PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

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• CASE REPORT •

Hepatitis B virus reactivation in a patient undergoing steroid-free chemotherapy

Daisuke Shimizu, Kenichi Nomura, Yosuke Matsumoto, Kyoji Ueda, Kanji Yamaguchi, Masahito Minami, Yoshito Itoh, Shigeo Horiike, Masuji Morita, Masafumi Taniwaki, Takeshi Okanoue

Daisuke Shimizu, Kenichi Nomura, Yosuke Matsumoto, Kyoji Ueda, Shigeo Horiike, Masafumi Taniwaki, Molecular Hematology and Oncology, Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kyoto 602-0841, Japan
Kanji Yamaguchi, Masahito Minami, Yoshito Itoh, Takeshi Okanoue, Molecular Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kyoto 602-0841, Japan
Masuji Morita, School of Nursing, Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kyoto 602-0841, Japan
Masafumi Taniwaki, Clinical Molecular Genetics and Laboratory Medicine, Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kyoto 602-0841, Japan
Correspondence to: Dr. Kenichi Nomura, Molecular Hematology and Oncology, Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kawaramachi-Hirokoji, Kamigyo-Ku, Kyoto 602-0841, Japan. nomuken@sun.kpu-m.ac.jp
Telephone: +81-75-251-5521 **Fax:** +81-75-251-0710
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Abstract

A 62-year-old Japanese man who was positive for hepatitis B surface antigen (HBsAg) and anti-HBe antibody, underwent chemotherapy for non-Hodgkin's lymphoma (NHL). Mutations were detected in the precore region (nt1896) of HBV. Because steroid-containing regimen may cause reactivation of hepatitis B virus (HBV) and hepatitis may progress to be fulminant after its withdrawal, we administered CHO (CPA, DOX and VCR) therapy and the patient obtained complete response. However, he developed acute exacerbation of hepatitis due to HBV reactivation. Recovery was achieved with lamivudine (100 mg/d) and plasma exchange. The present case suggests that acute exacerbation of hepatitis can occur with steroid-free regimen. Because the efficacy of the prophylactic use of lamivudine has been reported and the steroid enhances curability of malignant lymphoma, the steroid containing regimen with prophylaxis of lamivudine should be evaluated further.

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INTRODUCTION

CHOP regimen consisting of cyclophosphamide (CPA), doxorubicin (DOX), vincristine (VCR), and prednisolone (PSL) is performed as the first line therapy for non-Hodgkin's lymphoma (NHL) because of its high response rate and less incidence of side effect. However, CHOP regimen for hepatitis B virus (HBV) carrier may cause reactivation of HBV due to prednisolone and hepatitis may progress to be fulminant after its withdrawal. On the other hand, it has already been proven that steroid containing-regimens show higher complete response and survival rate than steroid free regimens[1]. Thus, it is difficult to choose which chemotherapeutic regimen for NHL carrying HBV.

We described an asymptomatic HBV carrier patient with NHL who received CHO therapy. Although he achieved complete response, hepatitis acutely exacerbated. Lamivudine and plasma exchange improved hepatic failure.

CASE REPORT

A 62-year-old man complained of tonsil swelling, redness and sore throat. He was referred to our hospital in August 2003. Needle biopsy from tonsil revealed him as having NHL (diffuse large B-cell lymphoma). He was admitted to our hospital on August 21 because tonsil swelling developed rapidly. Two enlarged cervical lymph nodes were palpable and right tonsil swelled. Hematological studies showed WBC 5 600/mL, Hb 15.4 g/dL and platelet 7.2×10^4/mm^3, LDH 167 IU/L, GOT 25 IU/L, GPT 15 IU/L, ALP 392 IU/L, Ch-E 163 IU/L, T-bil 1.82 mg/dL, prothrombin time (PT) 14.7 s, IL-2 receptor 564 U/mL, indocyanine green test (ICG) 25%. Serological tests showed HBsAg (+), HBeAg (-), HBeAb (+). HBV-DNA level was 4.7 LGE/mL (TMA method). Mutant virus having mutation at precore and core promoter region was detected by enzyme-linked mini-sequence assay (Smitest HBV Pre-C ELMA, Roche Diagnostics, Tokyo, Japan) and enzyme-linked specific probe assay (Smitest HBV core promoter mutation detection kit, Genome Science Laboratory, Tokyo, Japan). Ultrasonography revealed cirrhotic pattern of liver and mild splenomegaly. Neck magnetic resonance imaging revealed swelling of right tonsil and two cervical lymph nodes. Computed tomography scanning revealed no lymph node swelling in chest and abdomen. Bone marrow aspiration revealed involvement of abnormal lymphocytes. Thus, we diagnosed he was at stage IV.

He received first course of CHO regimen on August 22. Although tonsil swelling improved, liver dysfunction gradually developed after the third course. After the forth course, liver dysfunction got severe, as serum LDH level was 499 IU/L, GOT 650 IU/L, GPT 422 IU/L, T-bil 1.49 mg/dL, PT 25.9 s and HBV-DNA level increased 6.2 LGE/mL. We diagnosed it as acute exacerbation of HBV and started both lamivudine (100 mg/d) and plasma exchange. Liver dysfunction improved gradually. In January 2004, hematological data improved as LDH 328 IU/L, GOT 98 IU/L, GPT 54 IU/L, T-bil 3.66 mg/dL, PT 19.6 s, HBV DNA 2.8 LGE/mL. He was following good clinical course and remained complete response for NHL.

DISCUSSION

It has been reported that steroid may induce exacerbation of hepatitis after cessation of steroid therapy or during tapering of steroid. Cheng *et al*. reported that 50 NHL patients carrying HBV were randomized to receive either ACE (epirubicin, CPA and etoposide) or PACE (predonisolone+ACE). The cumulative incidence of HBV reactivation was 38% and 73%, respectively. On the other hand, it is clear that PACE chemotherapy was

more effective than ACE arm in the treatment of NHL, because CR rate was 46% and 35%, overall survival rate at 46 mo was 68% and 36%, respectively[1]. Thus, there is no consensus regarding the best therapy for NHL with HBV.

Regarding to HBV-DNA, cases with a point mutation from G to A at nucleotide 1896 of the precore region of HBV tended to develop fulminant hepatitis with steroid containing treatment[2-5]. Because we detected the mutant HBV in peripheral blood before chemotherapy, we performed CHO regimen and obtained CR for NHL. However, hepatitis acutely exacerbated.

Recently, several reports have shown promising results for the prophylactic use of lamivudine in cancer patients before chemotherapy[6-8]. However, we did not administer prophylaxis of lamivudine in the present patient, because (1) he was an asymptomatic HBV-carrier, (2) lamivudine-resistant virus might appear after lamivudine treatment or acute exacerbation after discontinuation of lamivudine, and (3) in Japan, adefovir dipivoxil was not available. Theoretically, the steroid containing regimen with lamivudine prophylaxis for NHL patients carrying HBV may be the best therapy. To prove the efficacy of this therapy, further studies are required.

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