Translational Medicine
ISSN: 2161-1025

Yue-Meng et al., Transl Med (Sunnyvale) 2016, 6:3
DOI: 10.4172/2161-1025.1000173

Case Report Open Access

The Strategy of Combining Antiviral Agent, Plasma Exchange and Transarterial Mesenchymal Stem Cell Transfusion in a Patient with Hepatitis B Virus (HBV) Related Acute-on-Chronic Liver Failure

Yu-Hua Li, Hua-Mei Wu, Zhi-Yuan Xu, Jing Yang, Ying Xu, Li-Hong Yang, Wan Yue-Meng*

Gastroenterology Department II, The Second Affiliated Hospital of Kunming Medical University, China

***Corresponding author:** Yue-Meng W, Gastroenterology Department II, The Second Affiliated Hospital of Kunming Medical University, China, Tel: +86-0871-6535128; Fax: +86-0871-65361017; E-mail: august19840820@163.com

Received date: May 06, 2016; **Accepted date:** May 11, 2016; **Published date:** May 21, 2016

Abstract

Acute on chronic liver failure (ACLF) is a newly recognized clinical entity with diverse etiology and an extremely high mortality rate. It may be rapidly fatal due to multi-organ failure. Liver transplantation (LT) is the best strategy for rescuing patients with ACLF. However, LT is not always possible due to donor shortage and/or high operation cost. The search for a strategy to provide temporary liver support and bridge the patients with ACLF to LT remains an important issue. Here, we report a case of hepatitis B virus (HBV) related ACLF patient who was successfully treated by repeated plasma exchange (PE) and umbilical cord-derived mesenchymal stem cell transfusion (UC-MSC) in combination with antiviral therapy with entecavir (ETV).

Keywords: Acute on chronic liver failure (ACLF); Plasma exchange (PE); Umbilical cord-derived mesenchymal stem cell transfusion (UC-MSC)

Introduction

Acute-on-chronic liver failure (ACLF) is an acute and severe deterioration of liver function in a patient with chronic liver disease, and it has a high mortality [1,2]. So far, liver transplantation (LT) is identified as the most useful approach for ACLF; however, few patients benefit from this treatment due to the extreme lack of healthy livers and/or the costly operation [3].

In the last decade there has been renewed interest in artificial liver support systems (ALSs), which have emerged as a potential tool for management of patients with ACLF [4]. Plasma exchange (PE) has been reported to improve the survival of patients with ACLF [5,6]. Umbilical cord-derived mesenchymal stem cell (UC-MSC) transfusion was also reported to increase the survival rates in ACLF patients [7]. Here, we report a case of hepatitis B virus (HBV) related ACLF (HBV-ACLF) who was successfully treated by a combination of repeated PE and UC-MSC transfusions in combination of antiviral therapy with entecavir (ETV).

Case Report

A 48-year-old man was admitted to our department due to progressive jaundice, fatigue and poor appetite for 3 weeks. He was diagnosed with HBV-related cirrhosis five years ago, but received no antiviral treatment. He denied alcohol consumption (forbidden in his Zang ethnicity), drugs or herbal remedies prior to the onset of this disease.

The patient was afebrile and jaundiced. Heart and lung examinations were unremarkable. The abdomen was slightly distended. Edges of the liver and the spleen descended 1.5 cm and 3 cm below the costal margin, respectively. Shifting dullness was detected upon abdominal percussion. Murphy's sign was negative. Peripheral edema was also noticed. Finger glucose was 5.6mmol/L at admission.

