

## Decompensated chronic liver disease

### Definition of decompensated chronic liver disease

Patients with chronic liver disease can present with acute decompensation due to various causes. The decompensation may take the form of any of the following complications:

- Oesophageal variceal bleed
- Ascites
- Spontaneous bacterial peritonitis
- Hepatic encephalopathy
- Hepatorenal syndrome
- Hepatocellular carcinoma

### Oesophageal variceal bleed

#### Definition of a variceal bleed

- Oesophageal varices are dilated oesophageal veins secondary to portal hypertension.
- Responsible for 5% of episodes of GI bleeding in the UK.

#### Causes of variceal bleeds

- Pre-hepatic
  - Portal vein thrombosis / obstruction
  - Increased portal blood flow: fistula
- Hepatic
  - Cirrhosis
    - 90% of cirrhotic patients get varices, 30% bleed
  - Acute hepatitis (esp. alcoholic)
  - Schistosomiasis
  - Congenital hepatic fibrosis
- Post-hepatic
  - Compression (e.g. from tumour)
  - Budd-Chiari syndrome
  - Constrictive pericarditis (and rarely right-sided heart failure)

#### Management of variceal bleeds

- Resuscitation
  - ABC
    - Oxygen, blood tests (VBG, FBC, U+Es, LFTs, clotting, X-match)
    - Erect CXR
    - Fluid resuscitation
    - HDU/ITU
    - Monitoring
      - CVP line and catheter
- Correct anaemia and coagulopathy
  - Transfusion trigger should be 7 (aim 7-9)
    - Using a trigger of 9 significantly increases mortality at 45 days (NEJM 2013).
- Terlipressin (glypressin) 2g IV
  - Vasopressin analogue. Reduces portal pressure. Contraindicated in shock and peripheral vascular disease
  - Octreotide (a somatostatin analogue) can also be used second line
- Antibiotics

- Broad spectrum. IV Tazocin 4.5g. Blood is an excellent culture medium so these patients often end up septic without antibiotics. It may also be a subacute bacterial infection that has brought the patient into hospital initially.
- Endoscopy (once stable and not bleeding)
  - Band ligation
    - This is the first choice of treatment
  - Sclerotherapy
    - In this therapy the varices are sclerosed
    - Various sclerosants can be used
    - Complications include transient fever, dysphagia, chest pain, ulceration and stricture.
  - Variceal obturation with glue
    - This involves embolisation of varices with a glue-like substance (N-butyl-2-cyanoacrylate)
    - Particularly good for gastric or gastro-oesophageal variceal bleeding
    - However, there is a risk of embolisation to the lung, spleen or brain
- Transjugular intrahepatic portosystemic shunt (TIPSS)
  - Where bleeding is not controlled by endoscopy
  - Patient needs to be transferred to a specialist liver unit
  - Hepatic vein is cannulated percutaneously via the internal jugular vein using a needle under ultrasound guidance and a tract is created through the liver from the hepatic to the portal vein reducing portal pressure.
  - High success rate but encephalopathy found in 25% cases (as portal blood diverted from the liver) and shunt occludes within 1 year in up to 50% cases
- Prevention of variceal bleeding
  - Beta blockers
    - These lower portal blood pressure and risk of further bleeding by reducing portal blood flow.
  - Nitrates
    - Just for secondary prophylaxis.
    - Nitrates can also be used in the acute variceal haemorrhage with vasopressin and terlipressin.
  - Endoscopic screening
    - All patients with newly-diagnosed cirrhosis should have screening endoscopy, looking for oesophageal varices. In the long-term, repeated endoscopic screening is usually required, e.g. 2 to 3-yearly in cases of small varices.

## Ascites

### Causes of ascites

- Cirrhosis (75%)
- Malignancy (10%)
- Heart failure (3%)
- TB (1%)

### Investigations in ascites

- Blood
  - FBC (anaemia and platelets), U&E, LFT, clotting, gas for pH
- Imaging
  - Abdominal USS
    - Liver mets, hepatic vein and artery Doppler, splenomegaly (portal HTN)

- Chest x-ray may show pleural effusion or HF
- Ascitic Tap
  - A diagnostic paracentesis, when only about 20 ml is required, is standard in the investigation of ascites
  - Ascitic fluid should be sent for measurement of:
    - Albumin or protein
    - Neutrophil count
    - Amylase (>2000 is pancreatitis)
    - Culture and sensitivity
    - Cytology where malignancy is suspected
  - Transudate vs exudate
    - Use serum-ascites albumin gradient (SA-AG)
      - SERUM ALBUMIN MINUS ASCITIC ALBUMIN
    - If low (<11g/l [or 1.1g/dl]) = non-portal hypertensive (sort of =) exudate
    - High = portal hypertensive = fluid leaking into peritoneum

### Management of ascites

- Non-drug
  - Avoid ETOH (no matter what the cause)
  - Salt restrict (<90 mmol = 5.2g)
- Drugs
  - Diuretics
    - Spironolactone at higher doses than for heart failure
      - Start at 50-100mg and can go up to 400mg daily
    - Aim for weight loss of 1kg/day initially
    - Loop diuretics may be used as an adjunct to spironolactone
- Therapeutic paracentesis
  - Patients with diuretic-refractory ascites or who are intolerant to diuretics should undergo regular large-volume paracentesis
  - This can be done in a day-case setting
  - Human albumin solution (20%) should be given alongside all large-volume paracentesis where more than 5L is removed (AASLD guidelines 2012)
  - Caution if patient is encephalopathic. Ensure platelets >50
- Transjugular intrahepatic portosystemic shunt (TIPSS)
  - Can be used in patients with refractory ascites needing frequent paracentesis (>3/month).

