

understanding of risk. Active surveillance for ICD and knowledge of local epidemiology are critical to minimizing the deleterious effects of this secondary infection.

Note

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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), ORF1b (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

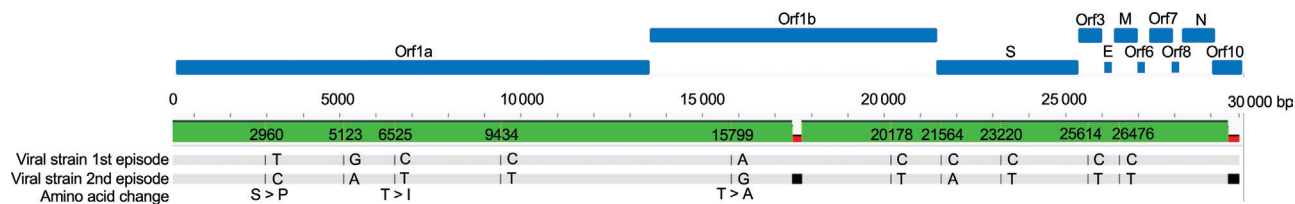


Figure 1. Sequences of the severe acute respiratory syndrome coronavirus 2 strains of the first and second coronavirus disease 2019 episodes. The black lines indicate the differences in nucleotides between the 2 strains. The black boxes indicate that these were locations of the genome that could not be determined reliably (1.85% of the genome).

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.

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.

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More Evidence Is Warranted to Establish the Role of ¹⁸FDG-PET/CT in Fever of Unknown Origin (FUO) Investigations Among Children

TO THE EDITOR—We read with great interest the article by Wright et al entitled “Imaging a Fever—Redefining the Role of ¹⁸FDG-PET/CT in FUO Investigations” [1]. The paper aims at providing an

overview of the clinical benefits and cost-effectiveness of 2-deoxy-2-[¹⁸F] fluoro-D-glucose positron emission tomography/computed tomography (¹⁸FDG-PET/CT) in the investigation of fever of unknown origin (FUO). We complement this article by raising a discussion about applying ¹⁸FDG-PET/CT in FUO investigations in the pediatric population, for which evidence is insufficient and relatively weak.

Evidence in adults is unsuitable to support the use of ¹⁸FDG-PET/CT in children, since the definition, etiology, and evaluation of FUO differ between children and adults. While FUO is well defined in adults, no consensus has been achieved in children. Various definitions have been applied throughout the years, and fevers lasting from 5 days to 3 weeks are acceptable to diagnose FUO in children [2, 3]. Moreover, the disease spectrum in children is highly age dependent, with 3 traditionally considered age groups: neonates or infants to 1 month of age, infants from 1 month to 3 months of age, and children from 3 months to 3 years of age [4]. Furthermore, children, especially young children, are not able to fully participate in the interaction with doctors, and hence objective information acquired from ¹⁸FDG-PET/CT might reveal more clues than that in adults. However, children are more sensitive to radiation than adults. Consequently, the benefits from ¹⁸FDG-PET/CT should be carefully re-examined in pediatric patients with FUO.

Very limited evidence is available on the role of ¹⁸FDG-PET/CT in pediatric FUO. We rescreened a literature database to include all cohort studies examining the