Acute Liver Failure

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Rapidly progressive (<8 wks/UNOS), often fatal syndrome characterized by
- Altered mentation/encephalopathy
- Coagulopathy (INR >2.0)
- Jaundice

Time frame <24-26 weeks
- Hyperacute: <7 days from presentation to encephalopathy
- Acute: 7-21 days to encephalopathy
- Subacute: 21 days-26 weeks to encephalopathy, often developing renal failure and portal hypertension

No prior history of chronic liver disease or cirrhosis
- Wilson’s disease can be considered ALF for listing purposes even with known history or cirrhosis
- Autoimmune hepatitis or vertically acquired HBV often presents with ALF
  - Not previously recognized
  - Recognized but medications stopped
ALF: Summary of a Workshop

- Relatively rare disease: 2000 cases/year
- Accounts for ~4-5% of all transplant listings
- Etiology not identified 15% adults/50% peds
- Course variable with high mortality
- 45% spontaneously recover
- 25% transplanted
- 30% death (sepsis and cerebral edema)

Etiology of ALF in Adults

Lee WM et al, Hepatol 2008

Bari et al, Prac Gastro & Hep 2016
Baseline Characteristics

<table>
<thead>
<tr>
<th>Feature</th>
<th>Acetaminophen (n = 532)</th>
<th>Drugs (n = 133)</th>
<th>Indeterminate (n = 161)</th>
<th>Hepatitis A (n = 31)</th>
<th>Hepatitis B (n = 83)</th>
<th>All Others (n = 297)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>37 (28-45)</td>
<td>46 (33-56)</td>
<td>38 (26-50)</td>
<td>47 (40-57)</td>
<td>42 (29-54)</td>
<td>42 (29-56)</td>
</tr>
<tr>
<td>Female Sex</td>
<td>76%</td>
<td>67%</td>
<td>58%</td>
<td>45%</td>
<td>42%</td>
<td>76%</td>
</tr>
<tr>
<td>Jaundice to Coma (days)*</td>
<td>0 (0-1)</td>
<td>9 (3-20)</td>
<td>9 (2-20)</td>
<td>3 (1-8)</td>
<td>7 (2-14)</td>
<td>7 (1-17)</td>
</tr>
<tr>
<td>Coma grade ≥ 3</td>
<td>52%</td>
<td>38%</td>
<td>50%</td>
<td>55%</td>
<td>54%</td>
<td>41%</td>
</tr>
<tr>
<td>ALT (U/L)*</td>
<td>4067 (2138-6731)</td>
<td>600 (260-1537)</td>
<td>847 (396-2111)</td>
<td>2404 (1367-3333)</td>
<td>1707 (745-2815)</td>
<td>650 (172-1867)</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)*</td>
<td>4.5 (2.9-6.6)</td>
<td>20.2 (12.1-28.3)</td>
<td>23.0 (9.2-25.7)</td>
<td>11.9 (9.7-27.5)</td>
<td>19.7 (12.4-26.6)</td>
<td>15.3 (6.3-26.7)</td>
</tr>
<tr>
<td>Spontaneous Survival</td>
<td>65%</td>
<td>29%</td>
<td>25%</td>
<td>58%</td>
<td>25%</td>
<td>34%</td>
</tr>
<tr>
<td>Transplantation</td>
<td>9%</td>
<td>41%</td>
<td>43%</td>
<td>29%</td>
<td>47%</td>
<td>33%</td>
</tr>
<tr>
<td>Death Without</td>
<td>26%</td>
<td>31%</td>
<td>32%</td>
<td>13%</td>
<td>28%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Summated and updated (after the workshop) from the AIF Study Group database, 1998-2007.1,4

* Median values (Q1, Q3).

