العدد (٤١)

المجموعة الرابعة

المرحلة الثالثة
فايروسات

Hepatitis Viruses:

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Five medically medically important Viruses are commonly described as "hepatitis viruses" because their main site of infection is the liver. Thes five are: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV, delta virus) & hepatitis E virus (HEV). other viruses, such as Epstein-Barr virus (The cause of infectious mononucleosis), Cytomegalo virus & yellow fever virus, infect the liver but also infect other sites in the body & therefore are not exclusively hepatitis viruses. Viral hepatitis is a sytemic disease primarily involving the liver.

Hepatitis type A:

Its 27-32 nm spherical particle with cubic symmetry, SSRNA., non-enveloped. It is picornavirus. It has one serotype & there is no antigenic relationship to HBV or other hepatitis viruses.

Clinical finding:

The clinical picture of hepatitis is the same. fever, anorexia, nausea, vomiting & jaundice are typical. Dark urine, pale feces & elevated transaminase levels are seen. Most cases resolve spontaneously in 2-4 weeks. Hepatitis A has a short incubation period (3-4 weeks) in contrast to that of hepatitis B, which is 10-12 weeks. Most infections are asymptomatic & are detected solely by the presence of IgG antibody. No chronic hepatitis or chronic carrier state occurs, & there is no predisposition to hepatocellular carcinoma.

Epidemiology:

Transmitted by fecal-oral route. Humans are the reservoir for HAV.. Virus appears in the feces roughly 2 weeks before the appearance of symptoms, so quarantine of patients is ineffective. Children are the most frequently infected group. Common-source outbreaks arise from fecally contaminated water or food. HAV is rarely transmitted via the blood, because the level of viremia is low & chronic infection does not occur.

Pathogenesis:

Virus replicates in the gastrointestinal tract & spreads to the liver via the blood. Hepatocytes are infected. HAV infection of Cultured cells produces no cytopathic effect. It is likely that attack by Cytotoxic T cells causes the damage to the hepatocytes. The infection is cleared, the damage is repaired & no Chronic infection ensues. Hepatitis Caused by the different viruses Cannot be distinguished pathologically.

Immunity:

The immune response Consists initially of IgM antibody, which is detectable at the time jaundice appears. It is therefor important in the laboratory diagnosis of hepatitis A. The appearance of IgM is followed 1 to 3 weeks later by the production of IgG antibody which provides lifelong protection.

Laboratory Diagnosis:

The detection of IgM antibody is the most important test. A four-fold rise in IgG antibody titer Can also be used. Isolation of the virus in cell Culture is possible but not available.

Treatment:

No antiviral therapy is available.

Prevention & Control:

Active immunization with a vaccine Containing inactivated HAV is available. Two doses, an initial dose followed by a booster 6–12 months later, should be given. If an unimmunized person must travel to an endemic area within 4 weeks, then passive immunization should be given to provide immediate protection & the vaccine given to provide long term protection. This is an example of passive-active immunization. For cost-effective we should determine antibody before giving the vaccine. The vaccine is also effective in posterposure prophylaxis if given within 2 weeks of exposure. A combination vaccine that immunizes against both HAV & HBV Called Twinrix is available. Passive immunization prior to infection or within 14 days after exposure Can prevent or mitigate the disease. observation of proper hygiene (e.g., sewage disposal & hand washing after bowel movements, is of prime importance)

Hepatitis B Virus:

Cause chronic infections, especially in those infected as infantr & may lead to. hepatocellular Carcinoma. Human only natural host. It is a member of hepadnavirus family. 42nm, enveloped, Icosahedral, DSDNA genome envelope contain protein Called the surface antigen (HBsAg), which is important for laboratory diagnosis & immunization. Other two antigens: The core antigen (HBcAg) and the e Antigen (HBeAg). The core antigen is the nucleocapsid core of the virion, whereas the e Antigen is secreted from infected cells into the blood. The e antig; is an important indicator of transmissibility.

For vaccine purposes, HBV has one serotype based on HBsAg. However, for epidemiolog; purposes, there are four serologic subtypes of HBsAg based on a group-specific antigen, "a" and two sets of epitopes, d or y & w or r. This leads to four serotypes - adw, adr, ayw; & ayr - which are useful in epidemiologic studies because they are concentrated in certai; geographic areas.

Clinical Findings:

Many HBV infections are asymptomatic & are detected only by the presence of antibody to HBsAg. The mean incubation period for hepatitis B is 10 to 12 weeks which is much longer than that of hepatitis A (3-4 weeks). The clinical appearance of acute hepatitis B is similar to that of hepatitis A. However, with hepatitis B, symptoms tend to be more severe, and life-threatening hepatitis can occur Most chronic carriers are asymptomatic, but some have chronic active hepatitis, which can lead to cirrhosis & death.

