Viral hepatitis and transmissible spongiform encephalopathies

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Abstract

Here, we provide an overview of viral hepatitis, the risks of transmission and new developments in the treatment of infected individuals. Acute hepatitis is a potentially fatal disease and, when not fatal, can lead to a chronic viral carrier status with the attendant risks of cirrhosis and hepatocellular carcinoma. Liver transplantation is often the only hope for survival, but advances in antiviral therapies are improving the outlook for those with chronic viral hepatitis. There are challenges to the anaesthetist who necessarily undertakes invasive procedures in such patients and may need to anesthetize them at any stage of their illness. There are complications relevant to intensive care management, and safety measures that clinicians need to adopt in the clinical environment. The majority of infectious agents, including the hepatitides, contain either DNA or RNA. In recent years, however, prion proteins have emerged as novel transmissible agents, lacking in nucleic acids. Transmissible spongiform encephalopathies are rare but, owing to the durability of prions, the associated mortality and the potential for iatrogenic transmission, significant changes to medical practice have ensued.

Keywords anaesthesia; transfusion; variant Creutzfeldt–Jakob disease; viral hepatitis

Learning objectives

After reading this article, you should:

- understand the differences between the various forms of viral hepatitis
- know what current prophylaxis and treatment of viral hepatitis is available
- know the epidemiology and pathogenicity of prion-related diseases.

Hepatitis

Hepatitis can be caused by infectious and non-infectious agents. Of the latter, alcohol, drugs and metabolic disorders are responsible, but the overwhelming global burden of hepatitis is caused by hepatotropic viral infection. An increasing number of hepatotropic viruses have been identified and may be acquired either from faecal contamination (hepatitis A and E) or parenterally via body fluids (hepatitis B, C, D and G). These hepatotropic viruses preferentially cause hepatitis and exhibit this preference to a greater (hepatitis A and B) or lesser (hepatitis G) degree (see Table 1).

Symptoms and signs

These may appear suddenly or follow a more insidious course. They may be so mild that the patient mistakes them for flu. Nearly all patients experience mild fever and fatigue with gastrointestinal symptoms of nausea, vomiting and abdominal discomfort being prominent features; some patients describe a sharp right hypochondrial pain. Thereafter follows anorexia, weight loss and dehydration. After approximately two weeks, jaundice with dark urine and pale stools can occur in a proportion of patients, but not all. Less specific symptoms of muscle pains, joint pains, itchiness or drowsiness can also occur. The liver may be tender and enlarged, and splenomegaly can occur in approximately 10% of patients.

Laboratory tests

The transaminases rise, often exceeding 1000 IU, between 7 and 14 days before the onset of jaundice and start falling with the onset of jaundice. These will usually normalize over the next 6–10 weeks. Plasma bilirubin peaks after approximately 2 weeks and falls over the next 2–4 weeks. Elevated fluctuating transaminase levels are suspicious of developing chronic hepatitis. A low albumin and prolonged prothrombin time suggest severe acute hepatitis and imply significant liver dysfunction.

Clinical course

In most cases of acute viral hepatitis there is complete recovery within 2–8 weeks. Rarely, fulminant liver failure occurs with progressive encephalopathy, coma and cerebral oedema. Occasionally, a sub-fulminant course with progressive ascites and encephalopathy results. Approximately 80% of these patients will die without liver transplantation. A small proportion of patients with certain types of viral hepatitis may go on to develop chronic carrier status with or without demonstrable hepatitic features.

Hepatitis A virus (HAV)

Spread by the faeco-oral route, HAV is a common cause of both sporadic and epidemic hepatitis. The infective agent is a small RNA virus and symptoms appear approximately 2 weeks after infection, with an associated rise in transaminase levels and excretion of viral particles in the faeces. At the same time, IgG anti-HAV and IgM anti-HAV antibodies appear; the former persist for life and the latter disappear within 3–12 months of infection. The features of acute hepatitis and the presence of IgM anti-HAV and HAV antigenaemia are usually diagnostic. The disease is self-limiting, seldom leading to fulminant hepatic failure. It is possible to become infected with HAV after transfusion from a donor in the viraemic phase (estimated risk 1/1 million units of blood transfused).

