

LIVER CIRRHOSIS

Clinic of Internal Medicine,
Faculty Hospital Prague - Motol

This Lecture

- Definition
- Pathology
- Epidemiology
- Etiology
- Pathogenesis
- Diagnosis
- Treatment
- Complications
- Follow-up

Definition

- Final common histological pathway of different chronic liver diseases.
- Fibrosis + transformation of normal liver structure into nodules.
- Manifestation through
 1. decreased synthetic function
 2. decreased detoxification capability
 3. portal hypertension

Pathology

- Fibrosis = excessive deposition of EC matrix
- Cirrhosis = fibrosis + nodular transformation

Poor correlation histology – clinical state

Epidemiology

USA:

- Incidence: 72.3/100.000/year
- Prevalence: 5.5 million cases.
- Mortality: 35.000 (1.2 %) deaths/year
- Gender: 60% male x 40 % female
- Costs (yr.2000): 1.5 billion \$ direct costs
- Hospitalizations: 421.000 in 2002

Etiology

- a) **Inflammatory** – viral hepatitis, sarcoidosis
- b) **Toxic** – alcohol, drugs (methotrexate, alpha-methyldopa, amiodarone)
- c) **Metabolic disorders** – NASH, hemochromatosis, Wilson disease, alpha-1 antitrypsin deficiency, glycogen storage disease
- d) **Obstructive** – secondary biliary cirrhosis
- e) **Autoimmune** – autoimmune hepatitis, PSC, PBC
- f) **Venous congestion** – right-sided heart failure, Budd-Chiari syndrome, tricuspid regurgitation
- g) **Cryptogenic (idiopathic)**

Etiology II (USA)

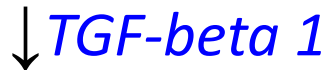
1.	Hepatitis C	26 % \	
2.	Alcohol	21 %	} 62 %
	Alcohol + hepatitis C	15 % /	
3.	Cryptogenic causes	18 %	
4.	Hepatitis B (+D)	15 %	
5.	Others	5 %	

Pathogenesis

Chronic liver injury (variable duration)



Stimulation of hepatocytes, Kupffer cells, sinusoidal endothelium



Paracrine stimulation of *stellate cells*



Increased production and deposition of EC matrix
(*collagen I*)



Fibrosis (potentially reversible)



Cirrhosis (usually irreversible)

Clinical presentation

Pathogenesis:

1. Lowered detoxification capability
→ Hepatic encephalopathy
2. Decreased synthetic function
→ Coagulopathy, hypoproteinemia, immunodeficiency, ...
3. Portal hypertension
→ Ascites, varices

Clinical presentation

Signs

1. Jaundice, flapping tremor, hair changes, gynecomastia,
 2. Edemas, bleeding signs, muscle atrophy, thrombotic events, infections
 3. Ascites, caput medusae, variceal bleeding
- + Dupuytren, palm reddening, teleangiectasias (“spider nevi”)

Symptoms

Fatigue, feeling of sickness, sleep disorders, loss of strength and power, dyspepsia, weight gain / loss, pruritus, dyspnea

Diagnostic workup

1. Patient history
2. Physical examination
3. Laboratory examination
 - Hematology: BC, PTT, APTT
 - Biochemistry: electrolytes, liver enzymes, bilirubin, albumin, CRP, ESR, Fe, ferritin, (Cu, ceruloplasmin)
 - Immunology: IgG,A,M, ANA,ANCA,AMA,ASMA,LKM
4. Imaging
 - US, CT, MRI, endo-US
5. Histology
 - Liver biopsy – a) percutaneous, b) transjugular
6. Endoscopy – screening for complications (varices)

Severity assessment

- Child-Turcotte-Pugh scoring system
 - INR, bilirubin, albumin, encephalopathy, ascites
 - Score 5-15 points → grade A-C
 - A – conservative treatment, follow-up
 - B – consider liver transplantation
 - C – 1-year mortality 50%
- Model for End-Stage Liver Disease (MELD)
 - 6-40 pts., → 3-month survival rate

Complications

- Variceal bleeding / other GI bleeding
- Hepatocellular carcinoma (HCC)
- Hepatorenal syndrome
- Spontaneous bacterial peritonitis (SBP)
- Other infections
- Surgical
- Acute liver failure

Therapy

A. Treatment of the underlying disease

B. Treatment of cirrhosis

- Nutrition
- Adjunctive therapies – pruritus, osteoporosis, training, vaccination
- Treatment of complications
- Liver transplantation

Follow-up

Specialist / GP, regular visits (stable 3-4/yr)

- Cirrhosis stage assessment:
 - Laboratory – CBC, PT, biochemistry → C-P score
- Screening for complications
 - Gastroscopy – varices (every 2 yrs?)
 - HCC – abd. US and/or AFP (2/yr?)

Liver transplantation

- Donor – living / deceased
- Indication
- Contraindication: cardiovascular, pulmonary, alcohol, neoplasm, sepsis, psychosocial
- Waiting list – MELD, PELD, CTP, extra
- Immunology: ABO system
- Technique: orthotopic,
- Survival rates: 1 yr 85-90%, 5 yrs 70%

Future

- Hepatocyte transplantation
- Bioartificial liver
- Xenotransplantation
- Genetic technology – stem cells