Case Report

REACTIVATION OF HEPATITIS B VIRUS (HBV) FOLLOWING CANCER CHEMOTHERAPY

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Abstract

Reactivation of Hepatitis B virus (HBV) may occur after immunosuppressive therapy and cancer chemotherapy. Some of these cases may develop liver failure in a previously compensated disease. Aim of this case report is to make an awareness of this reactivation of HBV in Bangladeshi society after cancer chemotherapy or immunosuppressive therapy. A forty-five-year old lady, mother of one child was found to have positive Hepatitis B surface antigen (HBsAg) since 1994 when the test was done for vaccination. She was asymptomatic and clinically unremarkable. She was treated with standard Interferon for 24 weeks in 2000 when Alanine aminotransferase (ALT) was high, Hepatitis B envelope antigen (HBeAg) & HBV deoxyribonucleic acid (DNA) were positive. After treatment HBeAg & HBV DNA were negative and ALT was normal. She developed carcinoma of the left breast which was operated in July 2008. Combination cancer chemotherapy started. After 5th cycle of chemotherapy she developed rise of ALT (1200 i.u/L) and HBV DNA (> 10^5 copies/ml). Patient was treated with tablet Lamivudine 100 mg/day. After one year of follow up she had no symptoms. HBV DNA and ALT became normal. Reactivation of HBV may occur after cancer chemotherapy or immunosuppressive therapy. At present recommendation of Asian Pacific Association for Study of Liver (APASL), European Association for the Study of Liver (EASL) and American Association for the Study of Liver Diseases (AASLD) is to start prophylactic Lamivudine, Entecavir or any other antiviral drugs in all patients who are positive for HBsAg irrespective of HBeAg, ALT or HBV DNA status before starting chemotherapy or immunosuppressive therapy. So, HBsAg and Anti HBc (Hepatitis B core) should be tested in all such cases.

Key words : Hepatitis B virus reactivation, chemotherapy.

Introduction

Hepatitis B virus is the commonest cause of chronic liver disease in Bangladesh[1]. Hepatitis B virus carrier (HBsAg) rate is about 5.2% to 7.8% in this country[2-3]. Usually asymptomatic carriers remain inactive but in case of immunosuppressed state, cancer chemotherapy and immunosuppressive therapy, there may be reactivation of the virus leading to acute flare up of hepatitis and liver failure[4].

Case Report

A forty-five-year old lady was detected to have positive Hepetitis B surface antigen (HBsAg) since 1994 when screening test was done for vaccination. At that time Hepetitis B envelope antigen (HBeAg) was positive but alanine aminotransferase (ALT) was persistently normal. After that, the patient was under constant follow up. In the year 2000, she developed rise of ALT (90 i.u/L), HBeAg was positive and HBV deoxyribonucleic acid (DNA) was positive (> 10^5 copies /ml). Liver biopsy showed chronic hepatitis with moderate activity (Hepatiris activity index [HAI] score 10/18). Ultrasonography of liver revealed coarse hepatic echotexure. Prothombin time and serum albumin were normal. She was treated with injection standard interferon 4.5 million units subcutaneously thrice a week for 24 weeks. After treatment her ALT became normal, HBV DNA became negative and she developed HBeAg seroconversion (HBeAg negative and Anti HBe positive). She was reasonably in good health. In July 2008, the patient developed carcinoma of the left breast. Total mastectomy was done. Combination chemotherapy was started with 5-Fluorouracil, Adriamycin and Cyclophosphamide. After 5th cycle of chemotherapy she developed anorexia, nausea and fatigability. Her ALT raised to 1200 i.u/L, HBeAg and HBV DNA (>10^7 copies /ml) were positive. Ultrasonography showed coarse hepatic echotexure. Prothombin time was 18 sec (control 13 sec), serum albumin 34 gm/L. Chemotherapy was stopped and she was treated with tablet Lamivudine 100 mg /day. After 3 weeks of treatment her ALT became normal. HBeAg became negative again after 3 months. HBV DNA remained persistently negative at 6 and 12 months of treatment. Tablet Lamivudine was stopped after one year. Patient remains symptom free after 1½ years of follow-up.

Discussion

Reactivation of HBV with increase in serum HBV DNA and ALT may occur in 20% to 50% hepatitis B carriers

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undergoing cancer chemotherapy or immunosuppressive therapy[5-6]. In most cases, hepatitis B flares are asymptomatic but icteric flares and even hepatic decompensation and death have been reported[7]. Reactivation of HBV replication is more common when chemotherapeutic regimens include corticosteroids or rituximab. Reactivation has also been reported following infliximab and other anti tumor necrosis factor (TNF) therapies for rheumatoid arthritis and inflammatory bowel disease[8-9]. Clinical studies including two controlled trails showed that prophylactic therapy with Lamivudine can reduce the rate of HBV reactivation, severity of hepatitis flares and mortality[10]. The reported case developed HBV reactivation following cancer chemotherapy. Following reactivation patient may develop acute flare-up of hepatitis and hepatic decomposition. To prevent this reactivation and hepatitis flare anti viral therapy should be given. Present recommendation of Asian Pacific Association for the Study of the Liver (APASL), European Association for the Study of the Liver (EASL) and American Association for the Study of the Liver Disease (AASLD) is to start prophylactic anti viral therapy (Lamivudine, Entacavir etc.) in all patients who are positive for HBsAg before chemotherapy/ immunosuppressive therapy. Anti viral therapy is to be started one week before Chemotherapy/ immunosuppressive therapy and is to be continued at least 6 months after discontinuation of chemotherapy[11].

Conclusion

Inactive HBV carrier should be followed up regularly. They should be looked for reactivation, liver failure, development of cirrhosis and hepatocelullar carcinoma. Reactivation commonly occurs following chemotherapy and immunosuppressive therapy. So, HBsAg and Anti HBc should be tested in all cases before every chemotherapy/ immunosuppressive therapy. Prophylactic therapy with anti viral drugs should be given in all HBsAg positive cases before starting chemotherapy/ immunosuppressive therapy irrespective of the status of HBeAg and HBV DNA.

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