OBSERVATION: CASE REPORT

SARS-CoV-2 RNAemia in a Healthy Blood Donor 40 Days After Respiratory Illness Resolution

Background: Asymptomatic donors infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may pose a risk to the safety of the blood supply (1). Although a previous report described detection of viral RNA in donor plasma, these donors tested positive for SARS-CoV-2 in a respiratory specimen or developed fever shortly after donation, suggesting that the donation occurred early in the course of their infection (2). To our knowledge, the persistence of SARS-CoV-2 RNA in plasma from an eligible donor after recovery from illness has not yet been described.

Objective: To report the case of a volunteer blood donor, healthy on the day of donation, who had detectable SARS-CoV-2 RNA levels in their blood at least 40 days after resolution of coronavirus disease 2019 (COVID-19)-like symptoms.

Case Report: In mid-April 2020, we implemented a research SARS-CoV-2 real-time, reverse transcriptase polymerase chain reaction (RT-PCR) test on our blood donations (Stanford Institutional Review Board protocol 55550) targeting the SARS-CoV-2 *envelope* gene in plasma mini-pools of 6 donors (3). The RT-PCR has a 95% lower limit of detection of 123 copies/mL (95% CI, 100 to 146 copies/mL) by probit analysis. Positive pools were resolved by retesting the individual samples they comprised. This testing algorithm is in line with current U.S. Food and Drug Administration–approved nucleic acid tests used to screen for infectious diseases in blood donors, which also use mini-pool testing. The index donation was collected on 23 April 2020 after approximately 700 negative donations. The cycle threshold value (Ct) for the positive mini-pool sample was 40.9, and the subsequent individual sample was positive at a Ct of 42.1—both results at the limit of detection for the assay. We further confirmed SARS-CoV-2 RNA detection by RT-PCR targeting the *nucleocapsid* gene (N2 region: Ct, 37.8) (4) from a separate sample drawn from the donor on the day of donation, thereby making cross-contamination highly unlikely. Negative plasma controls were included on each run, and SARS-CoV-2 RNA was not detected.

Serologic testing for antibodies against the SARS-CoV-2 spike protein receptor-binding domain revealed the donor to have positivity at the assay cutoff for IgG (wavelength, 450 nm; optical density, 0.30; cutoff, 0.30), but negativity for IgM and IgA. Additional serologic testing (IgM, IgG, and IgA) against the SARS-CoV-2 spike (S1 domain) and nucleocapsid proteins yielded negative results. Given these equivocal and negative findings, neutralization assays were not performed.

The donor had symptoms of upper respiratory infection in early March, including body aches and sore throat without fever. The donor did not seek medical attention and was not tested for SARS-CoV-2 at that time. After the donor was notified about the results, and 5 days after the donation date, RT-PCR assay of the donor's nasopharyngeal swab specimen showed no SARS-CoV-2 RNA.

Discussion: The confirmation of donor RNAemia more than 1 month after symptom resolution is concerning in light of current guidelines, which do not recommend SARS-CoV-2 screening in the general allogeneic donor population (5). In this case, plasma viral RNA was reproducibly detected at a time point that exceeded recommendations for deferral based on time since symptom resolution (14 days). Of importance, these results are unlikely to be false-positive given that 2 different regions of the SARS-CoV-2 genome were detected in separate specimens collected on the day of donation and that quality control passed on all runs, including the absence of amplification in the negative controls.

Of note, however, the infectivity of SARS-CoV-2 from blood remains unknown and, to date, we are not aware of cases of transfusion-transmitted COVID-19. Furthermore, the risk for transmission of other transfusion-transmitted viral infections, such as HIV-1, is correlated with virus load, indicating that if bloodborne transmission is possible, the low level of SARS-CoV-2 detected in this case was unlikely to be transmitted. Taken together, these data suggest that this donor posed a limited but uncertain risk to the safety of the blood supply.

Nevertheless, this case should be taken into consideration as blood donation policies are being crafted, particularly as infections increase with the relaxation of shelter-in-place orders worldwide. Although this case is insufficient to recommend universal SARS-CoV-2 blood screening, out of an abundance of caution and in the interest of further defining the risk to the local blood supply, our institution plans to continue donor screening for SARS-CoV-2 RNA and has extended the deferral period from 28 to 56 days after resolution of symptoms.

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References

1. Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfus Med Rev. 2020;34:75-80. [PMID: 32107119] doi: 10.1016/j.tmrv.2020.02.003

2. Chang L, Zhao L, Gong H, et al. Severe acute respiratory syndrome coronavirus 2 RNA detected in blood donations. Emerg Infect Dis. 2020;26:1631-1633. [PMID: 32243255] doi:10.3201/eid2607.200839

3. Hogan CA, Sahoo MK, Pinsky BA. Sample pooling as a strategy to detect community transmission of SARS-CoV-2. JAMA. 2020. [PMID: 32250394] doi: 10.1001/jama.2020.5445

4. Bulterys PL, Garamani N, Stevens B, et al. Comparison of a laboratory-developed test targeting the envelope gene with three nucleic acid amplification tests for detection of SARS-CoV-2. J Clin Virol. 2020;129:104427. [PMID: 32535398] doi:10.1016/j.jcv.2020.104427

5. AABB. AABB's Resources for: FDA's Updated Information for Blood Establishments Regarding the Novel Coronavirus (COVID-19) Outbreak. Accessed at www.aabb.org/advocacy/regulatorygovernment/Documents/COVID-19-Toolkit.pdf on 26 May 2020.