Risk of hepatitis B virus (HBV) reactivation in patient receiving rituximab: Results from Taiwan National Adverse Drug Reaction Reporting System

Shan-Hu Lin, Pi Huei chao, Wen-Wen Chen, Angela On
Taiwan National ADR Reporting Center, Taiwan Drug Relief Foundation, Taipei, Taiwan

Background

The use of rituximab in non-Hodgkin's lymphoma (NHL) is known to be associated with increased risk of hepatitis B virus (HBV) reactivation and the possible relationship could be explained by the depletion of B cells, which leads to occurrence of hepatitis B within 4 month after the initiation of and 1 month after the completion of therapy[1]. Since hepatitis viral infection is a high-prevalent disease in Taiwan, serologic testing for prior viral HBV exposure and antiviral agents have been covered by National Health Insurance (NHI) for rituximab-containing chemotherapy in NHL patients for the prophylaxis of HBV reactivation since 2009. However, it's still unclear whether the same risk exists when used for other indications, such as autoimmune disorders which have been widely used in Taiwan.

Objectives

The aim of this study is to review the pattern of HBV reactivation cases in patients receiving rituximab in Taiwan National ADR reporting database.

Methods

We collected rituximab cases containing MedDra Lower Level Term (LLT) coded with hepatitis B reactivation from Dec 2005 to Dec 2012 in Taiwan National ADR reporting database. Characteristics of the cases were further reviewed and analyzed.

Results

From a total of 358 rituximab reported cases, 27 (7.54%) were suspected of having HBV reactivation. Median age was 58.0±10.9 years (13 males vs. 14 females). The average days between the last dose of rituximab and HBV reactivation was 64.4 days(range, 7-135 days). 22 cases (81%) were reported as HBV carriers (HBsAg positive) or with histories of hepatitis B (HBcAb positive). Of the 27 HBV reactivation cases, 21 cases (77.8%) were indicated for NHL ; 4 cases (14.8%) for rheumatoid arthritis (RA) and 1 case (3.7%) for Idiopathic thrombocytopenic purpura (ITP). 9(33%) and 2(33%) fatal cases were indicated for NHL and non-NHL respectively. All patients indicated for NHL had HBV serologic testing (HBsAg at least) before treatment of rituximab ; however, only one patient treated for non-NHL indication was tested.

Table 1. Demographic characteristics of rituximab-related HBV reactivation cases

Item	NHL	Non-NHL (RA,ITP)
No. of cases (%)	21 (77.8)	6 (22.2)
Age	57.2±11.6	62.5±4.7
Gender		
Male	10	3
Female	11	3
Onset time* (day)	50.8	89.0
Range	7-105	7-135
Baseline		
HBsAg positive	14	0
HBsAg negative	7	1
Unknown	0	5
Seriousness		
Death	7	2
Hospitalization	1	2
Require intervention to prevent permanent damage	12	1
Non-serious	1	1
Mortality (%)	33	33
Antiviral prophylaxis		
Yes**	5	0
No/Not reported	16	6

*** Time to reactivate from the last dose of rituximab**

****Antiviral agents: Lamivudine or Entecavir**

Conclusions

The risk of rituximab associated HBV reactivation in patients treated for autoimmune disorders (eg: RA, ITP) cannot be overlooked. Routine lab tests (HBsAg and HBcAb) are suggested to be performed before the treatment of rituximab. HBV carriers should be monitored closely during therapy and for at least 6 months after completion of therapy[2]. When treated for HBV positive patients, antiviral therapy should be considered for prophylaxis.

Reference

1. Rituximab Package Insert. South San Francisco, CA: Biogen Idec, Inc. and Genentech, Inc., 2012.
2. Zelenetz AD, Abramson JS, Advani RH et al. NCCN Clinical Practice Guidelines in Oncology: Non-Hodgkin's Lymphomas. J Natl Compr Canc Netw 2010;8:288-334