LIVER DISEASES

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- Viral Hepatitis
- Cirrhosis of liver
- Liver cancer
Viral Hepatitis
Primary hepatic infections are caused by a group of specially hepatotropic viruses and characterized by degeneration and necrosis of hepatocyte morphologically.
ETIOLOGY

1. Hepatitis A virus (HAV)
   short-incubation, not lead to chronicity or carrier state, fecal-oral transmission

2. Hepatitis B virus (HBV)
   long-incubation, may result in fulminant hepatitis, a chronic carrier, chronic hepatitis, cirrhosis, parenteral transmission
3. Hepatitis C virus (HCV)
   similar to HBV, but higher propensity for transition to chronicity

4. Hepatitis D virus (HDV)
   delta agent (δ): cause hepatitis only in the presence of HBV

5. Hepatitis E virus (HEV)
   similar to HAV, high mortality in pregnant women (20%)
Pathogenesis

1. A direct cytopathic effect
2. Immune responses

The induction of immune responses against viral antigens or virus-modified hepatocyte antigens that damage virus-infected hepatocytes.
Morphology
Degeneration of hepatocytes

1) Swelling and ballooning degeneration
   hepatocytes swelling

2) Acidophilic degeneration
   the cell shows increased cytoplasmic eosinophilia, and appears shriveled

3) Fatty degeneration
Swelling and ballooning degeneration
Fatty degeneration
Acidophilic degeneration
1) Acidophilic body

The body is deeply eosinophilic, generally round and small in outline, and is usually extruded from liver-cell plate into the sinusoidal space.

- Now it is regarded as a form of apoptosis.
Acidophilic body
2) Spotty (focal) necrosis

Focal necrosis of single or a group of the liver cells, accompanied by inflammatory cell infiltration.
Spotty (focal) necrosis
3) Piecemeal necrosis

The necrosis at the interface between parenchyma and connective tissue and accompanied by destruction of the limiting plate and inflammatory infiltration.

Morphologically, it show a moth-eaten appearance.
Piecemeal necrosis
4) Bridging necrosis

Confluent necrosis of hepatocytes leading to collapse of the reticulin framework, linking portal-central, portal-portal or/and central-central areas.
Bridging necrosis
5) Massive necrosis

many bridging necrosis or whole lobule, leaving islands of hepatocytes.

The lobules are destroyed, collapse and disappear.
Massive necrosis X400
Inflammatory cell infiltrate

- **Cells**: principally lymphocytes and monocytes, lesser plasmocytes, neutrophils,
- **location**: portal tracts and necrotic areas of the lobules.
Stroma reactive proliferations and hepatocytes regeneration

1) Kupffer cell reactive changes:
   Kupffer cells reveal hypertrophy, hyperplasia and active phagocytosis

2) Regeneration of parenchymal cells

3) Hyperplasia:
   fat-storing cell and myofibroblast-like cell
Acute hepatitis

Grossly

The liver is slightly enlarged and more or less green, depending on the degree of hepatocellular damage and jaundice.
Figure 6.38. Normal liver.
Figure 6.39. Acute viral hepatitis.
Histologically

(1) Ballooning change
(2) Acidophilic bodies and spotty necrosis
(3) Regeneration of liver cells
(4) Infiltration of inflammatory cells in portal tracts and lobules.
(5) Kupffer cell proliferative reaction
Figure 5.19 Acute viral hepatitis; HE stain.
Clinicopathological correlation

(1) Hepatomegaly
(2) Pain under the right costal margin
(3) Jaundice
(4) Elevation of serum transaminases
About 5-10% HBV 50% HCV infection hepatitis develop into chronic hepatitis.

About 1% or less of cases of acute hepatitis run a fulminant course with submassive or massive liver necrosis and a high mortality rate.
Chronic hepatitis

Definition

Inflammation of the liver continuing without improvement for at least 6 months.
Classification and morphology

Chronic mild hepatitis
Chronic moderate hepatitis
Chronic severe hepatitis
Chronic mild hepatitis

1) the hepatic lobular structure keeps intact
2) proliferation of fibrous tissue in portal areas
3) spotty necrosis and occasional piecemeal necrosis of hepatocytes.
Chronic moderate hepatitis

1) piecemeal necrosis and bridging necrosis
2) fibrous septa formed but the hepatic lobule structure mostly preserved
3) Portal and lobular inflammatory infiltration
Chronic severe hepatitis

1) diffuse and widespread necrosis:
   severe piecemeal necrosis
   extensive bridging necrosis

2) irregular regeneration and formation
   of pseudolobule
Severe hepatitis (fulminant hepatitis)

Etiology

Viral hepatitis accounts for 50 to 65% of cases. But it may also result from drugs, poisoning.
Acute severe hepatitis

Gross

1) Size: shrunken,
2) Consistency: flaccid
3) Color: cut surface shows yellow or brown-red
4) Time: Ten days
Figure 6.23. Acute necrosis (yellow atrophy).
Histologically

1) Diffuse, widespread and massive necrosis of hepatic cells
2) The reticulum framework collapsed
3) Inflammatory infiltration of lymphocytes and macrophages in necrotic areas and portal tracts.
Subacute severe hepatitis

1) Size: shrunken,
2) Consistency: flaccid
3) Color:
   cut surface shows yellow or brown-red
4) Time: 3 weeks to 3 months
5) Nodules of regeneration: varying size on the surface and sections.
**Histologically**

1) Bridging, submassive *necrosis* of hepatic cells.

