Hepatic Coma

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Thanks for Invitation

Nothing to declare

We will cover

Definitions: HE vs H Coma
2 Types of HE in ER
Urgent mx in ER
Practical points

WE will NOT cover

Detailed Physiology and Pathophysiology

MECHANISM OF COMA

DIFFICULT ALGORRHYTMS

ABC MX IN ER

Post liver transplant HE

Patterns of Coma

Structural Brain leasion

Supretentorial Pattern

Infratentorial Pattern

Metabolic

Psychogenic

Causes of Metabolic Coma

Hepatic Encephalopathy

Uremic Encepahalopathy

Septic Encepahlopathy

Hypoglycemia

Resp: hypoxia or hypercarbia

Electrolyte imbalance: hyponatremia, hypercalcemia

Endocrine: myxedemic coma

Toxins and drugs

Metabolic Pattern of Coma

- Generally have no localizing sign that can be explained by specific area of the brain
- Pathology affect the brain a whole
- Same area of brain may do well one f and do bad other f
- EEG findings is generalized slowing – no localization
- Many times has motor component ex tremor, asterexis

Hepatic Encephalopathy vs Coma

Hepatic encephalopathy (HE) is defined as

Mental or neuromotor dysfunction

Due to

Acute or chronic liver disease

ALF is much less frequent that Cirrhotic CLF

Hepatic encephalopathy occurs with both acute and chronic liver failure

HE is more common and rapidly progressive in ALF

HE in Acute Liver Disease

Rare Disease

6-7 cases / day in US

Commonest causes

Drug overdose Paracetamol

Fulminant viral hepatitis

HE in Acute Liver Disease

Classical

Coagulopathy
Abnormal LFT
? High lactate
? Jaundice
+/- CNS

HE can rapidly progress to
Seizures
Coma
Death

HE in Acute Liver Disease

Adminster NAC

Oral NAC:

140 mg/kg loading dose, then 70 mg/kg every 4 hours until discontinued by GI physician

IV NAC:

150 mg/kg loading dose, then 50 mg/kg IV over 4 hr, then 100 mg/kg IV over 16 hr until discontinued by GI physician

Safe

SE Nausea, vomiting, bronchospasm

HE complicating Cirrhosis

Cirrhosis

Ranking 12th cause of death in US

6% of all deaths in US

Primarily needs long-term outpatient mx

HE complicating Cirrhosis

How often

Common

1/3 overt

1/3 subclinical

1/3 no HE

Cirrotics Present to ED because of

Hepatic Encephalopathy

Variceal Hemorrhage

Spontaneous Bacterial Peritonitis

Symptomatic Ascites

Hepatorenal Syndrome

Hepatopulmonary Syndrome

Other cause not related to Liver

HE complicating Cirrhosis

Acute encephalopathy on top of chronic disease

Commonly there is a precipitating factor

Medications

GI hemorrhage

Infection ex SBP

Big Protein Meal (Meat Intoxication)

Electrolyte disturbance (low K)

Pathophysiology

Ammonia increase in the 2 types of HE

No strong correlation between ammonia levels and stage or degree of encephalopathy

Tip of iceberg ?

Relation between GUT, Liver, Kdneys and BBB

Ammonia

Production:

Mainly in the intestine:

- colonic breakdown of nitrogenous compounds
- enterocytic catabolism of amino acids

Less: kidneys and skeletal muscle

Metabolism: Mainly in the Liver

Excretion: Kidneys and colon

Ammonia increased in Renal Diseases

Shunting of blood around the liver increases serum ammonia levels in cirrhotic patients

Various Clinical Scenarios of HE

Form	Precipitating Factors	Clinical Course	Reversibility
Acute	+	Short*	± ***
Recurrent	±	Short	+
Persistent	--	Continuous	--
Subclinical	--	Insidious	--

*** May be fatal or irreversible as in fulminant hepatic failure.

Grades of Hepatic Encephalopathy

Grade I: Changes in behavior
Minimal change in consciousness

Grade II: Gross disorientation
drowsiness
possibly asterixis and inappropriate behavior

Grade III: Marked confusion
Incoherent speech
Sleeping most of the time but arousable to vocal stimuli

Grade IV: Hepatic Coma
Unresponsive to pain
Decorticate or decerebrate posturing

Adapted by the American Association for the Study of Liver Diseases from criteria of **Conn et al**

West Haven Criteria of Altered Mental Status in HE

Stage	Consciousness	Intellect and Behavior	Neurological Findings
0 **Subclinical**	Normal	Normal	Normal examination Impaired psychomotor testing
1	Mild lack of awareness	Shortened attention span Impaired addition or subtraction	Mild asterixis or tremor
2	Lethargic	Disoriented Inappropriate behavior	Obvious asterixis Slurred speech
3	Somnolent but arousable	Gross disorientation Bizarre behavior	Muscular rigidity and clonus Hyperreflexia
4	Coma	Coma	Decerebrate posturing

If GCS = or < 11

Severe HE

DD of HE

Metabolic

- ↑↓ Glucose
- ↑↓ Ca
- ↓ K
- ↓ O2
- ↑ CO2
- ↑ Urea

Toxic

- Alcohol intoxication
- Alcohol withdrawal
- CO poisoning
- Drug Abuse
- Medications

CNS

- **Stroke**
  - Bleed or infarction
- **Infection**
  - Absces meningitis
  - Encephalitis
- **TBI**
- **Br Tumor**

Diagnosis of HE

Usually Clinical Picture very Sugestive

Asterexix

ABG – Resp Alkalosis

Lactate

Diagnosis of Exclusion

CBC

Biocemistry

CT

EEG

LP ?

