Understanding liver cirrhosis and its complications

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Agenda

• Complications of cirrhosis
  – Loss of functional liver tissue
  – Portal hypertension
  – Hepatocellular carcinoma

• Anatomy and normal function of the liver
• HCV-induced inflammation and fibrogenesis
Biliary system
Liver blood flow

Portal vein
Normal liver tissue

- Portal vein
- Cords of hepatocytes
- Central vein
The function of the liver.....

• Detoxification and metabolism
The function of the liver…..

• Detoxification and metabolism

• Energy metabolism
The function of the liver…..

• Detoxification and metabolism

• Energy metabolism

• Synthesis
  – Proteins
  – Lipids
  – Carbohydrates
  – Bile
  – Cholesterol
The function of the liver.....

- Detoxification and metabolism
- Energy metabolism
- Synthesis
  - Proteins
  - Lipids
  - Carbohydrates
  - Bile
  - Cholesterol
- Part of the immune system
Consequence of HCV infection

- HCV infection
  - 70% Clearance of virus
  - Chronic HCV infection
    - Chronic hepatitis
      - Liver fibrogenesis

Grade of inflammation and rate of fibrogenesis depends on:
- Age
- Genotype
- Gender
- Obesity
- Alcohol consumption

30% develop cirrhosis within 30 years
Stages of fibrosis in HCV

- **Stage 0**: No Fibrosis
- **Stage 1**: Portal Fibrosis
  - Few septa
- **Stage 2**: Cirrhosis
  - Stage 3
- **Stage 4 = liver cirrhosis**
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• Complications of cirrhosis
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Disturbed detoxification and metabolism

- Accumulation of bilirubin $\rightarrow$ icterus/jaundice

- Altered pharmacokinetics $\rightarrow$ unpredictable response to medications

- Accumulation of ammonium $\rightarrow$ Hepatic encephalopathy
Hepatic encephalopathy (HE)

- Neuropsychiatric abnormalities observed in cirrhosis
- HE may be acute or chronic

<table>
<thead>
<tr>
<th>Grade</th>
<th>West Haven classification</th>
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<tbody>
<tr>
<td>1</td>
<td>Trivial lack of awareness, euphoria.............................</td>
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<tr>
<td>2</td>
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Hepatic encephalopathy (HE)

• Neuropsychiatric abnormalities observed in cirrhosis
• HE may be acute or chronic

<table>
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• Minimal HE is defined as less than grade 1.
  – Common (50-80%)
  – May interfere with daily life

• Drug-induced personality change or HE?
Disturbed energy metabolism

• Diabetes mellitus 50-70%

• Muscle waisting

• Reduced tolerance for fasting
  – Cirrhosis: Protein breakdown after 12 hours
  – Normal: Protein breakdown after 72 hours
Reduced synthetic function

- Coagulation factors ↓ → increased risk of bleeding

- Anti-coagulation factors ↓ → increased risk of thrombosis (x 2)
Reduced immune function

- Increased risk of sepsis (x 2)
- When sepsis occurs → increased mortality (x 2)
- Infections are a main cause of death in cirrhosis
Agenda

• Complications of cirrhosis
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  – Circulatory changes - portal hypertension
  – Hepatocellular carcinoma
Liver blood flow

Portal vein
Circulatory changes

- Vascular resistance within the liver ↑
- Arterial vasodilatation in GI-tractus
- Blood volume within GI-tractus ↑
- Portal hypertension
Porto-systemic shunting
Development of varices
Development of varices

Oesophagus

Stomach
Varices

- Prevalence among cirrhotics: 40-80%
- Annual risk of bleeding: 5-15%

- Bleeding episodes imply high risk of complications and significant mortality

- Therapeutic options:
  - Medications (Nonselective betablockers....)
  - Endoscopic procedures
  - Radiological procedures

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Endoscopic band ligation
Endoscopic inj. of histoacryl
Endoscopic stent placement
TIPS (intrahepatic stent)
Circulatory changes

Vascular resistance within the liver ↑

Arterial vasodilatation in GI-tractus

Blood volume within GI-tractus ↑

Portal hypertension
Circulatory changes

- Vascular resistance within the liver $\uparrow$
- Portal hypertension
- Blood volume within GI-tractus $\uparrow$
- Arterial vasodilatation in GI-tractus
Circulatory changes

- Vascular resistance within the liver $\uparrow$
- Arterial vasodilatation in GI-tractus
- Blood volume within GI-tractus $\uparrow$
- Portal hypertension
- «Effective blood volume» outside GI-tractus $\downarrow$
Circulatory changes

- Vascular resistance within the liver $\uparrow$
- Arterial vasodilatation in GI-tractus
- Portal hypertension
- Blood volume within GI-tractus $\uparrow$
- «Effective blood volume» outside GI-tractus $\downarrow$
- Systemic blood pressure $\downarrow$
Circulatory changes

- Vascular resistance within the liver ↑
- Arterial vasodilatation in GI-tractus
- Blood volume within GI-tractus ↑
- Portal hypertension
- «Effective blood volume» outside GI-tractus ↓
- Systemic blood pressure ↓

Activation of renin/angiotensin and increased levels of ADH
- Salt and water retention
- ascites and hyponatremia

Activation of sympathetic nervous system
- Hyperdynamic circulation
- Vasoconstriction
- Renal hypoperfusion
Agenda

- Complications of cirrhosis
  - Loss of functional liver tissue
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  - Hepatocellular carcinoma
Hepatocellular carcinoma

- Annual risk in cirrhosis: 1-5%
- Prognosis is poor when the cancer is symptomatic
- Early detection improves survival
  - Ultrasound/ AFP is recommended every 6 months
Summary

• With cirrhosis the filter is destroyed

• Complications are caused by
  – Loss of functional liver tissue
  – Portal hypertension
  – Oncogenic effect of the chronic inflammatory state

• Prognosis may improve significantly after eradication of the virus
Liver blood flow

- Aorta
- Hepatic vein
- Portal vein
- Hepatic artery
- Inferior vena cava
- Liver blood flow
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<th>Prophylaxis</th>
<th>Direct treatment of varices</th>
<th>Reduction of portal pressure</th>
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<td>Band ligation</td>
<td>Non-selective Beta-blockers</td>
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<td>Histoacryl injection</td>
<td>Terlipressin, somatostatin</td>
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<td>Oesophageal stent</td>
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