

Spontaneous Clearance of Hepatitis C Virus after Liver Transplantation, A Report of Two Cases

Abstract

Background: End-stage liver cirrhosis due to HCV is the main indication for liver transplantation worldwide. Recurrence and rapid replication of HCV after liver transplantation is universal and leads to decreased graft and patient survival. Among patients exposed to HCV, spontaneous clearance of the virus is rare. Here we report two patients with spontaneous clearance after liver transplantation.

Case Reports: We report two female patients, with HCV cirrhosis, received liver transplantation (one DDLT and one LDLT), they cleared HCV on average of 20 days post liver transplant, one remained negative throughout while the other patient showed relapse on re-testing 2 years later.

Conclusion: Spontaneous clearance of HCV is rare when the patient is immunosuppressed. Here, we reported two patients with spontaneous clearance of HCV after liver transplantation. One has relapsed which highlights the need for serial testing in these patients

Background

Chronic hepatitis C is one of the main causes of chronic liver disease and estimated to affect 2-3 % of the world population, with 130-170 million people infected with HCV worldwide [1]. The outcome of HCV infection is variable and can range from minimal changes to advanced liver fibrosis and cirrhosis. End-stage liver disease and hepatocellular carcinoma secondary to HCV is the main indication for liver transplantation worldwide. Recurrence and accelerated replication of HCV due to immunosuppression after liver transplantation is common and leads to decreased graft and patient survival [2,3]. Spontaneous clearance of acute hepatitis C virus (HCV) occurs in the nontransplant population at a rate of approximately 10% to 50%, usually clear HCV during first 6 month after infection, some patients experience clearance of HCV many years after chronic HCV infection has been already established [4,5]. Termination of immunosuppression, HCV-specific cellular immunity has been shown to play a critical role in the spontaneous resolution of HCV infection [6,7], acute viral infection, or immune reconstitution following receipt of HAART [8-10]. Spontaneous clearance of HCV is rare in the immunocompromised patients post liver transplantation. There are only few case reports about spontaneous clearance of HCV after liver and renal transplantation particularly after withdrawal of immunosuppressive agents [8,11-14]. Here we report on the clinical features of two patients with spontaneous clearance after liver transplantation.

Case Presentation

Case 1

A 69-year-old female patient received a live donor liver transplant (LDLT) for hepatitis C virus cirrhosis and hepatocellular

carcinoma (HCC) on April 7, 2013. Before liver transplant, HCV RNA was 2,873 IU/mL, genotype 1b. Early postoperative course was complicated with biliary leak treated conservatively and methicillin resistant staphylococcus aureus (MRSA) respiratory infection treated with antibiotics. Liver enzymes remained high after liver transplant, Explant showed 2 cm well differentiated HCC without evidence of microvascular invasion. Abdominal sonogram was unremarkable and MRCP showed anastomotic stricture treated with PTC. On April 27 2013 and May 2, 2013, HCV RNA was undetectable. Liver enzymes normalized May 27, 2013. On 8/2/2015, HCV RNA became positive, 142,448 IU/ml, same genotype.

Case 2

A 59-year-old female patient with Hepatitis C virus-end-stage liver disease, HCC received a cadaveric liver transplantation (DDLT) on April 16, 2010. Pre-operatively, HCV RNA was 7,687 IU/ml, and HCV genotype was not reported. The patient had exploration for bleeding and sepsis due to small jejunal perforation. On May 7, 2010 HCV RNA was undetected and last HCV RNA in 31/3/2016 confirmed that it remained undetected.

Discussion

Recurrence of HCV after liver transplantation is universal and leads to decreased graft and patient survival [15]. While

Research Article

Volume 6 Issue 1 - 2017

Najwa Mohammad¹, Faisal Abaalkhail^{1,2}, Mohamed Omar³, Hany Elbeshbeshy², Waleed Al-Hamoudi^{2,4}, Yasser Elsheikh^{2,5}, Wael Al-Kattan¹, Mohamed Al Sebayel² and Hussien Elsiesy^{1,2*}

¹Alfaisal University, Saudi Arabia

²Department of Liver transplantation, King Faisal Specialist Hospital & Research Center, Saudi Arabia

³Department of Hepatology, National liver Institute, Egypt

⁴Department of Gastroenterology, King Saud University, Saudi Arabia

⁵Department of surgery, Fayoum University school of Medicine, Egypt

***Corresponding author:** Hussien Elsiesy, Department of Liver transplantation, King Faisal Specialist Hospital & Research Center, Althakhasusi Street, Riyadh, Saudi Arabia 11211, Tel: +966114647272; Ext: 33523; Email: helsiesy@gmail.com

Received: October 31, 2016 | **Published:** January 10, 2017

spontaneous clearance of acute hepatitis C virus occurs in the non-transplant population at a rate of approximately 10% to 50% [5], spontaneous clearance of HCV after liver transplant is rare. Studies showed that female gender, a history of acute icteric hepatitis [16], serologic evidence of HBV coinfection [17,18], and the rs12979860 CC genotype [19-22], are variables associated with spontaneous HCV clearance.

