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Case report

Hepatitis C transmission from viremic donors in hematopoietic stem cell transplant

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Abstract: Transmission of hepatitis C virus (HCV) to recipients of hematopoietic stem cell transplant (HSCT) occurs frequently from HCV viremic donors and causes complications. Here, we report the outcomes of 3 cases from our 265 allogeneic HSCTs, whose donors had HCV infections. Successful prevention of HCV transmission was noted in 1 recipient by pretreatment of the donor with peginterferon/ribavirin to undetectable levels of HCV viremia before stem cell harvest. This case stressed the important role of effective antiviral therapy and HCV RNA seronegativity before cell harvest for prevention of HCV transmission in HSCT.

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Transmission of hepatitis C virus (HCV) to recipients in hematopoietic stem cell transplant (HSCT) occurs frequently through HCV viremic donors and causes complications (1–5). Here, we report the outcomes of 3 cases from our 265 allogeneic HSCTs, whose donors had HCV infections. Successful prevention of HCV transmission was noted in 1 recipient by pretreatment of the donor with peginterferon/ribavirin to undetectable levels of HCV viremia before harvest.

Case reports

Case 1

A 35-year-old man was diagnosed with acute myeloid leukemia and underwent HSCT in January 1994 after treatment. His human leukocyte antigen-matched sibling donor had an HCV infection (genotype 2a) with a detectable viral load (Table 1). The donor took no anti-HCV therapy, and the recipient suffered from impaired liver function followed by anti-HCV seroconversion 1 month after HSCT. Persistent liver function fluctuation and HCV genotype 2a viremia developed thereafter. He survives for now, but with significant necroinflammatory activity and moderate fibrosis of the liver histopathologically.

Case 2

A 34-year-old man was diagnosed with chronic myeloid leukemia (CML) with blast crisis and had HSCT in September 2003, with complete remission status after

Characteristics and outcomes of 3 cases

	Case 1	Case 2	Case 3
Age in years	35	34	37
Gender	Male	Male	Female
Underlying disease	AML, remission	CML blast crisis, remission	ALL, refractory
Donor			
Gender	Male	Male	Male
HCV subtype	2a	1b	1b
Histology		Cirrhosis	
Anti-HCV therapy	No	Peginterferon-α-2b 100 μg/week subcutaneously plus oral ribavirin 1200 mg/day for 6 days	Peginterferon-α-2a 180 μg/week subcutaneously plus oral ribavirin 1200 mg/day for 25 days
Initial HCV load (KIU/mL)	42.112	0.665	334.346
HCV load before HSCT (KIU/mL)		–	3.693
HCV load in HSCT bag (KIU/mL)			9.785
Outcomes of recipients			
HCV infection	+	Negative for 10 years	+ (8 days after HSCT)
HCV load (KIU/mL)		Undetectable for 2 years	0.223 (1 week) 13,459.358 (1 month) 57,998.765 (2 months)
Liver function	Dysfunction 1 months later	No impairment	Dysfunction 2 months later
Outcome	Survive to now with fibrosis of liver	Relapse of CML, but survive to now without liver complications	Died of sepsis 6 months later

AML, acute myeloid leukemia; CML, chronic myeloid leukemia; ALL, acute lymphoid leukemia; HCV, hepatitis C virus; HSCT, hematopoietic stem cell transplant.

Table 1

treatment. The sibling donor was found to have HCV (genotype 1b) and detectable viremia (Table 1). The donor received peginterferon-α-2b (PEG-Intron, Schering-Plough Inc., Kenilworth, New Jersey, USA) 100 μg/week subcutaneously plus oral ribavirin 1200 mg/day for 6 days before HSCT. His serum HCV RNA declined to polymerase chain reaction (PCR) seronegative at day −4 and thereafter. Although a weak level of anti-HCV was detected in the recipient 1 month later, it disappeared at month 5. Also, HCV RNA was PCR seronegative all throughout the 2-year follow-up period (Fig. 1), although the CML relapsed 1 year later. The recipient survives for now without HCV infection, under targeted therapy for his CML.

