

Chronic Hepatitis C Virus Infection, Why Not Treat Now?

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Biologics are widely used in the treatment of rheumatoid arthritis (RA) these days and have shown excellent therapeutic effect. However, they tend to weaken the immunity and increase the susceptibility to infection. This becomes more problematic in patients with chronic infection of hepatitis B virus (HBV) and hepatitis C virus (HCV) because biologics can lead to the reactivation of these hepatitis viruses.

The reactivation of HBV can cause fatal outcomes in some patients and preemptive antiviral therapy is strongly recommended in all HBV-infected patients undergoing immunosuppressive therapy including biologics for RA. However, there are no specific guidelines about the management of chronic HCV infection in patients treated with immunosuppressive therapy.

In contrast to HBV, HCV reactivation usually follows a mild clinical course and rarely causes severe hepatitis or hepatic decompensation. Lee et al. [1] reported that enhanced HCV replication or increase in HCV RNA level was relatively common (27%) in HCV-infected patients treated with systemic chemotherapy or immunosuppressive therapy, but it did not lead to serious sequelae. Even patients with liver cirrhosis had relatively good liver function in spite of enhanced HCV replication. Torres et al. [2] reported that HCV reactivation occurred in 23% of HCV-infected patients receiving cancer treatment and most had an unremarkable clinical course with no liver failure or liver-related death.

Presence of HCV infection is not contraindication to therapy with tumor necrosis factor- α (TNF- α) inhibitors. Although TNF- α inhibitors potentially increase HCV replication, only a few cases of drug with-

drawal due to suspected recurrence of liver disease related to HCV were reported so far [3]. This suggests that TNF- α inhibitors are safe in patients with HCV infection in short term although there are insufficient data to assess their long term safety.

In this edition of the journal, Kwon et al. [4] reported the result of their retrospective study about the changes in the transaminase and viral load associated with biologic therapy in 17 RA patients with HCV infection. Transaminase was increased in 4 patients (2 in adalimumab and 2 in tocilizumab). Two adalimumab-treated patients also showed increase in HCV RNA level. One patient stopped adalimumab and the other patient received anti-viral therapy using interferon (IFN) and ribavirin, which was very effective. One tocilizumab-treated patient with the increase in HCV RNA level received anti-viral therapy using ribavirin and sofosbuvir and, in the other tocilizumab-treated patients, transaminase was normalized within 2 months. Authors said that use of biologics in HCV-infected patients could lead to changes in transaminase and viral load and regular follow up of liver function and viral RNA is necessary.

HCV infection is confirmed by simultaneous presence of anti-HCV antibody and HCV RNA. However, HCV RNA level does not correlate with either the severity of liver disease or the risk for progression to cirrhosis or hepatocellular carcinoma (HCC) in previous studies [5,6] and it is controversial whether it is essential to follow up HCV RNA levels in HCV-infected patients treated with immunosuppressive agents [3].

As for the treatment, HCV is very different from HBV in that HCV is a curable disease. Once antiviral treatment

Received : May 2, 2018, Revised : May 9, 2018, Accepted : May 10, 2018

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leads to sustained virologic response (SVR) which is defined by undetectable HCV RNA 12 to 24 weeks after the end of therapy, reappearance of the HCV RNA is very rare [5]. IFN-based regimens have long been used for the treatment of HCV but are only moderately effective [7]. Furthermore, these regimens have significant adverse effects, which made them difficult to use in patients being treated with immunosuppressive agents.

However, recently introduced direct-acting anti-virals (DAAs) (ledipasvir/sofosbuvir, sofosbuvir, daclatasvir, asunaprevir, ombitasvir/paritaprevir/ritonavir, dasabuvir, elbasvir/grazoprevir) changed the approach to HCV hepatitis [7]. These oral regimens are much tolerable compared to IFN-based therapies. They have shown SVR rates greater than 90% and are rapidly replacing IFN-based therapies. Because of high tolerability and efficacy of DAAs, many patients on immunosuppressive therapy after organ transplantation have been simultaneously treated with DAAs for HCV infection. Furthermore, there is a report that DAAs can be used concomitantly with anti-neoplastic agents and this therapeutic intervention may prevent delay in the administration of chemotherapy in HCV-infected cancer patients [8].

When it comes to the treatment of HCV-infected patients with RA, concomitant treatment with biologics and DAAs seems to be promising. When etanercept, a TNF- α inhibitor, was used with IFN and ribavirin for the treatment of HCV, SVR rate was higher than in the control group who were treated with IFN and ribavirin only (63% versus 32%) [9]. There has been a concern of RA flare followed by IFN treatment, but DAAs can avoid this problem.

Cirrhosis caused by HCV is a leading indication for liver transplantation and HCV is the most common cause of HCC in most industrialized countries [5]. When patients achieve a SVR to treatment, HCV does not recur in greater than 99% of patients, even in those who are immunosuppressed or receive chemotherapy and HCC is less likely to develop in these patients. Considering the sequelae of chronic HCV infection and the effectiveness and tolerability of recent DAAs, it looks like that time has come to think about simultaneously treating HCV through close cooperation with the hepatologists rather than just following up liver function and HCV RNA level

in HCV-infected RA patients on biologic treatment.

ACKNOWLEDGMENTS

The author is grateful to Prof. Woo-Im Chang (Department of Internal Medicine, The Catholic University of Korea, St. Vincent's Hospital) for her critical advice for this manuscript.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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