CLINICAL APPROACH TO ASCITES

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CLINICAL PRESENTATION

• De Novo OR during follow-up of chronic disease
  • Presentation: Increased abdominal girth, abdominal distension

• Physical Examination
  • Shifting dullness (500mls)
  • Fluid thrill
  • Puddle sign (100 mls)
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Causes of Abdominal Distension

• Fat
  • Faeces
  • Fluid
  • Flatus
  • Fetus
  • Full bladder
  • Fibroids
  • Full sized tumours
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CAUSES OF ASCITES

Peritoneal

Non-Peritoneal
CAUSES: PERITONEAL ("EXUDATIVE")

Malignant
- Primary mesothelioma
- Metastases

Miscellaneous
- Eosinophilic gastroenteritis
- Whipple’s disease
- Endometriosis

Granulomatous Peritonitis
- Tuberculous
- Chlamydia
- Fungal
  - Candida, histoplasma, cryptococcus, coccidioides
- Parasitic
  - Schistosomiasis, strongyloidosis, amoebiasis
CAUSES: NON-PERITONEAL ("TRANSUDATIVE")

Portal Hypertension
- Intrahepatic
  - Cirrhosis
  - Acute alcoholic hepatitis
  - Acute liver failure
  - Massive liver metastases
- Extrahepatic
  - CCF
  - Constrictive pericarditis
  - Budd Chiari Syndrome

Non-Portal Hypertension
- Hypoalbuminaemin
- Nephrotic syndrome
- Protein losing enteropathy
- Miscellaneous
  - Myxoedema
  - Ovarian diseases
    - Carcinoma
    - Benign (Meig’s syndrome)
  - Ovarian hyperstimulation syndrome
  - Pancreatic, bile, chylous ascites
CAUSES OF PORTAL HYPERTENSION

POST-HEPATIC

HEPATIC

PRE-HEPATIC
CAUSES OF PORTAL HYPERTENSION

POST-HEPATIC

HEPATIC

PRE-HEPATIC
CAUSES OF PORTAL HYPERTENSION

POST-HEPATIC

HEPATIC

PRE-HEPATIC
Cirrhosis

Increase Splanchnic Blood Flow

Splanchnic Vasodilation (Nitric Oxide)

Decrease SVR → Decrease BP

Activate
- R.A.A.S
- S.N.S.
- ADH

Water & Na Retention, Increase Cardiac Output

PATHOPHYSIOLOGY OF PORTAL HYPERTENSION
Cirrhosis

Increase Splanchnic Blood Flow

Splanchnic Vasodilation (Nitric Oxide)

Decr SVR → Decr BP

Activate
• R.A.A.S
• S.N.S.
• ADH

Water & Na Retention, Increase Cardiac Output

Compensated Cirrhosis

Increased intrahepatic vascular resistance
Moderate portal hypertension

Splanchnic arterial vasodilation

Low effective arterial blood volume

Increased cardiac output
Increased plasma volume

Restoration of effective arterial blood volume
Cirrhosis

Increase Splanchnic Blood Flow

Splanchnic Vasodilation (Nitric Oxide)

Decr SVR → Decr BP

Activate
• R.A.A.S
• S.N.S.
• ADH

Water & Na Retention, Increase Cardiac Output

Decompensated Cirrhosis

Disease progression
Severe portal hypertension
Bacterial translocation

Severe splanchnic arterial vasodilatation

Markedly reduced effective arterial blood volume
Increased cardiac output and plasma volume insufficient to normalize effective arterial blood volume
Activation of sodium-retaining and vasoconstrictor systems

Sodium and water retention and ascites formation

Further activation of vasoconstrictor systems
Impairment in cardiac output

Renal failure
WHERE IS THE SOURCE OF ASCITES?

Freeman (1953) & Mallet-Guy (1954)
WHERE IS THE SOURCE OF ASCITES?

Freeman (1953) & Mallet-Guy (1954)
WHERE IS THE SOURCE OF ASCITES?

Freeman (1953) & Mallet-Guy (1954)
Liver bed:
- Low pressure system: portal vein pressure 8-10mmHg,
- Pressure gradient across sinusoids 2-5 mmHg
- Sinusoids: fenestrae, no basement membrane → very porous

Hepatic Lymph → peritoneal cavity
- Normal 0.5L/day

Clinically evident ascites
- Lymph production > lymph return
- Abdominal lymphatic return
  - Thoracic duct 10-25 L/day
  - Right lymphatic duct 1.5 L/day
CLINICAL EVALUATION OF ASCITES

• QUESTIONS TO ANSWER

1. Is it peritoneal or non-peritoneal?
2. Is there portal hypertension?
3. Is there liver cirrhosis?
4. What is the aetiology of PHT/cirrhosis?
5. How severe is the cirrhosis?
6. Is there an acute precipitant?
HISTORY TAKING
PHYSICAL EXAMINATION: TIPS