Lee WM et al, Hepatol 2008

Clinical Pearls

- HEV: travel to Eastern Europe, Asia, India, Mexico. More severe in pregnancy
- HSV: neonates or pregnancy, steroid use, HIV, cancer, myelodysplastic syndromes. URI and hepatitis, no rash in 50%. Treat early with acyclovir
- VZV: immunosuppressed, hepatitis may predate rash or occasionally no rash
- Aminita phalloides: severe GI symptoms (N/V/D) within hours to a day from ingestion, liver injury 2 days later
- Wilsons: very low alk phos or uric acid, Bili: alk phos >2, Coombs negative hemolytic anemia with bili >20 ng/mL
Role of Liver Biopsy

- Always do transjugular route
- Unreliable in predicting clinical outcomes
- Not recommended in most cases
- Consider when autoimmune hepatitis, metastatic cancer (breast, small cell lung, melanoma), myeloma, lymphoma, or HSV suspected

Lee et al, Hep 2011; Flamm et al, Gastro 2017

Therapies

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Potential therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOXIC</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>N-acetyl cysteine</td>
</tr>
<tr>
<td>Amanita poisoning</td>
<td>Charcoal, penicillin, silibinin</td>
</tr>
<tr>
<td>VIRAL</td>
<td></td>
</tr>
<tr>
<td>Herpes simplex virus</td>
<td>Acyclovir</td>
</tr>
<tr>
<td>Acute hepatitis B</td>
<td>Nucleos(t)ide</td>
</tr>
<tr>
<td>METABOLIC</td>
<td></td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>Copper chelation, plasmapheresis, antioxidant</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>VASCULAR</td>
<td></td>
</tr>
<tr>
<td>Acute Budd Chiari</td>
<td>Directed thrombolysis, TIPS</td>
</tr>
<tr>
<td>PREGNANCY</td>
<td></td>
</tr>
<tr>
<td>Acute fatty liver of pregnancy/HELLP</td>
<td>Urgent delivery</td>
</tr>
</tbody>
</table>
Acetaminophen

- Still a large problem in US (especially combination narcotic/APAP)
- ~50/50 suicidal vs unintentional
- Relatively low mortality compared to other ALF cases
- 19% of indeterminant cases had APAP adduct level at 7 days

Table 2. Comparison of Intentional and Unintentional Acetaminophen Overdose

<table>
<thead>
<tr>
<th>Feature</th>
<th>Intentional (n = 122)</th>
<th>Unintentional (n = 131)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>34 (17-68)</td>
<td>38 (18-76)</td>
<td>NS</td>
</tr>
<tr>
<td>Female Sex</td>
<td>74%</td>
<td>73%</td>
<td>NS</td>
</tr>
<tr>
<td>Total Dose (grams)*</td>
<td>25 (1.2-90)</td>
<td>20 (2.5-180)</td>
<td>NS</td>
</tr>
<tr>
<td>Dose per day (grams)*</td>
<td>25 (1.2-90)</td>
<td>7.5 (1.0-7.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Coma Score ≥ 3</td>
<td>39%</td>
<td>55%</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum ALT (U/L)*</td>
<td>5326 (179-19,826)</td>
<td>3319 (176-18,079)</td>
<td>NS</td>
</tr>
<tr>
<td>History of depression</td>
<td>45%</td>
<td>24%</td>
<td>NS</td>
</tr>
<tr>
<td>Antidepressant use</td>
<td>38%</td>
<td>37%</td>
<td>NS</td>
</tr>
<tr>
<td>Narcotic compound</td>
<td>18%</td>
<td>63%</td>
<td>NS</td>
</tr>
<tr>
<td>Multiple preparations</td>
<td>5%</td>
<td>38%</td>
<td>NS</td>
</tr>
<tr>
<td>Spontaneous use</td>
<td>66%</td>
<td>64%</td>
<td>NS</td>
</tr>
<tr>
<td>Transplantation</td>
<td>7%</td>
<td>9%</td>
<td>NS</td>
</tr>
<tr>
<td>Death without</td>
<td>27%</td>
<td>27%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Summarized from reference 50 on a prospective consecutive series of 275 cases of ALF due to acetaminophen overdose, in 22 of whom the intent could not be determined.

* Median values (range).
Treatment of APAP Hepatotoxicity

- Activated charcoal if within a few hours
  - Best of <1 hour, reasonable up to 3-4 hours
  - 1 gm/kg oral slurry
- Initiate NAC (preferably IV)
  - No prospective studies to support benefit if >24 hours
  - Often given up to 72 hrs after ingestion
  - 150 mg/kg IV load followed by gtt
  - Controversial stop at 72 hrs vs liver recover
  - Side effects: allergic reaction, bronchospasm, asthma

NAC for Non-APAP ALF?

