

### Confirmed Reinfection With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Variant VOC-202012/01

TO THE EDITOR—We have detected a confirmed case of reinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with the second episode due to the “new variant” VOC-202012/01 of lineage B.1.1.7. The initial infection occurred in the first wave of the pandemic in the UK and was a mild illness. Eight months later, during the second wave of the pandemic in the UK, reinfection with the “new variant” VOC-202012/01 was confirmed and caused a critical illness.

A 78-year-old man with a history of Type 2 diabetes mellitus, diabetic nephropathy on hemodialysis, chronic obstructive pulmonary disease (COPD), mixed central and obstructive sleep apnea, ischemic heart disease, with no history of immunosuppression, presented with fever during hemodialysis on 2 April 2020. There were no other symptoms and he was discharged home. He had a mild illness with an uneventful recovery. Combined nose and throat (NTS) swab tested positive for SARS-CoV-2 RNA. Testing was performed on the Roche cobas<sup>®</sup> 8800 System, targeting the E gene and ORF1a gene targets. E gene cycle threshold (Ct) value was 26.8, ORF1a Ct value was 26.4. Our service has been routinely screening all hemodialysis patients under our care since the first surge of infections in London; a total of 22 routine NTS swabs were sent between 5 May 2020 and 1 December 2020 and all tested negative for SARS-CoV-2 RNA. SARS-CoV-2 antibodies (using the Roche anti-SARS-CoV-2 IgM/IgG assay detecting antibodies targeting viral nucleocapsid “N” antigen) were detectable on 6 occasions between 4 June 2020 and 13 November 2020 with no evidence of antibody waning seen.

On 8 December 2020, a routine repeat NTS was sent. Testing was performed on the Hologic Panther SARS-CoV-2

platform using the proprietary Aptima Transcription-Mediated Amplification (TMA) assay targeting ORF1a and ORF1b targets. The Relative Light Unit (RLU) value was 1348. On 14 December 2020, a repeat sample was tested with reverse transcription polymerase chain reaction (RT-PCR) using the Roche cobas<sup>®</sup> 8800 platform targeting the E gene and ORF1a targets, with Ct values of 27.5 and 27.9, respectively. On 14 December 2020, he presented to A&E with a 3-day history of shortness of breath (SOB) which had worsened overnight. He was brought in by ambulance *in extremis*, very short of breath (SOB) and unable to talk, with severe hypoxia, leading to emergency intubation. Severe COVID-19 pneumonia complicated by myocardial infarction with resulting trifascicular block and atrio-ventricular (AV) dissociation and pulmonary edema was diagnosed. He was admitted to ITU, treated with co-amoxiclav, clarithromycin, and dexamethasone, and required cardiac pacing, hemodynamic vasopressor support, hemofiltration.

Whole Genome Sequencing (WGS) of the viral genome was performed *in house* on stored aliquots of the samples collected on 2 April and 8 December. Briefly, samples were sequenced with a multiplex PCR-based approach according to the modified ARTIC protocol with version 3 primer set. Amplicon libraries were sequenced using Illumina MiSeq. Genomes were assembled with reference-based assembly and a bioinformatics pipeline with 10x minimum coverage cut-off for any region of the genome and 50% cut-off for defining single nucleotide polymorphisms (SNPs). The generated FASTA files were uploaded to the CoV-GLUE web platform for further analysis. 85.92% genome coverage was obtained on the sample dated 2 April. Phylogenetically, the isolate belonged to lineage B.2, with no mutations observed in the S region. 95.6% genome

coverage was obtained on the sample dated 8 December 2020. Phylogenetically, the isolate belonged lineage B.1.1.7 and accumulated 18 amino acid replacements across the genome. The following amino acid replacements were observed in the “S” region: N501Y, A570D, D614G, P681H, T761I, S982A, and D1118H. Also, deletions were present in the spike region: Y144 (21991–21993) and HV 69–70 (21765–21770).

The WGS results confirm reinfection with a different lineage 8 months after initial infection in the absence of significant immunocompromise. The reinfection was with the “new variant” VOC-202012/01. This variant has been recently identified in the UK, and is rapidly spreading, especially in London and the South East of England and South Wales and may be responsible for a surge in new cases here [1]. The “new variant” is characterized by numerous mutations in the spike region which causes diagnostic escape in PCR assays using the “S” gene as a target for amplification [1, 2]. The numerous spike region mutations also raise questions about possible immune escape and/or vaccine evasion and likelihood of reinfection.

Reinfection has been confirmed before in a handful of cases worldwide, but confirmation of reinfection relies on WGS and so cases may be drastically underreported. Regular PCR screening of our dialysis cohort and access to in-house WGS allowed reinfection to be confirmed in this instance. The development of reinfection in this case may just reflect waning immunity after 8 months since primary infection in a high-risk individual with multiple comorbidities. Anti-SARS-CoV-2 antibodies were still present shortly before onset of reinfection, with no evidence of antibody waning. This may raise some concerns about immune evasion by this new variant, which is a concern with the high number of spike region mutations seen. We have no assay for SARS-CoV-2

antibodies recognizing spike antigen, and neutralizing antibody studies are pending. The antibodies detected recognise “N” antigen, so drawing conclusions is difficult. The group of mutations identified in VOC-202012/01 appears to have significantly increased transmissibility compared to previously described mutations or haplotypes, but there is as yet no evidence of increased pathogenicity associated with these mutations [1]. In this case the initial illness was mild, and the reinfection with the new variant was critical/life-threatening. More severe illness on the second episode has been reported before in confirmed reinfections not caused by VOC-202012/01 [3, 4]. Rapid work on learning about immune, vaccine, and diagnostic escape is needed, as are data on severity of illness caused by VOC-202012/01.

## Notes

**Author contributions.** All authors confirmed they have contributed to the intellectual content

of this paper and have met the following 4 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; (c) final approval of the published article; and (d) agreement to be accountable for all aspects of the article thus ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.

**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Nonstandard Abbreviations: Ct, cycle threshold; NTS, nose and throat swab; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SOB, shortness of breath; WGS, whole genome sequencing.

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