### Prognosis in ascites

- 50% mortality over two years, and signifies the need to consider liver transplantation.
- Refractory ascites carries an even poorer prognosis, 50% patients dying within six months.
  - Therapeutic paracentesis and TIPSS do not improve long term survival

### Spontaneous bacterial peritonitis (SBP)

#### Epidemiology of SBP:

- 10-30% of patients with ascites and has mortality rate of 20%.
- Organisms are usually *E. coli*, streptococci and enterococci.

#### Symptoms of spontaneous bacterial peritonitis (SBP)

- Generalised abdominal pain
- Hepatic encephalopathy, renal impairment or peripheral leucocytosis without any obvious precipitating factor.

### **Investigations in suspected SBP**

- Diagnostic paracentesis
  - Mandatory in all patients with cirrhosis requiring hospital admission
  - Ascitic fluid contains >250 cells/mm.

### **Treatment spontaneous bacterial peritonitis (SBP)**

- Prompt broad spectrum iv antibiotics
  - e.g. Tazocin 4.5g three times daily
  - Treat as soon as ascitic tap has been sent if high index for suspicion
- If fluid resuscitation needed for septic shock then try to avoid colloid/crystalloid and use plasma expander such as human albumin solution instead.
- Good evidence for prophylactic antibiotics after one episode of SBP
  - E.g. Ciprofloxacin 250mg twice daily

### **Hepatorenal syndrome (HRS)**

#### **Epidemiology of hepatorenal syndrome (HRS)**

- 10% of patients with cirrhosis and ascites.

#### **Pathogenesis hepatorenal syndrome (HRS)**

- Renal vasoconstriction leading to renal failure.
- The renal vasoconstriction is a compensatory effect of RAAS and ADH, triggered by an extreme underfilling in the arterial circulation.

#### **Types of hepatorenal syndrome (HRS)**

- Type 1
  - Rapidly progressive
  - Triggered by an event such as SBP and requiring urgent intervention
- Type 2
  - Occurs gradually, as a consequence of aggravation of end-stage liver disease

#### **Treatment hepatorenal syndrome (HRS)**

- Plasma expander, normally human albumin solution
- Terlipressin 0.5-2mg IV four times daily

## Hepatic encephalopathy

### Common precipitants of hepatic encephalopathy

- Renal failure
- Gastrointestinal bleeding
- Infection
- Constipation
- Sedative drugs e.g. opiates, benzodiazepines, antidepressants and antipsychotic drugs
- Diuretics
- High protein intake

### Presentation of hepatic encephalopathy

- Mild
  - Impairment of attention and decision-making, and may have impaired fitness to drive. These patients usually have normal function on standard mental state testing but abnormal psychometric testing.
- Moderate
  - Confusion
  - Asterixis
  - Fetor hepaticus
  - Hypothermia
  - Hyperventilation

- Grade 0: subclinical; normal mental status, but minimal changes in memory, concentration, intellectual function, coordination.
- Grade 1: mild confusion, euphoria or depression, decreased attention, slowing of ability to perform mental tasks, irritability, disorder of sleep pattern such as inverted sleep cycle.
- Grade 2: drowsiness, lethargy, gross deficits in ability to perform mental tasks, obvious personality changes, inappropriate behaviour, intermittent disorientation.
- Grade 3: somnolent but rousable, unable to perform mental tasks, disorientation to time and place, marked confusion, amnesia, occasional fits of rage, speech is present but incomprehensible.
- Grade 4: coma, with or without response to painful stimuli.

### Investigations in hepatic encephalopathy

- Full septic screen
- Ascitic tap to check for SBP
- DRE to check for faecal impaction
- Ammonia levels are raised and can help with diagnosis. The sample needs to be collected and then stored on ice and sent directly to the laboratory.
- EEG
  - High-amplitude low-frequency waves and triphasic waves - not specific for hepatic encephalopathy.
- MRI/CT can help to exclude other causes of altered mental function such as intracranial lesions
- Visual evoked responses show classic patterns associated with hepatic encephalopathy.

### Management of hepatic encephalopathy

- Lactulose or enemas
  - To clear the nitrogen load
- Antibiotics
  - To stop nitrogen breakdown

- Metronidazole
- Prophylactic antibiotics
  - Rifaximin 550mg twice daily is licensed for prevention of hepatic encephalopathy

## Hepatocellular carcinoma (HCC)

- **Risk factors for HCC**
  - Hepatitis B or hepatitis C infection.
  - Alcoholism.
  - HH
  - PBC > PSC
  - Alpha-1-antitrypsin deficiency
  - Steroids
- **Investigations in HCC**
  - USS
    - First line and very sensitive
  - AFP
    - If a >2 cm mass is detected on USS and AFP is also raised, this is diagnostic
  - CT
    - Can look for local spread and CT of the thorax can look for metastases.
    - MRI or FNA if diagnosis still in doubt
- **Prognosis in HCC**
  - Estimated survival based on CLIP score