Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2

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ABSTRACT

Reinfection of SARS-CoV-2 is an apparently rare entity and only a few cases have been reported from across the world with the genetic characterization of the virus, differentiating reinfection from persistent virus shedding. These cases, therefore, provide unique insights into the long term protective immunity to SARS-CoV-2. The earlier reports suggest that patients were symptomatic in either one or both the episodes of infection. Here we report a unique case of asymptomatic SARS-CoV-2 reinfection in two healthcare workers from India identified in routine surveillance. Genome sequencing of the virus suggests that genetically distinct SARS-CoV-2 caused the infections. Our analysis demonstrates that asymptomatic reinfection could potentially be an under-reported entity with implications in long term surveillance of SARS-CoV-2 infections. This report also highlights the need for genomic surveillance of healthcare workers who are potentially not only at higher risk for primary infections but also for reinfections.

KEYWORDS

SARS-CoV-2, reinfection, genome, genetic variant, RT-PCR, healthcare worker, surveillance

INTRODUCTION

To et al [1] recently reported a case of SARS-CoV-2 reinfection confirmed by genome sequencing. Additional reports of genetically characterized reinfections have emerged [2, 3] raising pertinent questions on the longevity of immune response in SARS-CoV-2 infection. In all previous reports, patients had symptoms in one or both of the episodes. Here we report asymptomatic SARS-CoV-2 reinfection in two healthcare workers detected during routine surveillance. The report highlights the possibility of undetected SARS-CoV-2 reinfections and the need for surveillance of SARS-CoV-2 reinfections in healthcare systems.

CASE DETAILS

We describe two individuals, 25 year-old male (I1) and 28 year-old female (I2) healthcare workers posted in the COVID-19 unit of a tertiary hospital in North India, who tested positive for SARS-CoV-2 by reverse transcription-polymerase chain reaction (RT-PCR) on 5th May and 17th May, 2020 respectively. Though both individuals were asymptomatic, they were hospitalised as per institutional policy on 5th May and 17th May respectively. Subsequently, they tested negative for SARS-CoV-2 by RT-PCR on 13th May and 27th May, respectively. After resuming duties in the hospital, both I1 and I2 tested positive again for SARS-CoV-2 on 21st August and 5th September respectively. Eventually, on the 14th (I1) and 6th days (I2) of reinfection, they both tested negative. Both individuals were asymptomatic but had a higher viral load in the second episode of reinfection (C_T values were 36 and 16.6 for I1 and 28.16 and 16.92 for I2 for the first and second episodes, respectively). The timeline of the two episodes of infection in I1 and I2 is summarised in Figure 1A.

(A)

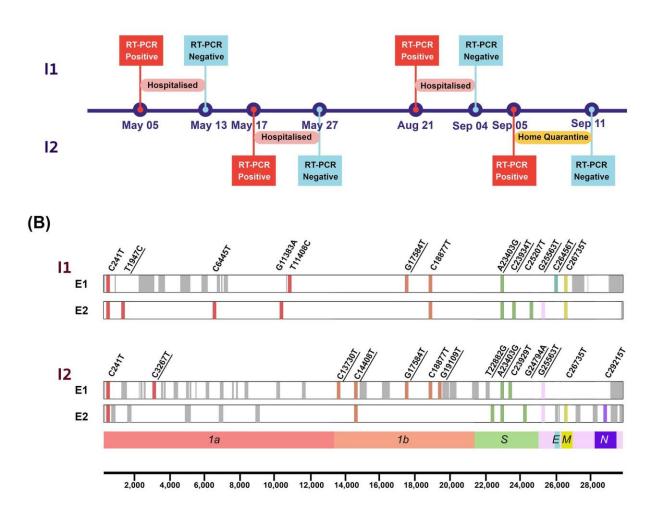


Figure 1. A. The timeline of SARS-CoV-2 infection in the two individuals I1 and I2. **B.** The genetic variants in isolates of the 2 episodes (E1 and E2) for individuals I1 and I2. Non-synonymous variants have been underlined and the gaps in the genome are marked in grey.

SEQUENCING AND GENOME ANALYSIS

Since RNA from the nasopharyngeal/oropharyngeal swabs were archived, after informed consent (IHEC-CSIR-IGIB/IHEC/2020-21/01) the sequencing-ready libraries were prepared using capture-based (TWIST Biosciences) as well as amplicon-based (COVIDSeq, Illumina) approaches. The libraries were sequenced on 75 bp x 2 paired-end recipe on Illumina MiSeq. Genomes were assembled at an average of 13,684X coverage after merging the datasets,

partially covering the SARS-CoV-2 reference genome (NC_045512.2) at 89.08% and 99.96 % respectively for the two episodes for I1 and 85.60% and 92.14% for I2. Analysis of the genomes using a previously published protocol [4] for loci covered in both the genomes revealed 9 and 10 unique variant differences between the virus isolates from the two episodes of infection for I1 and I2 respectively (**Figure 1B**). Of the unique variants between the pair of samples, seven variants each for the two individuals mapped to predicted immune epitopes [5].

DISCUSSION AND CONCLUSION

Taken together, our analysis suggests that asymptomatic reinfection may be a potentially under-reported entity. Genetically distinct SARS-CoV-2 rules out persistent viral shedding or reactivation. Both individuals had a higher viral load during reinfection highlighting the need for continuous surveillance. It is noteworthy that a genetic variant 22882T>G (S: N440K) found during reinfection in I2 possibly confers resistance to neutralising antibodies [6]. To the best of our knowledge, this is one of the earliest reports of genetically characterized reinfection from India.

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CONFLICT OF INTEREST

Vivek Gupta - No Conflict

Rahul C. Bhoyar - No Conflict

Abhinav Jain - No Conflict

Saurabh Srivastava - No Conflict

Rashmi Upadhayay - No Conflict

Mohamed Imran - No Conflict

Bani Jolly - No Conflict

Mohit Kumar Divakar - No Conflict

Disha Sharma - No Conflict

Paras Sehgal - No Conflict

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