Fulminant Viral Hepatitis

Saumya Jayakumar, MD, FRCPC[a], Raiyan Chowdhury, MD, FRCSC[b], Carrie Ye, MD[c], Constantine J. Karvellas, MD, SM, FRCPC[b,c,*]

KEYWORDS

• Acute liver failure • Cerebral edema • Fulminant viral hepatitis • Hepatitis A • Hepatitis B • Liver transplantation

KEY POINTS

- Fulminant viral hepatitis (FVH) is the predominant cause of acute liver failure (ALF) in developing countries.
- Hepatitis A and B are the most common causes of FVH, whereas other causes (hepatitis E, Epstein-Barr virus, herpes simplex) tend to occur in special patient populations (pregnancy, immunocompromised patients).
- All patients with FVH-induced ALF should receive N-acetylcysteine because evidence suggests that this agent improves spontaneous survival.
- Patients with ALF should be transferred to an intensive care unit at an institution with expertise in liver failure/transplantation.
- Although large studies are lacking, the primary focus of the management of critically ill patients with ALF/FVH is the prevention of cerebral edema and infection, which may greatly improve outcomes, either spontaneous recovery or a bridge to successful liver transplantation.

BACKGROUND

Fulminant hepatic failure or acute liver failure (ALF) is a condition wherein the previously healthy liver rapidly deteriorates, resulting in jaundice, encephalopathy, and coagulopathy. There are approximately 2000 cases per year of ALF in the United States,[1,2] averaging approximately 1 in 6 cases per million annually throughout the world.[3–5]

Funding Sources: S. Jayakumar, R. Chowdhury, C. Ye: None. C.J. Karvellas: Alberta Transplant Fund, Shering-Merck, Gambro.
Conflict of Interest: None.
[a] Faculty of Medicine and Dentistry, Division of Gastroenterology, University of Calgary, TRW Building, 3280 Hospital Drive NW, Calgary, Alberta T2N 4Z6, Canada; [b] Division of Critical Care Medicine, University of Alberta, 130 University Campus NW, Edmonton, Alberta T6G 2X8, Canada; [c] Division of Gastroenterology (Liver Unit), University of Alberta, 1-40 Zeidler Ledcor Building, Edmonton, Alberta T6G 2X8, Canada
* Corresponding author. Division of Critical Care Medicine, University of Alberta, 1-40 Zeidler Ledcor Building, Edmonton, Alberta T6G-2X8, Canada.
E-mail address: dean.karvellas@ualberta.ca

Crit Care Clin 29 (2013) 677–697
http://dx.doi.org/10.1016/j.ccc.2013.03.013 **criticalcare.theclinics.com**
0749-0704/13/$ – see front matter

Although acetaminophen hepatoxicity (APAP) is the most common cause of ALF in the United States, viral causes (fulminant viral hepatitis [FVH]) are the predominant cause of ALF in developing countries. Approximately 3% of liver transplants in the United States are caused by ALF.[6] Given the ease of spread of viral hepatitis and the high morbidity and mortality associated with ALF, a systematic approach to the diagnosis and treatment of FVH is required.

Hepatitis A

The hepatitis A virus (HAV) is an RNA virus that is transmitted through fecal-oral spread (**Table 1**). It is associated with poor sanitation, cohabitation or sexual contact with an infected individual, or contaminated food sanitation.[7,8] In the developed world, the advent of HAV vaccines has led to a dramatic decrease in the rates of acute HAV infection.[9] HAV has an incubation period of 30 days, after which the prodromal symptoms of fatigue, malaise, vomiting, anorexia, fever, and right upper quadrant abdominal pain are present.[10] Approximately a week after the onset of these symptoms, patients will experience jaundice, pruritus, and hepatomegaly. Other physical findings include splenomegaly, lymphadenopathy, rash, and arthritis.[11]

Most HAV infections in immunocompetent adults result in self-limited illness, with ALF occurring in less than 1% of cases.[12] HAV infection accounts for 3.1% of all patients with ALF in the United States.[13] HAV-induced ALF often follows a hyperacute (encephalopathy within <7 days of jaundice) course. Of 29 patients presenting with ALF from HAV over a 7-year period in the United States, 55% made a spontaneous recovery, whereas others either died or went on to require an emergency liver transplant (LT).[13] In this study by the US Acute Liver Failure Study Group (ALFSG), the presence of 2 of the following predicted poor survival without transplant: day 1 serum creatinine of 2.0 mg/dL or more, alanine aminotransferase (ALT) less than 2600 IU/mL, and intubation status and pressor support (sensitivity 92%, specificity 88%, and positive predictive value of 86%).[13] Mortality rates increase with age (0.1% of children, 0.5% in individuals aged 15–39 years, and 1.1% in those more than 40 years of age).[14]

The diagnosis of acute HAV infection is made through the presence of anti-HAV immunoglobulin M (IgM) in the setting of typical symptoms as well as the exclusion of other causes. Anti-HAV is present at the onset of symptoms and remains positive for 4 to 6 months afterward. Unfortunately, testing for HAV RNA in the setting of ALF is likely to yield false-negative results.[15] The treatment of acute HAV infection is supportive (see the intensive care unit [ICU] management section), and there is full recovery in 3 to 6 months in 85% of cases.[14] Patients with severe disease or evidence of ALF should be transferred to an LT center for supportive management and assessment for LT.

Hepatitis B

Hepatitis B (HBV) is a DNA virus transmitted through exposure (both vertical and horizontal) to infected blood or other bodily fluids. The incubation period is 1 to 4 months. During the prodromal phase, patients may experience a serum sicknesslike reaction, which is then followed by anorexia, nausea, right upper quadrant abdominal pain, and jaundice. Hepatocyte damage occurs mostly through a host immune-mediated response, and ALF develops when there is an immune-mediated lysis of infected hepatocytes.[16] Acute HBV accounts for nearly 30% of ALF cases in parts of Europe and is the main cause of ALF in Asia, sub-Saharan Africa, and the Amazon basin,[17,18] although only 0.1% to 4.0% of acute HBV infections lead to ALF.[16] The advent of HBV vaccination has led to dramatically decreased rates of HBV infection and associated morbidity and mortality.[19] In patients who do develop ALF, both ALT and