2) Collapse and *disorganization* of hepatic lobular structure.

3) Hepatocytes *nodular regeneration*.

4) *Proliferation* of fibrous tissue, bile ductules and cholestasis.

5) Inflammatory *infiltration* of lymphocytes, plasma cells and macrophages.
Outcome

1) Healthy young adults fare better than older individuals.
2) Long immunity
3) Some cases may progress to chronic hepatitis or cirrhosis.
Alcoholic liver disease

1. Hepatic fatty degeneration, Fatty liver

2. Alcoholic hepatitis
   (1) degeneration of hepatocytes
   (2) spotty necrosis with infiltration of neutrophils
       and portal infiltration of lymphocytes
   (3) fibrous proliferation around sinus and central vein

3. Alcoholic cirrhosis
CIRRHOSIS
Definition

Cirrhosis is applied to a diffuse fibrosis and nodular condition of the liver associated with a spectrum of clinical findings that include portal vein hypertension and hepatic failure.
Classification

Morphological

Micronodular cirrhosis
Macronodular cirrhosis
Mixed-nodular cirrhosis
Etiology

Portal cirrhosis
Post hepatitic cirrhosis
Biliary cirrhosis
Alcoholic cirrhosis

Mallory’s body: focal hyalinization of the cytoplasm of the liver cells, consist of filaments 14 to 20nm long
Chemical cirrhosis
metabolic cirrhosis
congestive cirrhosis
Cryptogenic (隐源性) cirrhosis
Pathogenesis

1) Necrosis and degeneration of hepatocyte
2) Hyperplasia of connective tissue and formation of fibrous septa
3) Nodous regeneration of residual hepatocytes and reconstruction of lobule and vessel
Morphology

Gross appearance:

Histological change:

1. Destruction of normal hepatic lobule structure

2. Formation of pseudolobule surrounded by fibrous septa.

3. Inflammatory infiltration et al.
Posthepatitic cirrhosis
Biliary cirrhosis
Pseudolobule

Normal hepatic lobule are destroyed and subdivided by hyperplastic fibrous tissue and form regenerative hepatic cellular nodule surrounded by fibrous septa. In the nodule, the central vein is missing or peripheral-located, the hepatic cord falls into disorder and some hepatic cells have atypia.
This trichrome stain demonstrates the collapse of the liver parenchyma with viral hepatitis. The blue-staining areas are the connective tissue of many portal tracts that have collapsed together.
Pseudolobule
Clinicopathological association
Portal hypertension

The major cause

Compression of central veins and sinusoids by nodules and fibrosis

Shunting of hepatic arterial blood into the portal vein system
Consequences

1. Splenomegaly and hypersplenism
2. Gastrointestinal congestion and edema
3. Ascites (腹水)

Mechanisms:

* Gastrointestinal congestion, Increased permeability of vessel wall
* Increased hepatic lymph formation
* Retention of sodium and water
* Hypoalbuminemia and reduced plasma osmotic pressure
4. Formation of bypass channels

Esophageal varices

Periombphalic and abdominal Varices:

Caput medusae “海蛇头”或“水蛇头”

Anorectal varices
“海蛇头”
Hepatic failure

**Hypoalbuminemia** (血白蛋白减少)

**Anemia and bleeding diathesis** (贫血、出血)

**Dysfunction of hormone inactivation**

  - **Spider angioma** (蜘蛛痣)
  - **Palmar erythema** (肝掌)

**Jaundice** (黄疸)

**Hepatic encephalopathy** (肝性脑病)
Outcome and complication

- Infection
- Gastrointestinal Dysfunction
- Development of hepatocellular carcinoma
- Hepatic coma
Primary carcinoma of liver

Classification:

- hepatocellular carcinoma
- cholangiocarcinoma
- mixed hepatocholangiocarcinoma
Hepatocellular carcinoma

Etiology

- chronic hepatitis
- cirrhosis
- Aflatoxin (黄曲霉毒素)
- alcohol and others
Morphology

Gross appearance

- nodular type $\leq 5\text{cm}$
- massive type $>5\text{cm}$
- diffuse type
- small hepatocellular carcinoma $\leq 3\text{cm}$
Nodular type
Nodular type
Massive type
small hepatocellular carcinoma
hepatocellular carcinoma
hepatocellular carcinoma
hepatocellular carcinoma
Cholangiocarcinoma
THANKS