There are several reports of spontaneous HCV clearance after liver transplantation [8,11-13,23-28]. Different reports had identified different speculative factors for viral clearance; withdrawal of immunosuppression [8,24], renal impairment, proteinuria, pretransplant exposure to interferon, and change of immunosuppression, antiretroviral therapy given for HIV coinfection or HBV coinfection [23], liver transplantation from homozygous IL28B CC donors [11].

Restoration of host immunity against HCV may be the mechanism for spontaneous HCV clearance. Lauer and Kim, propounded two conceivable scenarios for improved anti-HCV immunity: one was CD4+ and CD8+ T-cell reactivation, and the other was a massive release of type 1 IFN, which activates the dormant innate immune response. The exact mechanism for restoration of host immunity against HCV is unclear. Here we report two cases of spontaneous HCV clearance after liver transplantation. Patients were females with pre-liver transplantation viral load, both were transplanted for HCV ESLD with HCC and both patients had post-transplant sepsis treated by antibiotics and reduction of immunosuppression doses. The mechanism for spontaneous clearance of chronic HCV infection observed in our patients post-liver transplant, however, remains unclear. Reduction of immunosuppression with reconstitution of the immune system may have played a role. One patient had HCV recurrence diagnosed 2 years after spontaneous HCV clearance. One of the two patients most likely has viral relapse rather than new infection as the genotype was the same genotype before viral clearance. However, this underlines the need for long term follow up for patients with spontaneous HCV clearance. Prospective studies to identify factors associated with spontaneous HCV clearance may be difficult in the era of direct acting HCV antiviral therapy which is highly effective and well tolerated for HCV treatment as it should be given for all patients with HCV recurrence post liver transplant. Meanwhile, cases of spontaneous HCV clearance both in the transplant and nontransplant setting should be investigated in details as understanding the mechanism of HCV clearance might open new avenues for the development of future HCV therapies.

References

- Global Burden Of Hepatitis CWG (2004) Global burden of disease (GBD) for hepatitis C. *J Clin Pharmacol* 44(1): 20-29.
- Gane EJ, Portmann BC, Naoumov NV, Smith HM, Underhill JA, et al. (1996) Long-term outcome of hepatitis C infection after liver transplantation. *N Engl J Med* 334(13): 815-820.
- Berenguer M (2002) Natural history of recurrent hepatitis C. *Liver Transpl* 8(10 Suppl 1): S14-S18.
- Kamal SM (2008) Acute hepatitis C: a systematic review. *Am J Gastroenterol* 103(5): 1283-1297.
- Micallef JM, Kaldor JM, Dore GJ (2006) Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. *J Viral Hepat* 13(1): 34-41.
- Grakoui A, Shoukry NH, Woollard DJ, Han JH, Hanson HL, et al. (2003) HCV persistence and immune evasion in the absence of memory T cell help. *Science* 302(5645): 659-662.
- Shoukry NH, Grakoui A, Houghton M, Chien DY, Ghrayeb J, et al. (2003) Memory CD8+ T cells are required for protection from persistent hepatitis C virus infection. *J Exp Med* 197(12): 1645-1655.
- Somsouk M, Lauer GM, Casson D, Terella A, Day CL, et al. (2003) Spontaneous resolution of chronic hepatitis C virus disease after withdrawal of immunosuppression. *Gastroenterology* 124(7): 1946-1949.
- Fialaire P, Payan C, Vitour D, Chennebault JM, Loison J, et al. (1999) Sustained disappearance of hepatitis C viremia in patients receiving protease inhibitor treatment for human immunodeficiency virus infection. *J Infect Dis* 180(2): 574-575.
- Gruener NH, Jung MC, Ulsenheimer A, Gerlach TJ, Diepolder HM, et al. (2002) Hepatitis C virus eradication associated with hepatitis B virus superinfection and development of a hepatitis B virus specific T cell response. *J Hepatol* 37(6): 866-869.
- Chin JL, Nicholas RM, Russell J, Carr M, Connell J, et al. (2012) Spontaneous clearance of hepatitis C infection after liver transplantation from IL28B rs12979860 CC donors. *Eur J Gastroenterol Hepatol* 24(9): 1110-1112.
- Doughty AL, Zekry A, Spencer JD, Turhan S, Painter D, et al. (2000) Spontaneous clearance of hepatitis C virus infection post-liver transplantation is associated with rapidly changing quasispecies: a single case report. *Liver Transpl* 6(5): 648-653.
- Elsiesy H, Abaalkhail F, Al Sebayel M, Broering D, Al Hamoudi W, et al. (2015) Spontaneous clearance of hepatitis C genotype 4 after liver retransplantation. *Transplantation proceedings* 47(4): 1234-1237.
- Haque M, Hashim A, Greanya ED, Steinbrecher UP, Erb SR, et al. (2010) Spontaneous clearance of hepatitis C infection post-liver transplant: A rare but real phenomenon? A case report and review of the literature. *Annals of hepatology* 9(2): 202-206.
- Berenguer M (2007) Recurrent hepatitis C: worse outcomes established, interventions still inadequate. *Liver Transpl* 13(5): 641-643.
- Barrett S, Goh J, Coughlan B, Ryan E, Stewart S, et al. (2001) The natural course of hepatitis C virus infection after 22 years in a unique homogenous cohort: spontaneous viral clearance and chronic HCV infection. *Gut* 49(3): 423-430.
- Sagnelli E, Coppola N, Messina V, Di Caprio D, Marrocco C, et al. (2002) HBV superinfection in hepatitis C virus chronic carriers, viral interaction, and clinical course. *Hepatology* 36(5): 1285-1291.
- Wietzke-Braun P, Manhardt LB, Rosenberger A, Uy A, Ramadori G, et al. (2007) Spontaneous elimination of hepatitis C virus infection: a retrospective study on demographic, clinical, and serological correlates. *World J Gastroenterol* 13(31): 4224-4229.

