

## Case Report

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# Enhanced immune response after SARS-CoV-2 vaccination in a healthcare professional with recurrent COVID-19 episodes: A case report

Zina Hakim<sup>1\*</sup>; Saba Gargouri<sup>2</sup>; Imen Sellami<sup>1</sup>; Fadwa Hour<sup>3</sup>; Amel Chtourou<sup>2</sup>; Salma Mhalla<sup>4</sup>; Lamia Feki-Berrajah<sup>2</sup>; Mounira Hajjaji<sup>1</sup>; Kaouthar Jmal Hammami<sup>1</sup>; Maha Mastouri<sup>1</sup>; Mohamed Larbi Masmoudi<sup>1</sup>; H la Karray<sup>2</sup>

<sup>1</sup>Occupational Medicine Department, Hedi Chaker University Hospital, Faculty of Medicine, University of Sfax, Sfax, Tunisia.

<sup>2</sup>Laboratory of Microbiology, Habib Bourguiba University Hospital, Faculty of Medicine, University of Sfax, Sfax, Tunisia.

<sup>3</sup>Faculty of Medicine, University of Sfax, Sfax, Tunisia.

<sup>4</sup>Laboratory of Microbiology, Fattouma Bourguiba Hospital, Monastir, Tunisia.

### \*Corresponding Author: Hakim Zina

Occupational Medicine Department, Hedi Chaker University Hospital, Faculty of Medicine, University of Sfax, Sfax, Tunisia.

Tel: +21695684003; Email: hakim-zina@hotmail.fr

### Abstract

The present case highlights the possibility of multiple SARS-CoV-2 reinfections in highly exposed health care workers. The humoral immune response after natural infection seems to closely determine this phenomenon and to be boosted by vaccination in previously infected persons.

**Keywords:** COVID-19 disease; Reinfection; Occupational health; Virology; Vaccines.

**Abbreviations:** Ab: Antibodies; HCW: Health Care Worker; Ig: Immunoglobulin; NP: anti-Nucleocapsid; RT-PCR: Reverse Transcription Polymerase Chain Reaction; S1: anti spike.

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### Introduction

COVID-19 has rapidly become a global pandemic since the first case reported in China in December 2019 [1]. It has been previously suggested that natural SARS-CoV-2 infection could potentially induce a strong natural immunity with persistent, neutralizing anti-SARS-CoV-2 Immunoglobulin G (IgG) antibodies, a development of specific IgG memory B cells and a durable, functional, spike reactive memory CD4 T cells [2,3]. However, cases of confirmed reinfection were reported worldwide, primarily in Health Care Workers (HCW) [4,5], even with symptomatic clinical presentation despite the presence of antibodies. Reinfection episodes could be related to the continuous emergence of mutated variants of SARS-CoV-2 and/or the waning of antibody levels. In this context, several studies have assessed the effectiveness of vaccination of previously infected individu-

als in preventing substantial SARS-CoV-2 infection. In one study, it was concluded that both previous infection and vaccination provide substantial protection against COVID-19, and that vaccination of previously infected individuals does not provide additional protection against COVID-19 for several months [6]. Similarly, others have argued that HCW who recovered from natural SARS-CoV-2 infection should be exempt from vaccine mandates indefinitely, based on the power of natural immunity [7]. Here, we describe a case of a HCW who achieved the production of a humoral immunity response (detectable anti-spike (S1) IgG) only after receiving the vaccine, despite three recurrent episodes of SARS-CoV-2 infection.

### Case presentation

We report a case of a 32-year-old female healthcare worker, who was working as a medical doctor in the COVID-19 intensive

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**Table 1:** Characteristics of SARS-CoV-2 reinfections.

