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In Shortly about Hepatitis A

Research Article

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Abstract

Hepatitis A is mainly transmitted by consuming food and water contaminated with feces or by direct physical contact with an infected person. It is also called "dirty hand disease". It can also be transmitted by consuming raw shellfish from sewage–contaminated water and by consuming frozen fruits and vegetables, and sexual transmission is also possible. Symptoms can range from mild to severe and can include fever, loss of appetite, diarrhea, nausea, abdominal pain, dark color of urine, light stools, and jaundice. Not all infected people have symptoms, and they occur more often in adults than in children. Hepatitis A is contagious two to four weeks before symptoms develop and for several days thereafter. People with hepatitis B or C can become carriers of the virus after recovery, even if chronic disease does not develop and symptoms are not present. Hot water and thorough cleaning of items used by patients is important to prevent the spread of infection.

Keywords: HAV; RNA; ALF; Treatment.

Introduction

Although the hepatitis viruses have been characterized extensivey, the pathogenesis, diagnosis, and treatment of chronic vira hepatitis continue to be the focus of research [1]. Sensitive and specific assays are available for a five forms (A–E) of viral hepatitis. Nevertheless, at least approximately 5–10% of cases of acute and chronic hepatitis cannot be attributed to any of the known forms of viral hepatitis and do not appear to result from toxic, metabolic, or genetic conditions. A specific cause cannot be identified for approximately 50% of cases of fulminant hepatitis. Whether additional unidentified viruses cause acute or chronic liver disease remains an unanswered question; to date, despite intense investigation, no other hepatitis viruses have been identified.

Infection with HAV causes hepatitis A (infectious hepatitis) [2]. Hepatitis A is responsible for 20–25% of clinical hepatitis in the developing countries of the world but the incidence is much lower in the developed countries. Hepatitis A is usually a benign, self–limiting disease and has an incubation period of 15–45 days. The disease occurs in epidemic form as well as sporadically. It is almost exclusively spread by faeco–oral route. The spread is related to close personal contact such as in overcrowding, poor hygienic and sanitary conditions. Frozen and stored contaminated foods and water have been blamed in many epidemics. Most frequently affected age group is 5–14 years; adults are often infected by spread from children.

Hepatitis A virus is present in the liver and replicates there. It is present in the liver, bile, blood and stools in the pre–icteric incubation period but viraemia and viral shedding in stool is diminished after jaundice appears.

Acute hepatitis is commonly caused by one of five major viruses: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV) [3]. Other viral agents that can cause acute hepatitis, though less commonly, include the EpsteinBarr virus (cause of infectious mononucleosis), cytomegalovirus, varicella virus, measles virus, herpes simplex virus, rubella virus, and yellow fever virus. A newly discovered DNA virus, SEN virus, may be associated with transfusion–associated acute hepatitis not attributable to other viruses. HAV, a small RNA virus, causes liver disease both by direct killing of hepatocytes and by stimulating the host's immune response to infected hepatocytes. It is spread by the fecal–oral route from infected individuals. Although most cases are mild, hepatitis A occasionally causes fulminant liver failure and massive hepatocellular necrosis, resulting in death. Regardless of the severity, patients who recover do so completely, show no evidence of residual liver disease, and have antibodies that protect them from reinfection.

HAV

Hepatitis A virus (HAV) is a 27–nm nonenveloped RNA virus (genus Hepatovirus) that is transmitted by the fecal–oral route through ingestion of contaminated food (eg, she fish, strawberries, onions) or water [1]. The incubation period is 2–6 weeks, the duration of viremia is short (5–7 days), and chronic infection does not occur; therefore, percutaneous transmission is exceedingly rare.

Infection is more prevalent in areas of low socioeconomic status characterized by insufficient sanitation and poor hygienic practices, which facilitate the spread of enteric infections. In developing countries, hepatitis A is endemic, infecting most

children before the age of 5–10. In developed countries, improved socioeconomic conditions and sanitation have led to an increase in the mean age of infection and a reduction in the prevalence of HAV exposure, as reflected by serum antibodies to HAV (anti–HAV) in the population.

Hepatitis A occurs throughout the world and is endemic in countries with poor sanitation [4]. At special risk of infection are persons traveling abroad who have not been vaccinated or previously exposed to the virus. HAV has a brief incubation period, with an average of 25 to 30 days. The virus replicates in the liver, is excreted in the bile, and is shed in the stool. The fecal shedding of HAV occurs for 2 to 3 weeks before the development of symptoms and ends about 1 week after the onset of jaundice. Because young children are asymptomatic, they play an important role in the spread of the disease. Oral behavior and lack of toilet training promote viral spread among children attending day care centers, who then carry the virus home to older siblings and parents. Infected workers in food industries may also be a source of spread. HAV usually is not transmitted by transfusion of blood or plasma derivatives, presumably because its short period of viremia usually coincides with clinical illness, so that the disease is apparent and blood donations are not accepted.

