CORRESPONDENCE

Evidence for Transmission of Zika Virus by Platelet Transfusion

TO THE EDITOR: Zika virus (ZIKV) is a mosquito-borne virus that has important secondary means of transmission that include perinatal and sexual modes.[1-3] The potential for transmission in transfused donated blood components has been a concern owing to the detection of ZIKV viremia in healthy blood donors.[4]

This report from Brazil describes two cases of likely ZIKV transmission by blood transfusion from one presymptomatic infected person who donated platelets by apheresis on January 16, 2016. The two leukodepleted platelet units were irradiated with 25 Gy delivered by an IBL-437C gamma irradiator (Cis Bio International) and were transfused in different patients on January 19 (day 0). On January 21, the donor called the blood bank to report a cutaneous rash, retro-orbital pain, and pain in both knees that had begun on January 18. An investigation was initiated under the hospital's clinical protocol for transfusion-associated adverse events, with the donor and both patients providing written informed consent.

Two samples that were obtained from the donor before and after donation were negative for chikungunya virus (CHIKV) and dengue virus (DENV) on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay, but the index plasma and urine samples 14 days later were positive for ZIKV (Table 1). (Details of the methods that were used and results are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org.) Serologic analysis by means of point-of-care testing, in-house indirect immunofluorescence assay (IFA), and plaque-reduction neutralization testing (PRNT) confirmed the presence of acute ZIKV infection in the donor.

The first recipient (Patient 1) was a 54-year-old woman with the primary myelofibrosis syndrome. The second recipient (Patient 2) was a 14-year-old girl with acute myeloid leukemia who had undergone haploidentical bone marrow transplantation on January 6, after which she had been receiving continuous immunosuppressive therapy. Routine pretransfusion samples obtained from the two patients were negative on PCR assay for CHIKV, DENV, and ZIKV, but samples collected 6 days after platelet transfusion in Patient 1 and 23 to 51 days after platelet transfusion in Patient 2 were positive for ZIKV on PCR assay.

Molecular sequencing and phylogenetic analysis of ZIKV RNA isolated from the donor and from the two patients confirmed the identity of their ZIKV isolates, with nucleotide changes in the envelope gene (codons 11 and 186) shared only by the donor and platelet recipients among available isolates from Brazil (GenBank accession numbers, KX173840, KX173841, KX173842, and KX173844) (Table S1 in the Supplementary Appendix). Against a backdrop of a high degree of conservation (>99% nucleotide identity) of ZIKV isolates in the Western Hemisphere,[5] the possibility of a single spatiotemporal cluster of mosquito-acquired cases was further undermined by the fact that Patient 2 lived 200 km away from Rio de Janeiro. Although neither patient was hospitalized in the period immediately preceding viral detection and thus could have been exposed to aedes mosquitoes contemporaneously with the platelet transfusions, the temporal coincidence of the infection (shortly after ZIKV diagnosis in the donor) and the phylogenetic identity of ZIKV samples that were recovered strongly favor transfusion as the source of the infection.

Serologic data supported the findings from the molecular analysis. All the samples obtained from Patient 1 showed antibody reactivity to DENV-2 on both IFA and IgG-capture enzyme-linked immunosorbent assay, findings that were consistent with her report of a history of dengue fever. Seroconversion to ZIKV was evident in both IFA IgG and point-of-care results; her PRNT titer on day 31 was 1:2560. For Patient 2, reactivity on IFA developed between 23 and 51 days after transfusion, as did a modest neutralizing antibody titer. The limited cross-reactivity to DENV-2 suggests ZIKV as the primary flavivirus infection. The limited antibody response in Patient 2 was

Table 1. Results of Molecular and Serologic Testing of Samples Obtained from the Platelet Donor and the Two Recipients.*

Donor or Patient†	Molecular Testing				Serologic Testing						
	ZIKV (Ct)‡		CHIKV	DENV	PRNT§	IFA IgG¶		ZIKV POC‖		DENV-Capture ELISA**	
	Plasma	Urine	Plasma	Plasma	ZIKV	ZIKV	DENV	IgM	IgG	IgM	IgG
Donor											
Day –3	Pos (23)		Neg	Neg							
Day 11	Neg	Pos (33)	Neg	Neg	1:1280	++	+/–	Pos (143)	Pos (239)	Pos (1.4)	Neg (0.5)
Patient 1											
Day –4	Neg		Neg	Neg		–	+++	Neg (7)	Pos (57)	Neg (0.6)	Pos (5.0)
Day 6	Pos (33)		Neg	Neg		+	++++	Neg (9)	Sus (32)	Neg (0.7)	Pos (4.9)
Day 31	Neg				1:2560	++++	++++	Sus (33)	Pos (335)	Pos (2.3)	Pos (5.4)
Patient 2											
Day –1	Neg		Neg	Neg							
Day 1	Neg		Neg	Neg							
Day 23	Pos (36)	Neg	Neg	Neg	1:40	–	–	Neg (7)	Sus (20)	Neg (0.1)	Neg (0.3)
Day 51	Neg/Pos††				1:20	++	+/–	Neg (4)	Neg (17)	Neg (0.2)	Neg (0.3)
Day 71	Neg							Neg (12)	Neg (5)		

* CHIKV denotes chikungunya virus, DENV dengue virus, ELISA enzyme-linked immunosorbent assay, IFA indirect immunofluorescence assay, Neg negative, POC point of care, Pos positive, PRNT plaque-reduction neutralization test, Sus suspected infection, and ZIKV Zika virus.
† Day 0 was January 19, 2016, the date of transfusion for both recipients.
‡ Ct denotes the threshold cycle (indicated by the values in parentheses) at which the result on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay was positive.
§ PRNT values represent the serum dilution causing plaque reductions of 90%.
¶ IFA intensity ranges from low (+) to high (++++).
‖ The values in parentheses are measures of test-band intensity in arbitrary units, with results classified as negative (<20 units), suspected infection (20 to 39 units), and positive (≥40 units).
** The values in parentheses are the sample optical density divided by the assay cutoff.
†† The positive result on day 51 was obtained in a sample that had four times the starting volume on RT-PCR.

presumably due to her ongoing immunosuppressive therapy. Although neither patient reported symptoms associated with ZIKV infection during the investigation, these data show evidence for ZIKV transmission by means of platelet transfusion.

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