Case 3

A 37-year-old woman with a refractory acute lymphoid leukemia after salvage chemotherapy underwent HSCT in April 2010. Her sibling donor had HCV infection (genotype 1b) with a high viremia on pre-HSCT survey (Table 1). The donor received peginterferon-α-2a (Pegasys®, Genentech, San Francisco, California, USA) 180 μg/week subcutaneously plus oral ribavirin 1200 mg/day for 25 days before stem cell harvest. HCV RNA viremia declined to 3.69 KIU/mL 1 day before the harvest, but was still detectable in the harvested sample. One week after HSCT, the recipient showed HCV infection with a low HCV RNA viremia. The viral load went up dramatically 1 month later with elevated liver function tests. Because of complications of HSCT, the HCV was not treated. The patient died of disease relapse and sepsis 6 months after HSCT.

Discussion

Transmission of HCV to allogeneic HSCT recipients occurs frequently through HCV viremic donors, such

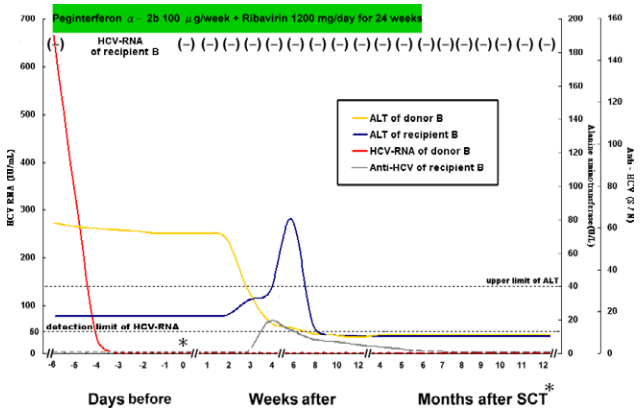

Fig. 1. Course of Case 2: A 34-year-old man with chronic myeloid leukemia (CML) with blast crisis had hematopoietic stem cell transplant (HSCT) in September 2003 in complete remission status after treatment. The sibling donor had hepatitis C virus (HCV) (genotype 1b) and detectable viremia. The donor received peginterferon-α-2b 100 μg/week subcutaneously plus oral ribavirin 1200 mg/day for 6 days before HSCT. His serum HCV RNA declined to be polymerase chain reaction (PCR) seronegative at day −4 and thereafter. Though a weak level of anti-HCV was detected in the recipient 1 month later, it disappeared at month 5. HCV RNA was also PCR seronegative throughout the 2-year follow-up period, even though the CML relapsed 1 year later; the recipient survives without HCV infection, under targeted therapy for CML. ALT, alanine aminotransferase.

as our Cases 1 and 3, and it puts recipients in high risk of hepatic complications and mortality after HSCT (1–5). The optimal strategy for treatment and monitoring of donors before HSCT is still uncertain. We herein report our 3 cases and showed peginterferon/ribavirin therapy, to give an undetectable viral load, could be effective to prevent HCV transmission.

A previous study demonstrated a successful prevention of HCV transmission from an HCV viremic donor after a 6-month treatment with interferon-α (6). Surapaneni et al. (7) also reported a similar case study, in which 5 weeks of peginterferon-α/ribavirin treatment could prevent donor-to-recipient HCV transmission. We also showed here that combined therapy was effective to decrease HCV virus within a shorter treatment course and, most important of all, that an undetectable viremia before stem cell harvest could be effective to prevent transmission. From 416 recipients in 121 centers, Tomblyn et al. (8) also reported 1 recipient who had undetectable HCV viremia from a donor with HCV whose viral load was undetectable before donation. These results, as with our cases, stress the important role of both anti-HCV therapy and an undetectable viremia.

Transient seropositivity of low anti-HCV titer was observed after HSCT in Case 2. Whether or not HCV transmission occurred with spontaneous remission was uncertain, but the likelihood is low, because no concomitant HCV viremia was detected and anti-HCV seropositivity was too short, with regard to the incubation time. Most babies from HCV-infected mothers acquired maternal anti-HCV at birth, with antibodies disappearing or diminishing in strength thereafter (9). The anti-HCV of Case 2 might have been acquired passively during HSCT, rather than coming from active infection.

Though anti-HCV therapy is effective and tolerable in HSCT recipients, the therapy still has side effects, and not all recipients are suitable for the therapy because of complications of HSCT (10, 11). Therefore, preventing HCV transmission during the transplant procedure is very important.

In conclusion, we demonstrated that effective antiviral therapy, which quickly lowers the viral loads, and HCV RNA seronegativity before stem cell harvest could successfully prevent transmission of HCV infection in HSCT recipient from an HCV viremic donor.

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