The onset of symptoms usually is abrupt and includes fever, malaise, nausea, anorexia, abdominal discomfort, dark urine, and jaundice. The likelihood of having symptoms is related to age. Children younger than 6 years often are asymptomatic. The illness in older children and adults usually is symptomatic and jaundice occurs in approximately 70% of cases. Symptoms usually last approximately 2 months. HAV infection does not cause chronic hepatitis or induce a carrier state, and only rarely causes acute fulminant hepatitis.

Pathogenesis

As is true for a hepatitis viruses, viral replication of HAV occurs primarily within hepatocytes [1]. Except in extraordinary circumstances, hepatitis viruses are not cytopathic; instead, liver cell damage results from host cell–mediated cytotoxicity. In hepatitis A, the necroinflammatory changes and mononuclear cell infiltrates are prominent in periportal areas, but lobular focal necrosis, ballooning hepatocytes, and apoptosis are regular features as well. In some cases, centrilobular cholestasis may be severe, particularly in adults. Serum neutralizing antibodies protect against HAV infection. HAV antigen can be demonstrated by immunohistochemica staining as fine granules in the cytoplasm of hepatocytes and Kupffer cells.

The only reservoir for HAV is the acutely infected person, and transmission depends primarily on serial passage from person to person by the fecal–oral route [5]. Epidemics of hepatitis A occur under crowded and unsanitary conditions, such as exist in warfare, or by fecal contamination of water and food. Edible shellfish in contaminated waters concentrate the virus and may transmit infection if they are not adequately cooked. In the United States, about 10% of the population younger than 20 years of age has serologic evidence of previous HAV infection. This circumstance indicates that most infections with HAV are anicteric and remain undetected. Hepatitis A is common in day care centers and among international travelers and male homosexuals. However, in about half of all cases of hepatitis A, no source can be identified. Vaccination confers long–term protection against the disease. Universal vaccination programs have significantly reduced acute HAV infection in the United States.

Concomitantly, liver injury is evidenced by a rise in serum aminotransferase activity. As the activities of aminotransferases begin to decline, usually 5 to 10 days later, jaundice may appear. It remains evident for an average of 10 days but may persist for more than a month. In most cases, the elevated levels of aminotransferases return to normal by the time jaundice has disappeared. Hepatitis A never pursues a chronic course. There is no carrier state, and infection provides lifelong immunity. Fatal fulminant hepatitis occurs only rarely, and virtually all patients recover without sequelae.

Hepatitis A usually has a mild course similar to that of a typical flu–like infection and often goes unrecognized [6]. It is spread most often by the fecaloral route by fecal contamination either from person–to–person contact (e.g., oral–anal sexual activity) or by consuming contaminated food or water. Common sources of infection include shellfish caught in contaminated water and food contaminated by food handlers infected with HAV. The disease is usually not life threatening, but its course may be more severe in people older than 40 years and those with pre–existing liver disease such as hepatitis C.

In a small percentage of hepatitis A cases, severe illness with extrahepatic manifestations can occur. Advanced age and conditions such as chronic liver disease may cause widespread damage that requires a liver transplant. In some cases, death may occur. The incidence of hepatitis A is particularly high in non–affluent countries in which sanitation is poor. However, over 35,000 cases are diagnosed each year in the United States. Some adults have hepatitis A and do not know it. The course is similar to that of a GI illness, and the disease and recovery are usually uneventful.

Alcohol

Symptoms of early alcoholic liver disease include weakness, fatigue, and weight loss [7]. In advanced disease, the patient develops anorexia, nausea and vomiting, swelling of the abdomen and the lower extremities, and central nervous system symptoms related to the cirrhotic liver disease. Other symptoms that may occur include loss of libido in both sexes, gynecomastia in men, and menstrual irregularities in women.

The liver of patients with alcoholic hepatitis and cirrhosis is usually enlarged, palpable, and firm. In advanced cirrhosis, the liver may actually shrink. Dermatologic manifestations include spider nevi, palmar erythema, telangiectasia on exposed areas, and occasional evidence of vitamin deficiencies. Although jaundice is rarely an initial sign, it usually develops later. Other later developing signs include ascites, lower extremity edema, pleural effusion, purpuric lesions, asterixis, tremor, delirium, coma, fever, splenomegaly, and superficial venous dilation on the abdomen and thorax. There appears to be a genetic predisposition to the development of these complications. Of patients with advanced cirrhosis, 50% will be dead in a period of 2 years; 65% will be dead in 5 years. Hematemesis, jaundice, and ascites are unfavorable signs.

