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LETTER TO THE EDITOR

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Re-infections with SARS-CoV-2 require a clarification of favourable risk factors

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Letter to the Editor

We were intrigued to read Shimada et al.'s paper [1] on a 36-year-old man who experienced reinfection with the SARS-CoV-2 alpha-variant (B1.1.7 lineage) 4 months after having been infected with the variant F484K (lineage R.1). Both infections were moderately severe, necessitating hospitalization but not oxygen supplementation, mechanical ventilation, or extra-corporal membrane oxygenation (ECMO) [1]. Methylprednisolone, azithromycin, and ceftriaxone were given to the patient for the second infection [1]. Although the study is wonderful, it also highlights issues that need to be considered.

It would be interesting to know the titres of neutralizing antibodies following the first and second SARS-CoV-2 infection in order to determine the aetiology of re-infection. Knowing the titres of neutralizing antibodies may be able to shed light on the pathophysiology and causation of re-infection. First, it is possible that neutralizing antibody titres were generally low following the initial infection. Second, it is possible that antibodies produced following the first infection were ineffective against the virus that caused the second infection. Third, it is possible that immunocompetence was impaired prior to the second infection, resulting in reinfection. Fourth, it is possible that the patient had an immune deficiency prior to the first infection. Fifth, neutralizing antibody titres were high after the first infection but rapidly declined, so not enough neutralizing antibodies were available when the second infection occurred.

It is unknown why the patient was given methylprednisolone to treat the re-infection [1]. The disease course was described as mild, with a low risk of progression [1]. The use of methylprednisolone in SARS-CoV-2 infections, particularly in mild cases, is being debated. A meta-analysis of 33 studies found that using methylprednisolone was associated with lower short-term mortality, fewer ICU admissions and mechanical ventilation, and longer days off the ventilator [2]. However, in a study of 113 COVID-19 patients with acute respiratory distress syndrome (ARDS), methylprednisolone use was associated with a shorter time to intubation and a faster progression to mortality in 51 patients than dexamethasone use [3]. Furthermore, in a study of 199 hospitalized COVID-19 patients, only dexamethasone could reduce the length of stay, but not methylprednisolone [4]. Has the patient been given methylprednisolone to help prevent the onset of multisystem, inflammatory syndrome in adults (MIS-A)?

We disagree with the case description's claim that a body temperature of 38.2 °C constitutes a "high fever" [1]. "Low grade fever" should be the new classification for a body temperature of 38.2 °C. The term "low grade fever" should be also used to describe a body temperature between 37.5 °C and 38 °C.

Why the patient experienced an episode of dyspnoea in between the two SARS-CoV-2 infections, as shown in Figure 1 of Shimada et al.'s paper [1], is still unknown. Was there any sign of heart failure, lung infection, or pulmonary embolism?

The study's inability to give reference limits in Table 1 of Shimada et al.'s paper [1], is another drawback. It

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is challenging to comprehend the results given in the absence of reference limits.

Overall, the intriguing study contains flaws that cast doubt on the conclusions and how they should be interpreted. Clarifying these flaws might enhance the study's findings and conclusions. SARS-CoV-2 re-infections are prevalent, and risk factors for reinfection should be carefully examined.

Disclosures
The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Compliance with ethics guidelines
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JF: design, literature search, discussion, first draft, critical comments, final approval.

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Declarations

Competing interests
The authors declare that they have no competing interests.

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