

Liver cirrhosis

Liver cirrhosis

- Liver cirrhosis is a consequence of **usually long lasting liver disease** leading to advanced changes in the structure of liver tissue
- The progression of fibrosis to cirrhosis:
 1. Distort hepatic architecture and vasculature
 2. Deleterious effect on hepatic function
 3. Increase propensity for neoplastic transformation

Liver cirrhosis: sequence of events

- Inflammation, increase of TGF-B1, IL1B, TNF
- Activation and migration of stellate cells
- Fibrosis
- Cirrhosis: irreversible changes

Definition WHO 1978:

- A diffuse process characterized by fibrosis and the conversion of normal liver architectures into structurally abnormal nodules

Liver cirrhosis: macroscopic changes

- Micronodular (nodules upto 3mm) - ALD
- Macronodular (nodules upto 3-4cm) - HepB
- Mixed

Liver cirrhosis: aetiology

- Alcohol
- Viral (HCV, HBV)
- PBC
- Secondary BC
- Metabolic problems:
 - Hemochromatosis
 - Wilson`s disease
 - alfa1-antytrips. deficiency
- Drugs:
 - MTX, Amiodarone, Isoniazid, Methyldopa
- Cystic Fibrosis
- Budd-Chiari syndrome
- Autoimmune
- Cryptogenic

Liver cirrhosis: history

- Cirrhosis can be clinically silent
- General complains: malaise, fatigue, weight loss, depression, loss of appetite, pruritus
- Digestive tract: nausea, vomiting, diarrhoea, black or pale stools, abdominal swelling
- Peripheral oedema
- Other complains: bruising, nasal and gingival bleeding, decreased libido, oligomenorrhoea

Liver cirrhosis: (clinical examination)

- Cachexia, muscle wasting
- Skin: jaundice, scratch marks, spiders, xantelasma, bruises, collateral veins and caput medusae, hair loss
- Hands: clubbing, leuconychia, palmar erythema, Duputrien`s contractions
- Abdomen: ascites, hepatosplenomegaly, caput medusae
- Other symptoms: testicular atrophy, hair loss, gynecomastia, peripheral oedema, foetor hepaticus

Liver cirrhosis – lab tests:

- History (alcohol, drugs, operations – iatrogenic injury of biliary tree, other diseases – metabolic syndrom, IBD)
- HBsAg, anti-HCV
- Metabolic disorders: ceruloplasmin, AA1T, ferritine and transferrin saturation
- Autoimmune hepatitis (AIH)
- Cholestatic diseases (PBC, PSC)

Liver cirrhosis – lab tests:

- Transaminases (AST,ALT) can be depressed, normal or elevated
- GGTP, ALP – nonspecifically raised, cholestasis
- Serum albumine – diminished level is a hallmark of cirrhosis
- Bilirubin – elevated, parenchymal pattern
- Prothrombin time – marker of synthetic function

Liver cirrhosis: Child-Pugh score

	1	2	3
bilirubin	<2.0	2.0-3.0	> 3.0
albumin	> 3.5	2.8-3.5	< 3.0
INR	<1.3		>1.5
ascites	-	-/+	+++
encefalopathy	-	I/II	II-IV

A: 5 – 6

B: 7 – 9

C: 10 - 15

Imaging technics valuable in cirrhosis:

- USG – size, texture and vascular patency of the liver, tumors, lymph nodes, ascites, splenomegaly, biliary problems
- Doppler ultrasound – measure blood flow in the portal vein, hepatic artery and hepatic veins
- CT, NMR – tumors, volumetry
- CT-angiography – thrombosis
- Endoscopy

Liver cirrhosis diagnosis

- Liver biopsy – gold standard
- Various histological classifications for the grading of fibrosis and cirrhosis: Scheuer, Ishak, Knodell, Metavir
- Blind technic, image-guided transabdominal approach, transjugular approach, laparoscopic or open
- To elucidate aetiology, to stage the severity of fibrosis and presence of cirrhosis, to find inflammation as a prognostic marker (HCV)

Liver biopsy limitations:

- Invasive procedure (pain, heamorrhage,)
- Sampling error (1:50 000 of the organ, non-homogenous distibuted diaseases)
- Not always possible – clotting problems
- Surrogate markers – elastography, hyaluronic acid, collagen IV, procollagen of PIIIINP, leptin, adiponectin, TGF-beta 1

Liver cirrhosis complications:

- **Portal hypertension:**

Ascites (and SBP)

Oesophageal and gastric varices

Hypersplenism

Renal dysfunction

- **Hepatopulmonary syndrome**
- **Cirrhotic cardiomyopathy**
- **Hepatocellular carcinoma**
- **Encephalopathy**
- **Malnutrition**
- **Haematological complications**
- **Endocrine disturbances**
- **Sepsis**

Portal hypertension:

- Elevated portal pressure greater than normal value of 1-5 mmHg. Clinically significant above 12 mmHg
- The major complications of portal hypertension include ascites, gastrointestinal haemorrhage and renal dysfunction

90% of patients with cirrhosis will develop oesophageal varices and 1/3 of these will bleed

Gastrointestinal haemorrhage carries a short-term mortality rate as high as 50% in the group with most severe liver dysfunction.

Ascites:

- May be clinically detectable after the accumulation of 2 l of fluid
- In 10% of cases accompanied by pleural effusion (right sided due to defect in the diaphragm)
- Fluid is transudative – protein in ascites is below 25 g/L or
Serum/Ascites Albumin Gradient greater than 1.1g/dL

Portal hypertension:

- Hypersplenism

Variable pancytopenia
with sequestration of
red, white cells and
platelets in the splenic
tissue

- Renal dysfunction

Abnormal salt retention as
the initiating event

Plus splanchnic

vasodilatation, increased
cardiac output, decreased
peripheral resistance and
renal vasoconstriction

= HRS

Hepatic encephalopathy

- also known as **portosystemic encephalopathy**) is the occurrence of confusion, altered level of consciousness and coma as a result of liver failure.
- In the advanced stages it is called **hepatic coma** or **coma hepaticum**. It may ultimately lead to death

Hepatic encephalopathy

- It is caused by accumulation in the bloodstream of toxic substances that are normally removed by the liver.
- The diagnosis of hepatic encephalopathy requires the presence of impaired liver function and the exclusion of an alternative explanation for the symptoms.
- Hepatic encephalopathy is reversible with treatment.

Hepatocellular carcinoma:

- 80% of tumors occur in cirrhotic liver
- Most clinical features is indistinguishable in patients with cirrhosis
- Screening –abdominal USG every 6 months
- Liver transplantation if within Milan criteria
- Surgical resection, Percutaneous ethanol injection (PEI), Radiofrequency ablation (RFA)
- Transarterial chemoembolization (TACE), Intra-arterial Chemotherapy
- SORAFENIB (anti-VEGF)

Liver cirrhosis: complications
definitive treatment

LIVER TRANSPLANT