Laboratory results(with the normal range in brackets) revealed a lower white blood cell (WBC) count, 2.97 × 109/L (3.5-9.5), lower hemoglobin, 90 g/L (130-175), and lower platelet count, 69 × 109/L (125-350), Prothrombin time (PT) 24.6 seconds (11.0 to 15.0), and international normalized ratio (INR) 2.32 (0.80 to 1.30). Hepatic function parameters at admission were presented. Viral serologies (hepatitis A, C, and E viruses; human immunodeficiency virus; Epstein-Barr virus and cytomegalovirus) and autoimmunity markers (antinuclear antibody, antimitochondrial antibody, antineutrophil cytoplasmic antibody, anti-smooth-muscle antibody, and anti-liver-kidney microsome antibody) were all negative. Markers for HBV infection including HBsAg, anti-HBe, anti-HBc were positive, and HBV-DNA was 2.64 × 105 copies/L (<500). ETV was immediately administered to the patient when he was tested positive for HBsAg on day 1.

Abdominal ultrasonography of the abdomen revealed signs of hepatic parenchymal injury, portal vein dilation, moderate ascites and splenomegaly, mildly distended gallbladder without calculi, and no biliary ductal dilatation. Abdominal computed tomography (CT) showed irregular liver edge, enlarged left lobe, ascites, enlarged spleen and gastric and esophageal varices (Figure 1).

In total, this patient was admitted to our department 3 times. The hospital stays were 45 days, 13 days and 24 days at the first, second and third time, respectively. During the first hospital stay, 13 sessions of PE and one session of UC-MSC transfusion were performed. One session of UC-MSC transfusion was implemented at the second and third hospital stay, respectively. His hepatic function improved gradually.

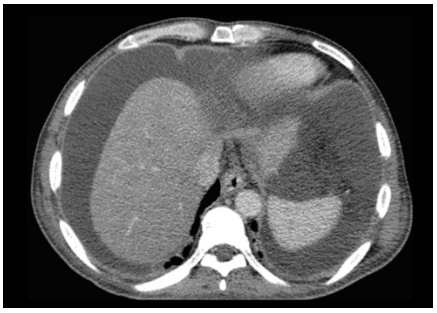

Figure 1: Abdominal computed tomography (CT) showed ascites, enlarged spleen, esophageal varices in a patient with ACLF.

Procedure Description

PE Procedure

A thorough description of PE protocol was previously presented in our recent published report [5]. Briefly, vascular access was established with a double-lumen central venous catheter inserted into a femoral vein. PE was performed with plasma separator multifiltrate 3MUG7581 (Fresenius Medical Care AG & Co. KGAa, Furth Germany). The total volume of exchanged plasma was about 3000 ml, and the exchange rate of plasma was 20-30 ml/min. Heparin was used as anticoagulant during PE. At the beginning of PE, 10mg dexamethasone was administered to avoid an allergic reaction and 20 ml 10% calcium gluconate was infused during the procedure to prevent hypocalcemia. Hepatic function before and after each PE session was tested. In total, this patient received 13 sessions of PE on day 3, 8, 9, 13, 16, 18, 20, 23, 25, 29, 34, 38, 40. The changes of hepatic function before and after each PE session were shown in Figure 2.

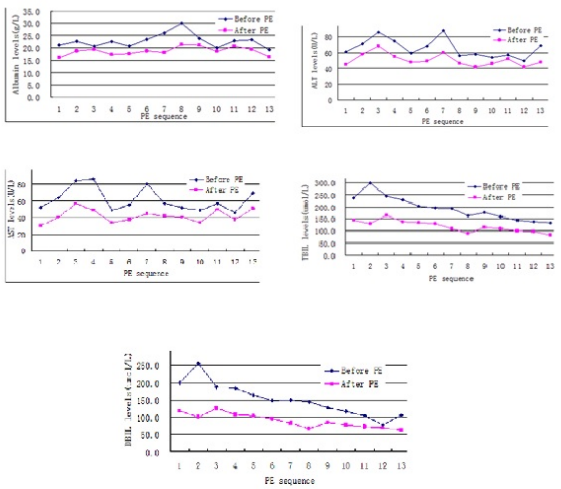

Figure 2: Changes of hepatic function parameters before and after each session of PE.

