CHRONIC HEPATITIS

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Chronic Hepatitis

Definition

It is chronic inflammation involving mainly the liver parenchyma of more than six months continuous without improvement.

PATHOLOGY

- There is infiltration of both portal tracts and parenchyma with lymphocytes and plasma cells.
- The swollen liver cells become isolated in the inflammatory cell infiltrate. This process of hepatocyte destruction is called piecemeal necrosis. The severity can be graded.

Etiology

1. Viral hepatitis: only the parenteral types (hepatitis B, C and Delta).
2. Autoimmune (lupoid hepatitis): Rare.
3. Drugs and toxins as methyl dopa, INH, ketokonazole and nitrofurantoin, toxins like aflatoxin and alcohol.
4. Metabolic as Wilson's disease, alpha-1-antitrypsin deficiency.

Clinical manifestations

- **Symptoms:**

1. Asymptomatic (in many cases).
2. Frequent fatigue (relieved by rest).
3. Onset: insidious, fever, arthralgia & pruritus, bleeding tendency.
4. Anorexia, amenorrhea.

- **Signs :**

1. 1-Jaundice, (sometimes, arthritis).
2. 2-Spider naevi, bruises, bleeding.
3. 3-Breast atrophy in females.
4. 4-Gynaecomastia in males.
5. 5-Abdominal striation, thyroiditis, haemolysis, etc. in autoimmune.
6. 6-Smooth palpable liver (±), splenomegaly (±).

Investigations

1. Liver function tests:

- a- Mild elevation in serum bilirubin.
- b- Raised transaminases (ALT,AST).

2. Hepatitis markers and PCR (HCV& HBV), studies for Wilson's disease and α-1 antitrypsin.

3. Liver Biopsy: is important for diagnosis, degree of severity, progression to cirrhosis and sometimes suggestion of etiology.

4. Antinuclear antibodies (ANA) and anti-smooth muscle (ASA) high gamma globulin in autoimmune hepatitis.

COMPARISON BETWEEN HBV AND HCV

	HCV	HBV
Virus type	**RNA, Fragile**	DNA
Integration to hepatocyte	No	Yes
Level of viraemia	Low	High
Antibody titre	Low	High
Infectivity	Low	High
Progression to Cirrhosis and HCC	Late Decades	Frequent in early infection And severe
Symptoms of acute attack	Rare	(±)

	HCV	HBV
Fulminant failure	Rare	(±)
Prognosis	Variable	worse in infants
Prevalence in Egypt	18%	5%
Progression to chronic hepatitis	Need decades 80%	2-10%
Age	Older	Younger
Transmission by sex and vertical	Rare	Common
Vaccine and I.G.	No	Yes

Chronic hepatitis B

- More in males.
- 90% of infected infants develop chronic hepatitis.
- Positive HBeAg &/or delta hepatitis are bad prognostic features.

- **Drug therapy for Hepatitis B**
  - **Lamivudine and adefovir** are beneficial for oral administration and safe, but only a few of the patients treated experience a sustained response after therapy withdrawal.

- **Entecavir** is a potent inhibitor of chronic hepatitis B virus DNA polymerase. The approved dosage in treatment-naive patients is 0.5 mg per day orally, whereas in patients who have failed lamivudine therapy or are known to harbor lamivudine-resistant mutants, the approved dosage is 1.0 mg per day.

CHRONIC HEPATITIS C

- Identification of chronic hepatitis (C) is accidental; the course is slow with marked fluctuation in transaminases over years.
- **Clinical picture:** see chronic hepatitis.

Investigation

1. ELISA-detected antibodies to HCV (anti-HCV) is the screening test of choice. RIBA assays are more accurate and are used to confirm the result. Antibodies are detectable 6-8 weeks after active infection and remain positive for life.
2. Detection of HCV RNA by PCR implies infectivity and chronicity (rather than simply previous exposure), the test is used to confirm ELISA test or diagnose acute disease in the first week.

