HIV Transmissions From a Window-Period Platelet Donation

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Abstract

Recently, blood centers began investigational testing for HIV RNA by pooled nucleic acid testing (NAT). A 35-year-old frequent platelet donor tested HIV p24 antigen positive, antibody negative before implementation of NAT. He made 2 platelet donations (day –4 and –11) immediately before testing positive for HIV. The donor’s HIV seroconversion was monitored, and stored samples were tested retrospectively for HIV RNA. Platelet recipients were tested for HIV infection. The day –4 sample tested positive for HIV RNA by pooled and individual sample NAT. The day –11 sample tested negative for HIV RNA by both NAT tests. The 2 recipients of the day –4 platelets tested HIV RNA and p24 antigen positive. The recipient of the day –11 platelets could not be tested because he had died. HIV NAT would have prevented transmission of HIV had it been available at the time of this donor’s HIV seroconversion.
A medical intervention is typically considered cost-effective at or below a threshold of $50,000 per quality-adjusted life-year.\textsuperscript{5,6}

Since implementation of HIV p24 antigen testing in the United States, only 10 volunteer blood donations have tested HIV antibody negative and HIV p24 confirmed positive.\textsuperscript{7} One of these donations was not transfused because the donor instructed the blood center not to use the blood after the donation process was completed. During this period, 12 to 14 million allogeneic blood donations were collected annually in the United States.

The original calculations of the effectiveness of HIV p24 antigen testing were overestimated because it was assumed that HIV-infected blood donors were equally likely to donate on each of the 22 days of the infectious or viremic phase of the window period. In practice, blood donors seem less likely to be able to donate successfully during the brief period of HIV p24 antigenemia. Possible reasons for this include self-deferral, owing to a recent HIV risk, or to signs and symptoms from the acute retroviral syndrome.\textsuperscript{8,9} In addition, the incidence of HIV among blood donors is declining, thus further reducing the number of HIV p24 antigen–positive donations.\textsuperscript{8,10}

In an effort to reduce even more the minute risk of transmission of HIV by transfusion, most blood centers in the United States began to screen blood donations for HIV RNA via nucleic acid testing (NAT) in late 1999 or early 2000. (Hepatitis C RNA NAT testing was implemented in early 1999. Testing for hepatitis B DNA by NAT is in the planning phase.) NAT detects the presence of HIV RNA. NAT is not licensed for blood donor screening and, thus, is being performed under investigational new drug applications with the Food and Drug Administration (FDA). Approximately 95% of the blood supply in the United States is being screened for HIV RNA. There are different methods of NAT in use; however, they are all based on multiple amplification cycles of HIV RNA. The test has been performed in the United States on sample pool sizes of 16 to 128 donations. Unlike all other blood donor screening, a pooled testing strategy is used because NAT is not sufficiently automated to accommodate the volume of individual samples that need to be processed.\textsuperscript{11} In addition, it is technologically possible to use pooled testing owing to the powerful amplification process of NAT.

It is not known what additional effect NAT will have on closing the window period. It has been estimated that it will only reduce the window period by an additional 5 days, leaving an infectious or viremic window period of 11 days.\textsuperscript{11} However, experiments in chimpanzees suggest that the infectious window period may be closed even further. Murthy et al\textsuperscript{12} infected a chimpanzee with HIV and removed blood in a serial manner. HIV RNA and DNA were detected 5 weeks after inoculation. HIV antibody and HIV p24 antigen were present 8 weeks after exposure. A second chimpanzee was sequentially inoculated with blood removed from the first animal 3 and 4 weeks after exposure to HIV. The chimpanzee was monitored for HIV infection for 24 weeks after each inoculation. No evidence of HIV infection was found. The chimpanzee was then inoculated with blood drawn from the first chimpanzee at week 5. The inoculated animal developed HIV RNA 4 weeks after exposure and HIV antibody 8 weeks after exposure. Although this experiment is confined to a set of 2 animals, it suggests that there may not be an infectious window period of significant duration before detection of HIV nucleic acid.

