Case Report

Liver Transplantation in Hepatitis B Patients

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Abstract | Hepatitis B patients are required to be managed to avoid any additional infection that could come from surgical procedures or through unhygienic conditions. In this case report, we demonstrate the management, care and complication of liver transplantation in patients with pre-established hepatitis B infections. Information gained through this study would be helpful to have better management and life style in these deadly infections.

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Introduction

Management for a successful liver transplantation of hepatitis B (HBV) includes avoidance of reinfection. The huge expenditure related to hepatitis B immunoglobulin (HBIg) prophylaxis can be reduced with low dose intramuscular HBIg treatments along with lamivudine. But in patients with great viral load, this procedure has been allied with HBV recurrences. In this report, a successful liver transplantation during a HBV flare following discontinuation of an extended entecavir prophylaxis for lymphoma chemotherapy and successful management of primary graft re-infection using a combination of tailored low dose HBIg therapy and entecavir aided by quantitative HBsAg testing has been described.

Case report

A 64-year-old woman having HBeAg negative chronic HBV infection with extreme viral load (785,000 IU/ml). She had steadily normal liver ultrasound and normal liver function test (LFT) findings. She grew early stage (1A) Burkitt-like high grade non-Hodgkin's lymphoma. She took entecavir at 0.5 mg/day prior to chemo- radiotherapy. Chemotherapy contained of a hyper-CVAD regimen (vincristine, cyclophosphamide, dexamethasone and doxorubicin) which she took regularly after a radiotherapy. She attained total remission and continued her medication on entecavir with untraceable HBV DNA levels and normal LFTs for further 14 months following chemo-radiotherapy. Liver biopsy at this time revealed slight inflammatory activity and Scheuer fibrosis score-1. Entecavir was then stopped 14 months after chemo- radiotherapy. Four and a half months later, she was presented with clinical and biochemical flare associated to recurrence of HBV. The growth of viral loads is >100 million IU/ml and the lung function tests (LFT) were as follows: serum bilirubin 139 µmol/l; ALT 643 U/L; AST 638 U/L and INR 3.1.

She obtained encephalopathy and was then referred to department of hepatology for urgent liver transplant

where the Model for End Stage Liver Disease (MELD) score of 28 and entecavir resumed at 1mg/day. The decreasing state and small recurrence menace of lymphoma were confirmed with the treating oncologist before starting liver transplant. She took entecavir for a period of eight days prior to liver transplant. Though, the patient remained HBV DNA positive with a viral load of 205,000 IU/ml at the time of liver transplant.

The explant liver indicated sub-massive necrosis with initial nodular regeneration. During a hepatic phase she acquired 800IU of HBIg intramuscularly after 800IU everyday post-transplant with daily entecavir. Despite all this, she remained persistently HBV DNA and HBsAg positive and absent anti-HBs antibodies. Later, she was on azathioprine, tacrolimus and steroids as per the local routine. She retained normal liver function tests during the whole follow up period. Observation of HBsAg titres showed persistently high concentration in the post-transplant period for about five weeks, after a noteworthy drop thereafter. HBIg was given on daily basis for successive six weeks hence; it reduced to 800IU weekly for 16 weeks. A steady increase in the anti-HBs titre was monitored at the starting of week six after transplant and raised to 88mIU by week 12. HBsAg clearance was attained by week 12 and it sustained thereafter. After four months HBV DNA levels gradually dropped and became negative. Post-transplant the patient has completed 18 months and presently remains HBV DNA and HBsAg negative with normal LFT and is on entecavir and HBIG 800IU monthly. Adefovir was added at week seven after-transplant but stopped at 14 months due to worsening serum creatinine. Modifications in HBsAg, HBV DNA and anti-HBs titres and their link with clinical events events are depicted in Figure 1. Graph presentation sequential values of HBsAg, HBV DNA, anti- HBs antibodies before and 18 months after liver transplantation together with the details of antiviral remedy.

