Neurological Complications following Liver Transplantation

(How to provide them to unfollow ?)

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Research Article / [illegible]

Evaluation of Neurological Complications Following Living Donor Liver Transplantation

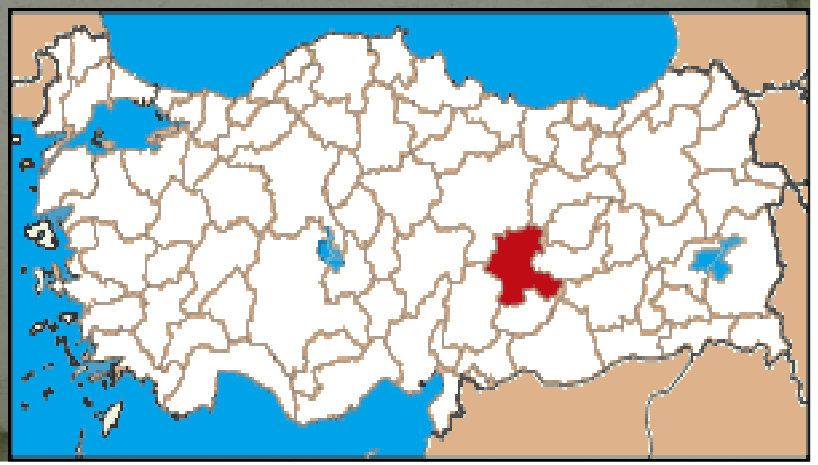
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A High Volume Liver Transplantation Center

- 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 (vasculary/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

*Guarino M, Benito-Leon J, Decruyenaere J. Neurological problems in liver transplantation. Europoan handbook of neurological management, vol 1, 2nd Ed., 2011 Blackwell Pub Ltd

**Liang BC, Neurologic complications of orthotopic liver transplantation.Hospitai 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
  - Cerebrovasculary disease

Results
Demographics & Clinical Characteristics

Characteristic	Group I (%)	Group II (%)
Age	44,5	34,33
Male	19 (65,5)	117 (62,73)
Female	10 (34,5)	71 (37,76)
HBV	13 (44,8)	55 (29,25)
Cryptogenic Cirrhosis	3 (10,3)	33 (17,55)
HCV	3 (10,3)	12 (6,38)

Results
neurological complications

Complication	N	%
Acute confusion/encephalopathy	19	65,5
Seizure	8	27,6
Cerebrovasculary disease (ischemic stroke)	2	6,9

Results
statistical analysis

Parameter	Group I (n=29)	Group II (n=188)	P value
MELD score	22,5	22,6	0,36
Postop hosp (days)	29,8	10,0	< 0,001*
Mortality	19,65	10,34	< 0,001*

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

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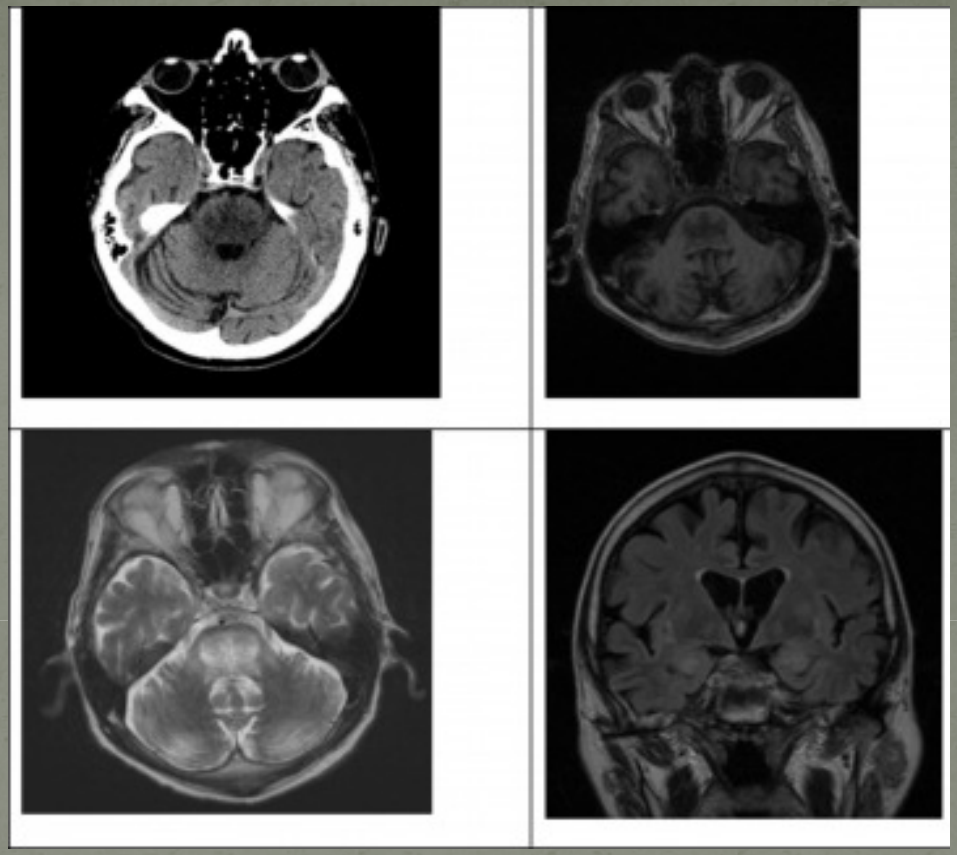
** Power C, Poland SD, Kassim KH et al. Encephalopathy in liver transplantation: neuropathology and CMV infection. Can Neurol Sci 1990; 17:378-81

