Haematology and Blood Transfusion Vol. 31
Modern Trends in Human Leukemia VII
Edited by Neth, Gallo, Greaves, and Kabisch

Transfusion-Acquired HIV Infection Among Immunocompromised Hosts

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Introduction

Since the surveillance definition of acquired immunodeficiency syndrome (AIDS) excludes patients who have other etiologies of immunodeficiency, transfusion – associated HIV disease in immunocompromised hosts has not been described. We have studied the transmission of HIV to 25 immunocompromised cancer patients through the transfusion of blood components harvested from a single asymptomatic seropositive donor prior to the initiation of blood bank serologic screening. Recipients and their intimate contacts/family members were traced, and serologic, virologic, immunologic, and medical evaluations were performed.

Results

In this study, we documented nearly uniform transmission of HIV via blood products from a single donor to immunocompromised patients with cancer. The asymptomatic index blood component donor, nine of ten living recipients of his blood products, and cryopreserved sera available from two decreased recipients demonstrate HIV seropositivity by all available serologic techniques at a median of approximately 1 year after transfusion. The recovery of HIV from cultures of peripheral blood mononuclear cells (PBMC) of seven of nine seropositive recipients, coupled with significant decreases in the T4:T8 ratio in seven of eight seropositive recipients, further confirms that these patients are infected with this retrovirus (Table 1).

The *only* recipient tested who remains seronegative at >2 years after transfusion received only one unit of fresh frozen plasma from the seropositive donor. Since fresh frozen plasma contains few leukocytes and is frozen then thawed prior to use, this patient may not have received a significant inoculum of infectious virus. Overall, HIV transmitted by transfusion to immunocompromised hosts appears to have an extremely high attack rate (Table 2).

Although many of the 25 recipients have died from their underlying cancer, HIV – related clinical sequelae have been noted in eight recipients (seven seropositive and one unable to be tested). To date, these sequelae have included hematologic abnormalities and opportunistic infections, together with lymphadenopathy and wasting (Table 3). The median time to development of these sequelae has been less than 1 year. This latent period in our adult immunocompromised patients resembles that of the pediatric HIV-infected population.

The HIV serologic profiles of the immunocompromised patients analyzed by native and recombinant gp41 Western blot (WB) and by radioimmunoprecipitation (RIP) were similar to serologic profiles of previously healthy high-risk seropositive individuals. Furthermore, as shown by RIP, the envelope proteins gp160 and gp120 appear to be the most immunogenic in this population.

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Table 1. HIV serologic and virologic studies

Recipient patient	Interval from transfusion to ELISA seropositivity for HIV antibodies (days)	Interval from transfusion to HIV culture positivity (days)	Interval from transfusion to death (days)	T4:T8[a] at time of ELISA seropositivity for HIV antibodies
1	686	714[b]	–	0.20
2	384	659[b]	–	0.21
3	423	(647) (culture-negative)	–	1.26
4	553	643[b]	–	0.57[d]
5	380	322[c]	–	qns[a]
6	331	387[b]	–	0.21
7	323	343[b]	–	qns
8	402	615[b]	–	0.30
9	237	(267 and 322) (culture-negative)	–	0.31
10[e]	(807) (seronegative)	(807) (culture-negative)	–	1.21
13	26	NT	43	NT
21	12	NT	55	0.02

NT, not tested.

[a] Anti-T4 and anti-T8 monoclonal antibodies were used to enumerate helper-inducer and cytotoxic-suppressor cells within recipient's PBMC. Normal T4:T8 ratio is 1.5–2.5.

[b] HIV culture positivity was not documented at the same time as ELISA evidence of HIV antibody was obtained, owing either to the time of testing or to the need for repeated cultures; but this does not imply a temporal sequence for viral culture positivity and seropositivity for HIV in recipient patients.

[c] Patient 5 underwent autologous bone marrow transplantation at 256 days after transfusion as treatment for neuroblastoma and was HIV culture-positive but ELISA-seronegative at 66 days after transplant (322 days after transfusion). ELISA seroconversion was documented 58 days after cultures were positive, at 380 days after transfusion.

[d] The quantity of PBMC available was not sufficient to permit accurate phenotypic analysis.

[e] Patient 10 is the only living recipient to have received fresh frozen plasma and remains HIV seronegative and culture-negative, as well as in good health, 807 days after transfusion.

The commercial enzyme-linked immunosorbent assays (ELISA) were false-negative in three cases (patients 5, 8, and 21) on the basis of concomitant positive native WB, recombinant gp41 WB, and/or RIP with banding indicative of HIV antibodies. This false-negative ELISA "window" was during seroconversion and may be prolonged in immunocompromised hosts.

