THE YELLOW PATIENT:
Acute Presenting Decompensated Chronic Liver Disease

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Topics we'll cover
• Alcoholic Hepatitis
• Ascites and Spontaneous Bacterial Peritonitis
• Hepatorenal Syndrome
• Hepatic Encephalopathy

Case
• 51yo unemployed man
• Resident from homeless shelter
• Nil past medical/drug history or previous admissions
• But Heavy alcohol dependence, 60 units/week, many years
• Trying to cut down recently
• Jaundiced and confused

O/E
• Febrile, Tachycardia
• Chest clear, Heart sounds normal
• Tense abdominal distension + lateral dullness to percussion
• 2 cm hepatomegaly
• Tremulous + asterixis
• No focal neurological abnormalities

Ix
• BR 220 Hb 10.8 Na 129
• ALT 130 MCV 100 K 3.7
• AST 250 Plat 90 Ur 12
• Albumin 30 WCC 17.0 Creat 89
• ALP 120 GGT 400 INR 1.9 CRP 35
• ECG: sinus tachycardia
• Blood/Urine culture: Negative
• CXR: Loss of lung volume, nil focal
• USS - Liver increased in size, coarse edge
  - Diffusely increased echogenicity
  - Free fluid throughout abdomen

Chronic Liver Disease: Screening Investigations
• Chronic Alcohol Abuse (History – collateral)
• Hepatitis B (Viral serology inc. HBeCore)
• Hepatitis C (Viral serology)
• Other Liver viruses: Hep A, Hep E, CMV, EBV, HSV
• Autoimmune Hepatitis/Primary Biliary Cirrhosis/Primary Sclerosing Cholangitis (Liver Antibodies Anti-LKM, ANCA, ANA, ASMA, AMA)
• Non-alcoholic Fatty Liver Disease (NASH) (Fasting lipids, glucose)
• Haemochromatosis (Ferritin/Iron Studies, Transferrin satn)
• Wilson's disease (younger patients) (Serum copper/caeruloplasmin and 24hr urine Copper)
• Alpha1-Antitrypsin Deficiency (Alpha1-AT levels)
• (Cystic fibrosis + other congenital diseases e.g. biliary artesia, glycogen storage disease)
• (Schistosomiasis)

Imaging
• EEG?
• Liver Biopsy?

Q for Discussion:
What immediate therapies should be instigated?
• IV fluids
• Pabrinex iv
• Vitamin K
• Vitamin B PO
• Thiamine PO
• Chlordiazepoxide PO: reducing dosage
• Address nutrition
Liver Biopsy (TJ) showed Alcoholic Hepatitis on background of cirrhosis

A clinico-pathological syndrome of Hepatitis (inflammation of liver) due to excessive intake of Alcohol
- EtOH chronic liver disease
- Recently cut down/stopped
- AST > ALT (both usually < 500 IU/L)
- Higher level suggests viral, ischaemic or drug hepatitis (e.g. paracetamol [acetaminophen])

Fever, hepatomegaly (tender), jaundice, anorexia


Alcoholic Hepatitis

- Steroids, Pentoxifylline – reduce mortality in selected cases
- Septic screen important

Discriminant function (Maddrey score):
\[ = (4.6 \times [\text{prothrombin time} - \text{control PT}]) + \text{serum bilirubin} \]
- Score > 32 associated with a high short-term mortality
- used to decide treatment
  - Prednisolone 40mg/d for 28 days
  - or Pentoxifylline 400mg tid for 28 days

GLASGOW ALCOHOLIC HEPATITIS SCORE:
- Age, Bilirubin (d1 and d6 to 9), Urea, PT, WBC
- Benefit from corticosteroids only in patients with score ≥9
  (Forest et al. Gut 2007)

- used to decide treatment
  - Prednisolone 40mg/d for 28 days
  - or Pentoxifylline 400mg tid for 28 days

Q for Discussion:

- What important bit of the septic screen don’t we know yet?

