A Review of Acute Viral Hepatitis in the Elderly

D’Arcy Little, MD, CCFP, Lecturer and Academic Fellow, Department of Family and Community Medicine, University of Toronto; Director of Medical Education, York Community Services; 2002 Royal Canadian Legion Scholar in Care of the Elderly, Toronto, ON.

Viral hepatitis is a major cause of acute and chronic liver disease worldwide. This article will review the epidemiology, etiology, presentation, diagnosis, management and prevention of acute viral hepatitis (Types A, B and C), with specific reference to the elderly population. Both similarities and differences between management in the elderly and the general population will be detailed. A cost-effective approach to diagnosis will also be formulated.

Key words: hepatitis A, hepatitis B, hepatitis C, acute viral hepatitis, elderly.

Introduction

Viral hepatitis remains a major cause of acute and chronic liver disease worldwide. However, although viral hepatitis affects the elderly, and while aspects of the illness in the elderly differ from those in their younger counterparts, most of the research and literature in this area does not specifically refer to the elderly. This article will review the epidemiology, etiology, presentation, diagnosis, management and prevention of acute viral hepatitis with specific reference to the elderly population.

There have been recent advances in knowledge about viral hepatitis, and known viruses currently include hepatitis A, B, C, D, E and G. This article, however, will focus on the viruses for which there is the most information—hepatitis A, B and C.

Hepatitis A

Hepatitis A (HAV) is a 27nm, non-enveloped RNA virus of the picornavirus family. It is thermostable, acid resistant and resistant to bile lysis. These features allow efficient fecal-oral transmission. As a result, HAV is the most common form of acute viral hepatitis in most parts of the world.

In developing countries, where the virus is endemic, most people are infected in childhood. At this age, the illness is mild or asymptomatic and results in life-long immunity. There is no chronic form of HAV. However, in non-endemic countries where living conditions and sanitation are such that enteral transmission is less likely, a larger proportion of the adult population is not immune to the virus. In these areas, there is an “upward shift” in the age at which this infection is acquired by adults. A 1994 serological survey in the U.S. documented the prevalence of anti-HAV antibodies at age 60, 70 and 80 years to be 40%, 60% and 80% respectively.

In addition, the severity of the illness associated with HAV increases with age. While jaundice occurs in less than 10% of affected children under six years, 70–80% of affected adults are icteric. Furthermore, the course of the illness in the elderly is often more prolonged. HAV also is associated with a greater mortality rate in adults than in children. The overall case fatality rate in the U.S. is less than one per 1,000, but this rate increases to 27 per 1,000 among cases older than 50 years. This is due to a higher prevalence of fulminant hepatitis in this age group.

In approximately one-half of HAV cases, the source of infection is unknown. However, the diagnosis of HAV should be suspected in the context of appropriate risk factors, such as interpersonal contact with an index case (22–26% of cases), exposure to daycare centres experiencing an outbreak (14–16%), international travel to endemic areas (2–6%), food and waterborne disease outbreaks (2–3%) and injection drug use (<2%).

Changes in liver enzymes are not specific for HAV. While aminotransferases (especially alkaline phosphatase) may reach 5000 U/L, the level of elevation does not correlate with severity or prognosis. Usually, alkaline phosphatase (ALT) is only minimally elevated and total bilirubin is rarely higher than 10mg/dL, except in the cholestatic form and in fulminant HAV. A prolonged prothrombin time reflects hepatocellular necrosis and can predict an increased mortality rate. Liver biopsy is not required to make a diagnosis.

The treatment of HAV is essentially supportive and undertaken on an outpatient basis. Bed rest and balanced nutrition are recommended; however, patients can resume their usual activities as soon as tolerated. Patients also should avoid alcohol and other hepatotoxins (i.e., more than 2g/day of acetaminophen). Virus-specific therapy is not available. Intravenous fluids may be needed if oral intake is substantially decreased, and hospitalization is mandatory if the patient exhibits signs of encephalopathy or severe coagulopathy. Patients at increased risk for poor outcome include the elderly and those with pre-existing chronic liver disease, such as hepatitis C. Most patients experience complete clinical and biochemical resolution within three to six months of onset.

