Case Report

A case considering utilization of potent antiviral agents in a hepatitis B virus-infected patient with high viral load receiving immunosuppressive therapy

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Abstract

In this case, we present a follicular non-Hodgkin lenfoma patient whose liver enzymes increased after withdrawal of chemotherapy and afterward hepatitis B virus (HBV) reactivation was occurred despite HBV surface antigen was negative before immunosuppressive therapy.

Introduction

Chronic hepatitis B virus (HBV), which is a major infection all of the world concerns, an average of about 7% of the world’s population is infected with this virus. It is estimated that approximately 400 million people are infected with HBV worldwide. The prevalence of HBV surface antigen (HbsAg) carrier is 0.5-10%. Reactivation can occur in HBV carriers who are under antineoplastic chemotherapy especially with removal of the immunosuppression. Due to the hepatocyte damage, not only asymptomatic liver enzyme elevation can be seen but also this condition may lead to severe liver failure and even death.

Chemotherapy-induced reactivation can be revealed not only in chronic HBV patients or HBV carriers but also in patients who had latent infection. In this case, we present a follicular non-Hodgkin lenfoma patient whose liver enzymes increased after withdrawal of chemotherapy and afterward HBV reactivation was occurred despite HbsAg was negative before immunosuppressive therapy.

Case Report

An 80-year-old male patient was diagnosed with follicular non-Hodgkin lenfoma after detection of multiple mass lesions in cervical, abdominal, axillary, and inguinal regions by positron emission tomography-computed tomography and by biopsy performed from the inguinal lymph nodes. The patient was decided to be performed chemotherapy. Before this treatment, HbsAg, anti-hepatitis C virus, antihuman immunodeficiency virus tests were performed, and these virologic markers were found to be negative. Chemotherapy with (rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone [R-CHOP]) regiment was commenced in May 2009 and completed in 2010 for a total of 6 cycles. After the withdrawal of chemotherapy, his liver enzymes increased and afterward HBV reactivation was occurred despite HbsAg of the patient was negative before chemotherapy. Laboratory study results were notable for anti-HBc immunoglobulin M (IgM): Positive, HBV DNA: 148. 203.779 IU/ml positive, alanine transaminase: 510 U/L, aspartate transaminase: 350 U/L. We evaluated the condition of the patient as acute hepatitis B caused by HBV reactivation due to immunosuppressive treatment. After following up of our patient for 6 months, relapsed NHL was occurred, and he was planned to be received chemotherapy again. For this reason, lamivudine at a daily dose of 100 mg was
Potent antiviral agents in an HBV-infected patient

Discussion

Following chemotherapy and radiotherapy, reactivation may appear in HBV-infected patients who have malignant neoplasms, and it may sometimes end up with serious hepatitis and even death (1). Reactivation is possible in patients diagnosed with previous hepatitis B infection (HbsAg positive, anti-HBc total, and HBV DNA-positive patients) and also occult HBV infection (HbsAg negative, anti-HBc total, and HBV DNA-positive patients) (2). Reactivation that is appeared during chemotherapy often occurs in the termination period of chemotherapy (3). Whereas 18 out of 27 HbsAg positive patients, which take an induction chemotherapy due to lymphoma, were recorded with acute hepatitis; only 10 out of 72 HbsAg negative patients were recorded with acute hepatitis in a previous study (4). Although reactivation seems to appear less in the HbsAg negative patients, it is identified in the 14-20% of the anti-HBc positive and anti-HBs positive patients who are under chemotherapy due to lymphoma (5). In our case, although HbsAg positivity was not detected in the investigations before chemotherapy, high levels of transaminases together with HbsAg, anti-HBc IgM, and high level of HBV DNA positivity was detected after chemotherapy and evaluating this as a reactivation, a treatment of lamivudine 100 mg/day was initiated as a result. On the other hand, when considered from the risk factors for reactivation, it has been detected that this risk is higher in men and the patients with lymphoma. The risk of reactivation is not the same in each patient who takes immunosuppressive therapy; it shows a variety according to the disease and the protocols used for treatment. For instance, as stated above, while this risk is high (30-60%) in the patients with lymphoma, it is lower (10-20%) in the patients with solid organ tumor. However, it has been revealed that as some medicines, used in the treatment of rheumatologic diseases and lymph cancer, stimulate HBV reactivation, they induce reactivation in the HCV infections as well. Particularly, it has been demonstrated that the treatment of rituximab in the non-Hodgkin lymphomas significantly accelerates the risk of reactivation and the mortality risk as a result of the occurred reactivation is also high (6). In our case, due to non-Hodgkin lymphoma, the treatment of R-CHOP was used. It has been thought that among those medicines especially rituximab, and prednisolone contributes to reactivation. Lamivudine is the most used antiviral agent in the patients who take an antineoplastic treatment and who are chronic HBV patients or hepatitis B carriers.

