Prevention of HIV Transmission with Post-Exposure Prophylaxis Following Transfusion of HIV-Infected Blood

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Background: Without intervention, 90% of recipients transfused with HIV-infected blood are expected to become infected. While post-exposure prophylaxis (PEP) is commonly prescribed in the setting of non-occupational HIV exposures, there is very limited evidence documenting efficacy in this setting. We report the successful use of combination PEP following transfusion of HIV infected blood from a viremic donor source.

Methods:A 12-year-old girl with vaso-occlusive sickle cell crisis received 1 unit of HIV-1 contaminated packed red blood cells from a donor with plasma HIV RNA viral load of 7500 copies/ml and not receiving antiretroviral therapy (ART). Longitudinal testing of the patient's plasma and peripheral blood mononuclear cells (PBMCs) was performed by both commercial laboratory tests and by highly sensitive research assays with thresholds of detection down to 0.07 DNA copies/10^6 PBMCs and 0.4 RNA copies/mL of plasma during directly observed combination antiretroviral therapy (cART) and up to 3 months after cessation of cART. Serial HIV-1 antibody measurements were also obtained.

Results: 24 hours after the transfusion, the patient had a positive HIV ELISA and confirmatory western blot (WB), but was negative for HIV DNA by PCR. The reactive bands on WB were identical in the donor and the recipient (GP120, GP41, GP31, P24 and P17). After prompt recognition of the infected transfusion and referral to a local medical center, she was started on tenofovir, emtricitabine, ritonavir-boosted darunavir (subsequently changed to lopinavir), and raltegravir. She demonstrated no signs or symptoms of acute HIV infection and received 13 weeks of cART in a tertiary care center under direct observation. Longitudinal testing of HIV-1 DNA and RNA by both commercial and highly sensitive research assays was negative during and 3 months after stopping cART. The patient's HIV antibody became undetectable 7 months after the initial transfusion exposure.

Conclusions: We demonstrate that PEP initiated shortly after direct non-occupational exposure to HIV-1 infected blood products can effectively prevent HIV transmission, even when exposure leads to positive antibody testing. The observation that no HIV DNA or RNA has been detected in her blood after stopping cART and that antibody levels disappeared over time strongly suggest that PEP prevented seeding of a viral reservoir. This case also cautions against not initiating or stopping PEP due to the presence of positive screening antibody reactivity immediately following exposure.

Introduction

While post-exposure prophylaxis (PEP) is commonly prescribed in the setting of occupational and non-occupational HIV-1 exposures, there is limited evidence documenting efficacy in the setting of transfusion with infected blood. Furthermore, there is a paucity of data regarding blood-borne exposures that lead to passive transfer of antibodies against HIV-1.

Objectives

- **Determine the efficacy of PEP using highly sensitive assays for HIV-1 DNA and low-level residual viremia and frequent post-exposure monitoring**
- **Describe the decay of HIV-1-specific antibodies following passive transfer from blood transfusion**

Methods

Frequent monitoring of the patient on ART and after cessation of prophylactic therapy by clinical HIV-1 antibody, viral load, and whole blood DNA tests was performed in addition to the following research assays:

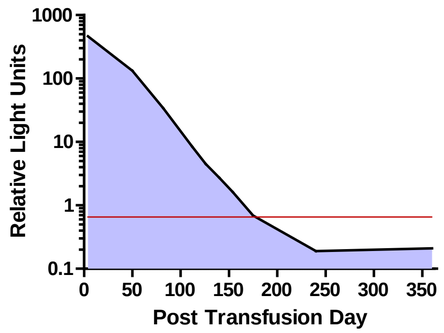
- Single-copy plasma HIV-1 RNA assay (lower limit of detection of 0.4 copies/mL)
- Real-time PCR method to quantify HIV-1 DNA from PBMCs

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Case History & Results

- Despite the standard practice of pre-screening blood products, the laboratory at the public hospital in the Kingdom of Saudi Arabia became aware that the PRBCs were contaminated with HIV-1 within hours of her transfusion as a result of human error involving mixing an un-screened with screened bags. Donor blood was discovered to be HIV-1 antibody positive and was not receiving antiretroviral therapy (ART).
- A 12 year-old girl (CCR5 wild-type) received one unit of infected packed red blood cells for sickle cell crisis.
- The Ministry of Health conducted an in-depth investigation and halted blood transfusions at the responsible blood blank.
- Approximately 24 hours after transfusion, the patient started tenofovir, emtricitabine, ritonavir-boosted darunavir (subsequently lopinavir) and raltegravir. Testing of donor blood revealed no HIV-1 resistance to the antiretrovirals chosen.
- The pattern of reactive bands on WB was identical for samples obtained from the donor and patient (gp120, gp41, gp31, p24 and p17).
- The patient demonstrated no signs or symptoms of acute infection during 13 weeks of ART in a tertiary care center.
- **HIV-1-specific Ab levels declined to undetectable levels 6 months after transfusion.**
- **No detectable HIV-1 RNA or DNA from patient samples at any time point.**
- **The patient stopped ART and no HIV-1 has been detected by ultrasensitive assays.**



Decay of HIV-specific Ab response after passive transfer from infected blood transfusion.
Relative light units from the Architect HIV-1/2 Ag/Ab Combo assay. Loss of confirmed antibody response by INNO-Lia HIV I/II line immunoassay observed on post-transfusion day 175. Horizontal line represents approximate threshold of Ab positivity.

HIV-1 DNA, Plasma RNA and Antibody Test Results Before and After Infected Blood Transfusion

		Clinical Laboratory Testing					Research Laboratory Testing		
Post-Transfusion Day		HIV Ab ELISA + Western Blot	Architect HIV-1/2 Ag/Ab Combo[a]	Immunoassay Ab Confirmation[b]	HIV-1 Blood DNA[c]	Quant. HIV-1 RNA PCR (copies/ml)	HIV-1 DNA (copies/10^6 PBMC)	HIV-1 plasma RNA (copies/mL)	VITROS Ab assay
Donor -1		Positive				9,740 copies/mL			
Patient -1		Negative							
0	Transfusion								
1	Start ART	Positive			ND	<40			
4			463.44	Pos	ND	<40			
34					ND	<40			
50			132.74	Pos	ND	<40			
78					ND	<40			
82			33.89	Pos	ND	<40		<0.4	1.7[d]
91	Stop ART								
98					ND	<40			
105					ND	<40			
112			8.43	Pos	ND	<40	<0.12	<0.4	0.35
119					ND	<40			
126			4.5	Pos	ND	<40			
133					ND	<40			
140			2.73	Pos	ND	<40	<0.1	<0.4	0.1
154			1.62	Pos	ND	<40			
175			0.69	Neg	ND	<40			
240			0.19	Neg	ND	<40			
360			0.21	Neg	ND	<40			

ND = not detected
[a] Abbot Architect HIV antibody/antigen combination chemiluminescentmicroparticle immunoassay. Value = relative light units (RLU)
[b] INNO-Lia HIV I/II Line Immuno Assay (LIA) used to confirm the presence of antibodies against the HIV-1/2
[c] HIV-1 proviral DNA qualitative detection by PCR (lower limit of detection = 66 copies/mL whole blood)
[d] signal/cutoff value from VITROS Anti-HIV-1 + 2 assay

Conclusions

- **ART PEP following large-volume transfusion of infected blood from a viremic donor prevented HIV-1 infection**
- **Passively transferred antibodies may persist for months after transfusion exposure**
- **Caution should be taken against presuming that individuals with positive HIV-1 serologies immediately post-exposure necessarily have pre-existing HIV-1 infection**