ALF

Acute liver failure (ALF) is a complex multisystemic illness that evolves after a catastrophic insult to the liver and leads to coagulopathy and encephalopathy within days or weeks [8]. The absence of recognized pre–existing liver disease is a requirement.

ALF is a heterogenous condition incorporating that is influenced by the underlying etiology, the age of the patient and the duration of time over which the disease evolves. These are not mutually exclusive factors and, as examples, hyperacute liver failure is more likely to be seen in younger patients with hepatitis A or B while subacute liver failure patients tend to be older and more likely to have seronegative hepatitis or idiosyncratic drug reactions.

ALF complicates 0.2–4% of cases of acute viral hepatitis, depending on the etiology, and is less likely with hepatitis A. Hepatitis B causes ALF through a number of scenarios. The classical ALF is caused by an aggressive immune response against the virus either at de novo infection or in chronic infections at the time of HBeAg clearance and seroconversion to HBeAb positivity. The alternative mechanism is aggressive viral replication, spontaneous or secondary to immunosuppression or chemotherapy; this may be amenable to therapy with antiviral agents. The incidence of the delta virus is decreasing. Hepatitis C is rarely recognized as the sole cause of ALF. Hepatitis E is common in parts of Asia and Africa. Unusual viral causes of ALF include herpes simplex 1 and 2, herpes virus–6, varicella zoster, Epstein–Barr virus and cytomegalovirus.

Diagnosis

Hepatitis A virus is an RNA virus that is transmitted by fecal–oral mode through ingestion of contaminated food (eg, shellfish) or water [9]. The incubation period is 2–6 weeks and the phase when virus is present in serum is short (5–7 days); hence, parenteral transmission is rare. Infection is sporadic and is associated with poor socioeconomic conditions, which can lead to epidemics. In several developing countries hepatitis A is endemic, with infection occurring in the majority of children before the age of 5 years. Improved socioeconomic conditions and sanitation have led to an increase in the mean age of infection in southern Europe. The liver cell damage probably results from cell–mediated cytotoxicity. Serum neutralizing antibodies protect against HAV infection. The necroinflammatory changes are prominent in periportal areas and are accompanied by many plasma cells. In some cases, centrilobular cholestasis may be severe, particularly in adults. HAV antigen can be demonstrated by immunohistochemical staining as fine granules in the cytoplasm of hepatocytes and Kupffer cells.

Diagnosis of HAV infection depends on detection of antibodies [immunoglobulin G (IgG) for prior infection, IgM for recent infection]. A positive anti–HAV result usually reflects total antibodies (both IgG and IgM) and cannot be used to distinguish between acute or prior exposure unless IgM is specified. Anti–HAV IgM may persist for 6–12 months after acute infection. Hence, in a patient with acute transaminase elevation, presence of anti–HAV IgM, does not always signify acute hepatitis A infection but may represent hepatitis A infection within the prior year, with a superimposed, unrelated hepatitis.

Most cases of acute hepatitis A are asymptomatic (particularly in children) or have nonspecific symptoms. When clinically apparent, patients present with jaundice, fatigue, and malaise. Uncommonly, HAV infection may result in a cholestatic picture.

Epidemiology

HAV is a member of the Picornaviridae family, genus Hepatovirus [10]. The hepatitis A viral particle is a 27–nm nonenveloped icosahedral nucleocapsid that expresses the hepatitis A antigen and contains a positive–stranded RNA genome approximately 7.5 kb long. Three different HAV genotypes have been described in humans (genotypes I, II, and III), with genotype I predominating worldwide. Other genotypes have been isolated in nonhuman primates. It is currently unclear to what extent different genotypes are associated with distinct clinical courses of infection.

HAV infection has a worldwide distribution, and infections can be sporadic or occur in epidemic outbreaks. The incidence of acute cases and the seroprevalence vary according to the hygiene, sanitation, housing, and socioeconomic standards of a given region, with a seroprevalence as low as approximately 13% in Sweden but up to 100% in many developing countries. In developing countries, infection generally occurs at a young age and most of the population has been exposed and is protected after age 10 years. In developed countries, however, infection can occur at any age, and the prevalence of exposed, immune subjects slowly increases with age. In the United States, according to the Centers for Disease Control and Prevention, the incidence of acute hepatitis A declined from 12.0 cases per 100,000 individuals in 1995 to 0.5 cases per 100,000 individuals by 2012. HAV is generally transmitted via the fecal–oral route, most often directly from person to person or through the ingestion of fecally contaminated food or water. Transmission by blood transfusion has been reported, and isolated cases of apparent perinatal transmission have been described. High–risk groups for acute hepatitis A include travelers to developing countries, children in daycare centers and their parents, men who have sex with men, injection drug users, patients who receive plasma products for hemophilia, and persons in institutions.

