学位の種類	博士（医学）
報告番号	甲第２０１０号
学位記番号	第１４１５号
氏名	萩原 真也
授与年月日	令和6年 3月 22日
学位論文の題名	Management of hepatitis B virus (HBV) reactivation in patients with resolved HBV infection based on a highly sensitive HB core-related antigen assay （高感度HBコア関連抗原アッセイに基づく、HBV既往感染患者におけるB型肝炎ウイルス(HBV)再活性化の管理） Hepatol Res. 2022;52(9):745-753
論文審査担当者	主査： 片岡 洋望 副査： 奥野 友介，林 香月

Abstract

[Background] Hepatitis B virus (HBV) reactivation after chemotherapy including anti-CD20 antibody therapy or hematopoietic stem cell transplantation can occur in patients with resolved HBV infection, those who are hepatitis B surface antigen (HBsAg) negative and HBc antibody (anti-HBc) or HBs antibody (anti-HBs) positive. Preemptive therapy with nucleos(t)ide analogs (NA) in these immunosuppressed patients with regular monitoring of HBV DNA can prevent HBV reactivation-related hepatitis. However, there is little evidence after NA administration (mainly the criteria for NA cessation). [Aims] To prevent HBV reactivation-related hepatitis, we examined the clinical usefulness of a highly sensitive HB core-related antigen (iTACT-HBcrAg) assay in patients with resolved HBV infection after NA treatment for HBV reactivation. [Methods] We retrospectively analyzed 27 patients with resolved HBV infection who experienced HBV reactivation (defined as HBV DNA levels of 1.3 log IU/ml or more), and who received systemic chemotherapies for hematological malignancies between 2008 and 2020. iTACT-HBcrAg, HBsAg-HQ and anti-HBs were measured using samples stored after HBV reactivation. The lower limit of quantification for iTACT-HBcrAg was 2.0 log U/ml. [Results] HBV reactivation was diagnosed at a median HBV DNA level of 1.8 log IU/ml, and then all patients received NA treatment. No patient had HBV-related hepatitis with a median maximum HBV DNA level of 2.0 log IU/ml. The positivities of iTACT-HBcrAg and HBsAg-HQ were 96% and 52% after HBV reactivation, respectively. Of 25 patients with detectable iTACT-HBcrAg at the initiation of NA treatment, 17 (68%) achieved iTACT-HBcrAg loss. Median durations from NA treatment to HBV DNA loss and iTACT-HBcrAg loss or the last follow-up were 35 and 175 days, respectively. Recurrence of HBV reactivation after NA cessation was not observed in seven of eight patients who achieved iTACT-HBcrAg loss or seropositive for anti-HBs during follow-up, except for one without anti-HBs after allogeneic transplantation. [Conclusions] iTACT-HBcrAg could be a potential surrogate marker for diagnosing early-stage HBV reactivation as well as safe cessation of NA treatment in patients with resolved HBV infection after HBV reactivation.