Reinfection or relapse of COVID-19 in health care workers; case series of 2 patients from Pakistan

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Abstract

During an ongoing pandemic of severe acute respiratory syndrome coronavirus 2, main question which has arisen in everyone's mind is about the immune response that may protect from reinfection. Coronaviruses are known for short-term immunity. Their ability of mutations enables them to escape host immunity, thus increasing chances of reinfection. Here we report two cases of reinfection among health care workers who presented with symptoms of COVID-19 disease, after 3 months of first infectious course. Such documentations are necessary for epidemiological purposes and also to monitor response of virus on re-exposure.

Keywords: Health care worker, health care–associated COVID-19 infection, reinfection, SARS-CoV-2
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Introduction

In 2020, the world was doomed under fear with the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) because of its rapid transmissibility and high mortality [1,8]. Also there is an extreme consternation about reinfection, as virus immune response assumed to be short lived in recovered patients, and cases of reinfection are being reported with increasing frequency [1,2].

Here we report two interesting cases of reinfection among health care workers (HCWs) who acquired SARS-CoV-2 from hospital settings.

Case report

The two HCWs of almost similar age bracket with no known comorbidities, presented to a medical emergency department on different occasions during this ongoing COVID-19 pandemic (timeline mentioned in Fig. 1). We took informed consent from both the individuals and their confidentiality was maintained by using codes.

The first patient is a nursing assistant who presented to medical emergency department on 19th June 2020 (12th day of quarantine after returning from leave following COVID policy by the Government of Pakistan), with complaints of arthralgia, generalised weakness, anosmia and ageusia. Patient was tested for SARS-CoV-2 on nasopharyngeal swab by using SARS-CoV-2-R-GENE® real-time polymerase chain reaction (r RT-PCR) assays (Biomerieux, France). These triplex assays can detect N-Gene/RdRp Gene, both specific to SARS-CoV-2 and E-Gene (generic for Sarbecoviruses) in patient's specimen. His PCR was positive with cycle threshold (CT) value 23.6 and detected both RdRp and N gene. His complete blood picture showed mild lymphocytosis with thrombocytopenia along with mildly raised C-reactive protein (CRP) and serum (S) ferritin as shown in Table 1. However, other inflammatory markers with baseline serum chemistry and chest X-ray were unremarkable. He

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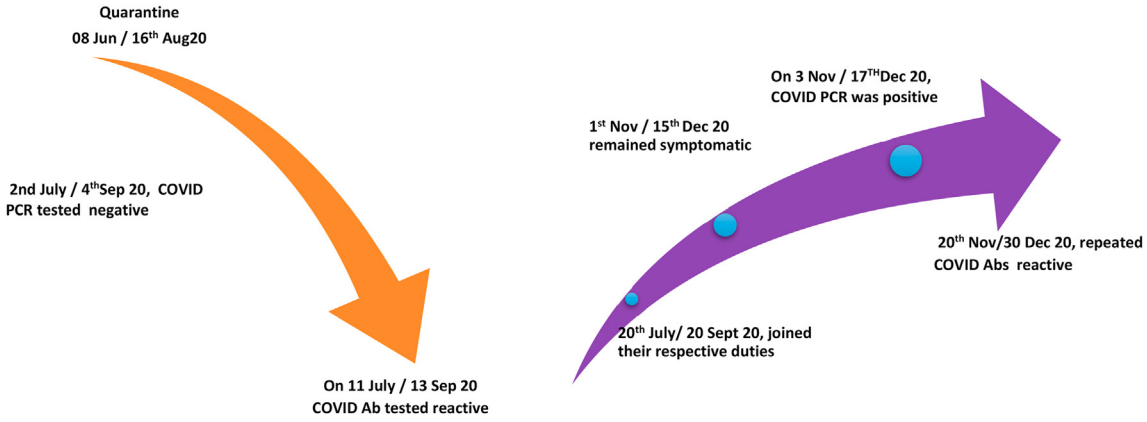