UC-MSC transfusions

Seldinger method was used to gain percutaneous transarterial access to the hepatic artery with an arterial sheath by puncturing the common femoral artery in the right groin and passing a 5F-RH catheter guided by a wire through the abdominal aorta, through the celiac trunk and common hepatic artery. At each session, 2 units of commercially available UC-MSCs (60 × 106 cells) (Shenzhen Baike Cell Engineering Research Institute) were suspended in 60ml saline solution and delivered via a pump to the liver through proper hepatic artery (Figure 3). In this case, the patient received 3 sessions of UC-MSC Transfusion on day 18, 87, 128. Alpha-fetpprotein (AFP) increased after each UC-SMC transfusion and returned to normal within 4 weeks (Figure 4).

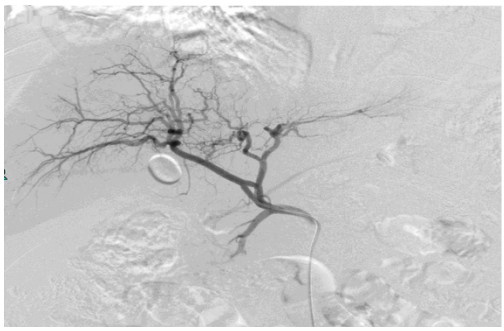

Figure 3: UC-MSC suspension was delivered to the liver through proper hepatic artery via a pump.

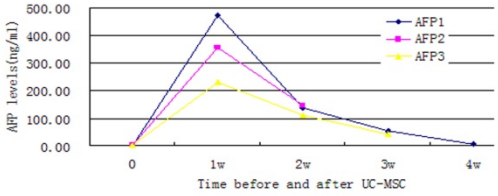

Figure 4: AFP levels before and after 3 sessions of UC-MSC transfusion.

Discussion

The ACLF criteria were as follows: serum bilirubin >5 mg/dl and an international normalized ratio (INR)>1.5 or prothrombin activity (PTA)<40%, complicated within 4 weeks by ascites and/or encephalopathy in patients with previously diagnosed or undiagnosed chronic liver diseases[1]. In this report, the patient fulfilled these criteria and thus diagnosed as ACLF. Despite the exact mechanism underlying ACLF was not clear, proinflammatory cytokines, neutrophil dysfunction and sepsis are believed to play a major role in pathogenesis and prognosis [2,8].

PE can improve the liver function by eliminating a wide array of accumulated toxins in patients with liver failure and providing an environment conducive to liver regeneration and can serve as an effective therapy for bridging the failing liver to LT [4,9]. Our previous retrospective study proved that PE improved the short-term survival of HBV-ACLF treated with ETV [5]. During PE procedure, the patient's plasma is removed and exchanged with fresh frozen plasma, which can facilitate correction of coagulopathy and removal of bilirubin and other toxic metabolites such as endotoxin as well as inflammatory mediators such as tumor necrosis factor (TNF)-alpha and interleukin (IL)-6 [10], which are known to be hazardous [11].

MSCs are multipotent cells that have self-renewing abilities and the potential to differentiate into various types of cells, including hepatocytes [12]. More importantly, these cells can interact with immune cells, leading to immunomodulation [13]. The UC-MSC transfusions has been reported to improve the hepatic function and increase the survival rates in ACLF patients [7].

Antiviral therapy is mandatory and life-long in patients with HBV-related decompensated cirrhosis irrespective of HBV DNA levels in order to prevent viral reactivation and hepatic decompensation [14]. Published data from 11 randomized controlled trials has demonstrated significant benefit of NAs on patients with ACLF for improving patient survival, HBeAg serologic conversion, and rapid reduction of HBV DNA levels [15]. ETV has both potent antiviral efficacy and better drug- resistance profile, thus it was applied to this patient.