• Stigmata of Chronic Liver Disease
• Signs of Decompensated Liver Function
• Signs of Portal Hypertension
• Clues to Aetiology
• Specific
  • Caput medusa
  • Elevated JVP
  • Diminished heart sounds
  • Loss of Hepatojugular reflex
PHYSICAL EXAMINATION: TIPS

- **Stigmata of Chronic Liver Disease**
- Signs of Decompensated Liver Function
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Stigmata of Chronic Liver Disease
- Palmar erythema
- Finger clubbing
- Pale nails
- Spider naevi (>5?)
- Gynaecomastia
PHYSICAL EXAMINATION: TIPS

- Stigmata of Chronic Liver Disease
- **Signs of Decompensated Liver Function**
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Signs of Decompensation
- Jaundice
- Asterixis/foetor hepaticus
- Presence of ascites
- Bruising
PHYSICAL EXAMINATION: TIPS

- Stigmata of Chronic Liver Disease
- Signs of Decompensated Liver Function
- **Signs of Portal Hypertension**
- Clues to Aetiology
- **Specific**
  - Caput medusa
  - Elevated JVP
  - Diminished heart sounds
  - Loss of Hepatojugular reflex

Signs of Portal Hypertension
- Splenomegaly
- Caput medusa
- Presence of ascites
PHYSICAL EXAMINATION: TIPS

• Stigmata of Chronic Liver Disease
• Signs of Decompensated Liver Function
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• Clues to Aetiology
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Clues to Aetiology
• Alcoholic cirrhosis
  • Dupuytren’s contractures
  • Parotidomegaly
• Wilson disease
  • K-F rings
• PBC
  • Xanthelesma
• Haemachromatosis
  • Slate grey pigmentation
PHYSICAL EXAMINATION: TIPS

• Stigmata of Chronic Liver Disease
• Signs of Decompensated Liver Function
• Signs of Portal Hypertension
• Clues to Aetiology
• Specific
  • Caput medusae
  • Elevated JVP
  • Diminished heart sounds
  • Loss of Hepatojugular reflex
• Caput medusae
  • Patent umbilical vein
• Elevated JVP
  • CCF/TR
• Diminished heart sounds
  • Constrictive pericarditis – also has paradoxical JVP (Kussmaul’s sign)
• Loss of HJ reflex
  • Hepatic outlet obstruction
DIAGNOSIS

INVESTIGATIONS

• Portal Hypertension
• Cirrhosis
• Severity of liver disease—MELD, CHILD
• Ascites – diagnostic tap
**DIAGNOSIS**

**INVESTIGATIONS**

- Portal Hypertension
- Cirrhosis
- Severity of liver disease—MELD, CHILD
- Ascites – diagnostic tap

**PORTAL HYPERTENSION**

- Platelet count
- Imaging
  - Spleno-portal-hepatic vein axis
- Fibrosis assessment
  - Fibroscan
  - MRE
- Hepatic Venous pressure studies
- Transjugular liver biopsy
**DIAGNOSIS**

**INVESTIGATIONS**

- Portal Hypertension
- Cirrhosis
- Severity of liver disease—MELD, CHILD
- Ascites – diagnostic tap

**CIRRHOSIS**

- Presence of portal hypertension
- ALT:AST ratio <1
- “Synthetic function”
  - Albumin
  - Bilirubin
  - Prothrombin time
- Imaging
  - Morphology – US, CT, MRI
- Liver biopsy
**DIAGNOSIS**

**INVESTIGATIONS**

- Portal Hypertension
- Cirrhosis
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**SEVERITY OF LIVER DISEASE**

**CHILD-PUGH SCORE**

- Bilirubin, albumin, INR, ascites, encephalopathy

<table>
<thead>
<tr>
<th>Points</th>
<th>Class</th>
<th>1-year surv</th>
<th>2-year surv</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6</td>
<td>A</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>7-9</td>
<td>B</td>
<td>81%</td>
<td>57%</td>
</tr>
<tr>
<td>10-15</td>
<td>C</td>
<td>45%</td>
<td>35%</td>
</tr>
</tbody>
</table>
**Diagnosis**

**Investigations**

- Portal Hypertension
- Cirrhosis
- Severity of liver disease—MELD, CHILD
- Ascites – diagnostic tap

**Severity of Liver Disease**

- Model for End Stage Liver Disease (MELD) Score
  
  \[3.78 \times \log_e \text{serum bilirubin} \text{ (mg/dL)} + 11.2 \times \log_e \text{INR} + 9.57 \times \log_e \text{serum creatinine} \text{ (mg/dL)} + 6.43 \times \text{aetiology} \text{ (0: cholestatic or alcoholic, 1- otherwise)}\]