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%*

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cpm



- 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

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SAH



- Non-enhanced CT after angiography, extensive SAH filling the right sylvian fissure, the interhemispheric fissure and the lateral and 3rd ventricles.

infection

- 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

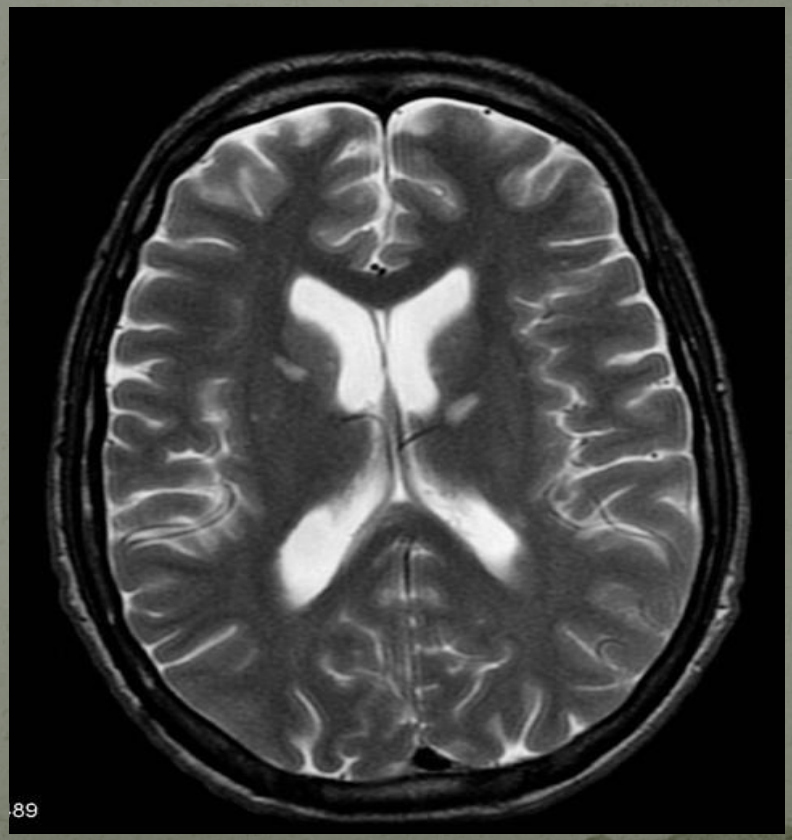
  - Aspergillus ……. usually not
  - CMV…… associated
  - HBV, HCV…… with haemorrhage

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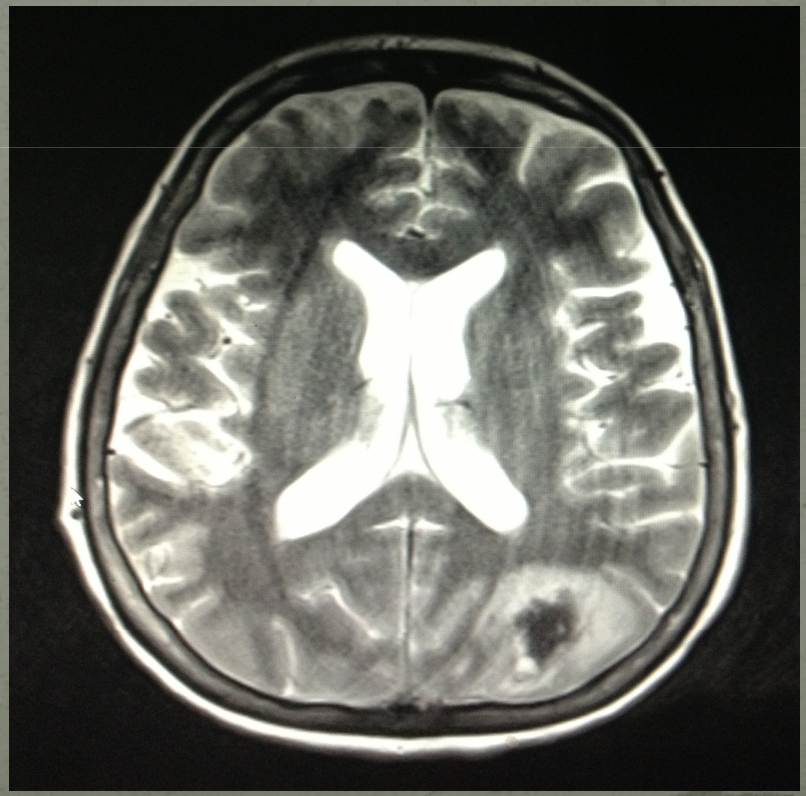
infection

- 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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** Choi EJ, Lee SA, Kim KH et al. New-onset seizures after liver transplantation: clinical implications and prognosis in survivors.Eur Neurol 2004; 52: 230-6



Cerebrovasculary 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 preceeded by transient/ varies of hypotension
- If haemorrhagic, often associated with bacteremia

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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%*

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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...