3. Serum transaminase levels fluctuate and correlate poorly with disease activity (ALT).
4. Liver biopsy: is essential for diagnosis. Disease activity and treatment options are best assessed on histological findings obtained by liver biopsy.
5. The patient must be HBs Ag negative to exclude associated chronic hepatitis B.
6. Exclude other etiology.

- **N.B.**

- 80% of cases develop chronic hepatitis, and an estimated 20%-30% develop cirrhosis and liver carcinoma within 30-40 years.
- ELISA is positive in about 20% of Egyptian but it has some disadvantages as it may be false positive or present in healthy carriers.
- The prognosis is variable, some patients may have spontaneous improvement and others may develop liver cirrhosis or hepatocellular carcinoma.

Treatment

- **Interferon:**
- Interferon Alpha with Ribavirin was used. However, the results were very unsatisfactory with high costs.
- **Side effects:**
- Bone marrow suppression
- Flu-like symptoms, headaches, fever, rigors, arthralgias and myalgia
- Depression
- Anxiety
- Sexual dysfunction
- Hair loss, insomnia
- Fatigue
- Hypothyroidism

- **Recent treatment regimens of chronic HCV**:
- Daily Ledipasvir + sofosbuvir (Sovaldi) for 12 weeks (Harvoni).
- Daily Daclatasvir + sofosbuvir (Sovaldi) for 12 weeks.
- Daily sofosbuvir (Sovaldi) +Simeprevir (Olysio) with or without Ribavirin for 12 weeks.
- Daily Ribavirin + sofosbuvir (Sovaldi) for 24 weeks.
- Daily Ribavirin + sofosbuvir (Sovaldi) + weekly PEG- INF for 12 weeks.

Sofosbuvir (Sovaldi): This is an HCV .١ nucleotide analog NS5B polymerase inhibitor. The recommended dose of sofosbuvir is 400 mg taken orally once daily. No dose adjustment is needed for mild-to-moderate renal impairment or with mild, moderate, or severe hepatic impairment. The most common adverse events observed in combination with pegylated IFN-α and ribavirin were fatigue, headaches, nausea, insomnia, and anemia.

CHRONIC AUTOIMMUNE (LUPOID)

Autoimmune HEPATITIS

It is a disease of disordered immune regulation marked by a defect in suppressor (regulatory) T-cell. This results in production of autoantibodies against hepatocyte surface antigens.

- **Clinical features:** It is very rare.

1- It is more in young (10-20 years) and three-quarters are females. Sometimes menopausal (has 2 peaks).

2- The patients feel unwell with easy fatigability.

3-Jaundice is often episodic.

4-Pulmonary infiltrates.

5-Epistaxis, bleeding gums, spider naevi, cutaneous striae and acne may occur.

6-Lupoid face. 7-Arthritis.

8-It is not confined to the liver.

9-The following associated conditions may occur: purpura, erythemas, arthralgia, lymphadenopathy, pulmonary infiltrates, pleurisy, ulcerative colitis, diabetes, lupus kidney, thyroiditis and hemolytic anemia.

- **Prognosis:**

Is variable, 60% of the patients may have 10 years survival.

- **Investigations:**

1-Serum transaminases are very high (> 10 times), gamma globulins are high and serum bilirubin is elevated.

2-Liver biopsy shows evidence of CAH.

3-All viral hepatitis markers are negative.

4-Antinuclear antibodies (ANA) and anti-smooth muscle antibodies (ASA) are positive.

- **Treatment:**

1- Corticosteroids: This condition responds dramatically to corticosteroids and it was shown that corticosteroid prolongs life.

Dose: 30 mg prednisolone for one week reduced to a maintenance dose of 10-15 mg daily. It can be maintained for 6 months.

2- Azathioprine: (50-100 mg daily) may be added if there is no response on 20 mg prednisolone daily.