HEPATITIS

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OBJECTIVES

At the end of this session each student will be able to:

1. Define hepatitis.
2. Describe the epidemiology of hepatitis.
3. Describe the cause of hepatitis.
4. Describe the clinical features of hepatitis.
5. Describe the complications of hepatitis.
6. Describe the differential diagnoses of hepatitis.
7. Investigate patients with hepatitis.
8. Treat patients with hepatitis.
9. Describe the prognosis of patients with hepatitis.
10. Describe the preventive measures to hepatitis.

Definition

- Hepatitis is a general term that refers to inflammation of the liver.

Causes

1. Infections.
- Viral.
- Non-viral.
2. Drugs.
3. Autoimmune diseases.

Cause

I. Infectious hepatitis:

A. Viral hepatitis:

- Hepatitis-A virus (HAV).
- Hepatitis-B virus (HBV).
- Hepatitis-C virus (HCV).
- Hepatitis-D virus (HDV).
- Hepatitis-E virus (HEV).

I. Infectious hepatitis

Other types:

- Non-ABCDE viral hepatitis (currently under investigation).
- Hepatitis-F virus .
- Hepatitis-G virus .
- Other viruses that may cause inflammation of the liver:
  - Cytomegalovirus.
  - Epstein-Barr virus.
  - Herpes simplex virus.
  - Varicella-zoster virus.

I. Infectious hepatitis

B. Non-viral hepatitis:

Liver abscess:

a. Amoebic liver abscess, caused by *Entamoeba histolytica*.

b. Pyogenic liver abscess:

- It tends to affect those at extremes of age (children and elderly patients).
- In neonates: It is caused by gram-positive aerobic cocci.
- In adults: It is caused by gram negative bacilli.
- In elderly: It is caused by the underlying malignancy.

II. Drugs-induced hepatitis

- Trimethoprim-sulphonamide combinations e.g. co-trimoxazole.
- Amoxycillin-clavulanate.
- Paracetamol.
- Amiodarone.
- Minocycline.
- Nitrofurantoin.
- Telithromycin.
- Trovafloxacin.

Drugs of abuse:

- Cocaine.
- Toluene.
- Alcohol.

III. Autoimmune hepatitis

- It is common in young women and girls.
- The cause is not known.
- They have elevated transaminase and serum globulins especially gamma globulin.
- They have other autoimmune diseases e.g. Graves' disease.

Clinical features

History:

Phase-1: Viral replication.

- Patients are asymptomatic.
- Laboratory studies demonstrate positive serologies and enzyme markers of hepatitis.

Phase-2: Prodromal phase.

- Anorexia, nausea, vomiting, an alteration of taste, arthralgia, malaise, fatigue, Urticaria and pruritus.
- Some even develop distaste to cigarette smoke.

History

Phase-3: Icteric phase.

- Darkening of urine, followed by pale-coloured stool.
- Right hypochondrial pain with hepatomegaly.

Phase-4: Convalescent phase.

- Symptoms and icterus resolves.
- Liver enzymes return to normal.

Physical examination

- Low-grade fever.
- Dehydration.
- Jaundice.
- Skin may have macular, papular or urticaria rashes.
- Liver is tender and diffusely enlarged with a firm, sharp and smooth edges.

Hepatitis-A

Epidemiology:

A. High risk areas:

- Developing countries.
- Areas of low socioeconomical status.
- Day care centers.
- Areas with inadequate sanitation.

B. High risk Individuals:

- International travellers.
- Users of injected drugs.
- Military personnel stationed abroad.
- Homosexual men.
- Close contacts of infected individual (20%).

Hepatitis-A

Transmission:

- Faecal-oral route (major) via contaminated water and food.
- Parenteral via infected serum (minor).

NB: HAV exists in highest concentration in the faeces of infected individuals.

Hepatitis-A

Clinical course:

- Incubation period of HAV infection is 2-7 weeks, with an average of 28 days.
- Nausea and vomiting.
- Hepatomegaly.
- Dark-urine.
- Jaundice.
- Anorexia.
- Fatigue.
- Fever.
- Rash.

Hepatitis-B

Epidemiology:

High risk individuals:

- Heterosexual persons with multiple sexual partners or a history of STD.
- Institutionalized persons.
- Recipients of multiple blood transfusions.
- Patients undergoing haemodialysis.
- Homosexual men.
- Sexual partners of HBV carriers.
- Person born in endemic areas.
- Intravenous drug users.
- Health care workers.
- Household contacts.

