Reinfection of Severe Acute Respiratory Syndrome Coronavirus 2 in an Immunocompromised Patient: A Case Report

To the Editor—Knowing the frequency and natural course of reinfections is important for strategies for control of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recently, To et al published a report of a 33-year-old Hong Kong resident with a SARS-CoV-2 reinfection, confirmed by whole-genome sequencing [1]. Here, we report a case of a reinfection in an 89-year-old Dutch woman suffering from Waldenström macroglobulinemia, treated with B-cell–depleting therapy. She presented to the emergency department with fever and severe cough and a lymphocyte count of 0.4×10^9 cells/L. An in-house SARS-CoV-2 reverse-transcription quantitative polymerase chain reaction (RT-qPCR) assay (E-gen) [2] on a nasopharyngeal swab was positive (cycle quantification value [Cq] = 26.2). She was discharged after 5 days; other than some persisting fatigue, her symptoms subsided completely.

Two days after a new chemotherapy treatment, 59 days after the start of the first coronavirus disease 2019 episode, the patient developed fever, cough, and dyspnea. At admission, her oxygen saturation was 90% with a respiratory rate of 40 breaths per minute. The SARS-CoV-2 RT-qPCR assay on a nasopharyngeal swab was positive (E-gen; Cq = 25.2). At days 4 and 6, serum was tested for SARS-CoV-2 antibodies using the Wantai SARS-CoV-2 total antibody and the immunoglobulin M enzyme-linked immunosorbent assays; both were negative. At day 8, the condition of the patient deteriorated, and she died 2 weeks later.

The viral genomes of both episodes were compared using SARS-CoV-2–specific multiplex qPCR and Nanopore sequencing [3]. The 2 strains differed at 10 nucleotide positions in the ORF1a (4), ORF 1b (2), Spike (2), ORF3a (1), and M (1) genes (Figure 1) and the sequences did not cluster in the phylogenetic tree (Supplementary Figure 1). Although we did not have PCR-negative samples in between episodes, with an average estimated SARS-CoV-2 mutation rate of 33 nucleotides per year (or 5–6 nucleotides per 2 months) [4], it is likely that the second episode was a reinfection rather than prolonged shedding.

In contrast to the Hong Kong resident, our patient experienced a more severe second episode. This has also been described in a 25-year-old Nevada resident with no underlying comorbidities [5]. Our patient was immunocompromised because of Waldenström macroglobulinemia treated with B-cell–depleting therapy, resulting in a declined humoral immunity [6]. However, it was shown that B-cell–depleting therapy does not necessarily result in life-threatening disease, suggesting that the innate immune response and T-cell immunity can be sufficient to eliminate SARS-CoV-2 [7].

SARS-CoV-2 reinfections are expected to occur once antibody titers decrease and immunity wanes. Although a recent population study in Iceland has shown that antibodies to SARS-CoV-2 did not decline within 4 months after infection [8], reinfections in seasonal coronaviruses, such as human coronaviruses NL63, 229E, OC43, and HKU1, were observed as early as 6 months postinfection. Frequent reinfections were shown from 12 months postinfection [9]. The Hong Kong resident did not have measurable antibodies at the start of the second episode, which occurred 4–5 months after the first. However, the second episode was asymptomatic, indicating sufficient immunological memory. Our patient and the Nevada patient suffered from an early reinfection within 2 months, unfortunately without serum samples in between episodes. The Nevada resident did develop a measurable antibody response after the second episode. Our patient did not have antibodies 6 days after start of the second episode, but seroconversion can take a few days longer.
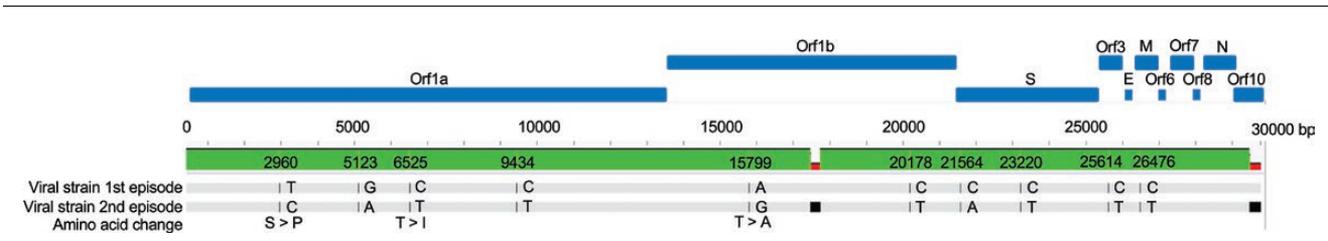
Figure 1. Sequences of the severe acute respiratory syndrome coronavirus 2 strains of the first and second coronavirus disease 2019 episodes. The black lines indicate the differences in nucleotides between the 2 strains. The black boxes indicate that these were locations of the genome that could not be determined reliably (1.85% of the genome).

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

Marlies Mulder,[1,2] Dewi S. J. M. van der Vegt,[2]
Bas B. Oude Munnink,[3] Corine H. GeurtsvanKessel,[3]
Jeroen van de Bovenkamp,[2] Reina S. Sikkema,[3]
Esther M. G. Jacobs,[4] Marion P. G. Koopmans,[3] and
Marjolijn C. A. Wegdam-Blans[2]

[1]Department of Medical Microbiology, Maastricht University Medical Center, Maastricht, The Netherlands, [2]Department of Medical Microbiology, PAMM Laboratories, Veldhoven, The Netherlands, [3]Department of Viroscience, Erasmus Medical Center, Rotterdam, The Netherlands, and [4]Department of Internal Medicine, Elkerliek Hospital, Helmond, The Netherlands

References

1. To KK, Hung IF, Ip JD, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clin Infect Dis 2020; doi:10.1093/cid/ciaa1275.
2. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill 2020; 25:2000045.
3. Oude Munnink BB, Nieuwenhuijse DF, Stein M, et al; Dutch-Covid-19 response team. Rapid SARS-CoV-2 whole-genome sequencing and analysis for informed public health decision-making in the Netherlands. Nat Med 2020; 26:1405–10.
4. Candido DS, Claro IM, de Jesus JG, et al; Brazil-UK Centre for Arbovirus Discovery, Diagnosis, Genomics and Epidemiology (CADDE) Genomic Network. Evolution and epidemic spread of SARS-CoV-2 in Brazil. Science 2020; 369:1255–60.
5. Tillett RS, Hartley P, Kerwin H, et al. Genomic evidence for a case of reinfection with SARS-CoV-2. SSRN [Preprint]. August 31, 2020. doi:10.2139/ssrn.3680955.
6. Karlsson J, Andréasson B, Kondori N, et al. Comparative study of immune status to infectious agents in elderly patients with multiple myeloma, Waldenstrom's macroglobulinemia, and monoclonal gammopathy of undetermined significance. Clin Vaccine Immunol 2011; 18:969–77.
7. Argudin MA, Deplano A, Meghraoui A, et al. Bacteria from animals as a pool of antimicrobial resistance genes. Antibiotics 2017; 6:12.
8. Gudbjartsson DF, Norddahl GL, Melsted P, et al. Humoral immune response to SARS-CoV-2 in Iceland. N Engl J Med 2020. Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa2026116.
9. Edridge AWD, Kaczorowska JM, Hoste ACR, et al. Coronavirus protective immunity is short-lasting. Nat Med. 2020; doi:10.1101/2020.05.11.20086439.