International Journal of Clinical Medicine, **2011, 2, 621-623**
doi:10.4236/ijcm.2011.25103 Published Online November 2011 (http://www.SciRP.org/journal/ijcm)

Occult Hepatitis B Flare-Up after Chemotherapy Treatment in HBsAg Negative Patient

Shoaib Ahmad, Vu Le, Tauseef Ali

Division of Digestive Diseases and Nutrition, University of Oklahoma Health Sciences Center, Oklahoma City, USA.
Email: shoaib-ahmad@ouhsc.edu

Received August 12th, 2011; revised September 24th, 2011; accepted October 18th, 2011.

ABSTRACT

Reactivation of Hepatitis B virus causing liver damage is a concern in patients with chronic HBV infections who receive immunosuppressive or cytotoxic treatments. HBV screening should be considered for all patients going to receive immunosuppressive regimens which have the potential to induce reactivation of HBV infection. We discuss here a case of occult Hepatitis B flare after chemotherapy in a patient who had negative acute hepatitis profile including HBsAg prior to therapy and baseline serum AST, ALT, INR, albumin, bilirubin and serum creatinine were within normal limits.

Keywords*: *Hepatitis B, Chemotherapy, Reactivation

1. Introduction

Hepatitis B virus (HBV) infection is by far the most common chronic viral infection affecting the liver in the world, with over 400 million subjects infected, and it is the leading cause of cirrhosis and hepatocellular carcinoma [1]. Reactivation of HBV in patients undergoing immunosuppressive therapy is a well-recognized complication of considerable clinical importance [2]. The majority of cases of HBV reactivation have been reported to occur shortly after the withdrawal of chemotherapy or during the interval between chemotherapy cycles [3]. HBV screening should be considered for all patients going to receive chemotherapy and other immunosuppressive regimens which have the potential to induce reactivation of HBV infection.

2. Case Report

A 70 year old Caucasian male with past medical history significant for hypothyroidism, hypertension and recently diagnosed Stage 4 Mantle Cell Lymphoma and had received 5 cycles of R-CHOP therapy, with recent PET/CT scans indicating great response to therapy, was admitted to our service with complaints of abdominal pain, nausea and vomiting after 5th cycle of R-CHOP. Prior to therapy, acute hepatitis profile including HBsAg was negative. Baseline serum AST, ALT, INR, albumin, bilirubin and creatinine were within normal limits.

After the 5th cycle of R-CHOP, patient developed abdominal pain, nausea and vomiting to the point that he could not tolerate the last chemotherapy. Gradually, the patient became jaundiced, and complete metabolic profile showed serum AST 423, ALT 307, Total bilirubin 1.9, alkaline phosphatase 82, albumin 3.3, platelets 258 and creatinine 0.95. Repeat Acute hepatitis profile came positive for HBsAg. The patient was admitted to the hospital 10 days later for worsening abdominal pain, jaundice, nausea, vomiting and diarrhea. On physical examination, the patient had normal vital signs, sclera were icteric, there was obvious jaundice, and the liver was mildly enlarged with mild to moderate tenderness to palpation in right upper quadrant. Laboratory data showed reactive HBcAg, HBsAg, HBsAb and positive HBV DNA by PCR. Serum ANA and H282Y gene mutation were negative. There was evidence of worsening of liver function tests with INR 1.77, serum AST 366, ALT 276, albumin 2.6, Creatinine 1.7 and platelets 158. Abdominal and Chest X-rays were normal. Ultrasound of the abdomen showed dilated pancreatic and common bile duct with grade 1 fatty and enlarged liver. MRCP showed no intrahepatic or extrahepatic ductal dilatation. Patient was treated with supportive care and fluid resuscitation. Entecavir was started one week later when liver function failed to normalize. Unfortunately, patient's condition worsened, and he developed hepatorenal syndrome 2 days after starting Entecavir, which was then discontinued. Lamivudine was recommended but patient did not have a chance to be on this medication. His liver and renal functions worsened gradually with peak total bilirubin 30.8, INR 5.6 and Creatinine 7.23. On the last two days of his life, he

Copyright © 2011 SciRes.

also developed disseminated intravascular coagulopathy and was placed on comfort care by family members. Autopsy report was consistent with chronic latent hepatictis B infection.

3. Discussion

Reactivation of HBV causing liver damage is a concern in patients with chronic HBV infections who receive immunosuppressive or cytotoxic treatments. Impairment of the immune response during chemotherapy may lead to resumption of virus replication and infection of more hepatocytes in the absence of an active host immune response. Once the immune response is restored after stopping treatment, a cytotoxic T-cell-mediated response directed against HBV-infected hepatocytes may induce severe liver damage [4,5]. Blanpain *et al.* showed that chronic HBV infection can be reactivated many years down the road when the host immune system is suppressed [6]. However, the term occult Hepatitis B infection was initially described by Cacciola *et al.* in 1999 who observed undetectable HBsAg in previously known HBV patients who were concurrently infected with HCV. However, they were able to demonstrate the presence of HBV DNA via PCR technique, hence the term occult hepatitis B infection [7].

