Covid19 Reinfection in Two Children with Cancer

Satya Yadav[1], Teena Wadhwa[1], Dhwanee Thakkar[1], Rohit Kapoor[1], Neha Rastogi[1], and Smita Sarma[1]

[1]Medanta The Medicity

September 11, 2020

Abstract

Reinfection after getting covid19 once was thought not to happen as patient would have developed immunity against the virus. But recently a case has been reported from Hongkong where the second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient. Epidemiological, clinical, serological and genomic analyses confirmed that the patient had re-infection with another strain of SARSCOV2 virus instead of persistent viral shedding from first infection. Here we report two children who got re-infected with SARSCOV2 after recovering fully and developing IgG antibodies it.

Introduction

Covid19 pandemic has affected >25 million people globally. It's very rare in children and mostly non-fatal. In children with blood and cancer disorders so far published data suggests most children are either asymptomatic or get mild disease (1,2). Reinfection after getting covid19 once was thought not to happen as patient would have developed immunity against the virus. But recently a case has been reported from Hongkong where the second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient. Epidemiological, clinical, serological and genomic analyses confirmed that the patient had re-infection with another strain of SARSCOV2 virus instead of persistent viral shedding from first infection (3). Here we report two children who got re-infected with SARSCOV2 after recovering fully and developing IgG antibodies it. Whole genome sequencing could not be performed for two episodes. Laboratory results, including RT-PCR Ct values and serum SARS-CoV-2 IgG, were analyzed.

Case 1

14-year-old boy with T-cell acute lymphoblastic leukemia was being treated as per BFM95 protocol for standard risk disease. He was in complete remission after end of induction. In the 3rdweek of consolidation phase, he was found to be SARSCOV2 positive by PCR (run on Thermofisher TaqPath kit) performed on nasopharyngeal & throat swab (Ct values; N-32.52 ORF-32, S-34.66) on screening test prior to giving chemotherapy. He was asymptomatic and his total leukocyte count (TLC) was low 1580/mm^3, Absolute neutrophil count (ANC) -140/mm^3 and absolute lymphocyte count (ALC) was- 990/mm^3. As he was asymptomatic so no specific treatment was given and he was isolated at home for next 2 weeks. After 2 weeks his SARSCOV2 PCR was negative. He was restarted on chemotherapy as per protocol and finished consolidation. Later he was given a course of high dose methotrexate (5 g/m2) and oral 6-mercaptopurine 25 mg/m2 daily for central nervous system prophylaxis which he tolerated well. Two weeks later he was again screened for SARSCOV2 prior to next chemotherapy and his PCR was positive (Ct values; N-19.25, ORF-18.7, S-18.02). This was 71 days after the first infection. This time his TLC was 7450/mm^3 and ANC was 3500/mm^{3}and ALC 2200/mm^3. He was asymptomatic so again he was isolated at home for 2 weeks and chemotherapy was stopped. After 2 weeks we rechecked his PCR and it was still positive (Ct values; N-31.25, ORF-31.57, S-30.48) so we treated him with tablet hydroxychloroquine 200 mg orally twice daily for 5 days and retested

PCR and it became negative. His IgG antibody (qualitative test by Orthoclinical diagnostic kit) against SARSCO2 was positive (1.75 cutoff value for positive >1)). He was given further chemotherapy as per protocol.

Case 2

A 3-year-old child with stage 4 neuroblastoma was being treated as per OPEC/OJEC protocol. After 4 cycles of chemotherapy he underwent surgical resection of primary right suprarenal tumor. He achieved very good partial remission. Two weeks after surgery on screening for SARSCOV2 prior to chemotherapy PCR test came positive (Ct values N-14.59 ORF-16.84 S-17.48). As he was asymptomatic so he was isolated at home for 2 weeks and chemotherapy was postponed. His TLC was 9630/mm^3 and ANC -7400/ mm^3 and ALC-970/ mm^3. Two weeks later repeat PCR test (using Siemens FTD SARSCOV2 RTPCR kit) was still positive (Ct value-32.39). We repeated test again after 1 week and it came negative. Child was given next course of chemotherapy OJEC. Three weeks later prior to next chemotherapy PCR (using Siemens Labgun exofast RTPCR kit) was again positive (Ct values, N-22.37 RdRp-22.15) and IgG antibody (quantitative assay by CLIA technology for quantitative determination of anti S1 and anti S2 specific IgG against SARSCOV2) was positive 306 AU/ml. Gap between first and second infection was 42 days. He was isolated at home for another 2 weeks and after that repeat PCR was negative. Child was restarted chemotherapy as per protocol.

Discussion

So, in these two patients as we did not perform sequencing of the virus in each episode so we can't prove that it's a reinfection from another strain of the virus. But both patients had IgG antibodies present when they got second infection so ideally, they should not have got reinfected. Immune suppression due to chemotherapy may have reactivated the virus but there are no reports of the same in the literature. Same infection may have persisted but we have no proof of that as in between two episodes virus was negative by PCR. Ct values in first case at first diagnosis were high >30 so was it a false positive? At the time of second infection Ct values were low <20. But patient had IgG antibodies against SARSCOV2 present when he had second infection suggesting first infection was real infection. In second patient Ct values are low in both infection episodes and also, he had IgG antibody against SARSCOV2 at onset of second infection suggesting first infection was real and second infection is also real and possibly because of another strain. Most neutralizing antibodies target the spike protein (4). Several mutations in the spike protein receptor binding domain and N-terminal domain have been shown to confer reduced susceptibility to neutralizing antibodies (5). Both our patients had IgG antibodies against SARSCOV2 at the time of onset of second infection so only way new infection could have happened is if they got infection from a new strain of virus which could escape these antibodies.

Our two cases raise more questions then give answers. More data is needed to confirm this phenomenon of reinfection in Covid19.

Disclosure – All authors have nothing to declare. All authors have contributed to the manuscript.

References

1. Yadav SP. COVID-19 in Children with Blood and Cancer Disorders: What Do We Know So Far? *J Pediatr Hematol Oncol* . 2020;42(6):413-414. doi:10.1097/MPH.0000000000001872
2. Boulad F, Kamboj M, Bouvier N, Maureen A, Kung AL. COVID-19 in Children with Cancer in New York City. *JAMA Oncology* . doi:10.1001/jamaoncol.2020.2028.
3. To KK, Hung IF, Ip JD, Chu AW, Chan W, Tam AR et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. *Clinical Infectious Diseases* , ciaa1275, https://doi.org/10.1093/cid/ciaa1275
4. Liu L, Wang P, Nair MS, Yu J, Rapp M, Wang Q, et al. Potent neutralizing antibodies against multiple epitopes on SARS-CoV-2 spike. Nature 2020;584:450-456. https://doi.org/10.1038/s41586-020-2571-7
5. Weisblum Y, Schmidt F, Zhang F, DaSilva J, Poston D, Lorenzi JCC, et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants. bioRxiv 2020;**doi:**

https://doi.org/10.1101/2020.07.21.214759