Abstract

Background: Hepatitis B reactivation is an important risk of rituximab therapy. As rituximab is used more widely by an increasing number of specialists, opportunities to prevent reactivation may be missed due to lack of awareness or protocolization. This study aimed to assess Hepatitis B screening in our rituximab patients.

Methods: All adult patients receiving rituximab therapy in 2014-5 at our centre (832 beds; catchment 850,000) were included. Available serology at the time of initiation were recorded. Patients found to have active hepatitis B (DNA/surface antigen) or core antibody were evaluated for evidence of monitoring or prophylaxis and for adverse outcomes.

Results: 318 patients received rituximab in the study period, 85% of whom received some form of hepatitis B serologic testing (Table 1). In the absence of Hepatitis B surface antigen, nearly 1 in 4 were not tested for core antibody. In those with core antibody, 32.5% did not have regular monitoring for or prophylaxis against reactivation. One (2.5%) of these patients developed a fatal fulminant hepatitis B flare. Of the patients not screened, one (2%) developed a clinical Hepatitis B reactivation. The majority of transaminase elevation was unrelated to hepatitis B.

Conclusions: A systematic protocol operationalizing hepatitis prevention guidelines in patients receiving rituximab is required in centres where one does not exist.

Background

In 2015, the American Society of Clinical Oncology released an updated clinician opinion regarding Hepatitis B Virus screening of patients undergoing anti-CD20 therapy (1). It was recommended that anyone undergoing anti-CD20 therapy or hematopoetic stem cell transplantation be screened with Hepatitis B core antibody and Hepatitis B surface antigen testing. This was based upon the increased risk of Hepatitis B reactivation in cancer patients undergoing these therapies.

The following study examined the Hepatitis B virus screening and management practices for patients receiving rituximab therapy at a large tertiary care centre, as well as the associated outcomes of viral reactivation.

Methods

Patient Selection

All patients who received rituximab therapy between August 2014 to March 2015 were included in the study.

Hepatitis B Screening Practices

Available hepatitis B tests (core antibody, surface antibody and surface antigen) resulted within 2 years of rituximab therapy were recorded. For patients with a positive core antibody we evaluated for: prophylactic therapy; serial measurements of Hepatitis B DNA and/or surface antigen; and the development of transaminis. The later was defined as twice the upper limit of normal according to the American Association for the Study of Liver Diseases (ALT >38 IU/mL for women and >60 IU/mL for men).

Results

318 patients received rituximab therapy during the study period for a wide variety of clinical indications.

87% of patients received some form of testing (Figure 1, Table 1). 25% of patients were not tested for the presence of core antibody. In those with a positive core antibody, 37% did not have regular monitoring for increases in Hepatitis B DNA levels nor did they receive prophylaxis against reactivation. One of these patients developed a fatal fulminant hepatitis B flare and another was found to have developed an asymptomatic Hepatitis B reactivation upon post-therapy screening.

The prophylactic regimens most commonly were lamivudine monotherapy (43%) and tenofovir (27%). 6 patients received HIV medication including one of these.

Discussion

Hepatitis B reactivation can cause morbidity and mortality in patients receiving rituximab. With an increasing number of indications for its use, the number of patients at risk is increasing concurrently. This study investigated our Hepatitis B screening practices and found that one third of patients were inadequately screened for Hepatitis B. Furthermore, of those identified as potentially infected, another third did not adequate prophylaxis or follow up. There were two serious adverse events including one death as a result. The potential causes for inappropriate screening could include:

- A lack of understanding of how to order and interpret HBV serologies
- Underestimation of the risk of Hepatitis B reactivation with rituximab
- An absence of a forcing function to prevent rituximab use without a full serological panel and management plan

There are several potential solutions to this issue:

- The prescription of rituximab must be coupled with orders for the appropriate serological tests and follow up. It should be impossible to deliver rituximab without proper testing, consisting of Hepatitis B core and surface antibody titres, as well as the surface antigen serology.
- Laboratory reporting should be improved to better allow end users to understand the patterns of results and their implications.
- The Infectious Disease physician or hematologist should play an important role in local protocol development.

References