Patients who receive chemotherapy are at risk for HBV reactivation after starting the treatment. In one prospective study, Yeo *et al.* reported reactivation of chronic HBV infection in 20% of the patients undergoing cytotoxic chemotherapy [8]. On the other hand, Lok *et al.* reported that 67% of patients who were HBsAg-positive developed reactivation during cytotoxic therapy for lymphoma and a small number of patients who were HBsAg-negative experienced the reactivation [9]. Currently, the consensus is to screen the patients for chronic hepatitis B infection with HBsAg prior to starting chemotherapy for cancer treatment [10]. There are no recommendations for further testing on patients who are screened HBsAg-negative. For patients who are HBsAg positive, the use of Lamivudine has been shown in several prospective studies to reduce reactivation of HBV significantly [11,12]. Currently, there are no clear

Recommendations on the management of the patients with previously known HBV infection who are seronegative for HBsAg prior the chemotherapy [10], since the incidence of reactivation is substantially lower than those who are HBsAg-positive [8].

4. Conclusions

Reactivation of HBV is a concern in patients with chronic HBV infections who receive immunosuppressive or cytotoxic treatments. HBV screening should be considered for all patients going to receive immunosuppressive regimens which have the potential to induce reactivation of HBV infection. In our case report, we have tried to bring to attention the need for further investigation or screening modality besides using HBsAg as the screening test in patients before starting antineoplastic or immunosuppressive therapy.

REFERENCES

[1] C. L. Lai, V. Ratziu and M. F. Yuen, T Poynard, "Viral Hepatitis B," *Lancet*, Vol. 362, 2003, pp. 2089-2094.

[2] R. P. Perrillo, "Acute Flares in Chronic Hepatitis B: The Natural and Unnatural History of an Immunologically Mediated Liver Disease," *Gastroenterology*, Vol. 120, No. 4, 2001, pp. 1009-1022.

[3] G. Rossi, A. Pelizzari, M. Motta and M. Puoti, "Primary Prophylaxis with Lamivudine of Hepatitis B Virus Reactivation in Chronic HbsAg Carriers with Lymphoid Malignancies Treated with Chemotherapy," *British Journal of Haematology*, Vol. 115, No. 1, 2001, pp. 58-62.

[4] M. Mondelli, G. M. Vergani, A. Alberti, *et al*., "Specificity of T Lymphocyte Cytotoxicity to Autologous Hepatocytes in Chronic Hepatitis B Virus Infection: Evidence That T Cells Are Directed against HBV Core Antigen Expressed on Hepatocytes," *The Journal of Immunology*, Vol. 129, No. 6, 1982, pp. 2773-2778.

[5] S. J. Leaw, C. J. Yen, W. T. Huang, T. Y. Chen and W. C. Su, C. J. Tsao, "Preemptive Use of Interferon or Lamivudine for Hepatitis B Reactivation in Patients with Aggressive Lymphoma Receiving Chemotherapy," *Annals of Hematology*, Vol. 83, No. 5, 2004, pp. 270-275.

[6] C. Blanpain, C. Knoop, M. L. Delforge, *et al*., "Reactivation of Hepatitis B after Transplantation in Patients with Pre-Existing Anti-Hepatitis B Surface Antigen Antibodies," *Transplantation*, Vol. 66, No. 7, 1998, pp. 883-886.

[7] I. Cacciola, T. Pollicino, G. Squadrito, *et al*., "Occult hepatitis B Virus Infection in Patients with Chronic Hepatitis C Liver Disease," *The New England Journal of Medicine*, Vol. 341, No. 1, 1999, pp. 22-26.

[8] W. Yeo, P. K. S Chan, S. Zhong, *et al*., "Frequency of Hepatitis B Virus Reactivation in Cancer Patients Undergoing Cytotoxic Chemotherapy: A prospective Study of 626 Patients with Identification of Risk Factors," *Journal of Medicine Virology*, Vol. 62, No. 3, 2000, pp. 299-307.

[9] A. S. F. Lok, R. H. S. Liang, E. K. W. Chiu, *et al*., "Reactivation of Hepatitis B Virus Replication in Patients Receiving Cytotoxic Therapy. Report of a Prospective Study," *Gastroenterology*, Vol. 100, No. 1, 1991, pp. 182-188.

[10] W. Yeo and P. J. Johnson, "Diagnosis, Prevention and Management of Hepatitis B Virus Reactivation during Anticancer Therapy," *Hepatology*, Vol. 43, No. 2, 2006, pp. 209-220. doi:10.1002/hep.21051

[11] W. Yeo, P. K. S. Chan, W. M. Ho, *et al*. "Lamivudine for the Prevention of Hepatitis B Virus Reactivation in HBV

Copyright © 2011 SciRes.

Seropositive Cancer Patients Undergoing Cytotoxic Chemotherapy," *Journal of Clinical Oncology*, Vol. 22, No. 5, 2004, pp. 927-934.

[12] G. K. K. Lau, H. H. Y. Yiu, D. Y. T. Fong, *et al*., "Early is Superior to Deferred Preemptive Lamivudine Therapy for Hepatitis B Patients Undergoing Chemotherapy," *Gastrterology*, Vol. 125, No. 6, 2003, pp. 1742-1749.

Copyright © 2011 SciRes.