- Predicts mortality within 3 months
  
  - > 40: 71% mortality
  - 30-39: 53% mortality
  - 20-29: 20% mortality
  - 10-19: 6% mortality
  - <9: 2% mortality
ASCITIC FLUID ANALYSIS

- Ascitic Tap
  - 15 cm lateral to umbilicus
  - No evidence for use of blood products for therapeutic procedure
    - ?platelet <20,000
  - Contraindication – uncooperative patient, overlying skin infection, severe bowel distension

- Ascitic tap improves outcome
  - Paracentesis is associated with reduced mortality in patients hospitalized with cirrhosis and ascites.
  - Delayed Paracentesis Is Associated With Increased In-Hospital Mortality in Patients With Spontaneous Bacterial Peritonitis.
ASCITES FLUID ANALYSIS

- Inspection
- SAAG
- Cell Count
- Cytology
- Culture and Sensitivity
- Others
ASCITES FLUID ANALYSIS

• SAAG - serum-ascites albumin gradient
• Better than traditional “transudate-exudate” concept
  • Ascitic fluid total protein concentration (AFTP)
  • Exudate: >25 g/L
  • Transudate < 25 g/L
  • Correctly classified in 56% (vs SAAG correct in 97%)

• Exudate or Low Gradient Ascites (Serum to Ascites albumin gradient <11 g/l)
  • Peritonitis
  • Neoplasm (Malignant Ascites, peritoneal carcinomatosis)
  • Pancreatitis
  • Vasculitis/Serositis
  • Nephrotic Syndrome
  • Biliary or chylous Ascites

• Transudate or High Gradient Ascites (Serum to Ascites albumin gradient >11 g/l)
  • Low ascitic fluid total protein (<10g/l)
    • Cirrhosis (Cirrhotic Ascites)
    • Alcoholic Hepatitis
  • High ascitic fluid total protein (>20 g/l)
    • Congestive Heart Failure
    • Budd-Chiari syndrome
    • Myxedema
    • Constrictive Pericarditis
ASCITES FLUID ANALYSIS

- **Cytology**
  - 60-75% sensitivity
  - Carcinomatosis – 100%
  - Liver mets, HCC – usually neg
  - Increase volume → increase sensitivity >100mls

- **TB Peritonitis**
  - Smear: 0-2% sensitivity
  - Culture: 1 liter yields 62-83% sensitivity (most labs can process 50cc)
  - Peritoneoscopy with biopsy: near 100%
  - Adenosine deaminase: falsely low when cirrhotic
ASCITES FLUID ANALYSIS

- **Total Protein**
  - Still useful < 1g/dL
  - risk for SBP
- **Cell count**
  - SBP definition: >250 neutrophils/mm³ (>500/mm³ without symptoms)
- **Culture**
  - Inject into culture bottles
  - Sensitivity 40% → 80%

**Appropriate Settings**

- Glucose – lower in infection
- LDH – infection, malignancy
- Amylase
  - ascites/serum ratio > 5 (normal 0.4) pancreatitis, perforated viscus
- TG - >200mg/dl chylous
- Bilirubin - ?biliary perforation
ASCITIC FLUID ANALYSIS

EXUDATE/TRANSUDATE PARADOX

• “Cardiac Ascites”

• Hepatic venous outflow obstruction

• Early alcoholic cirrhosis + alcoholic hepatitis

• Tuberculous ascites
IMAGING

• CT scan: Cirrhosis
IMAGING

• CT scan: Budd Chiari Syndrome
IMAGING

• Ultrasound: Hepatic Congestion
IMAGING

• CT Scan: Hepatic Congestion
IMAGING

• Constrictive Pericarditis
TREATMENT: BED REST & LOW NA DIET

• Bed Rest
  • Upright $\rightarrow$ activation of RAAS, SNS $\rightarrow$ reduce free water clearance, Na excretion
  • Increased responsiveness to diuretics

• Na restriction
  • “no added salt” - 88mEq/day
  • Useful for those who are still able to excrete Na
  • Also important where natriuresis impaired $\rightarrow$ reduces diuretics requirement
TREATMENT: DIURETICS

- **Distal Diuretics (spironolactone)**
  - inhibits aldosterone effect on tubule of distal nephron
  - 2 days before natriuretic effect seen (half life of aldosterone induced proteins)
  - 2 days before natriuretic effect stops after withdrawal (long half life)

- **Loop diuretics (frusemide)**
  - Inhibit Cl/Na reabsorption in Loop of Henle, no distal action → powerful
  - Must reach tubular lumen to be effective – i.e. urinary concentration correlates with response
  - Good natriuresis only in 50% of cirrhotics (reduced tubular delivery)
TREATMENT: DIURETICS