Based on the abovementioned reports, we came up with the strategy of combining oral NA with ETV, PE and UC-MSC transfusion to treat ACLF. In this case, our patient started entecavir 0.5 mg/day at admission and received 13 sessions of PE and 3 episodes of transarterial UC-MSC transfusions during 3 hospital stays. At 6 months, he survived with significantly improved hepatic function. Despite the limited data and evidence from a single case report, we believe that a PE and UC-MSC transfusion in combination of antiviral therapy was beneficial for improving the patient outcome in ACLF patients; this needs to be studied in larger randomized controlled clinical trials.

In summary, even though LT remains the primary treatment modality for patients with HBV ACLF, PE and/or UC-MSC transfusion can be considered as an effective form of bridging therapy in combination with antiviral therapy in ACLF patients.

References

1. Sarin SK, Kumar A, Almeida JA, Chawla YK, Fan ST, et al. (2009) Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the study of the liver (APASL). Hepatol Int 3: 269-282.
2. Olson JC, Kamath PS (2011) Acute-on-chronic liver failure: concept, natural history, and prognosis. Curr Opin Crit Care 17: 165-169.
3. Wlodzimirow KA, Eslami S, Abu-Hanna A, Nieuwoudt M, Chamuleau RA (2013) A systematic review on prognostic indicators of acute on chronic liver failure and their predictive value for mortality. Liver Int 33: 40-52.
4. Maiwall R, Maras JS, Nayak SL, Sarin SK (2014) Liver dialysis in acute-on-chronic liver failure: current and future perspectives. Hepatol Int 8 Suppl 2: 505-513.
5. Yue-Meng W, Yang LH, Yang JH, Xu Y, Yang J, et al. (2016) The effect of plasma exchange on entecavir-treated chronic hepatitis B patients with hepatic de-compensation and acute-onchronic liver failure. Hepatol Int 10: 462-469.
6. Mao W, Ye B, Lin S, Fu Y, Chen Y (2010) Prediction value of model for end-stage liver disease scoring system on prognosis in the acute on chronic liver failure patients with plasma exchange treatment. ASAIO J 56: 475-478.
7. Shi M, Zhang Z, Xu R, Lin H, Fu J, et al. (2012) Human mesenchymal stem cell transfusion is safe and improves liver function in acute-on-chronic liver failurepatients. Stem Cells Transl Med 1: 725-731.
8. Dirchwolf M, Ruf AE (2015) Role of systemic inflammation in cirrhosis: From pathogenesis to prognosis. World J Hepatol 7: 1974-1981.
9. Larsen FS, Schmidt LE, Bernsmeier C, Rasmussen A, Isoniemi H, et al. (2016) High-volume plasma exchange in patients with acute liver failure: An open randomised controlled trial. J Hepatol 64: 69-78.
10. Iwai H, Nagaki M, Naito T, Ishiki Y, Murakami N, et al. (1998) Removal of endotoxin and cytokines by plasma exchange in patients with acute hepatic failure. Crit Care Med 26: 873-876.
11. Hammami MM, Bouchama A, Al-Sedairy S, Shail E, AlOhaly Y, et al. (1997) Concentrations of soluble tumor necrosis factor and interleukin-6 receptors in heatstroke and heatstress. Crit Care Med 25: 1314-1319.
12. Lee KD, Kuo TK, Whang-Peng J, Chung YF, Lin CT, et al. (2004) In vitro hepatic differentiation of human mesenchymal stem cells. Hepatology 40: 1275-1284.
13. Shi M, Liu ZW, Wang FS (2011) Immunomodulatory properties and therapeutic application of mesenchymal stem cells. Clin Exp Immunol 164: 1-8.
14. European Association For The Study Of The Liver (2012) EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. J Hepatol 57: 167-185.
15. Xie F, Yan L, Lu J, Zheng T, Shi C, et al. (2013) Effects of nucleoside analogue on patients with chronic hepatitis B-associated liver failure: meta-analysis. PLoS One 8: e54773.