Episodes of CO-VID-19	RT-PCR dates (result, Cycle threshold)	Clinical presentation	Complementary exams	Treatment
1 <sup>st</sup> episode	October 01, 2020 (positive, 26)	<ul style="list-style-type: none"> <li>- Dyspnea, acute bronchitis with desaturation during exercise up to 92%</li> <li>- Paresthesia of all 4 limbs/heaviness of right leg with lameness</li> <li>- Asthenia, ageusia for 3 days without anosmia</li> </ul>	<ul style="list-style-type: none"> <li>- Thoracic radiography: minimal left basal atelectasis</li> <li>- Echo-Doppler of the right leg: no ultrasound signs of thrombophlebitis (giving the heaviness of the member)</li> </ul>	<ul style="list-style-type: none"> <li>- Hospitalization for 1 day on October 02, 2020 (Azithromycin, vitamins)</li> </ul>
Outcome	October 19, 2020 (Negative) November 13, 2020 (Negative)	<ul style="list-style-type: none"> <li>- Left otitis</li> <li>- Tendonitis of cervical muscles</li> <li>- Recurrent laryngitis and tendonitis after exposure to cold</li> <li>- Memory troubles, anxiety</li> </ul>	<ul style="list-style-type: none"> <li>- Biology: no abnormalities</li> </ul>	<ul style="list-style-type: none"> <li>- Muscle relaxant, Magnesium</li> </ul>
2 <sup>nd</sup> episode	December 10, 2020 (Positive, 36)	<ul style="list-style-type: none"> <li>- Sore throat</li> <li>- Dyspnea with desaturation on effort, thoracic burns, nasal burns, paresthesia</li> <li>- Sinusal tachycardia up to 140 bpm, hypoglycemic episodes</li> </ul>	<ul style="list-style-type: none"> <li>- Biology: lymphopenia at 900 Elements/mm<sup>3</sup>, respiratory alkalosis with bicarbonates at 21 mmol/l</li> <li>- Thoracic CT: no abnormalities</li> </ul>	<ul style="list-style-type: none"> <li>- Hospitalization for 3 days (antibiotics, colchicine, oxygen therapy, nebulization of pulmicort)</li> </ul>
Outcome	December 31, 2020 (Negative)	<ul style="list-style-type: none"> <li>- Asthenia</li> <li>- Tachycardia with palpitation</li> <li>- Shortness of breath on effort</li> <li>- Nasal and thoracic burns</li> </ul>	<ul style="list-style-type: none"> <li>- Normal auscultation hypotension at 90/60 (baseline BP at 120/60)</li> <li>- Electrocardiography: sinusal tachycardia</li> <li>- Cardiac ultrasound: Normal</li> </ul>	<ul style="list-style-type: none"> <li>- Magnesium, respiratory rehabilitation</li> </ul>
3 <sup>rd</sup> episode	January 28, 2021 (Positive, 17.7)	<ul style="list-style-type: none"> <li>- Dyspnea, chest pain</li> <li>- Paresthesia of the 4 extremities, tendonitis of neck muscles, asthenia</li> </ul>	<ul style="list-style-type: none"> <li>- Biological exams: normal</li> </ul>	
	February 17, 2021 (Positive, 33.1)		<ul style="list-style-type: none"> <li>- Nasal fibroscopy: deviation of the nasal septum, no polyps</li> <li>- CT scan of the facial sinuses: no sinusitis</li> </ul>	<ul style="list-style-type: none"> <li>- Vitamin B, Gabapentin, Magnesium</li> </ul>
Outcome	April 17, 2021 (Negative)	<ul style="list-style-type: none"> <li>- Shortness of breath on effort</li> <li>- Anxiety, depressive syndrome</li> <li>- Post-traumatic stress disorder</li> </ul>	<ul style="list-style-type: none"> <li>- Normal brain MRI</li> <li>- Immunological complementary tests: normal</li> </ul>	

**Table 2:** Results of serological testing performed.

	28/01/2021	18/02/2021	15/04/2021	08/06/2021	07/09/2021
<b>Anti-NP total Ab</b>					
Elecsys Anti-SARS-CoV-2, on the Cobas e411, Roche Diagnostics	Negative	Equivoqual	Positive	Positive	/
<b>Anti-S1 IgM</b>					
VIDAS®SARS-CoV-2 IgG and IgM, Biomérieux SA	Negative	Negative	Negative	Negative	/
<b>Anti-S1 IgG</b>					
VIDAS®SARS-CoV-2 IgG and IgM, Biomérieux SA	Negative	Negative	Negative	Negative	Positive

care unit since March 2020. She has no significant comorbidities except recurrent sinusitis during the past 2 years. She developed a first COVID-19 episode on October 01, 2020, confirmed by Reverse Transcription Polymerase Chain Reaction (RT-PCR) on a nasopharyngeal swab sample (Table 1). During this first episode, the patient developed pharyngitis with dyspnea and oxygen desaturation at 92%, requiring her hospitalization for 1 day on October 02, 2020. She also reported paresthesia of the four extremities. The patient returned to her professional activity 25 days later, although she continued to feel intermittent tendonitis of the cervical and thoracic muscles with asthenia. Two RT-PCR for SARS-CoV-2 detection were performed on October 19 and November 18, 2020, showing negative results (Table 1). Seventy days after the first infection, the patient showed severe symptoms that included fever, acute bronchitis, hypoglycemia, hypoxia and tachycardia, requiring her hospitalization for 3 days. Again, SARS-CoV-2 RT-PCR was positive (December 10, 2020), and the patient received antibiotics, glycolic serum perfusion, oxygen therapy and nebulization with corticoids. The RT-PCR performed on December 31, 2020 was negative, but she was still feeling fatigue and weakness, with persistent tachycardia. She performed cardiac explorations which returned normal. A serological testing was performed on January 16, 2021, showing negative results for anti-Nucleocapsid (NP) total Antibodies (Ab). Early after returning to work, the patient experienced weakness, pharyngitis, paresthesia and dyspnea. For the third time, the SARS-CoV-2 RT-PCR was positive on January 28, 2021 (49 days from the second episode). Surprisingly, serological testing performed at the same day has showed the absence of both anti-NP total Abs and anti-S1 IgG. Clinically, the patient reported an improvement after 2 weeks; however, she resumed her work despite the persistence of symptoms (tachycardia, hypotension, nasal burns feelings and headache). Of note, further serological testing showed that anti-S1 IgG were still negative, till June 2021 (Table 2). Therefore, the presence of an underlying immunodeficiency was suspected, but additional investigations revealed a normal B and T lymphocytes blood count and a negative result for HIV antibodies.