- Prospective trial of 173 patients with primary endpoint of overall survival at 3 weeks
  - 70% NAC vs 66% placebo (not significant)
- Transplant free survival 40% vs 72%
  - Confined to encephalopathy grade 1-2
    - 52% NAC vs 30% placebo
    - Worse in encephalopathy grade 3-4
      - 9% NAC vs 22% placebo
  - Transplant rate lower 32% NAC vs 45% placebo (not significant)

Lee WM et al, Gastro 2009
NAC for Non-APAP ALF?

- **NAC may improve spontaneous survival**
  - When given during early encephalopathy grade 1-2
  - DILI and HBV may benefit
  - Large amount of idiopathic cases are unknown APAP

- **Guidelines:**
  - AASLD: use in cases where it is possible APAP could be involved, for DILI may be beneficial
  - EASL: use in early stage in all ALF
  - AGA: use in non-APAP ALF only in context of clinical trials

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Drug Induced Liver Injury

- Most drug induced liver injuries occur within first 6 months of administration
- Generally patients present in a subacute fashion
  - Lower AST/ALT, higher bilirubin
  - Portal hypertension and shrunken nodular liver mimicking cirrhosis
  - Unfavorable transplant-free survival
  - 94% post transplant survival
- Corticosteroids are only indicated if there is also a hypersensitivity reaction (DRESS) or autoimmune reaction
Drug Induced Liver Injury

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### Table 3. Some Drugs Which May Cause Idiosyncratic Liver Injury Leading to ALF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Some herbal products/dietary supplements that have been associated with hepatotoxicity include:</td>
</tr>
<tr>
<td>Sulfaizaline</td>
<td>- Kava Kava</td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td>- Herbalife</td>
</tr>
<tr>
<td>Phenylpropanolide</td>
<td>- Hydroxycto</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>- Comfrey</td>
</tr>
<tr>
<td>Piroxicam sodium</td>
<td>- Senecio</td>
</tr>
<tr>
<td>Nifurtimone</td>
<td>- Greater celandine</td>
</tr>
<tr>
<td>Diethylamino</td>
<td>- He Shoon Wu</td>
</tr>
<tr>
<td>Didiostatol</td>
<td>- LipoKinetix</td>
</tr>
<tr>
<td>Didiostatol sodium</td>
<td>- Ma Huang</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>- Ceruloplasmin can be normal in up to 15% (and low in 50% of ALF from other causes)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>- Kayser-Fleischer rings present in 50%</td>
</tr>
<tr>
<td>Dapsone</td>
<td>- Treatment</td>
</tr>
<tr>
<td>Etodolac</td>
<td>- Can attempt to acutely lower copper to prevent further hemolysis with albumin dialysis, plasmapheresis, plasma exchange</td>
</tr>
<tr>
<td>Didanosine</td>
<td>- Do not attempt chelating agents</td>
</tr>
<tr>
<td>Darunavir</td>
<td>- Transplant</td>
</tr>
<tr>
<td>Darunavir sodium</td>
<td>- Combination agents with enhanced toxicity:</td>
</tr>
<tr>
<td>Carbenazepine</td>
<td>- Trimethoprim-sulfamethazine</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>- Rifampin-isonia</td>
</tr>
<tr>
<td>Amoxicillin-cavulanate</td>
<td></td>
</tr>
</tbody>
</table>

**Clues to diagnosis**

- Coombs negative hemolytic anemia and bilirubin >20 mg/dL
- Very low alkaline phosphatase and/or uric acid
- Bili:alk phos ratio >2
- Ceruloplasmin can be normal in up to 15% (and low in 50% of ALF from other causes)
- Kayser-Fleischer rings present in 50%

**Treatment**

- Can attempt to acutely lower copper to prevent further hemolysis with albumin dialysis, plasmapheresis, plasma exchange
- Do not attempt chelating agents
- Transplant