?improvent

Checking for Ammonia

Arterial better reflects BBB level

Inconsistent

No correlation between level and HE severity

Useful to confirm liver disease when suspected

DD

Renal failure

Precipitating Factor

After Dx

Look for in all cirrhotic with HE

Precipitating Factors in Hepatic Encephalopathy in Cirrhotic p

- **Gastrointestinal bleeding** (PR / gastric tube if confused + doubt)
- **Sepsis (UTI, spontaneous bacterial peritonitis)**
- **Post TIPSS**
- Anemia
- Azotemia, uremia
- Constipation
- Dehydration
- Excessive dietary protein
- Hepatocellular carcinoma
- Hypokalemia, metabolic alkalosis
- Hypoglycemia
- Hypothyroidism
- Hypoxia
- Medications (e.g., narcotics, sedatives)

HE Diagnostic Pearls

Diagnosis of exclusion

Ammonia can be helpful but not good for screening

Resp Alkalosis consistent

Hospitalized HE : precipitating factor search essential

Mx

Provide supportive care

Correct precipitating factors

Reduce nitrogen load in GIT

Assess the need for long-term therapy

Supportive Care

Ensure patient safety

Extra nursing

Frequent monitoring of mental status

Low grade HE patients to monitored Bed

ICU admission for higher grade and comatose

ALF with any degree of CNS dysf = ICU

ETT in ALF = avoid hypoventilation

Supportive Care

Feeding:

- Appropriate enteral nutrition as soon as feasible
- By mouth or by NGT
- Avoid prolonged fasting
- Restrict dietary protein in acute HE
- Long nitrogen restriction can cause malnutrition

Correct precipitating factors

Essential

Not always easy

Hepatic failure has multiorgan impact

Reducing Nitrogen Load in GIT

LACTULOSE — first line rx

Dosing

Immediate

Oral: 45 ml first dose
Followed by 45 ml q1-2 hr till b.m. occurs
After 1st motion aim is 2-3 soft motions / day
Usual dose 15-45 mls q6-12 hr

Or Enema: 300mL in 1L of water
Should be retained for 1 hr
Can be repeated q 4-6 hr

Chronic — Oral only 15-45 ml q 6-12 hr

Side Effects

Diarrhea, flatulence, cramps

Reducing Nitrogen Load in GIT

ANTIBIOTICS
Add-On Rx

	Dose Acute	Dose Chronic	Side Effects
Metronidazole	250 mg PO q8-12hr	Same dose Avoid high dose for long time	Peripheral Neuropathy Relatively common in long high doses
Rifaximin	400 mg PO q8hr	Same	Rare: flatulence, constipation, periph edema
Neomycin	(3-6 gm/d) 1000 mg PO q4-8hr	(1-2 gm/d) 500 mg PO q6-12hr	Rare: nephrotoxicity, ototoxicity on long term use

Summary of Treatment of HE

1. **Objectives:**
   - Supportive care
   - Correct any precipitating factors
   - Reduce the nitrogen load in the gastrointestinal tract
   - Refer to appropriate facility
2. **Lactulose** is generally considered first-line therapy for acute and chronic HE
3. **Antibiotics** are second-line therapy for HE, but they can have many potential side effects and complications
4. **Rifaximin** was FDA approved in 2004 for use in Traveller's diarrhea and in 2010 for PX of HE used in combination with lactulose, less side effects than other antibiotics
5. **Overt HE** is a poor prognostic indicator

Counseling

Precipitating factors avoidance: ex constipation and psychoactive medications

Medication compliance: ex lactulose, antibiotics

Higher risk of motor vehicle accidents

Referral to a liver specialist and to transplant center after the first episode of overt encephalopathy

The ultimate therapy for cirrhosis and HE is orthotopic liver transplantation

Prognosis

Some forms are reversible

Generally overt HE carries a poor prognosis

Recovery and recurrence rates are variable

Without liver transplantation only 40% alive at 1-year

Acute and chronic HE deteriorating to stage 4 (Hepatic Coma) is associated with an 80% overall mortality

PEARLS

Check for low sugar if sz or low GCS

HE and Liver failure not for ordinary ward

Checking for paracetamol even if p denies

No subclavian line if INR high

Piritoneal fluid culture even if afebrile

PEARLS

Antibiotics needed always with variceal hmg

Alcoholic ER reg visitor easily be missed when HE

Avoid Diazepam or lorazepam when agitated

All ALF should go to ICU even if looks stable

Transplant center informed ASAP if ALF

PEARLS

HE = Admission

Family story on baseline mental f essential to dx HE

Many Thanks