Bortezomib-associated late hepatitis B reactivation in a case of multiple myeloma

Multipl myelom'lu bir olguda bortezomib ilişkili geç hepatit B reaktivasyonu

To the Editor,

Bortezomib is a selective proteasome inhibitor that has a remarkable activity in relapsed/refractory multiple myeloma (MM) (1-7). Although it is well tolerated with a manageable toxicity profile, reactivation of viral infections emerges as a significant problem in this setting (1-4, 6, 7). Here, we present a case of MM who developed late hepatitis B reactivation after bortezomib therapy.

A 58-year-old male, with a diagnosis of lambda light chain MM, was considered to be in the replicative phase of chronic hepatitis B, revealing the presence of HBsAg and HBeAg, with a serum HBV DNA level of 350,000 copies/ml and normal aminotransferase levels. He was treated with four courses of VAD (vincristine, doxorubicin, dexamethasone) regimen on lamivudine prophylaxis. As he was determined to be refractory to VAD, he subsequently received up to eight three-weekly courses of bortezomib at a dose of 1.3 mg/m2/day on days 1, 4, 8 and 11, on lamivudine prophylaxis. HBV DNA was negative and aminotransferases were found to be normal during bortezomib therapy. However, the patient was lost to follow-up without lamivudine prophylaxis, after receiving the last course of bortezomib. Nine months after bortezomib therapy, HBV DNA was negative with normal aminotransferase levels. Hepatitis B reactivation was demonstrated with a HBV DNA level of 20,000 copies/ml 18 months after bortezomib therapy. Based upon the positivity of HBV DNA 18 months after the last course of bortezomib, this case might be considered as bortezomib-associated late hepatitis B reactivation.

Bortezomib, a potential inhibitor of nuclear factor kappa B (NF-κB) pathway, inhibits T-cell responses by increasing the apoptotic process of alloreactive CD4+ and CD8+ T-cells (1-4, 6, 7). Hence, antiviral prophylaxis is recommended to prevent herpes and varicella zoster infections in patients undergoing bortezomib therapy (4, 7). The combined treatment modalities of bortezomib with steroids or other cytotoxic agents might intensify the tendency to viral infections. To date, several reports have underlined the early concomitant reactivation of herpes infections in patients receiving bortezomib therapy (1, 2). Similarly, a case of severe toxic hepatitis, which was attributed to ongoing bortezomib treatment, was previously reported (5). Although inappropriate use of lamivudine might be a contributing factor for the late reactivation of hepatitis B in the present case, the role of bortezomib could not be excluded (5). Prolonged antiviral therapy might be considered in HBsAg carriers receiving bortezomib therapy; nevertheless, the optimal duration of antiviral prophylaxis remains to be defined. Bortezomib-associated late hepatitis B reactivation appears to be a novel topic which requires further confirmation.

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Manuscript received: 09.07.2009 **Accepted:** 04.02.2010

doi: 10.4318/tjg.2010.0087

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