

## Symptomatic SARS-CoV-2 reinfection by a phylogenetically distinct strain

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Dear editor:

To et al. reported the first documented case of a asymptomatic reinfection with SARS-CoV-2 after 4.5 months [1]. As the patient experienced only mild symptoms during the first episode, the question remains whether a weak immune response after the first episode might explain the reinfection. It has been suggested that patients with an asymptomatic or mild SARS-CoV-2 infection have a weaker immune response since their antibody titers are significantly lower than in patients with pneumonia [2]. An estimated 20% do not seroconvert [3]. It also remains unclear whether patients can have a symptomatic reinfection. A recent Italian study reported no clinical reinfections within 3 months after hospital discharge [4]. We here report a symptomatic reinfection 93 days after a moderate SARS-CoV-2 infection.

In March 2020, a 51-year-old women presented to the general practitioner symptoms of headache, fever, myalgia, coughing, chest pain and dyspnea. She also mentioned anosmia and a change in taste. She was not immunocompromised, but took a daily dose of inhaled corticosteroids for asthma. A nasopharyngeal swab tested positive with SARS-CoV-2 PCR. Routine biochemistry and complete blood count did not show any abnormalities besides mildly elevated liver enzymes. Oxygen saturation by capillary oximeter was 94%. Hospitalisation was not deemed necessary at the time and the patient was asked to self-quarantine for 2 weeks. Because of persisting symptoms of tiredness, muscle pains and dyspnoe, she stayed at home for 5 weeks before returning to work.

Three months after initial onset of symptoms, she experienced a relapse of symptoms with headache, cough and fatigue. Rhinitis was also present. There was no travel history. The patient told the general practitioner that the symptoms felt similar to the first episode in March, although milder. The nasopharyngeal swab was again positive for SARS-CoV-2, suggesting a reinfection (Table 1). The symptoms resolved after one week. At that time, the patient tested positive for anti-SARS-CoV-2 nucleocapsid antibodies (Roche total Ig signal/cut-off 134).

Full-length genome sequencing with ONT MinION revealed that the initial infection was caused by a lineage B.1.1 SARS-CoV-2 virus and the relapsing infection by a lineage A [5]. Eleven mutations were identified across the genome of the two strains (11/29903

differences, 99.7% identity; Table 1). This difference is in line with other circulating strains in Belgium [6]. Documenting reinfection requires full-length genome sequencing or viral culture as PCR can remain positive for up to 104 days [7]. Usually asymptomatic and mild cases exhibit longer RNA shedding than severe cases [2].

The fact that a symptomatic reinfection with SARS-CoV-2 can occur already 3 months after the first infection is not unexpected. Symptomatic reinfections with human non-SARS coronaviruses are common and not atypical within 1 year after initial infection, despite the presence of antibodies. Reinfections with human non-SARS coronaviruses are, however, typically milder as was the case in our patient [8–10]. The fact that clinical reinfection can occur shortly after the first infection further underlines the fact that both healthcare workers and patients who had a prior SARS-CoV-2 infection are not always protected against re-infection.

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## **Author contributions**

PM, KL and PV conceived the study. JVE, PV, TWB, BVM, EW and PM conducted experiments and drafted the manuscript. All other authors aided in collecting data and critically reviewed the manuscript.

## **Conflicts of interest**

Pieter Vermeersch reports personal fees from Roche, outside the submitted work. Katrien Lagrou reports personal fees and non-financial support from Pfizer, MSD, personal fees from SMB Laboratoires, Gilead, and FUJIFILM Wako outside the submitted work. The other authors state no conflicts of interests.

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**Table 1: RT-PCR and full-length genome-sequencing results**

	9th March 2020	10th June 2020	
<b>qPCR QuantStudio 7 (Applied Biosystems)<sup>1</sup></b>			
N-gene Ct	25.6 (N1) 27.2 (N2)	32.6 (N1) 33.2 (N2)	
<b>Full-length genome GISAID accession number</b>	EPI_ISL_522349	EPI_ISL_522350	
SARS-CoV-2 lineage <sup>2</sup>	B.1.1	A	
<b>Observed mutations of strain B.1.1 versus strain A</b>			
Position (bp)	Base change	Gene	Mutation type
3037	C / T	ORF1a	S
8782	C / T	ORF1a	S
11654	C / T	ORF1a	NS (Phe to Leu)
14408	T / C	ORF1b	S
17427	T / G	ORF1b	S
23403	G / A	Spike	NS (Gly to Asp)
23873	A / G	Spike	NS (Thr to Ala)
24726	C / T	Spike	NS (Ser to Leu)
28881	A / G	Nucleocapsid	NS (Lys-Arg to Arg-Gly)
28882	A / G	Nucleocapsid	
28883	C / G	Nucleocapsid	

NS: Nonsynonymous mutation; S: Synonymous mutation

<sup>1</sup>2019-nCoV CDC EUA kit, <sup>2</sup>nomenclature based on reference [5]