A correlation was noted between the clinical status of the patients and the presence of serum-neutralizing antibodies. The two transfusion recipients who manifested neutralizing activity (patients 1 and 3) remain asymptomatic, one after prolonged thrombocytopenia which has resolved. The one sexual partner of a recipient who has tested positive for seroconversion is also asymptomatic and has high neutralizing titers. The seropositive blood donor is also asymptomatic, repeatedly culture-negative for HIV, and has high titers of serum-neutralizing activity. In contrast, seven of nine seropositive recipients who lack neutralizing activity have manifested severe clinical complications indicative of HIV infection. These observations strongly support the view that an in vitro assay for neutralizing antibody, utilizing a stringent cut-off of $\geqq 90\%$ inhibition of HIV infection, may have clinical and prognostic significance.

Table 2. Characterization of HIV antibodies

Recipient patient	Day after transfusion	ELISA[a]	WB		RIP[d]	Neutralizing antibody[e]
			Native[b]	Recombinant gp41[c]		
1	714	+	+	+	+	+
2	384	+	+	+	+	−
	659	+	+	+	+	
3	423	+	+	NT	+	+
	647	+	+	+	+	
4	553	+	+	+	+	−
5	322	−	+	+	+	−
	380	+	+	+	+	
6	387	+	+	+	+	−
7	323	+	+	+	+[f]	−
	343	+	+	+	+	
8	267	−	−[g]	−	+	−
	296	−	NT	NT	+	
	337	−	NT	NT	+	
	402	+	NT	NT	+	
	443	+	+	+	+	
9	269	+	+	+	+[f]	−
10	807	−	−	−	−	−
13	43	+	+	+	+	−
21	2 days before transfusion	−	+	+	+[f]	−
	12	+	+	+	+	−
Intimate contact of recipient						
1	686	+	+	+	+	+
6	331	−	−	−	−	−
7	323	−	NT	NT	NT	NT
13	476	−	NT	NT	NT	NT
21	620	−	−	−	−	−
23	629	−	NT	NT	NT	NT
25	370	−	NT	NT	NT	NT

NT, not tested.

[a] Positive (+) or negative (−) by repeated ELISA.

[b] Presence of bands at p24 or gp41 and of at least one other band characteristic of HIV infection (gp 120, p64/53, p34, or p17) is positive on native WB.

[c] Presence of band at gp41 on recombinant gp41 WB is positive (+).

[d] Presence of definite bands in the envelope region gp 160–120 is positive (+). Other characteristic bands (p55, p27, p24, and p17) are usually also seen on RIP.

[e] Neutralizing activity of a patient's or family members sera against HIV is determined using a modification of the assay described by Robert-Guroff et al. Neutralization is arbitrarily defined using a stringent cut-off of $\geqq 90\%$ inhibition of HIV infection compared to control cultures with known HIV seronegative sera.

[f] Presence of band on RIP at gp 160/120 only.

[g] Presence of band on native WB at p24 only.

Table 3. HIV clinical sequelae[a]

Recipient patient	Status (day after transfusion)	Day after transfusion when HIV seropositive seropositive by ELISA	Manifestation of HIV infection (day after transfusion)
2	Alive (745)	384	*Pneumocystis carinii* pneumonia (745)
3	Alive (718)	423	Immune thrombocytopenic purpura, resolved (233)
5[b]	Deceased (411)	380	Persistent thrombocytopenia (286) *Pneumocystis carinii* pneumonia (411)
6	Alive (459)	331	Persistent thrombocytopenia (56)
7	Deceased (365)	323	*Pneumocystis carinii* pneumonia (365)
8	Alive (718)	402	Recurrent cryptococcal meningitis (266) Lymphadenopathy, wasting and lymphopenia (456)
14	Deceased (194)	NT	Lymphopenia and Candida esophagitis (169) Undefined pneumonia (194)
21[c]	Deceased (54)	12	Cytomegalovirus pneumonia (54)

NT, not tested

[a] HIV clinical sequelae observed by 1 March 1986.

[b] Patient 5 underwent autologous bone marrow transplantation at 256 days after transfusion as treatment for neuroblastoma and was HIV viral-culture-positive but ELISA seronegative at 66 days after transplant (322 days after transfusion). ELISA seroconversion was documented 58 days after cultures were positive, at 380 days after transfusion.

[c] Patient 21 underwent autologous bone marrow transplantation 18 days before the transfusion of platelets from the seropositive donor. At 30 days after transplant (12 days after transfusion) she was seropositive, and at 66 days after transplant (54 days after transfusion) she died of cytomegalovirus pneumonia.

Summary

This survey suggests that HIV infection in immunocompromised hosts is characterized by a high attack rate, short incubation time to clinical sequelae, and WB and RIP seropositivity which may precede evidence of antibodies by ELISA by weeks or months. The functional properties of patients' serum antibodies, such as neutralizing activity against HIV in vitro, may correlate with clinical course.

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