Epidemiology:

The three modes of transmission are: blood, during sexual intercourse, & perinatally from mother to newborn. Needle-stick injuries can transmit the virus indicates that only very small amounts of blood are necessary. It is likely that sexual transmission & transmission from mother to child during birth or breast feeding are the natural routes.

IBV found worldwide but is particularly prevalent in Asia. Globally, more 300 million people are chronically infected with HBV & about 75% of them ar sian. There is a high incidence of hepatocellular Carcinoma (hepatoma) in many sian countries – a finding that indicates that HBV may be a human tumor virus.

Pathogenesis:

After entering the blood, the virus infects hepatocytes & viral antigens are displayed on the surface of the cells. Cytotoxic T cells mediate an immune attack against the viral antigens & inflammation & necrosis occur. Immune attack against viral antigens on infected hepatocytes is mediated by cytotoxic T cells. The pathogenesis of hepatitis B is probably the result of this cell-mediated immune injury, because HBV itself does not cause acytopathic effect. Antigen-Antibody complexes cause some of the early symptoms (e.g., arthralgias, arthritis & urticaria) & some of the complications in chronic hepatitis (e.g., glomerulonephritis, cryoglobulinemia, & vasculitis).

About 5% of patients with HBV infection become chronic carriers. A chronic carrier is someone who has HBsAg persisting in their blood for at least 6 months. HBV DNA exists primarily as an episome in the cytoplasm of persistently infected cells; a small number of copies of HBV DNA are integrated into cell DNA. A high rate of hepatocellular carcinoma occurs in chronic carriers. HBV genome integrater into the hepatocyte DNA. Integration of the HBV DNA could activate a cellular oncogene, leading to a loss of growth control. Approximately 90% of infected neonates become chronic carriers this lead to high risk of hepatocellular Carcinoma.

Immunity:

lifelong immunity occurs after the natural infection & is mediated by humoral antibody against HBsAg. Antibody against HBsAg (HBsAb) is protective because it binds to surface antigen on the virion & prevents it from interacting with receptors on the hepatocyte. Antibody against the core antigen is not protective because the core antigen is inside the virion & the antibody can not interact with it.

atory Diagnosis:

The most important laboratory test for the detection of HBV infection is the immuno assay for HBsAg. HBsAg appears during the incubation period & is detectable in most patients during the prodrome & acute disease. It falls to undetectable levels during convalescence in most cases; its prolonged presence (at least 6 months) indicates the carrier state & the risk of chronic hepatitis & hepatic carcinoma. HBsAb is not detectable in the chronic carrier state. There is a period of several weeks when HBsAg has disappeared but HBsAb is not yet detectable. This is the window phase. At this time, the HBc Ab is always positive & can be used to make the diagnosis. HBcAb is present in those with acute infection & chronic infection, as well as in those who have recovered from acute infection. presence of HBeAg indicates a high likelihood of transmissibility. The detection of viral DNA (viral load) in the serum is strong evidence that infectious virions are present.

Treatment:

Interferon or nucleoside are used, these drugs reduce hepatic inflammation & lower the viral load but they do not cure HBV infection. In most patients when the drug is stopped, HBV replication resumes.

Prevention & Control:

Prevention involves the use of either the vaccine or hyperimmune globulin or both:

1) The vaccine (e.g., Recombivax) seroconversion is 95%, 3 doses are used. A vaccine called Twinrix that contains both HBsAg & inactivated HAV provides protection against both hepatitis B & hepatitis A.

2) Hepatitis B immune globulin (HBIG) contains a high titer of HBsAb. It is used to provide immediate, passive protection to individual known to be exposed to HBsAg positive blood. In needle-stick injury from a patient with HBsAg-positive blood & newborn whose mother is HBsAg positive, passive-active immunization is used of both vaccine & HBIG be given (at separate sites). This give both immediate & long term protection are provided.

All blood for transfusion should be screened for HBsAg. No one with a history of hepatitis (of any type) should donate blood.

hep

epatitis Type C:

This is ssRNA virus in the family Flaviviridae, genus Hepacivirus
hey are at least 6 major genotypes (clades) & more than 100 subtypes. enveloped virus
ost new infections are subclinical. The majority (70-90%) of HCV patients develop
chronic hepatitis, & many at risk of progressing to chronic active hepatitis & cirrhosis
10-20%). In some countries, HCV infection often leads to hepatocellular carcinoma.
It has genetic variability due to high mutation rate in the envelope gene.

linical finding:

Acute infection with HCV is milder than infection with HBV. Fever,
norexia, nausea, vomiting, & jaundice are common. Dark urine, pale feces, & elevated
ransaminase levels are seen. HCV resembles hepatitis B as far as chronic liver
isease, cirrhosis, & predisposition to hepatocellular carcinoma. Chronic carrier state
ccurs more often with HCV infection than with HBV. Many infections with HCV,
ncluding both acute & chronic infections, are asymptomatic & are detected only by the
presence of antibody. The mean incubation period is 8 weeks. Cirrhosis resulting from
chronic HCV infection is the most common indication for liver transplantation.
HCV infection also leads to significant autoimmune reactions, including vasculitis, arth
ralgias, purpura, & membranoproliferative glomerulonephritis. HCV is the main cause of
essential mixed cryoglobulinemia. The cryoprecipitates often are composed of HCV antigens &
antibodies
Epidemiology:

Transmitted via blood. 180 million worldwide are infected with HCV

Pathogenesis:

Infect hepatocytes with no cytopathic effect. Death of hepatocytes caused
by immune attack by cytotoxic T cells. Infection strongly predisposes to hepatocellular
Carcinoma. Alcoholism greatly enhances the rate of hepatocellular carcinoma in HCV
infected individuals.

Immunity:

Antibodies against HCV are made, but approximately 75% of patients are
chronically infected & continue to produce virus for at least 1 year. Chronic active hepatitis
& cirrhosis occur in approximately 10% of these patients.

Diagnosis:

Detection of antibodies by ELISA. Because false-positive results occur in the ELISA, a RIBA (recombinant immunoblot assay) should be performed as a confirmatory test. If RIBA positive, PCR should be done to detect the presence of viral RNA (viral load) in the serum should be performed to determine whether active disease exists. chronic infection is characterized by elevated transaminase levels, a positive RIBA, & detectable viral RNA for at least 6 months.

Treatment & Prevention

acute with alpha interferon decreases the number of patients who become chronic carriers. In chronic HCV a combination of preginterferon (Pegasys) & ribavirin pegmterferon is alpha interferon. Patients infected with genotypes 1 & 4 are treated for 12 months, whereas those infected with genotypes 2 & 3 are treated for 6 months. The addition of protease inhibitor, either boceprevir (Victrelis) or telaprevir (Incivek), to the Combination of preginterferon & ribavirin significantly improved the duration of the suppression of viral replication of HCV genotypes.

Blood found to contain antibody is discarded. No vaccine & hyperimmune globulins are not available. Patients with chronic HCV infection should be advised to reduce or diminate their consumption of alcohol, to reduce the risk of hepatocellular Carcinoma & Cirrhosis. Patient coinfected with HCV & HIV should take HAART

Hepatitis D Virus (Delta Virus):

It is defective virus. HDV replicate only in cells also infected with HBV because HDV uses the surface antigen of HBV (HBsAg) as its envelope protein. HBV is therefore the helper virus for HDV (defective virus). HDV is an enveloped SSRNA virus. The RNA genome of HDV is very small & encodes only one protein, the internal core protein called delta antigen. HDV has one serotype because HBsAg has only one serotype. It is often associated with the most severe forms of hepatitis in HBsAg-positive patients. Its classified in the Deltaviruses genus, which is not assigned to any virus family

Clinical finding:

hepatitis delta can occur only in a person infected with HBV. A person can either be infected with both HDV & HBV at the same time (coinfected) or be previously infected with HBV & then superinfected with HDV.

hepatitis

epatitis in patients coinfected with HDV & HBV is more severe than in those infected with HBV alone, but the incidence of chronic hepatitis is about the same in patients nfected with HBV alone. However, hepatitis in chronic carriers of HBV who become super-nfected with HDV is much more severe, & the incidence of fulminant, life-threatening epatitis, chronic hepatitis & live failure is significantly higher.

:pidemiology:

Transmitted by the same means as HBV. Occur worldwide similar to HBV

athogenesis: Same as HBV (virus infected hepatocytes are damaged by cytotoxic T cells)

here is some evidence that delta antigen is cytopathic for hepatocytes.

mmunity: IgG against delta not detected for long periods after infection.

aboratory Diagnosis: Detecting either delta antigen or IgM antibody to delta in patient sera

eatment & Prevention: No vaccine, No therapy. person immunized against HBV will not be nfected by HDV because HDV cannot replicate unless HBV infection also occurs.

epatitis E Virus:

Transmitted by fecal-oral route. Cause waterborne epidemics. Non envelope SSRNA. Disease resemble hepatitis A, With the exception of a high mortality rate in regnant women. No chronic, No carrier. No treatment & No vaccine

epatitis G Virus:

Isolated from patients with posttransfusion hepatitis. Its a member f flavivirus family as is HCV. HGV has not been documented to cause any of these inical findings. The role of HGV in the causation of liver disease has yet to be established ut it can cause a chronic infection lasting for decades. Approximately 60-70% of hose infected clear the virus & develop antibodies.

HGV is transmitted via sexual intercourse & blood. It is carried in the blood of millions of people worldwide. Patients coinfected with HIV & HGV have a lower mortality ate & have less HIV in their blood than those infected with HIV alone. It is hypothesized at HGV may interfere with the replication of HIV.