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Wilson Disease

- Nearly uniformly fatal without transplant
- UNOS exception 1A can be assigned even with known prior liver disease or cirrhosis present
- Clues to diagnosis
  - Coombs negative hemolytic anemia and bilirubin >20 mg/dL
  - Very low alkaline phosphatase and/or uric acid
  - Bili:alk phos ratio >2
  - Ceruloplasmin can be normal in up to 15% (and low in 50% of ALF from other causes)
  - Kayser-Fleischer rings present in 50%
- Treatment
  - Can attempt to acutely lower copper to prevent further hemolysis with albumin dialysis, plasmapheresis, plasma exchange
  - Do not attempt chelating agents
  - Transplant
Autoimmune Hepatitis

- May account for up to 30% of indeterminant cases
  - 25-39% ANA negative or weakly positive and normal IgG
  - Liver biopsy can be helpful
- Consider corticosteroids for some with early stage ALF without multi-organ failure
  - Prednisone or prednisolone 40-60 mg/d
  - Methylprednisolone 60 mg IV/d
  - Do not treat indefinitely
- Septic complications from steroids can jeopardize transplant
  - if multilobular necrosis and failure to improve within 2 weeks, stop steroids
  - Jaundice and failure to improve MELD by 2 points in 7 days, stop steroids

Aminita Phalloides Poisoning

- “Death Cap” mushroom, found mainly summer and autumn
- Ingestion of 30g (1 oz) or ½ cap likely lethal without transplant
- Severe GI symptoms within hours to 1 day of ingestion, then presents 1-2 days later with liver failure
- Amatoxin taken up by hepatocyte, inhibits RNA polymerase II, excreted in bile, and reabsorbed causing more damage
- Liver primarily affected, can also cause renal failure
- Treatment:
  - gastric lavage with activated charcoal
  - Nasobiliary drainage
  - Penicillin G 1 gm/kg/d IV plus NAC
  - Silibinin IV 30-40 mg/kg/d x 3-4 days (investigational in US)
Transplant Listing

- **UNOS Criteria for Status 1A listing**
  - Life expectancy without a liver transplant of less than 7 days and has at least one of the following conditions:
    - Fulminant liver failure, defined as the onset of hepatic encephalopathy within 56 days of the first signs or symptoms of liver disease. In addition, the candidate
      - Must not have a pre-existing diagnosis of liver disease
      - Must currently be admitted to the intensive care unit
      - Must meet at least one of the following conditions:
        - Is ventilator dependent
        - Requires dialysis, continuous veno-venous hemofiltration (CVVH), or continuous veno-venous hemodialysis (CVVHD)
        - Has an INR greater than 2.0
    - Anhepatic
    - Primary nonfunction of a transplanted whole liver or liver segment (with certain lab parameters)
    - Hepatic artery thrombosis within 7 days of transplant (with certain lab parameters)
    - Acute decompensated Wilson’s disease

King’s College Criteria

**KING’S COLLEGE HOSPITAL CRITERIA FOR LIVER TRANSPLANTATION**

**ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE**

<table>
<thead>
<tr>
<th>Current criteria*</th>
<th>Modified criteria 0</th>
</tr>
</thead>
<tbody>
<tr>
<td>List for transplantation if:</td>
<td>Strongly consider listing for transplantation if:</td>
</tr>
<tr>
<td>Arterial pH &lt; 7.3 after adequate fluid resuscitation</td>
<td>Arterial blood lactate concentration &gt; 3.5 mmol/L after early fluid resuscitation</td>
</tr>
</tbody>
</table>

List for transplantation if all three of the following occur within a 24-h period:

- Creatinine > 300 µmol/L (>3.4 mg/dl)
- PT > 100 s (INR > 6.5)
- Grade III/IV encephalopathy

List for transplantation if all three of the following occur within a 24-h period:

- Creatinine > 300 µmol/L (>3.4 mg/dl)
- PT > 100 s (INR > 6.5)
- Grade III/IV encephalopathy

**NON-ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE**

List for transplantation (regardless of grade of encephalopathy):

- Age < 10 yr or > 40 yr
- Acute liver failure (jaundice or encephalopathy) ± MELD > 15
- PT > 50 s (INR > 3.5)
- Serum bilirubin > 18 mg/dl