Given the absence of a detectable specific humoral response alongside the high exposure to SARS-CoV-2, eviction of the contact with confirmed COVID-19 patients in addition to vaccination were strongly recommended. Indeed, a notable clinical and psychological recovery was only achieved nearly 8 months after the first episode of COVID-19. The patient received her first dose of mRNA vaccine on June 15, 2021, and resumed her professional activity on July, 2021. Three months after the first dose, a new serological testing was performed, showing the

positivity of anti-S1 IgG. The second mRNA vaccine dose was received on November 2021. Since her vaccination, she is doing well and actively involved in the intensive care unit, with no more episodes of documented SARS-CoV-2 infection.

### Discussion

Here we present an interesting case of a HCW who failed to develop protective antibodies (anti-S1 IgG) against SARS-CoV-2 despite three laboratory-confirmed symptomatic episodes of COVID-19. The production of those antibodies was achieved only after her vaccination with 2-doses of mRNA vaccine.

Multiple SARS-CoV-2 reinfections (three episodes) were previously reported in immunocompetent HCW, and were considered as rare events with an estimated risk ranging from 0.008% to 0.16% [8-10]. SARS-CoV-2 reinfection may be defined as a positive RT-PCR or rapid antigen test in patients with recurrence of respiratory symptoms, more than 90 days after the onset of the primary infection [11]. Although the time course between COVID-19 episodes in our case were 70 and 49 days only, and no genomic information related to viral strains was available, we consider that our patient have experienced three distinct episodes of symptomatic SARS-CoV-2 infection, given the high exposure to the virus, the severe clinical presentation compatible with COVID-19, and the negative results by RT-PCR testing documented between the three episodes.

Interestingly, the serological profile of our patient also suggests that she was susceptible to recurrent infection, since no detectable anti-S1 IgG were observed till June 2021 (nearly 4 months after the third episode of COVID-19). Indeed, antibodies may not be produced by every individual after natural infection, or, if they do develop, they may not last long enough, hence, allowing the virus to enter the body and cause the disease again [12]. Of note, it has been reported in one study that most third infections in cases of thrice-infected HCWs occurred during the Omicron surge, a variant that is known to evade natural and post-vaccination immunity [8]. Nevertheless, our case has been observed even before the description of the first variants of concern of SARS-CoV-2. Again, this observation supports the close association between the reinfection and the immunity response of the host; the inadequate immunity (or the absence) after the first infection may predispose to early and multiple reinfections with severe clinical presentation, especially in case of HCWs who are frequently exposed to SARS-CoV-2 [5].

Notably, for our patient, the anti-S1 IgG production was enhanced after the first dose of mRNA vaccine. In a previous published study, it has been shown that anti-SARS-CoV-2 spike

protein IgG antibody level increased rapidly after the first mRNA vaccination, and this high antibody titer is maintained after the second vaccination in a previously re-infected individual [13]. Therefore, the authors in this study have suggested that a single booster shot may provide sufficient protection in patients with COVID-19 with history of re-infection. Indeed, no more episodes of SARS-CoV-2 infection were documented for our patient since her vaccination.

### Conclusion

The present case highlights the possibility of multiple symptomatic SARS-CoV-2 reinfections in HCWs. The absence of humoral immune response after natural infection may represent one of the causes of susceptibility to reinfection, especially in case of high exposure. Vaccination may boost immunity and offer better protection against reinfection with SARS-CoV-2.

### Declarations

**Consent for publication:** Written informed consent was obtained from the patient to publish this report. The patient has given his consent for clinical and laboratory information to be reported in the journal.

**Availability of data and materials:** The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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

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**Authors' contributions:** ZH and IS ensured the patient's medical follow-up, aptitude for work and legislative procedures. SG, AC and SM analyzed and interpreted the patient data regarding the hematological disease and the transplant. FH contributed to the availability of all datasets during the current study. LF, MH, KJH, MLM and HK supervised the medical and laboratory follow-up and ensured that the manuscript is eligible for publication.

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