Blood components with very low levels of viremia (5-39 copies/mL) have transmitted HIV. Although this level of viremia is detected inconsistently by minipool NAT, it is detected by individual NAT.\textsuperscript{13} The routine use of pooled HIV NAT has detected HIV RNA–positive, antibody-negative donations, thus preventing transmission of HIV.\textsuperscript{14}

Approximately 5 months before implementation of experimental HIV NAT, a frequent platelet donor was confirmed positive for HIV p24 antigen but negative for HIV antibody. Since plateletpheresis donors are allowed to donate up to twice a week, his frequent donor status meant that he likely donated platelets in the viremic portion of the window period before detection of either HIV p24 antigen or HIV antibody.

\section*{Case Report}

A 35-year-old man made a double plateletpheresis donation that tested positive for HIV p24 antigen (confirmed by neutralization) but negative for HIV-1 and HIV-2 antibodies. He was a frequent platelet donor who had made 2 donations in the 11 days before the index unit. The –11 day plateletpheresis was a single product, while the –4 day donation was a double plateletpheresis. Before the 3 platelet donations, he was a frequent whole blood donor with 8 donations in 21 months.

In-date components at the blood center were quarantined immediately. Hospitals that received the previous platelet products were notified that the donor was infected with HIV. Three patients had received platelets from this donor. The platelet recipients and their close contacts were offered HIV testing.

The donor was interviewed to determine his risk factors for contracting HIV. Serial blood samples were drawn from the donor to monitor his HIV seroconversion. Serum samples collected on the day of donation of the 3 plateletphereses subsequently were submitted for individual and pooled HIV NAT to determine whether they
contained HIV RNA and whether pooled NAT testing would have detected this donor’s HIV infection earlier than HIV p24 antigen.

Materials and Methods

Anti–HIV-1/2 (Abbott Laboratories, Abbott Park, IL) and HIV p24 antigen (Coulter/Ortho, Raritan, NJ) testing was performed using FDA-licensed enzyme immunoassay screening. HIV-1 Western blot was performed using an FDA-licensed test kit (Calypte Biomedical, Rockville, MD). Qualitative NAT was performed using polymerase chain reaction (PCR) under a clinical trial protocol. The donor screening test for this protocol uses a 24-member pooled sample. For this study, 41.7 µL of each of the donor’s samples was pooled with 23 donor samples previously tested and found negative for HIV-1 RNA. The protocol then requires RNA purification and extraction using a manual “MultiPrep” protocol, followed by PCR amplification and detection using target-specific oligonucleotide probes in a colorimetric assay (Cobas AmpliScreen, Roche Molecular Systems, Pleasanton, CA). Individual qualitative NAT of donor samples was performed using the companion protocol for individual testing, “standard preparation.” This protocol uses a 200-µL sample volume, and steps are similar to those listed previously. Levels of HIV RNA were determined using the HIV-1 Monitor Test (Roche Molecular Systems), an FDA-approved assay that uses PCR for quantitative HIV-1 RNA determination.

Results

Donor

The donor was interviewed 10 days after the index donation. He denied any risk factors for and exposure to HIV. He revealed that he was a caregiver for a person with AIDS. A second interview was performed 5 days later. During this interview, the donor stated that he had subsequently remembered he had been exposed to urine of the person with AIDS under his care. He stated that his hands had open cuts at the time of the exposure.

The donor’s serial HIV antibody and p24 antigen test results are given in Figure 1. The HIV p24 antigen became positive shortly before the appearance of HIV antibody. HIV p24 antigen reactivity decreased as the antibody titer increased and was absent 18 days after it first appeared. Individual and pooled NAT results are given in Table 1. The index and day –4 donations were both positive for HIV RNA in individual and pooled NAT. The day –11 donation was negative for HIV RNA in both types of NAT. The Western blot was indeterminate (±p24 antigen band) 10 days after the index donation but positive (p24, glycoprotein [gp]160, ±p51, ±gp120 bands) on day 15.

Recipient 1

A 61-year-old man with acute myeloid leukemia received the platelepheresis donated 11 days before the index donation. The patient died of his primary disease before notification. Family members declined HIV testing.