AGA guidelines recommend using MELD score over King’s College Criteria for prognostic scoring system
- MELD score > 30.5 predicts need for OLT
  - Pooled sensitivity 77%, pooled specificity 72%
- AASLD guidelines recommend King’s College Criteria over MELD
  - Sensitivity 68-69%, specificity 82-92%
- EASL notes even low grade encephalopathy may indicate extremely poor prognosis in subacute presentations, and prognosis worse in patients with more severe liver injury, extrahepatic organ failure, and subacute presentations

Management of the Patient with ALF

Fig. 2. Main organ specific complications in ALF.
Management of the Patient with ALF

- Foley, arterial line, central venous lines
- Avoid lactated ringers
  - Albumin preferred, especially if serum albumin <3 mg/dL
- Enteral nutrition when able
- PPI recommended for stress ulcer prophylaxis
- Norepinephrine is first pressor of choice (more predictable cerebral perfusion)
  - Vasopressin causes some cerebral vasodilation
  - Epinephrine decreases mesenteric blood flow, compromising hepatic function

Cerebral Edema in ALF

- Development of CE/ICH defines prognosis
  - 30% of patients with CE will herniate while awaiting an organ
- Possible long term neuro effects in survivors
  - 25-35% in grade 3 HE, 65-75% in grade 4 HE
- Related to cytokine release and inflammatory mediators, causing vasodilation and cerebral hyperemia, along with increased ammonia causing glutamine/alanine increase in astrocytes
Cerebral Edema in ALF

- Clinical signs not reliable, ICP can silently increase until late stages
- Arterial ammonia levels >100 mmol/L herald impending herniation and poor outcomes
- Transcranial dopplers can be useful, CT somewhat insensitive, and occasionally ICP monitor required
- Grade 3-4 encephalopathy patients should be intubated to prevent aspiration
- Continuous renal replacement therapy recommended even in setting of normal renal function for removal of fluid and ammonia

- Lactulose used but with little data; little data on Rifaximin
- Small doses of propofol preferred sedation
Infection

- Bacterial +/- fungal sepsis frequent cause of death
  - Often in absence of fever or leukocytosis
- Surveillance cultures recommended in all
- Empiric antibiotics not recommended until patient develops grade 3-4 encephalopathy, clinical signs of infection, or elements of SIRS
  - Based on local resistance profiles
- Consider antifungal therapy in patients with prolonged critical care support

Coagulopathy

- Do not correct coagulopathy prophylactically
  - Increases volume overload
  - Confuses/obscures clinical picture (INR for prognosis)
  - Does not reduce transfusion requirements
- Administer vitamin K 5-10 mEq SQ or IV x3 days
- Use thromboelastogram (TEG) for coagulation testing prior to procedures rather than INR, fibrinogen, PTT, or platelets
Acute liver failure is a rare emergency

Understanding the time to onset, etiology, and prognosis can help dramatically with knowing best steps in care

Multiple organ systems are involved and each one needs special understanding for care of these patients

Most care is best done in a transplant center where liver transplant can be offered in those cases with poor transplant free survival
A 32 year old man with Wilson’s Disease comes in to the hospital with confusion. He has had known Wilson’s disease for approximately 12 years, and was on therapy with Trientene. He recently had some difficulties with getting refills from the prescriber’s office, and has been out of his medications for two weeks. On presentation, he is confused but responsive. He has asterixis. His vital signs are stable.

### Laboratory Test

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin, serum</td>
<td>3.1 g/dL</td>
<td>3.5-5.5 g/dL</td>
</tr>
<tr>
<td>Aminotransferase, serum aspartate (AST, SGOT)</td>
<td>850 U/L</td>
<td>10-40 U/L</td>
</tr>
<tr>
<td>Aminotransferase, serum alanine (ALT, SGPT)</td>
<td>300 U/L</td>
<td>10-40 U/L</td>
</tr>
<tr>
<td>Alkaline phosphatase, serum</td>
<td>55 U/L</td>
<td>30-120 U/L</td>
</tr>
<tr>
<td>Bilirubin, serum (total)</td>
<td>14.1 mg/dL</td>
<td>0.3-1.0 mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>3.4 mg/dL</td>
<td>15–25 mg/kg body weight/24 hr</td>
</tr>
<tr>
<td>Sodium, serum</td>
<td>135 mEq/L</td>
<td>136-145 mEq/L</td>
</tr>
<tr>
<td>Hemoglobin, blood</td>
<td>7.5 g/dL</td>
<td>14-18 g/dL (male)</td>
</tr>
<tr>
<td>INR</td>
<td>2.3</td>
<td>1.0</td>
</tr>
</tbody>
</table>
QUESTION/ POLL