FIG. 1. Timeline of COVID-19 disease among HCWs.

remained afebrile with 98% oxygen saturation (SpO_2) during his entire hospital stay and was discharged on 5th July 2020 after his 2 consecutive nasopharyngeal swabs were negative. Patients' total COVID antibody (Ab) tested was performed after 23 days of first course of illness by electrochemiluminescence immunoassay (ECLIA) method on Cobas e-411 which was reactive against nucleocapsid protein (N) and he resumed his duties of nursing assistant in the COVID ICU. On 1st Nov 2020, the patient again developed fever, sore throat with dry cough, after 2 days, his RT-PCR was positive for SARS- CoV-2 with detection of single target, N-gene at CT value 33 with non-reactive COVID Abs. For confirmation, his sample was tested with another diagnostic kit of KHB®RT-PCR (Shanghai Kehua Bio-Engineering, China) which detected ORF ab1 region, N and E gene with CT value 33, 32 and 33, respectively. He had mild course of disease with mildly raised CRP, whereas rest of the findings were non-contributory. Patient was discharged after 7 days and remained asymptomatic during follow-up.

Our second patient laboratory technician presented in similar manner on 25th August 2020 with history of fever and sore throat and no other symptoms; he was tested for SARS-CoV-2 on nasopharyngeal swab using the same triplex assays. His PCR was positive with CT value 30.5 and detected for both RdRp and N gene, remained afebrile with 98% SpO_2 during his hospital stay and discharged on 7th September 2020 after his two consecutive nasopharyngeal swabs resulted negative testing. The patients' total COVID antibody (Ab) test was performed after 23 days of the first course of illness by (ECLIA) method on Cobas e-411 which was reactive. He resumed his duty on 20th September 2020 and was placed on COVID-19 screening centre for collection of nasopharyngeal swabs from suspected patients. On 15th December 2020, the patient presented with symptoms of sinusitis and his X-ray paranasal sinuses indicted right-sided sinusitis, he was given antibiotic cover with levofloxacin 750 mg OD but his symptoms persisted for 5 days, he was tested for SARS-CoV-2-R-GENE® r RT-PCR and found positive with CT values (N-gene = 33, RdRp-gene = 34), respectively, but his repeat COVID Abs were non-reactive, patient was admitted and his baseline chemistry and other markers were non-contributory and was discharged after 7 days.

Our both patients had shown mild course of diseases with mildly raised CRP whereas rest of the findings were non-contributory (mentioned in Table 1).

Discussion

Cases of SARS-CoV-2 reinfection has been reported globally; here we present two cases of reinfection in HCWs, one reported after 135 days while other after almost 100 days of first episode of COVID-19. This time it seems to be health care–associated COVID-19 infection, as supported by our patients' histories. Our cases are different in certain aspects from previously published reports, as in one study reinfection was reported after 2 months in a HCW of 58 years with severe course of illness and no serological evidence of COVID Ab formation from the previous episode [3], but as per the Centers for Disease Control and Prevention in settings of limited genomic testing facility higher suspicion of reinfection to be made only once duration is more than 90 days with positive symptoms [4,5]. Contrary to these regional and international reports [2,3], our patient had a mild course of disease with no oxygen dependency and showed complete recovery. Even though CT values can vary substantially, one can roughly depict the level of viremia. Like Singanayagam A et al. found the cultivable virus in only 8% positive samples with CT values greater than 35 [6]. In a resource poor settings with a limited amount laboratory setups, patient's clinical symptoms along with laboratory based evidence increased with the likelihood of reinfection with another variant of the SARS-CoV-2 virus and

