SUBMASSIVE LIVER NECROSIS IN A HEPATITIS B CARRIER WITH CUSHING’S SYNDROME

Pei-Ling Tsou, Hsuan-Shu Lee, Yung-Ming Jeng, and Tien-Shang Huang

Abstract: Reactivation of hepatitis B virus (HBV) replication in hepatitis B surface antigen (HBsAg)-positive patients is associated with immunosuppressive therapy. However, the interactions between endogenous glucocorticoid in Cushing’s syndrome and HBV-related hepatitis remain unclear. Here, we describe the management of a 32-year-old male HBV carrier with Cushing’s syndrome caused by an adrenal cortical adenoma, who developed severe hepatitis B. Repeated episodes of septicemia resulting from hypercortisolemia-related immunosuppression further compromised his hepatic condition. Adrenalectomy could not be performed due to coagulopathy. Lamivudine was not available at that time in Taiwan, and this patient died of hepatic failure and sepsis. At autopsy, his liver showed submassive necrosis with small regenerative nodules. The hepatocytes were positive for HBsAg (membrane and cytoplasmic) and hepatitis B core antigen (nuclear and cytoplasmic). Screening for HBsAg is of crucial significance for immunocompromised individuals. Once positive HBsAg is detected in immunosuppressed patients, liver function and viral status should be closely monitored to enable earlier diagnosis and prompt treatment with the newer nucleoside analogues that actively fight HBV.

Case Report

A 32-year-old man had been well until July 1995, when he developed lower leg edema followed by general malaise and jaundice. He had elevated serum bilirubin (3.7 mg/dL), aspartate aminotransferase (AST, 204 U/L), and alanine aminotransferase (ALT, 645 U/L), and HBV markers. HBV markers were HBsAg (+), anti-HBs (–), hepatitis B early antigen (HBeAg) (+) and anti-HBe (–). After that episode, he remained asymptomatic. On December 20, 1995, he developed fever, chills, and vomiting and was admitted to our hospital. Upon admission, hypotension, fever, hypoxemia, jaundice, puffy face, distended abdomen with purple striae, hepatomegaly (3 finger-breathds below right costal margin), and lower leg edema were noted. Blood culture revealed Klebsiella sepsis and biochemical tests showed poor liver function (prothrombin time 29.2 s, control 11.9 s; albumin 2.1 g/dL; bilirubin 6.4 mg/dL; AST 157 U/L; ALT 120 U/L). Abdominal sonography revealed no evidence of liver cirrhosis. On the other hand, serum cortisol showed no diurnal rhythm (16.4 µg/dL at 08:00; 16.25 µg/dL at 16:00) and plasma adrenocorticoto-
Reactivation of Hepatitis B in Cushing’s Syndrome

Fig. 2. A) Submassive necrosis with ductular transformation and cholestasis (arrow, a regenerative nodule) (original magnification, x 100). B) Hepatitis B core antigen (HBcAg) is present in the cytoplasm and nuclei of the hepatocytes (original magnification, x 200).

Discussion

This case illustrates a therapeutic dilemma. While repeated episodes of septicemia resulting from hypercortisolemia-related immunosuppression further compromised hepatic condition, the administration of ketoconazole to inhibit steroid synthesis risked deterioration of hepatic function. Adrenalectomy, the mainstay of therapy for adrenal Cushing’s syndrome, was withheld in this case because of the patient’s hepatic decompensation, coagulopathy, and uncontrolled sepsis. Even if this patient underwent adrenalectomy, the abrupt withdrawal of endogenous glucocorticoid after surgery (though exogenous steroid will be supplemented) may risk a flare of hepatitis or even hepatic failure.

Restoration of the immune function may result in the rapid destruction of infected hepatocytes. In theory, hepatic necrosis under these circumstances can be ameliorated by reinstatement of immunosuppressive therapy. Nevertheless, fatal hepatic failure has been reported even in patients who were treated with corticosteroids at the first sign of clinical hepatitis [3]. Neither gradual withdrawal of steroid or increasing the dose of steroid in the event of acute hepatitis appears to improve the outcome [4]. In addition, clinical rebound occurs more frequently in patients previously exposed to a high dose of corticos-
nucleoside analogues that actively fight HBV.

earlier diagnosis and prompt treatment with the newer viral status should be closely monitored to enable an
tected in immunosuppressed patients, liver function and
tory users of immunocompromising agents. This is
patients infected with HIV, as well as those who are obliga-
tocytes with increased viral load. Screening for HBsAg is
ted in HBV endemic areas. Once HBsAg is detected in immunosuppressed patients, liver function and

Reactivation of HBV replication, defined as reappearance of serum HBsAg, HBV DNA, or both, is a complica-
tion in HBsAg-positive patients receiving immunosuppressive therapy [13]. Immunosuppression may impair
the function of T cells, and reduce immune-mediated hepatocytolysis and viral clearance [14]. Glucocorticoid,
one of the most commonly used immunosuppressive agents, may activate the glucocorticoid responsive ele-
ment in the HBV genome to enhance HBV replication and gene expression [15]. Withdrawal of immunosuppres-
sants leads to restoration of immune function and a rebound of the T-cell mediated immune attack on hepa-
tocytes with increased viral load. Screening for HBsAg is of crucial significance for immunocompromised individuals, patients with Cushing's syndrome, and patients infected with HIV, as well as those who are obligatory users of immunocompromising agents. This is
mandatory in HBV endemic areas. Once HBsAg is detected in immunosuppressed patients, liver function and viral status should be closely monitored to enable an earlier diagnosis and prompt treatment with the newer nucleoside analogues that actively fight HBV.

References