Reinfection of SARS-CoV-2 in an immunocompromised patient: a case report

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

Marlies Mulder, department of Medical Microbiology, Maastricht University Medical Center
Maastricht, The Netherlands; department of Medical Microbiology, PAMM Laboratories Veldhoven,
The Netherlands. M.Mulder@pamm.nl.

Dewi S.J.M. van der Vegt, department of Medical Microbiology, PAMM Laboratories, Veldhoven, The
Netherlands. D.van.der.Vegt@pamm.nl

Bas B. Oude Munnink, department of Viroscience, Erasmus Medical Center, Rotterdam, The
Netherlands. b.oudemunnink@erasmusmc.nl

Corine H. GeurtsvanKessel, department of Viroscience, Erasmus Medical Center, Rotterdam, The
Netherlands. c.geurtsvankessel@erasmusmc.nl

Jeroen van de Bovenkamp, department of Medical Microbiology, PAMM Laboratories, Veldhoven,
The Netherlands. j.van.de.bovenkamp@pamm.nl

Reina S. Sikkema, department of Viroscience, Erasmus Medical Center, Rotterdam, The Netherlands.
r.sikkema@erasmusmc.nl
Esther M.G. Jacobs, department of internal medicine, Elkerliek hospital, Helmond, The Netherlands.
ejacobs@elkerliek.nl

Marion P.G. Koopmans, department of Viroscience, Erasmus Medical Center, Rotterdam, The Netherlands. m.koopmans@erasusmc.nl

Marjolijn C.A. Wegdam-Blans, department of Medical Microbiology, PAMM Laboratories, Veldhoven, The Netherlands. M.Wegdam@pamm.nl

**Corresponding author:**

Dr. Marjolijn C.A. Wegdam-Blans; department of Medical Microbiology, PAMM Laboratories, Veldhoven, The Netherlands. Email: M.Wegdam@pamm.nl
Dear Editor:

Knowing the frequency and natural course of reinfections is important for strategies for control of 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’s macroglobulinemia, treated with B-cell-depleting therapy. She presented to the emergency department with fever and severe cough and a lymphocyte count of 0.4x10^9/L. An in-house SARS-CoV-2 RT-qPCR (E-gen),[2] on a nasopharyngeal swab was positive (Cq 26.2). She was discharged after 5 days and besides some persisting fatigue her symptoms subsided completely.

Two days after a new chemotherapy treatment, fifty-nine days after the start of the first COVID-19 episode, the patient developed fever, cough, and dyspnea. At admission, her oxygen saturation was 90% with a respiratory rate of 40/min. The SARS-CoV-2 RT-qPCR 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 Ab and IgM ELISA, both were negative. At day 8, the condition of the patient deteriorated. She died two weeks later.

The viral genomes of both episodes were compared using SARS-CoV-2-specific multiplex qPCR and Nanopore sequencing.[3] The two strains differed at ten nucleotide positions in the ORF1a (4), ORF (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’s 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 HCoV-NL63, HCoV-229E, HCoV-OC43 and HCoV-HKU1 were observed as early as 6 months post-infection. Frequent reinfections were shown from 12 months post-infection.[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.

Notes

Conflicts of interests

The authors have no conflicts of interest to declare.
References

Figure legend

Figure 1. Sequences of the SARS-CoV-2 strains of the first (top) and second (bottom) COVID-19 episode. The black lines indicate the differences in nucleotides between the two strains. The black boxes indicate that these were locations of the genome that could not be determined reliably (1.85% of the genome).