Recipient 2

A 69-year-old man with plasma cell leukemia received half of the double platelepheresis donated 4 days before the index donation. The patient tested positive for HIV infection by p24 antigen and NAT approximately 2 weeks after transfusion. HIV antibody was negative at this time. He died of his primary disease 4 weeks after transfusion. Family members declined HIV testing.

Recipient 3

A 74-year-old man with aplastic anemia received the second half of the double platelepheresis donated 4 days
before the index donation. The patient tested positive for HIV infection by p24 antigen and NAT approximately 2 weeks after transfusion. HIV antibody was negative at that time. He died of his primary disease 4 months after transfusion. The patient’s wife tested negative for HIV antibody and HIV RNA at 1 month and 6 months after her husband’s transfusion.

Discussion

The frequency of platelet donation makes this case of HIV transmission by transfusion unique. Because plateletpheresis donors are allowed to donate up to twice a week, this donor made 3 donations while he was in the HIV window period. The last 2 donations were double platelet components (2 doses of apheresis platelets collected during a single donation). Therefore, up to 5 patients could have been at risk of receiving HIV-infected platelets. Two potential transmissions were prevented owing to HIV p24 antigen testing. If NAT for HIV RNA had been available at the time of the previous donation, 2 additional HIV transmissions would have been prevented. It is impossible to determine whether the plateletpheresis collected 11 days before the donor tested positive for HIV p24 antigen also would have transmitted HIV. This is somewhat unfortunate because it is not known whether HIV can be transmitted by transfusion if the donor is negative for HIV RNA by NAT. It is known that HIV can be transmitted by blood components with a very low level of detectable HIV RNA.13

Although 1 donation of platelets transmitted HIV to 2 patients, the practice of obtaining multiple apheresis products from 1 donor is analogous to component preparation from whole blood donation. Had this donor made a whole blood donation, he could have transmitted HIV to 3 patients via transfusion of the component RBCs, platelets, and fresh frozen plasma.

A recent report suggests that postexposure prophylaxis can prevent HIV transmission after the transfusion of an HIV RNA–positive unit.15 The recipient of an HIV RNA–positive, HIV-seronegative unit of packed RBCs began receiving antiretroviral therapy within 50 hours of transfusion. She continued receiving therapy for 9 months after the transfusion and remains HIV seronegative and HIV RNA negative. Although prophylaxis apparently was successful in that case, it was not likely to be effective in our situation. Both recipients who contracted HIV from transfused platelets received their transfusions approximately 1 week before our donor was confirmed positive for HIV p24 antigen.

The only exposure to HIV that the donor admits is a urine splash to his hands, which had an open cut, from a person with AIDS under his care. We suspect that the donor was not being completely truthful. When first interviewed, the donor denied any HIV exposure. It was only later that he “remembered” the urine splash. The timing of his switch from being a frequent whole blood donor (allowed to donate every 56 days) to a frequent platelet donor (allowed to donate as often as twice a week) is suspicious. He began donating by plateletpheresis 11 days before testing positive for HIV p24 antigen. It suggests that he may have been donating more frequently to obtain HIV testing after a recent exposure. Subsequent, independent information revealed that the donor had sexual exposure to high-risk persons. In addition, although the donor has repeatedly agreed to tests for HIV sequencing to determine whether he contracted HIV from the person with AIDS under his care, he has failed to assist us in obtaining a sample from that patient.

The only way to prove that this donor contracted HIV from the person with AIDS in question would be to perform sequencing of the HIV from both parties. However, even if we could prove by HIV sequencing that the donor contracted HIV from this source, it would not prove that the mode of transmission was a urine splash.

This case emphasizes 2 important points. The first is that a thorough, honest history, before blood donation, remains a cornerstone of prevention. This donor would have been deferred from donating blood for 1 year if he had admitted to a body fluid exposure from an HIV-infected person during the screening interview or permanently if he had told us about high-risk sexual activity. The second and more important point is that the motivation for blood donation should never be “free” HIV disease testing or testing of any other nature. It is vital for all physicians and blood donors to understand that HIV can still be transmitted by a blood or component transfusion even if the donor tests negative for HIV.

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References


