Hepatocellular Carcinoma and Hepatitis B e Antigen

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Hepatitis B e antigen serum persistence in an individual chronically infected with the Hepatitis B virus may be associated with a greatly increased risk of developing cirrhosis and hepatocellular carcinoma. This article presents an overview of the Hepatitis B e antigen and discusses the findings of a recent study evaluating its associated risk of hepatocellular carcinoma. A gross photographic image of hepatocellular carcinoma is provided.

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The Hepatitis B virus genetic code creates multiple proteins. The S region of this coding is responsible for the formation of viral envelop proteins, while the C region codes for 2 nucleocapsid proteins, the Hepatitis B e antigen (HBeAg) and the Hepatitis B core antigen (HBcAg). HBcAg serves as an intracellular core protein, while HBeAg is a soluble protein, which when manufactured binds to smooth endoplasmic reticulum within cells and is thereafter secreted into an infected individual’s circulation.

Since HBeAg is secreted into the circulation, it is an easily measured marker for active Hepatitis B viral gene replication. Its presence in serum suggests that the individual’s blood is highly infectious. Typically HBeAg occurs early in an acute initial infection with the Hepatitis B virus. Its appearance is usually transient, as the antigen is quickly cleared by the host’s immune response. However, in those with chronic persistent Hepatitis B viral infection, the HBeAg

Figure 1. A 2.0 cm hepatocellular carcinoma arising in the setting of chronic viral hepatitis. Copyrighted material used with permission of Dr. F. Mitros, The University of Iowa, and Virtual Hospital, www.vh.org.

Figure 2. Multiple irregular green areas of hepatocellular carcinoma in a cirrhotic liver. Copyrighted material used with permission of Dr. F. Mitros, The University of Iowa, and Virtual Hospital, www.vh.org.
may also persist, and if it does so, it likely indicates a high level of virus activity and replication.

The result of this continued replication is greater hepatic inflammation and subsequent necrosis and fibrosis. Ultimately, this can lead to cirrhosis and end-stage liver disease. It also may confer, upon those with chronic Hepatitis B, a much greater risk for the development of hepatocellular carcinoma (Figure 1).

A recent study by Yang et al examined a cohort of 11,893 men from Taiwan, who were enrolled during the period of 1991 to 1992 and followed for 9 years. They found that the relative risk of hepatocellular carcinoma in men age 30 to 65 that were positive for both Hepatitis B surface antigen (HBsAg) and HBeAg, as compared to those who were negative for both, was as high as 60.2 (95% C.I. 35.5 to 102.1). For those who were HBsAg positive alone, the relative risk of hepatocellular carcinoma, as compared to those who were seronegative for both antigens, was 9.6 (95% C.I. 6.0–15.2).

Given the prevalence of chronic Hepatitis B viral infections, particularly in the Far East, attention to HBeAg status may help identify those at greater mortality risk due to the development of either cirrhosis and end-stage liver disease or hepatocellular carcinoma.

REFERENCES