The genome serves as a messenger RNA and contains a single open reading frame that encodes both structural and nonstructural viral proteins. After attachment to a specific receptor at the surface of hepatocytes, the virus penetrates into cells and is uncoated. Subsequent events occurring exclusively in the cytoplasm include translation of the single open reading frame into a polyprotein that is later processed to generate the mature viral proteins; replication in a membrane–bound replication complex that generates new viral genomes, which are subsequently used for viral protein production and viral particle assembly; and packaging of newly formed genomes into new particles that are exported out of the cells. The virus is secreted into bile and, to a lesser extent, serum.

Treatment

Hepatitis A is rarely fulminant and never chronic [9]. Systemic manifestations are uncommon and include cryoglobulinemia, nephritis, and leucytoclastic vasculitis. Concomitant meningoencephalitis has been reported in some patients. Cholestatic hepatitis with protracted cholestatic jaundice and pruritus can occur as a variant of acute hepatitis A. It has been suggested that in genetically susceptible individuals, HAV infection may trigger an autoimmune hepatitis. Hepatitis A may have a relapsing course, symptomatic for 6 months or more. The relapses are generally benign, with eventual complete resolution. Chronic infection never ensues, and complete recovery is the rule. Rarely (less than 1% of cases), fulminant hepatic failure with encephalopathy and coagulopathy results from acute infection. Such patients should be referred for consideration of liver transplantation. Once profound encephalopathy develops in elderly patients, mortality is high (up to 80%). In younger

patients, the prognosis is better than in patients with fulminant liver failure of other causes. The overall case fatality rate with HAV infection is very low (about 0.1%), although in patients with chronic underlying liver disease, the morbidity and mortality are increased in the presence of a hepatitis A superinfection.

Treatment is largely supportive and consists of bed rest until jaundice subsides, a high caloric diet, discontinuation of potentially hepatotoxic medication, and restriction of alcohol intake. Most cases do not require hospitalization, which is recommended for patients with advanced age, serious underlying medical conditions, or chronic liver disease, malnutrition, pregnancy, immunosuppressive therapy, hepatotoxic medication, severe vomiting that excludes adequate oral intake, and clinical and laboratory findings that suggest fulminant hepatitis. The occasional patient with fulminant hepatic failure, defined as the onset of encephalopathy within 8 weeks of the onset of symptoms, should be referred for consideration of liver transplantation.

Prevention of hepatitis A is justified for public health reasons. General measures to prevent the spread of HAV include careful handwashing, safe water supply, and proper sewage disposal. Human trials with inactivated whole HAV vaccines have shown a protective efficacy of 94–100% after two or three doses and only minor side effects. Such a vaccine is licensed in several countries, including the United States, and is widely available. Immunoglobulin has also been shown to be safe and effective in preventing HAV infection in both pre– and postexposure situations. If immediate protection is required, travelers should receive passive immunization with immunoglobulin as well as vaccine to confer protection. Passive immunization is by a single intramuscular dose of immune serum globulin of 0.02–0.06 mL/kg. In postexposure setting, immune serum globulin, if given within 10–14 days of exposure, has an efficacy of about 85%, and usually aborts or reduces the severity of the HAV infection. The protection offered by immune serum globulin lasts only a few months.

HAV vaccine is very effective, and should be offered to: travelers to areas of increased risk; IV drug users; men who have sex with men; patients with hemophilia or chronic liver disease (including hepatitis C, who may have increased risk of acute liver failure); those at occupational risk (e.g., child care centre workers) [11]. 1 ml of vaccine given initially, and then at six to twelve months, provides 95% protection for > five years. Passive immunization, with human normal immunoglobulin (HNIG) has few indications, due to the rapid efficacy of HAV vaccine (even postexposure), and worries about transmission of prion disease (HNIG manufactured from pooled serum).

Conclusion

Anyone can be at risk of contracting viral hepatitis, which affects about 400 million people worldwide. and 1.4 million people die each year from the effects of viral hepatitis. It is estimated that 95% of people with viral hepatitis in the world do not even know they are living with this disease, given that the infection often causes very mild symptoms or none at all. If left untreated, viral hepatitis can cause liver damage and failure. Viral hepatitis is the leading cause of liver cancer and liver transplantation in Europe. Viral hepatitis varies according to the mode of transmission, the way it damages the liver and the effect on the condition of the organism. They are distributed throughout the world, with varying prevalence (percentage of infected), with types A, B and C accounting for 95% of cases.

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Conflict of interest

The author has no conflict of interest to declares.

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