Hepatitis-B

Transmission:

1. Parenteral.
2. Sexual.
3. Mucous membrane or percutaneous exposure with infectious body fluids e.g. saliva, serum and semen.
4. Perinatal.

Hepatitis-B

Clinical course:

The incubation period: 30-180 days (average: 75 days).

Prodromal phase:

- Anorexia, malaise and fatigue.
- The liver enlargement.
- Right hypochondrial pain.
- Fever, arthritis, arthralgia or urticarial rash (15%).

Hepatitis-B

Icteric phase:

- Liver becomes tender.
- Jaundice.
- Urine darkens and stool lightens in colour.
- Nausea, vomiting and pruritus.

From this point on, patients may have a variable course:

- Fairly rapid improvement in their symptoms.
- A prolonged disease course with slow resolution.
- Symptoms that periodically improve, only to worsen later (relapsing hepatitis).

  Finally, unfortunate patients may rapidly progress to fulminant hepatic failure. This may occur over days to weeks.

Hepatitis-C

Epidemiology:

- It is the most frequent cause of parenteral non-A, non-B hepatitis worldwide.
- Estimates suggest that 170 million people are chronically infected.
- The highest rates of disease prevalence are found in patients with haemophilia and in injection drug users.

Hepatitis-C

Transmission:

- Parenteral.
- Sexual.
- Perinatal.

Clinical course:

- Incubation period is 15-150 days, with symptoms developing anywhere from 5-12 weeks after exposure.
- Up to 80% of HCV infections are asymptomatic and do not develop icterus.

Hepatitis-D

Epidemiology:

- HDV, an incomplete virus, requires the presence of HBV to replicate; therefore, HDV infection develops only in patients who are positive for the hepatitis-B surface antigens (HBsAg).
- CDC estimates 7,500 infections to occur each year, of which 4% of cases are due to co-infection with HDV and HBV.

Hepatitis-D

- **Transmission:**

  Similar to those of HBV, although perinatal transmission rarely occurs.

Clinical course:

- Incubation period of HDV is approximately 35 days.
- Patients co-infected with HDV and HBV tend to have a more severe disease course than those infected with HBV alone.
- One third of those co-infected go on to develop fulminant hepatitis.

Hepatitis-E

Epidemiology:

- It is a primary cause of enterically transmitted non-A, non-B hepatitis.

Transmission:

- HEV is transmitted primarily by the faecal-oral route, via faecally contaminated water.
- Transmission by person to person contact is undocumented.

Hepatitis-E

Clinical course:

- Incubation period is 2-9 weeks with an average of 45 days.
- HEV causes an acute self-limited disease similar to HAV infection.
- Fulminant disease does occur in 10% of cases.
- No report of chronic HEV infection exists.

Complications

- Acute or subacute hepatic necrosis.
- Cholestatic hepatitis.
- Relapsing hepatitis.
- Chronic active hepatitis.
- Chronic hepatitis.
- Liver cirrhosis.
- Liver failure.
- Fulminant hepatic failure.
- Hepatocellular carcinoma (25-30 years after initial infection).

Differential diagnoses

- Hepatocellular carcinoma.
- Biliary obstruction.
- Pancreatic cancer.
- Pancreatitis.
- Liver abscess.
- Liver cirrhosis.
- Cholecystitis.
- Cholelithiasis.
- Cholangitis.

Investigations

- Urinalysis for Bilirubin.
- Total Bilirubin.
- Alkaline phosphatase.
- Prothrombin-time.
- Random blood glucose.
- Serum creatinine and BUN.
- Serum ammonia.
- Liver biopsy.
- Ultrasound or computed tomography scans.

Investigations

Serologies:

- Hepatitis-A antibody (IgM anti-HAV) test.
- Hepatitis-B core antibody (IgM anti-HBc) test.
- Hepatitis-B surface antigens (HBsAg) test.
- Hepatitis-C antibody (IgM anti-HCV) test.
- Hepatitis-D antibody (IgM anti-HDV) test.

Treatment

Goals of therapy:

- Reduce liver inflammation and fibrosis.
- Prevent progression to liver cirrhosis.
- Prevent complications of liver cirrhosis.

