

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

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Najwa Mohammad,¹ Faisal Abaalkhail,^{1,3}
Mohamed Omar,³ Hany Elbesheshy,²
Waleed Al Hamoud,^{2,4} Yasser Elsheikh,^{2,5}
Wael Al Kattan,¹ Mohamed Al Sebayer,²
Hussien Elsiey^{1,2}

¹Alfaisal University, Saudi Arabia²Department of Liver transplantation, King Faisal Specialist Hospital & Research Center, Saudi Arabia³Department of Hepatology, National liver Institute, Egypt⁴Department of Gastroenterology, King Saud University, Saudi Arabia⁵Department of surgery, Fayoum University school of Medicine, Egypt

Correspondence: Hussien Elsiey, Department of Liver transplantation, King Faisal Specialist Hospital & Research Center, Altakhasusi Street, Riyadh, Saudi Arabia 11211, Saudi Arabia, Tel 966114647272, Email helsiesy@gmail.com

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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 spontaneous clearance of acute hepatitis C virus occurs in the non-transplant population at a rate of approximately 10% to 50%,¹⁵ 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.

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Conflicts of interest

Authors declare that there is no conflict of interest.

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