Reactivation of Resolved Hepatitis B virus Infection before the Relapse of Lymphoma : Immunosuppressive effect of the Lymphoproliferative disorders ?

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Abstract

Hepatitis B virus (HBV) infection is a heterogeneous disease with distinct phases determined mainly by the interaction between virus replication and host immune response. HBV reactivation can occur spontaneously, developing resistance to antiviral treatment while the patient is undergoing treatment, after cessation of antiviral drugs, or be triggered by immunosuppressive drugs and chemotherapy. HBV reactivation can be severe and sometimes fatal because of liver failure. Here we report a patient with resolved HBV infection who presented with reactivation before being diagnosed with a relapse of non-Hodgkin lymphoma. (Acta gastroenterol. belg., **2016**, 79, **63-64**).

Key words : Hepatitis B virus (HBV), reactivation, immunosuppression, lymphoma.

To the editor,

Hepatitis B virus (HBV) infection is a heterogeneous disease with distinct phases determined mainly by the interaction between virus replication and host immune response. This interaction is important because HBV reactivation can be severe and sometimes fatal because of liver failure (1). Here we report a patient with resolved HBV infection who presented with reactivation before being diagnosed with a relapse of non-Hodgkin lymphoma.

A 73-year-old woman was admitted owing to weakness, nausea, and painless jaundice during the previous 3 weeks. Physical examination revealed scleral icterus but no splenomegaly or peripheral lymphadenopathy. Laboratory investigation showed increased aminotransferases (AST : 408 IU/mL ; ALT : 325 IU/mL) and hyperbilirubinemia (total bilirubin : 5.7 mg/dL ; direct bilirubin : 3.7 mg/d). She was positive for hepatitis B surface (HBs) antigen, hepatitis B e antigen, and anti-hepatitis B core antibody immunoglobulin M, and negative for anti-hepatitis C virus and HIV antibodies. Serum HBV DNA levels were 980,000 IU/mL ; as a result, the patient was diagnosed with reactivation of HBV infection. We learned from the patient's history that she was diagnosed with diffuse large B-cell lymphoma (DLBCL) and underwent chemotherapy with 6 cycles of cyclophosphamide, hydroxydaunorubicin, Oncovin, prednisone, rituximab regimens 5 years ago. The patient was known to have a resolved hepatitis B status with anti-hepatitis B core antibody immunoglobulin M and anti-HBs antibody positive serology. She achieved complete remission without HBV infection reactivation and remained disease-free for 5 years. She had been screened for disease relapse at regular intervals since being diagnosed with lymphoma. Her last clinic visit was 6 months ago where she showed normal aminotransferase levels with positive anti-HBs. Entecavir therapy was initiated. Both ultrasonography of the neck and computed tomography of the thorax and abdomen revealed no lymph nodes. At the sixth week of entecavir treatment, her serum aminotransferase levels returned to normal levels, HBV DNA decreased to 600 IU/mL, and symptoms improved significantly. However, 8 weeks after her presentation, she reported swelling on the right side of her neck. Neck ultrasonography detected multiple lymph nodes. A cervical lymph node excision biopsy revealed DLBCL, and the patient was referred to the oncology department.

HBV reactivation can occur spontaneously, developing resistance to antiviral treatment while the patient is undergoing treatment, after cessation of antiviral drugs, or be triggered by immunosuppressive drugs and chemotherapy (1). The risk is higher in patients with lymphoma than those with solid tumors. In addition, anti-HBs seroconversion after three vaccine doses has been reported in 57% of cancer patients, 15%-68% of bone marrow transplant recipients, but only in 10% of acute lymphocytic leukemia patients (2). This can be attributed to the hematological disease itself inducing a greater degree of immunosuppression or because chemotherapy is stronger in cases of hematological malignancies. The number of circulating naive and activated regulatory T cells has been found to be lower in patients with DLBCL than in healthy controls or patients with solid organ tumors (3). The levels of T- cell receptor rearrangement excision circles in peripheral blood mononuclear cell DNA show recent thymic output function is severely impaired in DLBCL patients before chemotherapy and has been reported to affect prognosis (4). A significant association

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between non-Hodgkin lymphoma and past or present HBV infection has also been reported ;this association was more powerful for patients with DLBCL, low education, and current HBV infection.Moreover, HBV is believed to be lymphotropic, affecting various target cells or tissues, besides being hepatotropic. B-cell lymphocytic leukemiais derived from memory B cells-antigen-experienced cells-therefore, HBV could act as an antigen for lymphoproliferation (5). To our knowledge, this is the first case of HBV reactivation preceding lymphoma relapse.

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