

LIVER FAILURE

Last reviewed 01/16/2020; Reviewers: Naresh Veerabattini, MBBS

PRESENTING COMPLAINT: Yellowish discoloration of skin and sclera, abdominal distention, abdominal pain

FINDINGS

- **A** Check ability to protect airways, secretions
- **B** Normal, ↑RR or ↓RR as part of Cushing's triad
- **C** ↓BP, ↓HR
- **D** Variable altered (V,P,U,D)* : confusion, agitation, slurred speech, disordered sleep, altered mental state, unresponsive to pain, coma, dilated pupils, asterixis
- **E** Abdominal distention +/- ascites, jaundice, vesicular skin lesions, RUQ tenderness, spider angiomas, asterixis, pruritus, fever
- **L_{PC}**
 - a) LFT- ↑PT&INR, ↑Aminotransferase levels, ↑Bilirubin
 - b) Other- ↑Creatine & BUN, ↑amylase & lipase, ↓ blood glucose, ABG, Hypophosphatemia, Hypomagnesemia, Hypokalemia, Hyponatremia, Acidosis or alkalosis, ↑NH₃, ↑LDH.
 - c) Specific diagnosis- Acetaminophen:- very high aminotransferase levels(>3500 IU/L), acetaminophen level, low bilirubin, high INR.
- **U_{PC}** Ascites, hepatomegaly/altered echotexture of the liver

***V** (verbal), **P** (pain), **U** (unconsciousness), **D** (delirious)

U_{PC} (point of care ultrasound) **L_{PC}** (point of care labs)

OTHER HISTORY

Nausea, vomiting, malaise, drowsy

DIFFERENTIAL DIAGNOSIS

Acute liver failure (drugs, poisoning), acute on chronic liver failure (underlying cirrhosis, usually precipitated by bleeding/infection), ischemic hepatic injury: very high aminotransferase levels (25 to 250 times the upper limit of normal), ↑ serum LDH levels, Hepatitis A, B (Aminotransferase levels of 1000-2000 IU/L are common, ALT>AST), acute fatty liver of pregnancy/HELLP syndrome (Aminotransferase levels<1000 IU/L, ↑ bilirubin, low platelet count)

OTHER INVESTIGATIONS

- **History:**(new) drug/medication intake, alcohol (ab)use, mushroom ingestion, herbal or dietary supplements, illicit drug use and other risk factors for hepatitis B, hematemesis/melena or signs of

gastrointestinal hemorrhage, diarrhea (hepatitis A?), malignancy, exposition (heat, trauma, surgery), pregnancy

- **Labs:** blood sugar, coagulation tests (\uparrow prothrombin time and INR >1.5), elevated liver enzymes, elevated ammonia level, serum lactate dehydrogenase, RFT (hepato-renal syndrome), blood count (low platelets), electrolytes, viral hepatitis serology, acetaminophen serum concentration, toxicology screen, blood gases, lactate levels, pregnancy test, multisite cultures, fungal cultures
- **Monitoring:** Hemodynamic and respiratory status, level of consciousness (GCS or AVPU), urine output, ICP monitoring, serial coagulation tests, serial glucose, serial lactate measurements
- **Imaging:**
 - **Doppler-sonography or abdominal computed tomography:** differentiate etiology (steatosis, cirrhosis, ascites, neoplasia, Budd-Chiari syndrome, portal hypertension)
 - **CT head, consider EEG:** assess cerebral impairment
 - **Chest radiographs:** assess for edema, aspiration, or infiltrates.
 - Transthoracic echocardiography with agitated saline/colloid: confirm transpulmonary right-to-left shunt in hepatopulmonary syndrome

Other Tests: Diagnostic paracentesis if ascites (white cell count, biochemical analysis, microbiological cultures)

Severity Scores: MELD/Child Pugh-Score (prognosis, need for liver transplantation)

Alcoholic hepatitis: consider Maddrey's Discriminant Function (steroids if >32 points)

THERAPEUTIC INTERVENTIONS

- **Based on findings/ etiology:**
 - **Hemodynamic instability/ shock:** Fluid resuscitation (consider 5% albumin) + vasopressors; consider hydrocortisone particularly in patients with septic shock and cirrhosis
 - **Airway compromise and/or respiratory insufficiency: endotracheal intubation**
 - **Reduced level of consciousness:** Prevent/minimize stimulation, avoid temperatures $>38^{\circ}\text{C}$, head of the bed elevation, optimal fluid balance, sedation/analgesia.
 - Lactulose + Rifaximin for encephalopathy in acute on chronic liver failure
 - If ICP crisis: hyperosmotic agents (e.g., mannitol or hypertonic saline), hyperventilation, barbiturate coma, indomethacin bolus (25 mg IV over one minute).
 - **Oliguria** (hepatorenal syndrome): terlipressin or vasopressin (or oral midodrine) plus albumin +/- octreotide
 - **Electrolyte** (hypokalemia, hyponatremia, hypophosphatemia) and metabolic abnormalities (hypoglycemia): correct (hypokalemia can aggravate encephalopathy! slow correction of hyponatremia to prevent osmotic demyelination syndrome)

