90838_Auto_Edited-check.docx

WORD COUNT 1002
TIME SUBMITTED 08-FEB-2024 07:39PM
PAPER ID 106766571

Name of Journal: *World Journal of Gastroenterology*

Manuscript NO: 90838

Manuscript Type: LETTER TO THE EDITOR

Risk of hepatitis B virus reactivation in oncological patients treated with tyrosine kinase inhibitors: A case report and literature analysis

Colapietro F *et al*. Risk of HBVr in TKI

Abstract

Hepatitis B virus (HBV) reactivation (HBVr) represents a severe and potentially life-threatening condition, and preventive measures are available through blood test screening or prophylactic therapy administration. The assessment of HBVr traditionally considers factors such as HBV profile, including hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen, along with type of medication (chemotherapy; immunomodulants). Nevertheless, consideration of possible patient's underlying tumor and the specific malignancy type (solid or hematologic) plays a crucial role and needs to be assessed for decision-making process.

Key Words: Chronic hepatitis B; Reactivation; Nucleoside analogue; Tyrosine kinase inhibitors; Onco-hematology

Colapietro F, Pugliese N, Voza A, Aghemo A, De Nicola S. Risk of hepatitis B virus reactivation in oncological patients treated with tyrosine kinase inhibitors: A case report and literature analysis. *World J Gastroenterol* 2024; In press

Core Tip: Hepatitis B virus reactivation (HBVr) is a clinical challenge among patients receiving chemotherapy for solid tumors or hematologic malignancies. The emergence of novel immunosuppressive and immunomodulatory agents requires expertise in delineating the risk of HBVr associated with each drug class. Classifying the risk of HBVr into low (< 1%), intermediate (1%-10%) and high (> 10%) allows physicians to understand in whom nucleos(t)ide analogues (NAs) are required to avoid potential progression to liver failure and death. To note, according to guidelines, patients without immediate indication for NAs should undergo serial monitoring of blood test for transaminases and HBV profile, including hepatitis B surface antigen status and HBV-DNA titer.

TO THE EDITOR

We were intrigued by the study conducted by Mak JWY *et al*[1], which aimed to provide an updated guidance for monitoring or initiating antiviral prophylaxis in patients at risk of developing hepatitis b virus reactivation (HBVr). When focusing on Bruton tyrosine kinase (BTK) inhibitors, successful in treating various lymphoid malignancies, the authors emphasized the current absence of guidelines for prophylaxis and management of HBVr. Existing data primarily stems from retrospective studies and show HBVr rates ranging up to 8.3% in previously resolved infection. We agree with authors' perspective that administering anti-HBV prophylactic treatment with nucleotide analogues is advisable for patients receiving tyrosine kinase inhibitors (TKIs) for hematologic malignancies who exhibit either positive hepatitis B surface antigen (HBsAg) or resolved HBV infection with detectable HBV DNA.

Papatheodoridis *et al*[2] recently raised awareness on the topic by conducting an analysis of available literature, identifying 4 studies including 268 chronic hepatitis B patients treated with TKI. Overall, 196 HBsAg+ patients and 72 HBsAg-/antibody to hepatitis B core antigen (antiHBc)+ patients were included; to note, HBV DNA status was not reported. The pooled rate of HBVr in HBsAg+ patients was 21/196 (11%), with no HBVr observed in the cohort of HBsAg-/antiHBc+ patients who did not receive nucleos(t)ide analog (NA) prophylaxis. Conversely, among HBsAg+ patients who did not receive NA treatment, 16 cases of HBVr-associated hepatitis were observed. No cases of HBVr hepatic decompensation or death were observed. Based on these figures, the authors recommend NA prophylaxis for HBsAg+ patients receiving TKI (high risk of HBVr), while close monitoring and on-demand NA therapy is warranted in HBsAg- (low risk of HBVr)[2].

Next to these papers, several cases of TKI-associated HBVr in HBsAg- patients with hematologic malignancies have been reported (Table 1). Innocenti *et al*[3], in a cohort of 108 chronic lymphocytic leukemia (CLL) patients, reported two cases of HBVr (1.9%) among HBsAg-/anti-HBc+ patients within the initial 6 months of second-line treatment with ibrutinib, a covalent BTK[3]. None of these cases experienced HBVr associated hepatitis, and both individuals responded effectively to entecavir treatment.

Additionally, Chiu *et al*[4] analyzed a series of 29 patients treated with TKIs, reporting 3 cases (10%) of HBVr, with 2 occurring in HBsAg-/anti-HBc+ patients receiving BKT inhibitors. Notably, all 3 experienced HBVr hepatitis, with 2 developing liver failure; all cases recovered with anti-HBV therapy[4]. To note, several cases of HBVr have been reported in patients with solid tumors. Lee *et al*[5] described the largest retrospective cohort, comprising 1960 anti-HBc+ patients with lung cancer treated with TKI. Among them, 1594 were HBsAg- and 521 received TKI as first-line treatment. One patient developed HBVr characterized by the reappearance of HBsAg, elevation of alanine aminotransferase (ALT) more than 10 folds upper limit of normal (ULN) and HBV DNA reaching up to 245000 IU/mL (undetectable at baseline).

We present here the case of a 67-year-old Caucasian male patient with CLL treated with acalabrutinib, a Food and Drug Administration-approved next-generation covalent BTK inhibitor[6]. His medical history included prior treatment for colorectal cancer through surgical intervention for bowel obstruction (TNMv8: pT4b N0 R0).

As the patient was HBsAg-/anti-HBc+, close monitoring of liver function blood tests and HBV profile was started. To note, HBV DNA was undetectable before starting treatment. After 8 months of therapy, a mild elevation of transaminases up to three times ULN was observed, with no coagulation impairment or elevation of total bilirubin. Subsequently, one week later the patient developed hepatic liver failure characterized by jaundice (total bilirubin 23 mg/dL), PT > 1.7 and ascites. At this point HBV DNA was 8.9 log IU/mL, ALT 497 U/L (ULN 50 U/L), aspartate aminotransferase 493 U/L (ULN 50 U/L); nucleos(t)ide analog treatment was started immediately. Two weeks following the onset of HBVr, HBV DNA reduced to 4.9 log IU/mL. Ascites was well controlled, no signs of hepatic encephalopathy developed, but bilirubin persisted at 43 mg/dL and the patient remained hospitalized. Acalabrutinib treatment was stopped.

Based on these reports, HBsAg-/antiHBc+ patients receiving TKI in the onco-hematological setting should be reclassified as intermediate risk for HBVr warranting consideration for antiviral prophylaxis. We advocate for regular updates on the risk of

HBVr associated to specific drug classes. Moreover, we think that type of tumor (solid or hematologic) should be analyzed as a possible risk factor for deciding when to start antiviral prophylaxis.

90838_Auto_Edited-check.docx

ORIGINALITY REPORT

0%

SIMILARITY INDEX

PRIMARY SOURCES

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 15 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 15 WORDS