- Ascitic tap: 2500 WC, polymorphs
- Patient is septic with spontaneous bacterial peritonitis

Ascites

- A major complication of cirrhosis: 50% over 10y
- 50% mortality in 2 years
- Signifies need to consider liver transplantation
Causes of Ascites

- Cirrhosis 75%
- Malignancy 10%
- Heart Failure 3%
- Tuberculosis 2%
- Pancreatitis 1%
- Others 9%

Pathogenesis of ascites in liver disease – Appendix 1

Ascites: Basic Investigations

Serum Albumin – Ascitic Albumin Gradient

High > 11g/L
- Cirrhosis
- Heart Failure
- Massive Liver metastases
- Fulminant Liver Failure
- Vascular Occlusion
- Alcoholic Hepatitis
- Acute Fatty Liver of Pregnancy
- Myxoedema

Low < 11g/L
- Peritoneal carcinomatosis
- Peritoneal tuberculosis
- Pancreatitis
- Biliary leak
- Nephrotic syndrome
- Serositis
- Bowel infarction/perforation

Ascites: Basic Investigations – WCC

Spontaneous Bacterial Peritonitis (SBP)

- Ascitic neutrophil count >250 cells/mm³
- 15% in-patients with ascites
- SBP develops in 25% patients within 1 year
- Subsequent prognosis < 40% at 1 year

Other Ix
- Ascitic fluid Cytology and Amylase

Management of Ascites

Dietary Salt Restriction to 90mM/day (5.2g)

- Lower diuretic requirement
- Faster resolution of ascites
- Shorter hospital stay

Achievable by:
- no-added salt
- avoid pre-prepared food

Management of Ascites: Diuretics

Diuretics and Regular Weights

- Spironolactone
  - Initially; aldosterone antagonist; distal tubules
  - 100-400mg/d; 3-5 day lag before natriuresis (urine Na > K)
- Then add loop diuretic (Furosemide 40 – 160mg/d)

Management of Ascites: Hyponatraemia

Hyponatraemia - Poor prognostic indicator

Na > 125mmol/l
- no need for H2O restriction
- continue diuretics if renal function stable

Na < 125mmol/l
- little data
- consider stopping diuretics esp if Na < 121mmol/l
- if creatinine rising (>150µmol/l), volume expansion
- maintaining renal function crucial
Management of Ascites: Therapeutic Paracentesis

- 8g albumin iv/L ascites after 5L removed
- Failure to volume expand risks circulatory dysfunction + renal failure
- Albumin better > artificial plasma expanders, which activate RAA system more
- Ascites recurs in 90% pts if diuretics not begun; in 20% despite diuretics
- Do NOT leave drain in situ overnight

Management of Ascites: Transjugular Intrahepatic Portosystemic Shunt - TIPS

- For refractory ascites and hepatic hydrothorax
- 25% risk encephalopathy
- May PPT heart failure (consider ECHO)

Management of Ascites: Spontaneous Bacterial Peritonitis (SBP)

- 70% due to
  - E. coli
  - Gram positive cocci (mainly strep)
  - Enterococci

- Taxo/3rd gen cephalosporins cover 95% flora isolated from ascites
- If asymptomatic, oral ciprofloxacin or augmentin

- Albumin (1.5g/kg for 6h then 1g/kg on d3)
  - reduces mortality (41% to 22%, 3m)
  - decreases renal impairment from 33% to 10% (Sort et al., NEJM 1999)

Management of Ascites: Spontaneous Bacterial Peritonitis (SBP)

- Those who survive SBP
  - 70% recurrence at 1 year
  - 30 to 50% mortality at 1 year
  - Prophylactic norfloxacin or ciprofloxacin reduces SBP recurrence to 20%
  - Consider transplantation

Patient given Taxo, Spironolactone, Frusemide and undergoes Paracentesis

LFTs better, sepsis settling, less confused

BUT renal function going off

Na 129—124
K 3.7—5.6
Ur 12—25
Creat 89—180

Urine output 30mls/hour

Hepatorenal Syndrome (HRS)