Acute HAV infection can be prevented by the administration of immune globulin within two weeks of exposure. This is used in cases of sexual or household contact with an index case. In addition, the use of HAV vaccine within three to four weeks of travel to an endemic area is recommended. The routine immunization of elderly patients is controversial, and experts have advocated further research into the immunogenicity of hepatitis A vaccines in frail older persons before a vaccination policy for nursing homes is established.

Hepatitis B

Hepatitis B (HBV) is a 42nm, enveloped member of the hepadnavirus family. It
Acute Viral Hepatitis

has a circular, double-stranded DNA genome. In North America, major risk factors for HBV include unprotected sex between males and intravenous drug use; hence, it is relatively uncommon in the geriatric age group. A recent survey of geriatric hospitals in Canada found the prevalence of hepatitis B surface antigen (HBsAg) positivity to be 0.6%, similar to that of the general population.

The incubation period for HBV lasts one to six months, with an average of approximately 50 days. Acute viral hepatitis is usually mild in older people, and in many cases may even be subclinical. Approximately 70% of patients have a subclinical, anicteric hepatitis, whereas 30% develop icteric hepatitis. The prodromal period consists of nonspecific constitutional symptoms including anorexia, myalgias and fatigue, as well as right upper quadrant pain.

Liver function tests reveal a pattern of hepatocellular injury with elevation in ALT higher than AST (aspartate aminotransferase). While the peak ALT level does not correlate with prognosis, those patients with a vigorous immune response, as indicated by higher aminotransferase levels, are more likely to clear the acute viral infection and to not progress to a chronic carrier state.

HBsAg, as well as markers of viral replication (HBsAg and HBV DNA), become detectable before symptoms and before biochemical abnormalities. Hepatitis B core antibody (anti-HBc) becomes positive with the onset of symptoms and continues to be detectable throughout the illness. Initially, IgM anti-HBc is present for months to one year; thereafter IgG anti-HBc is present as a marker of prior HBV infection. The disappearance of HBsAg and the appearance of anti-HBs are markers of infection resolution. With resolution of the acute infection, HBeAg and HBV DNA cannot be detected in the serum by hybridization assay, and HBe antibody (anti-HBe) develops.

While only 10% of young adults become chronic carriers after acute infection with HBV, 60% of older people become chronic carriers. This is thought to be secondary to the fact that cellular immunity, which is involved in viral clearance, declines with age. Furthermore, HBV is the most common hepatitis virus to lead to fulminant hepatic necrosis in the elderly.

Treatment of acute HBV is supportive. Alpha interferon is given to patients with chronic HBV infection with evidence of active viral replication to prevent progression to cirrhosis and possibly to hepatocellular carcinoma.

Response rates and antibody titers after immunization with hepatitis B vaccine depend on age, with the frequency of an inadequate antibody level (< 10mIU/mL) increasing with age. In order to prevent chronic liver disease secondary to hepatitis B, vaccination early in life and in healthy older people has been advocated by many, especially in those at risk of hepatitis B infection. The Canadian Association for the Study of the Liver (CASL) devised a consensus statement suggesting “the most appropriate vaccination strategy for Canada is universal vaccination of all neonates.” In addition, it has advocated a catch-up program for all children and young adults who have not yet been vaccinated.

Hepatitis C

Traditionally, hepatitis C (HCV) has been the most frequent cause of acute viral hepatitis in older people. Hepatitis C, an RNA virus, also is the most common cause of chronic viral hepatitis, which is a leading cause of liver transplantation as well as a leading cause of hepatocellular carcinoma.

HCV is transmitted mainly by the parenteral route; however, the route of transmission in some cases is unclear. Prior to 1992, blood and blood products were the major mode of transmission. Due to improvements in adequate blood system screening, injection drug use currently is the major route of transmission. Simor et al. found the prevalence of anti-HCV antibodies among 508 patients in a long-term care facility in Toronto to be 1.4%, similar to the prevalence in the general Canadian population.