Lamivudine which initiated before chemotherapy with the aim of prophylaxis decreases the risk of reactivation to a high level, and it can be said that the efficacy has been proved by clinical observations and experiences (7). However, during its usage, resistance may appear because its genetic barrier is low. The appearance of lamivudine resistance may trigger fatal hepatitis reactivations particularly in the patients with chronic HBV who undergo immunosuppressive treatment (8).

In our case, despite the decrease in HBV DNA level at the beginning of lamivudine treatment, breakthrough was occurred in the first year of lamivudine therapy and YMDD mutation was detected. Due to YMDD mutation, the treatment of the patient was switched with tenofovir which is a more potent antiviral agent than lamivudine. Other antiviral agents are also as effective as lamivudine yet the agents other than tenofovir and entecavir have lower genetic barrier. Therefore, potent antiviral agents with low risk of resistance (tenofovir and entecavir) should be preferred to the agents with low genetic barrier (lamivudine, telbivudine, adefovir) for the patients with high HBV DNA level.

Conclusion

As a result, every patient who is planned to be received immunosuppressive therapy should be screened for HBV infection. Tests should not only be limited to HbsAg but also anti-HBc IgG should be included in screening plan. Although HbsAg is negative in patients treated with rituximab, if anti-HBc IgG positivity was detected, antiviral agents should be immediately initiated.

References

1. Lubel JS, Angus PW. Hepatitis B reactivation in patients receiving cytotoxic chemotherapy: Diagnosis and
management. J Gastroenterol Hepatol. 2010;25:864-71.

2. Chen MH, Hsiao LT, Chiou TJ, Liu JH, Gau JP, Teng HW, et al. High prevalence of occult hepatitis B virus infection in patients with B cell non-Hodgkin’s lymphoma. Ann Hematol. 2008;87:475-80.

3. Cheng AL, Hsiung CA, Su IJ, Chen PJ, Chang MC, Tsao CJ, et al. Steroid-free chemotherapy decreases risk of hepatitis B virus (HBV) reactivation in HBV-carriers with lymphoma. Hepatology. 2003;37:1320-8.

4. Jang JW, Choi JY, Bae SH, Kim CW, Yoon SK, Cho SH, et al. Transarterial chemo-lipiodolization can reactivate hepatitis B virus replication in patients with hepatocellular carcinoma. J Hepatol. 2004;41:427-35.

5. Lok AS, Liang RH, Chiu EK, Wong KL, Chan TK, Todd D. Reactivation of hepatitis B virus replication in patients receiving cytotoxic therapy. Report of a prospective study. Gastroenterology. 1991;100:182-8.

6. Tsutsumi Y, Tanaka J, Kawamura T, Miura T, Kanamori H, Obara S, et al. Possible efficacy of lamivudine treatment to prevent hepatitis B virus reactivation due to rituximab therapy in a patient with non-Hodgkin’s lymphoma. Ann Hematol. 2004;83:58-60.

7. Hui CK, Cheung WW, Au WY, Lie AK, Zhang HY, Yueng YH, et al. Hepatitis B reactivation after withdrawal of pre-emptive lamivudine in patients with haematological malignancy on completion of cytotoxic chemotherapy. Gut. 2005;54:1597-603.

8. Law JK, Ali JA, Harrigan PR, Sherlock CH, Savage KJ, Yoshida EM. Fatal post-lymphoma chemotherapy hepatitis B reactivation secondary to the emergence of a YMDD mutant strain with lamivudine resistance in a noncirrhotic patient. Am J Hematol. 2006;81(12):969-72.