A Novel Antiviral Treatment of Hepatitis C Virus Reactivation in a Breast Cancer Patient Undergoing Chemotherapy

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To the Editor: Viral hepatitis is a major public health concern worldwide, and hepatitis B virus (HBV), with which two billion people infected globally, has been commonly reported to undergo reactivation during chemotherapy for malignancies.[1,2] Some literatures have reported hepatitis C virus (HCV) reactivation in hematological malignancies.[1,3] Breast cancer, the most common cancer in female, is increasing rapidly globally. Hence, oncologists would undoubtedly deal with breast cancer patients with asymptomatic HCV carrier who are prone to HCV reactivation.[3] HCV reactivation is defined as a minimum 3-fold increase in alanine transaminase (ALT) level in a patient with the absence of liver metastasis with careful exclusion of HCV reactivation from other causes.[1] An increase in HCV viral load of more than 1×10^3 U/L could be a sign of HCV reactivation.[1]

A 59-year-old female patient was admitted to our hospital complaining of right breast mass for the past 2 months. After admission, the patient was diagnosed with right breast infiltrating ductal carcinoma ($T_2N_2M_0$) by core needle biopsy, meanwhile liver function tests and ultrasonography were normal. HCV and HBV serological markers had no obviously abnormal. The patient was treated with four cycles of neoadjuvant chemotherapy of TEC regime (Docetaxel 75 mg/m^2, Epirubicin 75 mg/m^2, and cyclophosphamide 500 mg/m^2) every 3 weeks, followed by modified radical mastectomy. After surgery, the patient underwent two cycles of TEC chemotherapy. The liver function tests before the sixth cycle of chemotherapy revealed a significant elevation of liver enzymes: ALT 124 U/L and AST 180 U/L. Further serological examinations revealed HCV RNA obviously elevated. Autoimmune antibodies, hepatitis A, D, E virus, and EB virus antigen and antibody were negative. The patient had medical history of blood transfusion about 20 years ago for upper gastrointestinal hemorrhage due to gastric ulcer, but she had no knowledge of HCV infection before. After consultation with hepatologists, the patient was diagnosed with HCV reactivation and further advised to go for HCV genotyping. While the results of HCV genotyping were on waiting, we started her last cycle of chemotherapy. She successfully completed her sixth cycle of chemotherapy with active liver protection under the guidance of hepatologists. After chemotherapy, the patient received novel antiviral therapy of daclatasvir plus sofosbuvir for 12 weeks under the guidance of HCV genotyping (Genotype Ib), meanwhile she accepted postoperative radiotherapy for 5 weeks. After 2 weeks, the HCV reactivation was controlled effectively, and the patient's liver function and HCV RNA level returned to normal levels [Table 1].

HCV reactivation seems to be less common than HBV reactivation, however, once it occurs, severe hepatitis develops as a result of viral reactivation, and mortality rate seem to be similar to HBV reactivation.[1] Liver dysfunction due to hepatitis viral reactivation often leads to modification or disruption of anticancer treatment, which would negatively impact patients' prognosis.[1] Liver dysfunction after HCV reactivation generally occurs 2–4 weeks after chemotherapy. In this case, the HCV reactivation was detected at the initiation of the sixth chemotherapeutic cycle. This would be due to enhanced viral replication with increased number of infected hepatocytes after immunosuppressive treatment, and withdrawal of immunosuppressive therapy led to the restoration of the host immune function, resulting in rapid destruction of infected cells and hepatic injury. HCV is not directly cytopathic for infected host cells, and the immune response plays a central role in the pathogenesis of liver damage. Small quantities of HCV RNA may persist in liver or macrophages and lymphocytes even after antiviral treatment, this continuous viral presence could result in persistence of humoral and cellular immunity for many years and could present a potential risk for viral reactivation.[4]

In this case, a Stage III_A breast cancer patient occurred HCV reactivation during chemotherapy and received novel antiviral therapy of daclatasvir plus sofosbuvir. Daclatasvir and sofosbuvir, as novel direct-acting antiviral agents (DAAs), are currently recommended for chronic hepatitis C treatment. Before the recent approval of DAAs, triple therapy combining PEGylated interferon, ribavirin, and protease inhibitor was the standard regimen for HCV treatment.[5] It is suggested that all HCV-infected patients should undergo HCV genotyping for therapeutic guidance. In this case, the patient was confirmed to be infected with HCV of Genotype Ib. Current guidelines recommend HCV of Genotype Ib patients

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Table 1: The status of HCV and HBV serological markers

Time	HCV serological markers			HBV serological markers					
	HCV antigen	Anti-HCV	HCV RNA (U/L)	HBsAg	HBsAb	HBeAg	HBeAb	HBcAb	HBV DNA (U/L)
At admission	–	+	$<1.0\times10^3$	–	+	–	–	+	NA
During chemotherapy*	–	+	8.17×10^6	–	+	–	–	+	$<1.0\times10^3$
After antiviral	–	+	–	–	+	–	–	+	$<1.0\times10^3$

*During chemotherapy: Before the sixth cycle chemotherapy. –: Negative; +: Positive; Anti-HCV: HCV IgG antibody; HBsAg: HBV surface antigen; HBsAb: HBV surface antibody; HBeAg: HBV e antigen; HBeAb: HBV e antibody; HBcAb: HBV core antibody; NA: Data not available; HCV: Hepatitis C virus; HBV: Hepatitis B virus.

with 60 mg orally of daclatasvir and 400 mg orally of sofosbuvir with or without ribavirin once daily. However, the recommended treatment duration is 12 weeks for noncirrhotic patients.[5]

As more cytotoxic chemotherapy is carried out for various cancers, reactivation of hepatitis viruses during anticancer treatment has become a significant problem that cannot be ignored. Our case indicates that HCV should be screened before the initiation of systemic chemotherapy, and we should pay more attention to patients with elevated transaminase levels and liver dysfunction during chemotherapy for possible HCV reactivation. In addition, liver function tests should be undertaken strictly during systemic chemotherapy, especially for patients with the anti-HCV positive.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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