- **Active bleeding/before invasive interventions:** Fresh frozen plasma, platelet transfusion; cryoprecipitate if low fibrinogen; avoid administration of fresh frozen plasma in non-bleeding patients to allow for better prognostication; consider Factor VIIa if active bleeding in patients unresponsive to FFP or who are already fluid overloaded.
- **Ascites:** Therapeutic paracentesis with albumin replacement to decrease intraabdominal pressure and improve respiration/hemodynamics/renal perfusion pressure
- **Infection/Sepsis:** Early empiric broad-spectrum antibiotics/ antifungals (if suspected infection, or prophylactically if patient very sick/awaiting transplant)
- **Gastrointestinal Bleeding:** hemorrhage control and prevention of re-bleeding (e.g., terlipressin in variceal hemorrhage)
- **Therapeutic Drug-induced:** stop/avoid hepatotoxic drugs
- **(Suspected) Acetaminophen intoxication:** start early high-dose N-acetylcysteine therapy (IV dose: Loading dose: 150 mg/kg over 1 h; 50 mg/kg over 4 hrs; then 100 mg/kg over 16 hrs; may also be considered in non-acetaminophen-induced acute liver failure)
- **Hepatitis B, (C), D:** antiviral therapy
- **Mushroom (Amanita phalloides) poisoning:** charcoal, high-dose IV penicillin (1,000,000 IU/kg for the first day, then 500,000 IU/kg for the next two days) or IV silibinin (20–50 mg/kg/day for 48-96 hours)
- **HELLP/acute fatty liver of pregnancy:** delivery
- **Portal vein thrombosis/Budd-Chiari syndrome:** therapeutic anticoagulation, consider local thrombolysis in Budd-Chiari syndrome
- **Autoimmune hepatitis:** steroids and/or plasma exchange
- **Wilson's disease:** penicillamine, consider plasma exchange
- **Hemochromatosis:** phlebotomy, deferoxamine
- **Rejection:** immunosuppression, consult with the transplant surgeon
- **Experimental (for acute liver failure):** plasma exchange, MARS (acute on chronic liver failure)

Consult: Hepatology, Nephrology

MANAGEMENT AFTER STABILIZATION

- **Further Diagnostics:**
 - **Labs:** Serial coagulation tests; repeat blood counts, metabolic tests, and ABG; repeat cultures if worsening or suspected infection
 - **Non-emergent liver biopsy:** consider if indeterminate etiology
 - **Further Treatment:** Consider **lactulose** and/or selective digestive decontamination (if encephalopathy), **renal replacement therapy** (if acute renal failure, hyperammonemia, and/or

fluid overload), **treat alcohol withdrawal**, emergent liver **transplantation**, and transfer to transplant center if indicated (e.g., King's College criteria, factor V + encephalopathy grade), transcranial Doppler/ICP monitoring if acute neurological deterioration or persistent severe encephalopathy

- **Reassess antibiotics:** adapt treatment to Gram stain findings and culture results
- **Prophylaxis & Nutrition:** Stress **ulcer prophylaxis**; early initiation of enteral nutrition; avoid protein restriction and underfeeding (achieve the caloric target by enteral nutrition as soon as possible!)

CAUTIONS

- **Treatment: AVOID** 1. overhydration (cerebral edema and pulmonary edema), 2. oversedation (benzodiazepines and opioids may have markedly prolonged effects and can aggravate encephalopathy; use propofol), 3. therapeutic hypothermia (in patients with high-grade encephalopathy and increased ICP), 4. **too much lactulose** (can cause bowel distension, diarrhea, electrolyte abnormalities, and dehydration), 5. intravenous contrast for CT or nephrotoxic medications ((e.g. antibiotics) due to increased risk of renal failure (hepatorenal syndrome)), 6. sensorial stimulations: may increase intracranial pressure.
- **End-stage liver disease major complications**
 - Hepatic Encephalopathy: Give lactulose and rifaximin PO
 - Hepatopulmonary syndrome: Give O2 and consider shunt embolization
 - Portopulmonary hypertension: Give pulmonary vasodilators
 - Hydrothorax: Thoracentesis, TIPS, diuretics
 - Varices: EGD/banding, PPI, octreotide, TIPS, temporary balloon tamponade
 - Hepatorenal syndrome: Albumin, vasopressors, octreotide, midodrine, dialysis
 - Spontaneous bacterial peritonitis: Do an abdominal paracentesis, send the ascitic fluid bacterial culture and PMN count, if ascitic fluid PMN count >250/mm³, give empiric antibiotic like cefotaxime 2 gm IV q8hr, albumin 1.5 g/kg at diagnosis followed by 1 g/kg on day 3

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