Case 31

This 36-year-old male presented to the emergency department with a 5-day history of progressive jaundice, nausea, and vomiting. Review of systems was notable for dark urine but no diarrhea, hematemesis, abdominal pain, or fever. He had no history of pruritus or melena. The patient had traveled extensively to the Far East and South America and had returned from an 8-month trip to Mexico 2 weeks prior to evaluation. He gave no history of excessive alcohol use, denied use of intravenous drugs, had no history of blood transfusions, and had one sexual partner for the preceding 19 years. His only medication was an inhaler for asthma. No exposure to toxic chemicals was elicited.

On physical examination, he was thin and jaundiced. He was afebrile and had a normal pulse and blood pressure. Marked scleral icterus was present. His abdominal examination was notable for a palpable liver edge 2 cm below the right costal margin and a total liver span of 12 cm in the midclavicular line. He had a nontender abdomen. Skin exam was notable for jaundice, but there were no stigmata of chronic liver disease, nor were there any signs of bruising or hematomas. His neurologic examination was normal with no asterixis. Laboratory studies revealed markedly elevated serum total bilirubin levels of 21.6 mg/dl and direct bilirubin of 12.5 mg/dl, elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (1,718 U/liter and 2,436 U/liter, respectively), and a mildly elevated alkaline phosphatase of 241 U/liter.

Blood sent for serologic studies revealed the cause of this patient's liver disease.

1. Clinically, what does this patient have? What is the differential diagnosis of this condition?

2. Of the possible infectious causes of his illness, what are the possible risk factors that are present or absent in his history?

3. How can an acute infection with one of these etiologic agents be determined serologically?

4. For which of the viral causes of this condition is there a chronic carrier state? Which of the viral causes is associated with an increased risk of cirrhosis? Of hepatocellular carcinoma?

5. What methods can be used to prevent infectious liver disease?

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Case Discussion

1. This patient presented with a clinical picture of hepatitis. The markedly elevated levels of AST and ALT with a mildly elevated level of alkaline phosphatase are consistent with hepatocellular injury, rather than a biliary process. The causes of hepatitis include adverse events due to some drugs, chemicals, excessive alcohol use, and specific infectious agents. Among the infectious causes, nonviral causes of acute hepatitis include primary toxoplasmosis, leptospirosis, and syphilis (particularly during the secondary stages of syphilis). Viral causes include hepatitis A, B, C, D (in association with hepatitis B), E, or G (at least three variants) virus, Epstein-Barr virus, cytomegalovirus, and several other viruses. A number of other viral agents that are not endemic to the United States can also cause a clinical picture of hepatitis. These include such exotic viruses as yellow fever virus.

2. The history is not suggestive of a drug-induced hepatitis, and the patient's alcohol intake is likewise unremarkable. He had no known chemical exposures associated with hepatitis. The patient's recent travel history to Mexico is suggestive of hepatitis A virus (HAV). This virus is endemic to much of the world other than the United States, Canada, and Western Europe. It is spread by the fecal-oral route, and the incubation period is typically 25 to 30 days (but may be 15 to 50 days). Hepatitis E virus, which is less common than hepatitis A infection, has also been reported from Mexico and is transmitted by the fecal-oral route. The patient did not receive any blood transfusions, which would have placed him at risk for infection with hepatitis C and G viruses. Finally, the patient had only one sexual partner in the past 19 years and did not use drugs by injection. Hepatitis B virus (HBV) is spread sexually as well as via sharing of needles and via contaminated blood and body fluids.

3. Serologically, the presence of a specific immunoglobulin M (IgM) antibody response to a particular etiologic agent is diagnostic of an acute infection with that pathogen. In this patient, the presence of an IgM antibody to hepatitis B core antigen indicated that he had recently been infected with HBV. In some patients who are acutely infected with HBV, hepatitis B surface antigen (HBsAg) may be present in the serum, which would be diagnostic of this infection. The presence of antibody to HBsAg may occur only after the HBsAg has been cleared from the blood. During this "window," it is the demonstration of antibody to the hepatitis B core antigen that allows for the diagnosis of infection. An acute infection will be characterized by an IgM antibody response to the hepatitis B core antigen. Patients who have had a past infection with HBV may have detectable IgG antibody to the hepatitis B core antigen but will not have IgM antibody. Finally, a patient who has been immunized against HBV will have antibody to HBsAg only, which is present in the vaccine.

4. Although hepatitis A infection and hepatitis E infection do not result in chronic carriage, a chronic infection occurs in a minority of patients with hepatitis B infection and in the majority of patients with hepatitis C infection. Hepatitis D virus

(HDV), formerly known as hepatitis delta virus, requires the presence of HBV in order to replicate. Chronic infection may occur in a patient if both HBV and HDV infections occur at the same time, or it may occur when an acute HDV infection is transmitted to someone who has been a carrier of HBV.

Chronic carriage of HBV, either with or without HDV infection, can result in cirrhosis and is a risk factor for the development of hepatocellular carcinoma. Similarly, chronic carriage of HCV can cause cirrhosis and is associated with the development of hepatocellular carcinoma.

5. Commercially available vaccines are available for both HAV and HBV. In an acute setting, such as when a nonimmune health care worker has been exposed via needle stick injury to HBV, a commercial preparation of hepatitis B immune globulin can be given to the individual to prevent the development of infection. Large outbreaks of HAV, which is spread primarily by the fecal-oral route, frequently occur when an HAV-infected food worker contaminates commercially prepared foods. HAV-exposed individuals should receive injections of gamma globulin. Travelers who are going to areas endemic for HAV should be offered the HAV vaccine prior to the trip. Enough time should elapse between vaccination and exposure to assure the development of a protective antibody response. If this cannot be done, gamma globulin can be administered prior to the trip. Travelers to countries in which yellow fever is endemic should be offered the yellow fever vaccine.

Finally, blood products used in transfusion medicine are all screened serologically to prevent transmission of HBV and HCV as well as other infectious agents.

References

1. **Lau, J. Y. N., and T. L. Wright.** 1993. Molecular virology and pathogenesis of hepatitis B. *Lancet* **342:**1335–1340.
2. **Wright, T. L., and J. Y. N. Lau.** 1993. Clinical aspects of hepatitis B infection. *Lancet* **342:**1340–1344.