Acute HCV infection in the elderly is usually a mild disease with few, non-specific symptoms such as fever (34%), abdominal pain (38%) and jaundice (30%). In approximately 30% of cases, the liver enzymes exhibit a cholestatic picture, with high levels of ALT. While fulminant viral hepatitis is a rare complication of HCV, age over 50 years is an independent adverse prognostic factor. HCV is a common precursor for chronic liver disease. At least 50% of patients develop chronic hepatitis, and of those, 20–60% develop cirrhosis. HCV also is strongly associated with the development of hepatocellular carcinoma, and the risk of developing this cancer increases significantly with age, likely due to the longer duration of cirrhosis in such patients.

CASL recommends that patients with acute hepatitis C should be treated with interferon at a dose of at least 3mU three times a week for three to six months. However, acute hepatitis C is usually diagnosed only in specific circumstances, such as following a transfusion or in a health care worker with an accidental exposure to hepatitis C. Community-acquired hepatitis C infection, associated with injection drug use, is usually asymptomatic and therefore acute treatment is often not possible. Interferon is given primarily to patients with chronic HCV infection when the ALT elevation is more than 1.5 times the upper limit of normal for more than four to six months. In patients with normal ALT levels, interferon treatment often fails to clear the HCV RNA. However, most studies of treatment of chronic HCV have not included older patients. In such cases, comorbidity and life expectancy should be considered in treatment decisions.

A hepatitis C vaccine is not yet available. Hymervariable regions in the HCV genome and a high rate of mutation are some barriers to vaccine development.

A Cost-effective Approach to Differential Diagnosis and Follow-up

A reasonable, cost-effective approach to the diagnosis of patients with possible acute viral hepatitis has been proposed and is reproduced here in Figure 1. This algorithm is not applicable to the patient.
Acute Viral Hepatitis

with fulminant hepatic failure or with chronic viral hepatitis.8 This algorithm suggests that the initial laboratory investigation for acute viral hepatitis should include serologic tests to exclude HAV and HBV (IgM anti-HAV and HBsAg, IgM anti-HBc), since 75% of cases of acute viral hepatitis result from infection with either of these two viruses.8 If the results of these investigations are negative, further testing can be undertaken to rule out HCV, such as anti-HCV. Since HCV antibodies become detectable eight to 10 weeks following acute infection, the use of HCV PCR may be considered, as it can detect HCV one to two weeks after symptom onset.8 However, checking for HCV RNA by PCR is not felt to be cost effective unless there is a known history of blood exposure.8

It should be kept in mind that not all cases of acute hepatitis are viral in nature, and other causes of acute hepatitis should be considered, such as alcoholic hepatitis, drug toxicity, autoimmune hepatitis and Wilson’s disease.21 In addition, rarer causes of viral hepatitis can be considered in the appropriate epidemiological context. For instance, infectious mononucleosis and Hanta virus infection are possible causes. Hepatitis E is a form of acute viral hepatitis found in the Indian subcontinent and possibly in Latin America. However, in a patient without an appropriate travel history or without a history of immunosuppression, these diagnoses usually do not need to be pursued.21

Any patient who appears ill with acute hepatitis should have their prothrombin time measured and have an assessment for hepatic encephalopathy.21 Also, any patient with acute hepatitis, regardless of the cause, needs to be followed until the acute liver injury resolves.21

Figure 1
Algorithm for Cost-effective Laboratory Evaluation of Acute Viral Hepatitis

Patient with suspected acute viral hepatitis

IgM anti-HAV (32%)

HBsAg, IgM anti-HBc (43%)

Negative HAV and HBV serology

anti-HCV (8–10 weeks after onset of infection)

HCV PCR (1–2 weeks after onset of symptoms)


Conclusion

This article has reviewed the management of acute viral hepatitis in the elderly. Both similarities and differences between management in the elderly and the general population have been stressed. A cost-effective approach to diagnosis was detailed, and the importance of a broad initial differential diagnosis with reference to epidemiological factors was emphasized. The vast importance of resultant chronic viral hepatitis was alluded to, as old age is not necessarily an exclusion criterion for antiviral treatment in such cases.

No competing financial interests declared.

References