中文題目：使用惠立妥，貝樂克雙線抗病毒藥物合併靜脈注射甘草甜素複方來治療於一位Ｂ型肝炎復發併肝功能嚴重失常：一個治療成功之案例分享

英文題目：Dramatically improving liver function after using of dual antiviral drug plus intravenous SNMC in a patient of HBV reactivation with acute severe decompensation

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Abstract

Acute hepatitis B virus (HBV) is one of the most common causes of fulminant hepatitis, especially in the endemic area. In additional to antiviral drug, liver transplantation is usually the critical patients' only treatment choice for life-saving. Here we present a case of decompensated hepatitis resulted from HBV reactivation after Rituximab therapy, and improved after tenofovir and entecavir dual therapy, and intravenous SNMC(Stronger Neo-Minophagen C, main component: glycyrrhizin).

Case report

A 58 years old female was diagnosed diffuse large B cell lymphoma, Ann Arbor stage II and then received R-CHOP (Rituximab-CHOP) regimen for total six courses in half year. She had history of HBV/HCV co-infection without prior hepatitis history. HBV DNA was 386 IU/ml and HBsAg was 215.77 IU/ml before chemotherapy. We prescribed tenofovir (300mg) once daily both one week before starting chemotherapy and for six months after cessation of therapy, following the reimbursement indication by National Health Insurance in Taiwan. During this period, her HBV DNA was undetectable. However, she suffered from HBV reactivation with acute decompensated hepatitis after ceasing antiviral drug for 2 months. Elevated liver enzymes and bilirubin were noted. [aspartate aminotransferase (AST)/alanine aminotransferase (ALT): 951/1154 IU/L; normal reference limit: 34/40 IU/L. Total bilirubin (T-bil): 1.13 mg/ dL; normal reference limit: 1.2 mg/dL]. The profiles for viral hepatitis B markers were as follows: qHBsAg: 1593 IU/ml; HBeAg: negative; HBV DNA: $9.2x10^7$ IU/ml. We prescribed Tenofovir(300mg) once daily therapy. But progressive elevated liver enzyme and bilirubin with impending hepatic failure were still noted after 7-day therapy. (AST/ALT: 2703/2210 IU/L; T-bil: 8.5).

Liver transplantation was not indicated because of her malignancy history. We changed our treatment strategy, adding entecavir(1mg) once daily, together with tenofovir. We also prescribed intravenous SNMC 100ml daily. Her liver enzyme and bilirubin decreased dramatically after that. The level of AST/ ALT/T-bil declined from the peak:2703/2210/8.57 to 127/382/6.48 within 8 days and returned to normal limit within one month. After eight-day dual antiviral drug therapy, we held entecavir and left tenofovir alone for long-term treatment. SNMC were used for total 15 days. There was no special event or additional treatment after that.

Discussion

HBV reactivation after chemotherapy or immunotherapy was not uncommon, especially in high risk groups such as patients receiving Rituximab therapy or bone marrow transplantation, even under prophylactic antiviral drug use.[1] In these patients if they had poor response to antiviral drug, they may progress to decompensated hepatitis, even hepatic failure or death. Liver transplantation is usually not indicated because of their malignancy history. In this case we used two strategies in this difficult situation: dual antiviral drug therapy and SNMC use.

First, because of worsening liver function, we shifted Tenofovir monotherapy to tenofovir plus entecavir dual therapy. For most treatment naïve patients, the use of tenofovir plus entecavir does not offer any benefit compared with entecavir monotherapy.[2] But combination therapy may be effective in patients who have experienced treatment failure and/or have multi-drug resistant hepatitis B virus.[3] In our critical case who progressed rapidly, it was reasonable to combine both drugs in the golden treatment time, to avoid the possibility of treatment failure or having multi-drug resistant hepatitis B virus.

Secondly, we used SNMC for additional treatment. SNMC is a Japanese product, including glycyrrhizin, the main component, and the other two amino acids: Glycine and L-Cysteine Hydrochloride. Glycyrrhizin can interfere with complement pathways and inhibit phospholipase A2. It has anti-inflammatory and membrane protective effect.[4] Clinically it is indicated in drug-induced liver disease and subacute or fulminant viral hepatitis. In on recent published randomized trial, the early introduction of glycyrrhizin therapy in combination with NUCs might be beneficial and safe for patients with clinically severe acute

exacerbation of chronic hepatitis B.[5]

In our case, the patient with impending hepatic failure had rapid recovery of HBV reactivation after dual antiviral drug and glycyrrhizin use. Further large randomized control study is needed to prove the efficacy in such severe acute decompensated HBV patients.

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