19. Ezzikouri S, Alaoui R, Rebbani K, Brahim I, Fakhir FZ, et al. (2013) Genetic variation in the interleukin-28B gene is associated with spontaneous clearance and progression of hepatitis C virus in Moroccan patients. *PLoS one* 8(1): e54793.
20. Rao HY, Sun DG, Jiang D, Yang RF, Guo F, et al. (2012) IL28B genetic variants and gender are associated with spontaneous clearance of hepatitis C virus infection. *J Viral Hepat* 19(3): 173-181.
21. Shi X, Pan Y, Wang M, Wang D, Li W, et al. (2012) IL28B genetic variation is associated with spontaneous clearance of hepatitis C virus, treatment response, serum IL-28B levels in Chinese population. *PLoS one* 7(5): e37054.
22. van den Berg CH, Grady BP, Schinkel J, van de Laar T, Molenkamp R, et al. (2011) Female sex and IL28B, a synergism for spontaneous viral clearance in hepatitis C virus (HCV) seroconverters from a community-based cohort. *PLoS one* 6(11): e27555.
23. Bhagat V, Foont JA, Schiff ER, Regev A (2008) Spontaneous clearance of hepatitis C virus after liver transplantation in two patients coinfecting with hepatitis C virus and human immunodeficiency virus. *Liver Transpl* 14(1): 92-95.
24. Neumann UP, Neuhaus P (2004) Discussion on spontaneous resolution of chronic hepatitis C virus after withdrawal of immunosuppression. *Gastroenterology* 126(2): 627.
25. Samonakis DN, Cholongitas E, Triantos CK, Griffiths P, Dhillon AP, et al. (2005) Sustained, spontaneous disappearance of serum HCV-RNA under immunosuppression after liver transplantation for HCV cirrhosis. *J Hepatol* 43(6): 1091-1093.
26. Tamaki I, Kaido T, Yagi S, Ueda Y, Hatano E, et al. (2015) Spontaneous clearance of hepatitis C virus after liver transplantation: a report of four cases. *Surgical case reports* 1(1): 124.
27. Kogiso T, Hashimoto E, Ikarashi Y, Kodama K, Taniai M, et al. (2015) Spontaneous clearance of HCV accompanying hepatitis after liver transplantation. *Clin J Gastroenterol* 8(5): 323-329.
28. Urzua A, Poniachik J, Diaz JC, Castillo J, Saure A, et al. (2015) Spontaneous clearance of hepatitis C virus after liver transplantation: Report of two cases. *Rev Med Chil* 143(5): 663-667.