Treatment

Vaccines are available, but are not wholly effective in controlling outbreaks. They are not recommended for children under 2 years

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Key features of viral hepatitis

Virus	HepA 27 nmRNA	HepB 42 nmDNA	HepC 30–60 nmRNA	HepD 35–37 nmRNA*	HepE 32–34 nmRNA	HepG RNA
Incubation (days)	15–45	30–150	15–120	15–150	15–56	
Transmission						
Faeco-oral	+++	–	–	–	+++	
Percutaneous	Rare	+++	+++	+++	–	+
Perinatal	–	+++	± (?)	+	–	
Sexual	±	++	± (?)	++	–	
Fulminant	0.1%	0.1–1%	0.1%	5–20%	1–2%	Reports
Chronic	0%	5%	85%	5–70%	0%	Yes
Carrier	None	10–25%	0.5–1%	Variable	None	
Mortality	0.2%	0.5–2%	0.2%	2–20%	0.2%	Reports
Diagnostic markers						
Acute	IgM Anti-HAV	IgM Anti-HBc	Anti-HCV	HD-Ag	Anti-HEV	
Chronic	–	HBsAG	Anti-HCV	Anti-HDV	–	
Infective	HAV–RNA	HBe/sAg HBV–DNA	Anti-HCV HCV–RNA	Anti-HDV HDV–RNA	HEV–RNA	
Carrier	–	HBsAg	(Anti-HCV) (HCV–RNA)	Anti-HDV HD-Ag	–	
Recovery	None	Anti-HBe/s	None	None	None	

*HDV core, HBsAG coat.
Adapted from Rabin L. Hepatitis. In: Mandell GM, (ed). Atlas of infectious diseases, vol VII. Philadelphia: Churchill Livingstone, 1996. 2.01–2.54.

Table 1

of age, but can be given to pregnant women because the virus is inactivated.

Hepatitis B virus (HBV)

HBV has the smallest genome of any DNA virus infecting humans. It has four gene regions: the S or envelope region (HBsAg), the C or nucleocapsid region (HBcAg and HBeAg), the P region (DNA polymerase), and a fourth region that is a transactivator of HBV replication (HBxAg). UK prevalence is approximately 0.1%. As many as 10^{13} viral particles can be found in 1 ml of infected blood; this compares with 10^{1}–10^{4} particles in HIV-infected blood. HBV can survive in dry blood for up to 1 week. Transfusion-transmitted HBV has, however, been dramatically reduced since the introduction of third-generation screening tests in the mid-1970s and the estimated risk of HBV infectious blood entering the UK blood supply is now 2.2 per million.

It takes approximately 2 months after infection for symptoms to appear, with a concomitant rise in alanine aminotransferase (ALT) in the acute phase. HBsAg, HBeAg and HBV–DNA are all detectable in the blood slightly before the appearance of jaundice and other symptoms. Also, at this time, IgG anti-HBc and IgM anti-HBc become evident, denoting acute infection (see Figure 1). A month later, antibodies to HBe appear, resulting in clearance of HBeAg and a gradual reduction in HBV–DNA levels. Some months after this, HBsAg clears from the blood and anti-HBsAg antibodies become detectable. In 10–25% of patients, a chronic carrier state develops and there is persistence of HBV–DNA, indicating continuing viral replication, and HBsAg and HBeAg, which, if found together, indicate continuing viral replication with a high level of infectivity and active liver disease. The development of anti-HBe antibodies, which can occur at any time, implies disease resolution and quiescence of liver disease.

Vertical transmission is thought to occur at the time of delivery and is much more likely (from 5 to 90%) if the mother is HBeAg positive. Caesarean delivery does not offer any particular advantage in reducing transmission rates but immunoprophylaxis with both immunoglobulin and vaccine given to the neonate is crucial prevention. The exact regimen is dependent on maternal HBsAg and HBeAg status at the time.

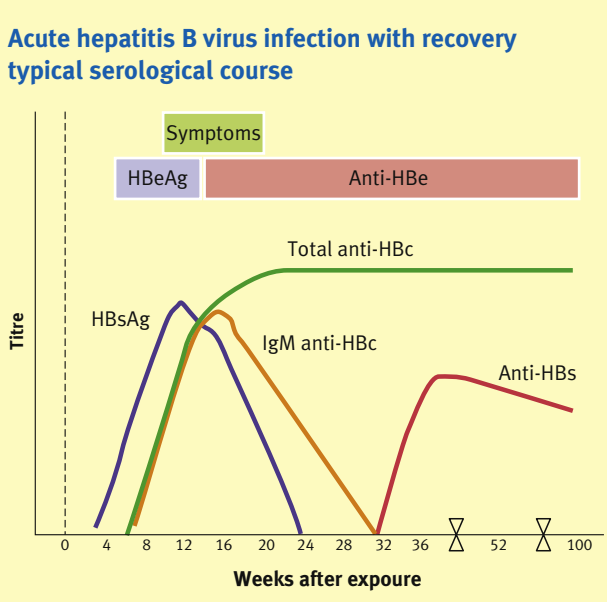

Figure 1 The relationship between antigen and antibody appearance in the serum and the course of the disease in acute hepatitis B infection.