DNA levels were recorded high prior to beginning of chemoprophylaxis and fell severely later on. After four months of cessation of chemoprophylaxis, the DNA levels elevated up and fell progressively four months following liver transplantation. HBsAg titres were high prior to liver transplantation and for six weeks following that. Rising levels of anti-HBs antibodies coincided with falling titres of HBsAg. The HBV sequence analysis of the polymerase region showed genotype B with no transmutation of forentecavir, adefoviror and lamivudine resistance. The HBV analysis of pre-core region showed a mutation at start codon (M1T), linked with no HBeAg synthesis and HBeAg negative chronic hepatitis B.

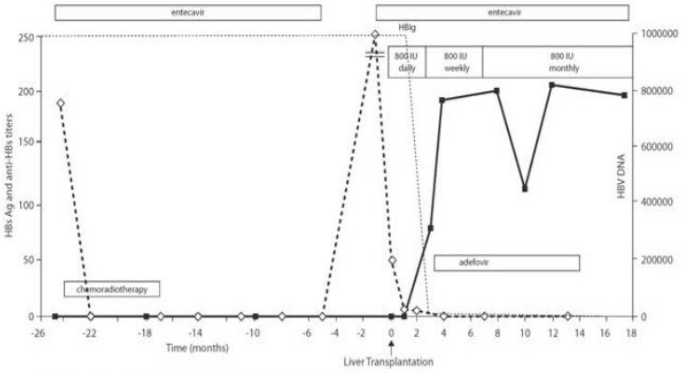

Figure 1: *Graph presentation sequential values of HBsAg, HBV DNA, anti- HBs antibodies before and 18 months after liver transplantation together with the details of antiviral remedy.*

Discussion

Although reinfections from extra hepatic sources of HBV may occur any time post-transplant, initial reinfections are frequently due to the high concentration of circulating HBV particles. This happens when the tire of anti-HBs antibodies is inadequate to neutralize circulating HBsAg particles (Terrault et al., 2005). Failure of low dose intramuscular HBIg in combination with lamivudine is normally related to high pre-transplant viral load (Gane et al., 2007). The patient had high pre-transplant HBV DNA load, which is a well-defined risk factor for post-transplant recurrence of (HBV) hepatitis B (Samuel et al., 1993). Instead of the regular protocol adopted in liver transplant unit, wherein HBIg treatment is given every day only for the initial seven days, this patient was given six weeks of HBIg every day. Common quantitative observation of HBsAg, anti-HBs and HBV DNA titres delivered valuable assistance. Monitoring of qualitative HBsAg alone cannot distinguish between an established recurrent hepatitis and a progressively resolving early recurrence. The combination of steadily rising anti HBs titers together with declining HBsAg and HBV DNA preceded HBsAg clearance. Several pre-core and promoter region changes have been related with recurrence of HBV in patients experiencing cytotoxic chemotherapy besides we do not know the accurate role of the M1T mutation in this case (Dai et al., 2001).

An additional motivating aspect of this case is the HBV recurrence following cessation of extended antiviral prophylaxis for non-rituximab based chemotherapy. Recurrence of HBV is a well-known snag in HBsAg positive patients, who receive immunosuppressive or cytotoxic therapy and may lead to fulminant hepatic failure in some patients (Hsu et al., 2008), but the ideal period of prophylaxis remains controversial. Present European guidelines propose antiviral prophylaxis for not less than 12 months following chemotherapy (Hepatol et al., 2009). Current American and Australian Society guidelines recommend patients with high baseline HBV DNA (>2,000 IU/ml) to carry on prophylaxis until they reach end points of chronic hepatitis treatment (Digestive Health Foundation. 2008). It is obvious from this case that even extended prophylaxis does not safeguard against withdrawal flares in some settings. It is also very much significant to have frequent ALT and viral load testing after cessation of antiviral treatment to identify early flares.

In short, this case is a recurrent quantitative scrutinizing of HBsAg, anti-HBs and HBV DNA aided in enhancing post-transplant HBV prophylaxis. This is a rare case of successful liver transplant for HBV recurrence precipitated by cessation of extended HBV prophylaxis for chemotherapy. Lifelong continuation of antiviral prophylaxis after chemotherapy in patients of liver transplant with high baseline viral load is recommended.

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