Received: 3 September 2020 | Revised: 16 September 2020 | Accepted: 17 September 2020

DOI: 10.1002/pbc.28744

Pediatric Blood & Cancer

SOCIÉTÉ INTERNATIONALE D'ONCOLOGIE PÉDIATRIQUE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

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LETTER TO THE EDITOR

Repeat-positive SARS-CoV-2 in a child with cancer

To the Editor:

We report a case of repeat positivity with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a child with cancer. The SARS-CoV-2 virus is responsible for the ongoing coronavirus disease 2019 (COVID19) pandemic. A 4-year-old male was treated for pre-B cell acute lymphoblastic leukemia (ALL) at our hospital. The patient was receiving treatment with the Indian Childhood Collaborative Leukaemia Group (ICiCLe) protocol under the high-risk arm.[1] On June 27, 2020, the patient and his caregiver tested positive for SARS-CoV-2 on the reverse transcriptase-polymerase chain reaction (RT-PCR) test of their nasopharyngeal and oropharyngeal swabs.They were asymptomatic but were tested as they were high-risk contacts of a COVID19 patient. The patient had started the interim maintenance phase of the protocol and was 5 days post the first 24-h high-dose methotrexate (HDMTX) infusion (3 gm/m^2) along with 6-mercaptopurine (6MP) when he tested positive for SARS-CoV-2. His white blood cell (WBC) count, absolute neutrophil count (ANC), and absolute lymphocyte count (ALC) were 2500, 650, and 1225/mm^3, respectively, on the day of the positive RT-PCR test. 6MP was stopped after the patient tested positive. The patient and the caregiver were quarantined in a COVID19-designated hospital. Both tested positive for SARS-CoV-2 on RT-PCR of their nasopharyngeal and oropharyngeal swabs on repeat testing on days 5 and 10, and tested negative on days 14 and 21. The patient's WBC count, ANC, and ALC were 12 900, 5547, and 6597/mm^3, respectively, on day 5 of SARS-CoV-2 positivity. The patient and the caregiver remained asymptomatic during their hospitalization for SARS-CoV-2 infection. The patient resumed his cancer treatment (second cycle HDMTX with 6MP) on July 22, 2020 after two negative RT-PCR tests of nasopharyngeal and oropharyngeal swabs for SARS-CoV-2. His WBC count, ANC, and ALC at reinitiation of the ALL protocol were 5400, 1566, and 3200/mm^3, respectively. We did not test the patient or the caregiver for antibodies to SARS-CoV-2.

It is our policy to screen the patient and the caregiver for SARS-Cov-2 infection by RT-PCR of their nasopharyngeal and oropharyngeal swabs before each block of chemotherapy or hospitalization. The patient and caregiver had tested negative for SARS-CoV-2 when they were admitted for the third block of HDMTX on August 12, 2020. However, both tested positive again for SARS-Cov-2 on September 1, 2020 during routine surveillance before admission for the fourth block of HDMTX. This was 65 and 51 days after their first positive and first negative RT-PCR test, respectively. The patient and the caregiver continued to remain asymptomatic. The patient had not received steroids for 8 weeks before (augmented BFM consolidation phase) the first positive test and thereafter (interim maintenance phase).

All the RT-PCR tests on patient's and the caregiver's samples were performed by laboratories accredited by the Indian Council of Medical Research (ICMR). The laboratories followed the guidelines issued by the Government of India for SARS-CoV-2 sample collection, transportation, testing, reporting, and quality control.[2] The nasopharyngeal and oropharyngeal swabs were transported in a viral inactivation medium for RT-PCR testing. The patient and caregiver samples were not stored but tested on the same day of taking the swabs.

There could be three possibilities for the repeat-positive SARS-CoV-2 in our patient and caregiver 2 months since the first infection. First, it could be a persistent carrier state and viral shedding with a possibility that the two negative reports in between were false negative.[3,4] The other possibility is of reinfection with SARS CoV-2. There have been recent reports of reinfection with SARS-CoV-2.[5,6] The reinfection was confirmed by showing genetic differences in the viral genome between the two infections using next-generation sequencing.[5] The third possibility could be a false-positive result due to contamination of the samples during collection, transportation, or testing.

Viral shedding up to 37 days (median 20 days) has been observed in adult patients infected with SARS-CoV-2, and patients with severe disease had prolonged viral shedding compared to patients who were asymptomatic or had mild disease.[7] Disease severity, corticosteroid therapy, fever (temperature >38.5°C), and time from onset to hospitalization were associated with prolonged duration of SARS-Cov-2 viral shedding in adult patients in a study from Beijing, China.[8] Our patient or the caregiver did not have any of the risk factors mentioned in this study.[8] The median duration of viral shedding in the above study was 11 days (interquartile range 8-14.3 days).[8] A study from Korea on children with SARS-CoV-2 infection reported a mean duration of viral shedding in nasopharyngeal swabs of 17.6 days (standard deviation 6 days).[9] It has been observed that positive RT-PCR tests in patients with prolonged viral shedding or those who turn positive after a negative RT-PCR test is due to viral ribonucleic acid (RNA) in dead cells, and these viral particles are inactive and noninfective.[10,11] Persistent SARS-CoV-2 positivity has been demonstrated in feces ranging from 1 to 33 days after a negative nasopharyngeal swab.[12] However, the transmission of SARS-CoV-2 through feces has not been documented.[12]

A prior study reports that the majority of repeat-positive cases after a negative SARS-CoV-2 PCR occur within 30 days of the first positive test.[9] Our patient and caregiver became positive 65 days after their first positive report, and this is one of the longest periods reported for repeat-positive cases and the first case report of a pediatric cancer patient developing repeat positivity or prolonged viral shedding with

SARS-CoV-2 infection. Since we did not do genetic sequencing of the virus or test the patient and the caregiver for antibodies, we cannot be sure if it was reinfection or a prolonged carrier state. Our report should alert physicians to continue testing pediatric cancer patients who previously tested positive for SARS-CoV-2 and recovered. Consent was obtained from the caregiver for publishing this case report.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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