepatic congestion*

Small for Size Syndrome

**Criteria**

Size and flow:
- Graft weight to recipient body weight ratio <0.8 & PVF>250 ml/min/100g

Two out of Four:
- Ascites
  - >1000 ml on 3 consecutive days post op week 1 or on day 14
  - >500 ml on POD day 28
- Hyperbilirubinemia
  - >5 on 3 consecutive days post op week 1 or on day 14
- Prolonged PT/INR
  - Uncorrected INR >2 on 3 consecutive days post op week 1
- Altered MS
  - Grade 3/4 hepatic encephalopathy

No other cause for the above

Small for Size Syndrome

**Treatment**

- Decreasing portal inflow
  - Medically
    - Octreotide 50-100 mcg/hr x 5 days
  - Surgically
    - Shunt operation: mesocaval shunt, portacaval shunt and splenorenal shunt
    - Splenectomy
- Increase hepatic vein outflow
  - Surgically
    - Include middle hepatic vein in right lobe grafts
- Hepatic Encephalopathy Tx
- Liver Growth
Steroid Psychosis

Steroid psychosis may manifest as depression, mania, psychosis and delirium
• Incidence is about 22% for neuropsychiatric events
  • 2 fold risk of depression
  • 4-5 x risk of developing mania
  • 4-5 x risk of developing confusion
• Increased risk with underlying psychiatric disorder
• Psychotic symptoms are dose dependent.
  (Fardet, Petersen, Nazareth, 2012)
• Symptoms have been noted to develop in as little as 40 mg /day, but become much more common at 80 mg/day
  (Boston Collaborative Drug Surveillance Program, 1972)
• Diagnosis is largely based on history of exposure.

Steroid Psychosis

Treatment

<table>
<thead>
<tr>
<th>Post-Op</th>
<th>Steroid Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (INTRA-OP)</td>
<td>1000 mg IV x 1</td>
</tr>
<tr>
<td>0 (INTRA-OP)</td>
<td>500 mg IV x 1</td>
</tr>
<tr>
<td>POD 1</td>
<td>200 mg IV x 1</td>
</tr>
<tr>
<td>POD 2</td>
<td>160 mg IV x 1</td>
</tr>
<tr>
<td>POD 3</td>
<td>120 mg IV x 1</td>
</tr>
<tr>
<td>POD 4</td>
<td>80 mg IV x 1</td>
</tr>
<tr>
<td>POD 5</td>
<td>40 mg PO x 1</td>
</tr>
<tr>
<td>POD 6</td>
<td>20 mg x 7 days</td>
</tr>
<tr>
<td>POD 7-13</td>
<td>15 mg PO x 7 days</td>
</tr>
<tr>
<td>POD 14-20</td>
<td>12.5 mg PO x 7 days</td>
</tr>
<tr>
<td>POD 14-20</td>
<td>10 mg PO x 7 days</td>
</tr>
<tr>
<td>POD 21-27</td>
<td>7.5 mg PO x 7 days</td>
</tr>
<tr>
<td>Thereafter</td>
<td>5 mg PO</td>
</tr>
</tbody>
</table>

• Steroid reduction
• Mood stabilizers and antipsychotic
  • Lithium
  • Olanzapine
  • Haloperidol
• SSRI
  • Fluoxetine

Calcineurin Inhibitor Toxicity

May manifest as headache, tremor, neuralgia, neuropathy, hallucinations, ataxia or seizures.
• Incidence for neurological event
  – 10-28% with cyclosporine
  – 21-32% with tacrolimus
  – 18% either
• Recipients of liver transplant more affected than other transplant patients
• Predisposing factors may include:
  – Hepatic encephalopathy pre transplant
  – High MELD going into transplant
  – Lower hgb preoperatively
  – Acute decompensation of chronic liver disease
  – Multiple surgeries
• Not related to dose

Calcineurin Inhibitor Toxicity

Treatment

• Acute alteration:
  – Removal of offending agent
  – Try another CI
  – see steroid psychosis
• Seizures:
  – Phenytoin
  – Levetiracetam
• Headaches/Tremors:
  -Propanolol

(Balderramo, Prieto, Cardenas, Navasa, 2011; Bechstein, 2000)
**PRES**

**Often presents with confusion, agitation. May have concurrent:**
- **Seizure:** Tonic Clonic
- **Headache:** constant, not localized, not relieved with analgesics.
- **Visual disturbances:** neglect, aura, hallucinations

**Physical Exam:**
- Papilledema may be present
- Deep tendon reflexes are brisk
- Babinski sign present
- May have incoordination of the limbs.

**Diagnosis:**
- MRI: hyperintense signal on fluid–attenuated inversion recovery image

**Differential Diagnosis:** PTLD, PML
- Can progress to cerebral edema or hemorrhage and death.

**Treatment**
- **Removal of offending agent**
- **Reduction of offending agent**
- **Substitute other CI with caution**
- **Seizures**
  - Levetiracetam
  - Topiramate
- **Hypertension:**
  - Lower diastolic blood pressure in 2-6 hours to <100 mm Hg, but not > 25% of presenting value
  - Labetolol is often first line

**Infection**

**Infections can result in altered mental status both inside and outside of the CNS. May presented with confusion, agitation, headache or weakness**
- Maybe fungal, viral or bacteria.
- Exposure may be donor-related, recipient-related, nosocomial or community

**Viral:**
- Herpes Simplex Virus (HSV)
- Cytomegalovirus Virus (CMV)
- Varicella zoster virus (VZV)
- Epstein–Barr virus (EBV)
- Human herpes virus 6 (HHV-6)

**Fungal**
- Aspergillosis
- Candida
- Cryptococcus

**Bacterial**

**Treatment**
- **Prophylaxis**
  - CMV: Valganciclovir 900 mg PO BID for 3 or 6 months based on recipient donor risk factors
  - PCP: Trimethoprim/sulfamethoxazole (TMP/SMX) three times weekly for one year
  - Fungal: Fluconazole 100 mg once per week for 6 weeks
- **Treatment**
  - Based on sensitivities
  - Often in collaboration with transplant ID
Dazed and Confused

- Take mental status changes seriously
- Subtle differences can be the beginning of something more serious
- Collaboration with the multidisciplinary healthcare team and patient’s support system is helpful for identification and treatment

References