• Combined Loop and distal diuretics
  • Increases natriuretic effect of both drugs
  • Reduce hypoK, hypeK issues of drugs

• Approaches
  • STEP-CARE or COMBINED
  • Depends on state of ascites
  • Always institute Na restriction
  • Water restriction when Na drops (impaired free water clearance – ADH & diuretic induced)
TREATMENT: DIURETICS

• **Dosing**
  • Spironolactone 50-100mg/day + Frusemide 40mg/day

• **Monitoring**
  • Daily weight: target 0.5kg (or 1kg if pedal oedema present)
  • Urine Spot Na (target >100 mmol/L, <70 - suboptimal)
  • Electrolytes

• **Step Up**
  • If poor response after 4-5 days
  • Max dose spironolactone 400mg, frusemide 160mg/day
TREATMENT: DIURETICS

• Complications
  • Hyperkalaemia
  • Hyponatraemia
    • Diuretic induced impaired free water clearance
  • Azotaemia
    • Pre-renal
  • Hepatic encephalopathy
    • Increased renal ammonia production (following diuretic induced hypoK and alkalosis), direct effect of diuretics on urea cycle
  • Anti-androgenic effects
    • Decreased libido, impotence, gynaecomastia
  • Muscle cramps
    • Quinine helps
**NEW DRUGS**

Aquaretics “VAPTANS”

- Vasopressin receptor antagonist
- Blocks production of aquaporins (water channels) in renal tubules
- Increases free water clearance; esp useful in setting of hypoNa
- Phase III
  - Tolvaptan, conivaptan, moxivaptan
  - Satavaptan (!)
NEW DRUGS

Aquaretics “VAPTANS

• Meta-analysis Dahl APT 2012
  • Vaptans increased serum sodium levels and lead to reductions in weight and the time to the first paracentesis.
  • Vaptans increased the risk of adverse events including an excessive urine volume).
Difficult to control Ascites

- **Tense Ascites**
- **Resistant Ascites**
  - Diuretic resistant
  - Diuretic intractable (unacceptable side effects from diuretics)

Large Volume Paracentesis

- 5L can be removed without colloids
- Larger volumes with colloid replacement – albumin 8g/L of ascites
- Concurrent treatment with diuretics, Na restriction
DIFFICULT TO CONTROL ASCITES

Resistant Ascites

Harbinger of end stage liver disease

Options

• Serial paracentesis
• TIPS
• Liver Transplant
• Peritoneovenous Shunts
DIFFICULT TO CONTROL ASCITES

Newer Shunts
Difficult to control Ascites

Resistant Ascites: TIPS vs Paracentesis

Table 5. Large-Scale Randomized Controlled Trials of TIPS Versus Serial Large-Volume Paracenteses

<table>
<thead>
<tr>
<th>Ref No</th>
<th>Inclusion Criteria</th>
<th>Method of Randomization and Analysis</th>
<th>N</th>
<th>Control of Ascites</th>
<th>Survival</th>
<th>Encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>99</td>
<td>Tense ascites &amp; failure of 4 weeks of therapy</td>
<td>No details</td>
<td>60</td>
<td>61% vs. 18% (P = .006)</td>
<td>69% vs. 52% (P &lt; .01)</td>
<td>58% vs. 48%*</td>
</tr>
<tr>
<td>100</td>
<td>Ascites refractory to medical therapy</td>
<td>Sealed opaque envelope Intention to treat</td>
<td>70</td>
<td>51% vs. 17% (P = .003)</td>
<td>41% vs. 35%* (P = .29)</td>
<td>All 77% vs. 66%</td>
</tr>
<tr>
<td>102</td>
<td>Refractory ascites</td>
<td>No details Intention to treat</td>
<td>109</td>
<td>58% vs. 16% (P &lt; .001)</td>
<td>40% vs. 37%*</td>
<td>Severe 60% vs. 34% (P = .03)</td>
</tr>
<tr>
<td>103</td>
<td>Refractory or recidivant</td>
<td>No details</td>
<td>66</td>
<td>79% vs. 42% (P = .0012)</td>
<td>77% vs. 52% (P = .021)</td>
<td>Severe (P = .039)</td>
</tr>
</tbody>
</table>

*P value not significant.
SUMMARY

1. **Cirrhosis** if the most common cause of ascites
2. **Other causes** need to be considered and excluded
3. **Ascites tap** is useful and underused
4. **Bed rest, Na restriction, diuretics** are mainstay for treatment
5. **TIPS** is useful for resistant ascites
6. **Liver transplant** should be considered when ascites becomes difficult to control