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

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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 occured 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.

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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).

Figure 1