What is the best next step in treatment?
A. List for liver transplant, Status 1A
B. List for liver transplant, MELD 37
C. Restart trientene
D. Urgent plasma exchange

A. List for liver transplant, status 1A
- Acute liver failure Wilsons disease can occur as a new presentation or after stopping therapy. Prognosis is poor without liver transplant, and Wilsons disease is one of the few cases where patients are listed as a status 1A even in the setting of known chronic liver disease rather than MELD score listing
- Restarting trientene is unlikely to result in significant recovery
- Plasma exchange is sometimes used to acutely lower serum copper and limit further hemolysis and liver damage, but is unlikely to result in recovery.
A 32 year old woman comes in with upper respiratory symptoms and fever. She is 28 weeks pregnant, and so far has had an uncomplicated pregnancy. She denied any sick contacts. She has well controlled systemic lupus erythematosus and is on hydroxychloroquine 200 mg daily and prednisone 5 mg daily. She denies any other medications or herbal supplements. She does not drink, smoke, or use illicit drugs. She reports family history of diabetes. Physical exam is notably for right upper quadrant abdominal tenderness, gravid uterus. Lung exam is normal. She has a fever to 39.2, and is lethargic.
Laboratory Test | Result | Reference Range
--- | --- | ---
Albumin, serum | 3.2 g/dL | 3.5-5.5 g/dL
Aminotransferase, serum aspartate (AST, SGOT) | 2607 U/L | 10-40 U/L
Aminotransferase, serum alanine (ALT, SGPT) | 2364 U/L | 10-40 U/L
Alkaline phosphatase, serum | 130 U/L | 30-120 U/L
Bilirubin, serum (total) | 3.1 mg/dL | 0.3-1.0 mg/dL
Creatinine | 3.4 mg/dL | 15–25 mg/kg body weight/24 hr
Sodium, serum | 135 mEq/L | 136-145 mEq/L
Hemoglobin, blood | 11.5 g/dL | 12-16 g/dL (female)
INR | 1.4 | 1.0

Ultrasound duplex of liver is normal. Ultrasound of uterus is normal with viable fetus. Hepatitis A, B, and C is all negative (IgM and IgG).

QUESTION/ POLL

Which of the following is the best step in treatment?

A. Urgent liver transplant
B. Urgent delivery of fetus
C. IV steroids
D. IV acyclovir
E. Anticoagulation
D. IV Acyclovir

- Herpes hepatitis requires a high index of suspicion and has a high mortality with progression to liver failure, with mortality rates approaching 90%. It most commonly affects women in the second and third trimester of pregnancy, and in up to 50% of cases is not associated with the characteristic skin rash. Therapy with IV acyclovir is life-saving, and must be instituted quickly. Patients present with a characteristic anicteric hepatitis with very high liver enzymes in the setting of relatively low or normal bilirubin, and often have fevers and concomitant upper respiratory symptoms. It is best diagnosed with HSV PCR or liver biopsy.
- Urgent liver transplant is not the best treatment as she may have a response to IV acyclovir and preclude the need for liver transplant. In addition, she does not yet meet the criteria for acute liver failure Status 1A transplant since her INR is less than 2.
- Delivery of fetus is not recommended as this does not change the outcomes of the acute herpes hepatitis and this liver injury is not pregnancy related.
- IV steroids would be appropriate for acute autoimmune hepatitis, which this patient is at risk for given her underlying lupus, but is not commonly associated with fevers and upper respiratory symptoms. She may require stress dose steroids because of her chronic prednisone use, but this is not the best answer.
- Anticoagulation may be required if she had acute thrombosis of hepatic veins or portal veins, which she is at risk for with pregnancy, but her ultrasound was normal so this diagnosis is very unlikely.

REFERENCES