- Acute renal failure in patient with cirrhosis, severe alcoholic hepatitis, or hepatic failure from any cause
- HRS represents the end-stage of a sequence of reductions in renal perfusion induced by increasingly severe hepatic injury
**Hepatorenal Syndrome (HRS)**

- Ascites and Hyponatraemia are harbingers of doom.....
- 40% of patients with cirrhosis and ascites develop HRS during the natural history of their disease
- Type 1
  - rapid and progressive renal impairment
  - most commonly precipitated by SBP (25% of patients)
  - characterized by diuretic resistant ascites
  - most patients **die within 10 weeks**
- Type 2
  - Moderate and stable reduction in the GFR
  - median survival of 3-6 months

**HRS Therapy**

- Terlipressin (iv 1-2g qds) and human albumin solution (40g/day)
- superior to placebo for HRS reversal (34% vs 13%, p=0.008)

**HRS Diagnosis**

- Creatinine > 130 µmol/L that progresses: days to weeks
- Absence of another cause for renal disease, inc:
  - shock
  - sepsis
  - acute tubular necrosis and other causes of prerenal disease
  - nephrotoxic drugs
  - absence of obstruction
  - no known parenchymal renal disease
- Must exclude spontaneous bacterial peritonitis, which is complicated by acute renal failure that may be reversible in 30% patients
- No improvement in renal function after volume expansion with i.v. albumin for at least 2d and withdrawal of diuretics

**Hepatic Encephalopathy (HE)**

- Spectrum of potentially reversible neuropsychiatric abnormalities in patients with liver dysfunction after exclusion of unrelated neurologic and/or metabolic abnormalities.
- Reversibility of symptoms after improvement of liver function considered to proof of causal relation to liver disease.
- **HE Grading: Appendix 2**
Hepatic Encephalopathy in CLD

- Not usually a cause of death ……if airway is managed
- Treat precipitating cause e.g. antibiotics, bleeding, fluids
- Lactulose and Enemas
- Decreasing ammonia therapies
  - (i) ornithine and (ii) benzoate
- CT head rules out bleeding
- EEG may help if diagnosis unclear

• Patient’s renal function improved
• LFTs improving (BR 85, INR 1.4)
• Ascites minimal (therapeutic drainage + low dose spironolactone)
• Sepsis eradicated
• Confusion gone
• Discharged

Qs for Discussion:
What important issues need to be addressed post-discharge?

• Support to prevent alcohol relapse
• Variceal screening (OGD)
• Hepatocellular screening (6-monthly AFP + liver USS)
• Vitamin D levels
• Early follow-up: consider liver transplant assessment

### Appendix 1: Pathogenesis of Ascites in Liver Failure

Portal (sinusoidal) Hypertension
- Abnormal Na + Water Retention

1. **Portal (sinusoidal) Hypertension**
   - Abnormal Na + Water Retention
   - Ascites rare if hepatic-venous portal gradient < 12mmHg
   - Consequence of structural changes in cirrhotic liver (↑ resistance to portal flow) and ↑ splanchnic blood flow

2. **Systemic/Splanchnic Vasodilation**
   - Key step in renal dysfunction + Na retention
   - 72-hour vascular synthesis NO, prostacyclin results in effective arterial blood volume + hyperdynamic circulation

3. **Renal v/constriction to systemic vasodilatation** is partly a homeostatic response:
   - ↑ renal sympathetic activity
   - Activation of renin-angiotensin system to maintain BP
   - ↓ renal blood flow → ↓ GFR, ↓ delivery and fractional excretion of Na
   - ↓ Na reabsorption in distal tubule (hyperaldosteronism)

### Appendix 2: Grades of Encephalopathy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms</th>
<th>Signs</th>
<th>GCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Short attention span</td>
<td>Tremor</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Lethargy</td>
<td>Asterixis</td>
<td>Ataxia</td>
</tr>
<tr>
<td>3</td>
<td>Confusion</td>
<td>Asterixis</td>
<td>Ataxia</td>
</tr>
<tr>
<td>4</td>
<td>Coma</td>
<td>Decerebration</td>
<td>&lt;8</td>
</tr>
</tbody>
</table>

Seizures can occur at any grade