Chapter 35

HEPATITIS B REACTIVATION AFTER CHEMOTHERAPY

Muhammed OKUYUCU[1]

INTRODUCTION

It is estimated that more than two billion people from all over the world have been infected with the hepatitis B virus (HBV) at some stage in their lifetime and around 350 million people have chronic hepatitis B infection (Pattullo, 2015). According to a study from Turkey, approximately 15 million people, corresponding to one-third of the adult population, have been exposed to HBV and carry ccc (covalently closed circular) DNA of the virus in their livers (Tozun & et al., 2015). Anyone who had been exposed to an HBV infection is at risk for reactivation of the infection. The hallmark of progressive liver disease in HBV infection is active viral replication. However, patients with low serum HBV DNA level (usually below 1000 IU/mL) and normal alanine aminotransferase (ALT) values are considered inactive carriers at low risk for clinical progression. Nevertheless, HBV reactivation may occur in these inactive carriers either spontaneously or after immunosuppression (Dienstag, 2008). Impaired host defense system due to treatment with chemotherapeutic or immunosuppressive agents increases the risk of HBV reactivation (HBVr) (Gupta & et al., 1990). HBVr may occur in patients with occult HBV (HBsAg negativity, HBV DNA<200 IU/mL, anti-HBC (total) negativity or positivity) or resolved HBV infection (both HBsAg and HBV DNA negativity, and anti-HBC (total) positivity) who receive cancer chemotherapy. Consequently, increased viral replication may cause elevation of liver enzymes, hepatic failure and severe clinical manifestations or even death. In addition, HBVr also leads to premature discontinuation of chemotherapy and delay in treatment schedules (Yeo & et al., 2003).

Given the high prevalence of chronic HBV infection globally, oncologists may encounter with patients with both cancer and chronic HBV infection. The most common approach to prevent HBVr is to start prophylactic treatment prior to administration of immunosuppressive medications or simultaneously. Almost all studies have demonstrated the effectiveness of this strategy (Liao & ark., 2015).

[1] Dr lecturer, Department of Internal Medicine, 19 Mayıs University Faculty of Medicine, Samsun, Turkey, muhammedokuyucu55@gmail.com

being a young male, has been considered as a risk factor for HBVr in many studies (Yeo & et al., 2000).

SCREENING AND TREATMENT

Considering that most patients are not aware of the fact that they have been infected with HBV, all patients should be screened before initiation of chemotherapy. In countries with a HBsAg prevalence greater than 2%, pretreatment screening must be conducted for HBsAg, anti-HBC (total) and anti-HBs. HBV DNA should be tested if HBsAg or anti-HBc (total) positivity is detected (EASL, 2012).

HBVr risk may be reduced markedly by implementing antiviral prophylaxis. The use of antiviral agents at the start of chemotherapy has been shown to be effective for decreasing the risk of HBV reactivation. Prophylaxis may also be initiated before starting therapy. In patients on immunosuppressive regimens, prophylaxis should be continued for at least 6 months after discontinuation of immunosuppressive drugs. Additionally, it was recommended that antiviral prophylaxis be continued for 12 months after stopping rituximab therapy (Evens & et al., 2010). Ideal antiviral agents to be used for prophylaxis are entecavir and tenofovir. Since lamivudine is associated with a high rate of drug resistance and many patients are at risk for HBV reactivation after 6 months of chemotherapy discontinuation, entecavir and tenofovir which provide rapid and strong suppression of HBV DNA should be used for long-term prophylaxis (Terrault & ark., 2016).

Treatment might be deferred or discontinued if HBVr is detected during chemotherapy. Cessation of chemotherapy due to reactivation can reduce HBV replication but poses a major risk for the primary disease in question. The decision to interrupt treatment depends on the severity of the clinical picture. Treatment should be interrupted in patients with elevated ALT levels 3 times the upper limit of normal (ULN) in the presence of persistent symptoms or jaundice (Köksal, 2016). Antiviral therapy should be started as soon as possible if HBVr occurs. Patients may be asymptomatic or progress to hepatic failure. Decision for treatment is based on the condition and renal function of the patient and recommended therapeutic options include tenofovir and entecavir (Lok & Bonis, 2016).

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