Treatment

Supportive therapy:

- Maintain adequate hydration.
- Instruct the patient to abstain from using any potential hepatotoxins e.g. alcohol, Paracetamol etc.
- Avoid vigorous or prolonged physical exertion until their symptoms improve.

Interferon alpha-2b

- It induces remission in patients with chronic HBV and HCV infection.
- Decreases abnormal aminotransferese concentration.
- It delays or prevents the development of Hepatocellular carcinoma in patients with liver cirrhosis.

Dose:

- 5 million IU/day or 10 million IU 3 times/week IM or SC for 16 weeks; reduce the dose by 50% if severe adverse reactions occurs.

Antiviral drugs

A. Amantadine:

Mechanism of action:

- **It prevents penetration of the virus into the host by inhibiting uncoating virus.**

Indication:

- **It may be useful in patients with HCV who do not respond to interferons.**

Dose: 100 mg PO BID for 6 months.

Antiviral drugs

B. Famciclovir:

Mechanism of action:

- It is a prodrug that, when transformed into active metabolite Penciclovir, may inhibit viral DNA synthesis or replication.

Dose: 500 mg PO TID for 6 months.

Corticosteroids

Prednisolone:

Dose:

- 5-60 mg/day PO OD or divided BID/TID; taper over 2 weeks as symptoms resolves.

Contraindications:

- Fungal or tubercular skin infections.
- Documented hypersensitivity.
- Connective tissue infection.
- Gastrointestinal disease.
- Peptic ulcer disease.
- Hepatic dysfunction.

Prognosis

- **Hepatitis-A:**
- It is mild and self-limited.
- It confers lifelong immunity against HAV infection.
- Mortality rate is 0.01%. It is the highest in children younger than 5 years and adults older than 50 years.

Prognosis

Hepatitis-B:

- The risk of chronic HBV infection in older children and adults is 5-10%.
- Patients with chronic HBV infection are at risk of developing chronic active hepatitis, liver cirrhosis and hepatocellular carcinoma.
- Fulminant hepatic failure develops in 0.5-1% of patients infected with HBV with case-fatality rate of 80%.

Prognosis

Hepatitis-C:

- Chronic HCV infection develops in 50-60% of patients with HCV infection.
- Chronically HCV infected patients are at risk for chronic active hepatitis, liver cirrhosis and hepatocellular carcinoma.

Prognosis

Hepatitis-D:

- Patients with chronic HBV infection who are co-infected with HDV also tend to develop chronic HDV infection.
- Chronic infection with HBV and HDV often leads to rapidly progressive subacute or chronic hepatitis with as many as 70-80% of these patients eventually developing liver cirrhosis.

Prognosis

Hepatitis-E:

- It is mild and self-limited.
- Case-fatality rate reaches 15-20% in pregnant women.
- HEV infection does not result in chronic disease.

Prevention

Hepatitis-A:

- Improve sanitation, strict personal hygiene and hand washing.
- Do not drink untreated water or ingest raw seafood or shellfish.
- Passive immunization:

  Post-exposure passive immunization with immune globulin 0.02 ml/kg can protect a person against HAV clinical illness.

Hepatitis-A

Active immunization:

Indications:

- Health care workers.
- Day care personnel.
- Travellers to endemic areas.
- Sewage and wastewater workers.
- Veterinarians working with imported non-human primates.

Hepatitis-B

Active immunization:

Indications:

- Children (routine).
- Non-immunized persons who are close contacts of patients with acute HBV infection or who suffer percutaneous exposure to HBV and infants born to potentially infectious mothers.

Passive immunization:

- Those exposed should receive HBV immune globulin in additional to active immunization.

Prevention

Hepatitis-C:

- Transmission is prevented by avoiding transfusion of infected blood, infected organs and contact with semen.
- No vaccine is available.

Hepatitis-D:

- Since the HDV infection can infect patients only when HBV is present, transmission of this disease can be decreased by effectively immunizing patients against HBV.

Hepatitis-E:

- No vaccine available.
- Administration of immune globulin does not prevent development of clinical disease.

Thank you for your attention

Reference

- Buggs A.M. and Lim J.K. Hepatitis; www.emedicine.com/emerg/topic244.htm Last uptodated: July 12, 2006.