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Immunosuppressants Induced Hepatitis B Reactivation - A Case Report

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ABSTRACT

Introduction: A greater number of cases of hepatitis B virus (HBV) reactivation have been reported in hepatitis B surface antigen (HBsAg) carriers as well as in HBsAg-negative patients who have recovered from HBV infection, coinciding with the increased use of biologicals and other immunosuppressants.

Case Report: A 54 year old male patient with complaints of abdominal pain, constipation, occasional vomiting and icterus ,on DMARDs and high dose of methylprednisolone for RA was examined. On investigation, he was diagnosed with immunosuppressant induced hepatitis B reactivation treated with antiviral and was on regular follow up with better clinical outcome.

Conclusion: High index of clinical suspicion should be there for patients receiving chronic Anti rheumatoid therapy with methotrexate, steroids and leflunomide in view of its systemic manifestation which results in HBV, HCV reactivation. Screening before beginning immunosuppressive therapy and Prophylactic antiviral medication were suggested in preventing Hbv reactivation in HBsAg-positive patients treated with biologicals or DMARDs.

Keywords: DMARDS;HBV; HBsAg

INTRODUCTION

Nearly 400 million individuals worldwide are affected with Hepatitis B virus. It is the most widespread chronic viral infection in human. It is prevalent in Asia (8%) when compared to Europe north America (0.1-2%), and South America (2-7%).[1] A greater number of cases of hepatitis B virus (HBV) reactivation have been reported in hepatitis B surface antigen (HBsAg) carriers as well as in HBsAg-negative patients who have recovered from HBV infection, coinciding with the increased use of biologicals and other immunosuppressants. Patients with chronic Rheumatologic condition may have an infection that has been resolved in 7.3% to 66% of cases.[2] Glucocorticoids, Methotrexate (Mtx), Hydroxychloroquine, Sulfasalazine, and Leflunomide are examples of conventional DMARDs that are used in the treatment of RA patients.

CASE REPORT

A 54 year old male patient was admitted with complaints of abdominal pain, constipation, occasional vomiting and icterus. He was on a high dose of methylprednisolone for RA and anti hypertensive drugs for hypertension. He was clinically examined and investigated, among them complete blood count and liver function test were found to abnormal, INR was high. Since the patient was on DMARDs Methotrexate, leflunomide and high dose steroid for the past seven years. A chance of hepatitis B reactivation due to immunosuppression were suspected. Hepatitis B surface antigen test were carried out which turned out positive, it revealed that the patient might already had an exposure to hepatitis B in the past and its reactivation following immunosuppression. Along with HBsAg, HBV DNA RTPCR and hepatitis B E (HBeAg) antigen were done. Among them HBV DNA RTPCR were detected and hepatitis B E antigen were non reactive. The patient was treated with anti viral drugs Tenofovir Alafenamideand clinical progress monitored.

DISCUSSION

The viral protein released by HBV known as HBeAg (Hepatitis B E-Antigen) is a marker of hepatitis B viral replication. HBV-DNA is an important marker for assessing the viral reactivation. However, prolonged use of immunosuppressants may lead to the reactivation of the hepatitis B virus.[3] There has recently been a rise in awareness of the occult hepatitis B virus, particularly in endemic areas, such as Indonesia, which is part of the Asia pacific region.[4] Reactivation of HBV and HCV may occur in rheumatologic diseases as a result of illnesses or the use of biological medications.[5,6] Patients who are either infected with HBV or recovered from HBV infection are susceptible for HBV reactivation. Yh Lee Et Al conducted a study in 122 HBsAg positive patients ,15 patient (12.3%)had virus reactivation when on treatment for rheumatic diseases.[7]

Before starting immunosuppressive medication, the centers for disease control and prevention (CDC) recommend screening patients for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb), and hepatitis B surface antibody (HBsAb) since it might reactivate the hepatitis B virus (HBV).[8,9] Japan college of rheumatology (JCR)suggested monitoring of ALT levels during antirheumatic therapy at monthly intervals and this monitoring be maintained for at least 12 months following the completion of medication.[10,11] Before receiving anti-rheumatic medication therapy, patients with RA should undergo a thorough examination that takes into account their age, sex and anti-HBs level. Patients who have a high risk of contracting HBV should routinely have their ALT and HBV DNA levels checked. Antiviral treatment should be started as soon as they meet the treatment criteria and the option is to use medications with potent antiviral activity and significant drug resistance barriers.[12] Approach to prevent the HBV reactivation suggested by Watanabe et al was preemptive antiviral therapy and concluded immunosuppressive medication can cause viral reactivation in individuals with chronic hepatitis B virus (HBV) infection and, less frequently, in patients with cured HBV infection. He reported a case of 57-year-old Japanese lady who underwent Methotrexate treatment for RA acquired de-novo hepatitis associated to the hepatitis B virus. Her liver function improved as a result of treatment with Entecavir and oral Prednisolone after steroid pulse therapy.[13]

Treatment with an antiviral agent, previously with Lamivudine, now with more potent Tenofovir or Entecavir, has evolved into a standard practice for HBsAg-positive patients who are candidates for chemotherapy or treatment with biologic agents.[14] Prophylactic or preventive antiviral treatment has long been known to lower the prevalence of reactivation of HBV, the severity of associated HBV hepatitis, and death.[15,16] The timing of beginning antiviral medication for reactivated HBV-caused hepatitis may be too late to completely eradicate the virus.[16] Antiviral prophylaxis of choice exist as lacunae in literature and Lamivudine resistance was observed 24% at one year.[17] Entecavir was superior to lamivudine in terms of virological response and the normalization of liver enzymes in HBV-infected individuals.[18,19] The level of HBV infection and the length of the scheduled biological or targeted treatment determine the suitable antiviral drug to use. Entecavir, tenofovir, or tenofovir alafenamide fumarate are the recommended first-line therapies.[20,21]

CONCLUSION

High index of clinical suspicion should be there for patients receiving chronic Anti rheumatoid therapy with methotrexate, steroids and leflunomide in view of its systemic manifestation which results in HBV, HCV reactivation. Screening the patients for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb), and hepatitis B surface antibody (HBsAb) before beginning immunosuppressive therapy and Prophylactic antiviral medication were suggested in preventing Hbv reactivation in Hbsag-positive patients treated with biologicals or DMRDs.

DISCLOSURE

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ABBREVIATION

RA - RHEUMATOID ARTHRITIS

HBV - HEPATITIS B VIRUS

MTX- METHOTREXATE

INR- INTERNATIONAL NORMALIZED RATIO.

PCR - POLYMERASE CHAIN REACTION

CDC - CENTERS FOR DISEASE CONTROL AND PREVENTION

HBsAg- HEPATITIS B SURFACE ANTIGEN.

HBcAb- HEPATITIS B CORE ANTIBODY.

HBsAb- HEPATITIS B SURFACE ANTIBODY

ALT- ALANINE TRANSAMINASE

DMARDs- DISEASE MODIFYING ANTI RHEUMATOID DRUGS

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