TABLE 1. Diagnostic details of patients reported with reinfection

Laboratory test performed	Specimen A			Specimen B	
First case (nurse assistant)	First infection			Reinfection	
Second case (laboratory assistant)	19 June 2020	2nd/5th July 2020	11 July 2020	3 November 2020	19 November 2020
	25 August 2020	4th/7th September 2020	13 September 2020	17 December 2020	30 December 2020
rRT-PCR (Argene®)	Positive	Both negative	……..	Positive (N gene only)	NT
Targets (N &RdRp gene)	Both detected	……	…..	CT value = 33	……
1st case	CT value = 23.6	…….	…….	Both gene detected	…….
2nd case	CT value = 30.5	—	1st case: NT	(CT value 33 and 34)	NT
rRT-PCR (KHB®)	1st case: NT	1st case:NT	2nd case: NT	1st case: All targets	NT
Targets (N,E &ORFab 1)	2nd case:NT	2nd case: NT	Reactive	detected,	Reactive
Immunoassay	NT	NT	Reactive	CT value = 33,32,33	Reactive
(IgM and IgG COVID Ab)	NT	NT		2nd case: NT	
1st case				Non-reactive	
2nd case				Non-reactive	
Other biomarkers	1st case: 45mg/l	24mg/l	Non-reactive	1st case: 14mg/l	Non-reactive
C-reactive protein (>6mg/l)	2nd case: 22mg/l	12mg/l	Non-reactive	2nd case:36mg/l	9mg/l
Serum ferritin (24-336nmol/l)	1st case: 448nmol/l	380nmol/l	Normal	1st case: 345nmol/l	Normal
S. creatinine kinase (25-190u/l)	2nd case: 395nmo/l	351nmol/l	Normal	2nd case: 415nmol/l	Normal
Thrombocytopenia	1st case: Raised	Raised	Normal	Normal	Normal
Normal (150-400 × 10^9/l)	2nd case: Raised	Raised	Normal	Normal	Normal
	1st case: 121 × 10^9/l	135 × 10^9/l	Normal	1st case:110 × 10^9/l	Normal
	2nd case: 115 × 10^9/l	133 × 10^9/l	Normal	2nd case:105 × 10^9/l	Normal
Coarse of disease (both cases)	Symptomatic in isolation ward	Mild disease	Asymptomatic/ discharged	Febrile admitted in isolation ward	Asymptomatic/ discharged

Note: inflammatory markers S. Lactate dehydrogenase, procalcitonin, interleukin 6,D-dimers along with liver function test and renal function test were also tested but within normal range. Therefore, they are not mentioned in the table.

less likely to be viral shedding from past infection. UmairM et al. and Awan UA et al. reported about the emergence SARS-CoV-2 variant B.1.1.7 (United Kingdom strain) identified in people travelled from UK to various parts of Pakistan, whole genomic sequencing of those strains in which Spike protein target (S gene) was not detected from oropharyngeal swabs. In above mentioned studied authors have also mentioned other types of mutations not related to S gene [7,8].

Major limitation of our study is non-availability of genomic sequencing facility in our setup. Therefore, it cannot be established whether the later infection reported in first HCW occurs with the same virus or the variant strain. As in his case of reinfection, PCR failed to pick the RdRp gene and there can be a probability of mutations. RdRp mutation reported in Pakistani isolates as the second-most common SARS-CoV-2 variant mentioned by Khan TM et al. [9]. Therefore, those patients who are symptomatic and presented with CT value $\geq$ 33 on single target detection should be reported cautiously and taken as presumptively positive. Therefore, even after 3 months of first episode, one should take standard, contact and droplet-based precautions in a true spirit irrespective of his previous status.

As Pachetti M et al. emphasised about the RdRp gene alteration, its mutation rate and role in the emergence of multiple drug-resistant phenotypes [10]. This information is not only important in diagnosing a case of reinfection but also helpful in better understanding of the effective diagnostic and therapeutic approach against such variants in future. Serological data are also essential to understand the protection provided by these antibodies.

In conclusion, based on the data and analysis above, increased surveillance efforts are required by both the public and government sector to improve screening and emphasis on skilled molecular testing with strong clinical and serological correlation, which can aid in establishing accurate statistics of reinfection. This way we can obtain precise data of reinfection/reactivation or secondary response. It is important not only for patient management but also for aid in early response and curtails its transmission of infection.

Transparency declaration

None to declare.

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