Journal of Associated Medical Sciences 2022; 55 (3): 105-108

JAMS
Journal of Associated Medical Sciences

Thai-Journal Citation Index Centre (TCI) & ASEAN Citation Index (ACI)

Journal of Associated Medical Sciences

Journal homepage: https://www.tci-thaijo.org/index.php/bulletinAMS/index

Reinfection of SARS CoV-2 in patients with relapse of symptoms after clinical recovery: A Case Series

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ARTICLE INFO

Article history:
Received 26 February 2022
Accepted as revised 1 July 2022
Available online 1 August 2022

Keywords:
COVID-19 infection, SARS CoV-2 reinfection, health care workers

ABSTRACT

Background: It has been more than a year, and still, we are battling with a novel coronavirus (SARS-COV-2). Initially, the interim guidelines by the World health organization (WHO) stated that infection ranges from asymptomatic to critical life-threatening pneumonia with the symptomatology of fever, cough and breathing difficulty.

Objectives: To observe the reinfection of SARS CoV-2 in patients with relapse of symptoms after clinical recovery.

Materials and methods: Three cases were observed during the isolation period. Reverse transcription polymerase chain reaction (RT-PCR) and severity of similar symptoms in the fourth week from the onset was monitored.

Results: All the three patients had health care exposure, and which pointed us towards health care associated reinfection could be a possible cause of step-up in the symptom severity.

Conclusion: Reinfection by SARS CoV-2 can be considered in patients with relapse of symptoms after clinical recovery after natural infections.

Introduction

It has been more than a year, and still, we are battling with a Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-COV-2). Initially, the interim guidelines by the World health organization (WHO) stated that infection ranges from asymptomatic to critical life-threatening pneumonia with the symptomatology of fever, cough and breathing difficulty.[1] Further, researchers contributed about extra-pulmonary manifestations for disease expression and potential sources of viral transmission.[2] The disease pattern never stopped surprising us with its atypical presentations like cerebral infarcts, rhabdomyolysis, acute coronary syndromes following full clinical recovery. As it is a novel disease with many faces, which mandates vigilant monitoring and regular follow-up by clinicians.[2] These rare cases are to be earmarked with patient-centric specific treatment strategies.

We observed the following three cases during the isolation period who tested positive for Reverse transcription polymerase chain reaction (RT-PCR), COVID test and developed increased severity of similar symptoms in the fourth week from the onset of desease symptoms. The basic idea to put present these cases is not only because of their atypical presentations but also because of paucity in the literature.

Case scenarios

Case 1: A 28-year-old male health care worker with no comorbidities presented with prodromal symptoms of fever, cough and tested positive for RT-PCR COVID test. The chest radiograph had normal lung fields and started on symptomatic treatment with favipiravir, levocetirizine, and

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doi: 10.12982/JAMS.2022.031
E-ISSN: 2539-6056

oral vitamin C. Patient was asymptomatic during the treatment period and discharged home on the 14th day after the RT-PCR negative report. The patient developed respiratory distress with a respiratory rate of 36/min, and saturation measured on pocket pulse-oximeter at home was 90% on room air on the 22nd day after discharge. The patient was admitted and started on oxygen therapy with a nasal cannula; High Resolution Computerized Tomography (HRCT) thorax done on the same day showed a CT severity Index (CTSI) of 20/25 and CORADS 5. On day 3 of admission patient had an increased requirement of oxygen and shifted on to venturi mask. He received Injection of Ramdesivir 200 mg 10 days regimen and injection dexamethasone 6 mg once a day. The patient was discharged after symptomatic improvement. The patient was being followed up periodically as a part of the institutional protocol. (Table 1 and 2)

Case 2: A 50-year-old male health care worker, a known diabetic and hypertensive with 10 years of duration, has presented with fever and cough. Tested to be COVID positive by RT-PCR with normal baseline vitals and was in home isolation for 14 days and took standard care regimen for mild disease (favipiravir, vitamin c, levocetirizine) then the RT-PCR report was negative on day 14th of illness. Day 26th after the RT-PCR report was negative for the patient, he developed tachypnea with a respiratory rate of 34/min and presented to casualty. On examination, he was hemodynamically stable with room air saturation of 89%, and CT thorax revealed subpleural opacities with CTSI of 18/25. He fitted to the moderate category as of our institutional protocol and started injection Dexamethasone 6 mg OD. The patient stayed in the hospital (ICU, Ward) for 10 days and discharged on the 11th day. (Table 1 and 2).

Case 3: A 22-year-old female, a known case of thalassemia, had come for routine blood transfusion. As a protocol for admission, COVID RT-PCR was done, and it turned out to be positive. The patient had a history of recurrent admission. The patient has admitted to the COVID ward. The patient was asymptomatic and fitted into a mild-grade disease category, received multivitamins and vitamin C, and was discharged home on day 14 after tested negative for RT-PCR. The patient developed severe dyspnea and come to a casualty with room air saturation of 86% on room air. She was admitted in Isolation ICU and CT severity index 20/25 14 days after discharge. The patient received Injection Ramdesivir 200 mg (Viral replication inhibitor, used for COVID- 19 Pnemonia) and Injection Dexamethasone 6 mg, iv for 10 days. She was discharged home after clinical improvement on the 14th day of readmission. (Table 1 and 2).

Table 1 Tabular representation of the case details .

	Case 1	Case 2	Case 3
Age (years)	28	50	22
Symptoms on Day 1	Fever with cough	Fever with cough	Asymptomatic
Relapse of symptoms	Shortness of breath with room air saturation 90%	Tachypnea with Room air saturation of 89%	Dyspnea
CT severity Day 1	3/25	5/25	4/25
CT severity (readmission) Comorbidities	20/25 Obesity (BMI 28 kg/m^2) (Quetelets Index)	18/25 Diabetes and hypertension	20/25 Thalassemia on frequent blood transfusions
Probable anticipated source of infection	Health care associated	Health care associated	Health care associated
Treatment received on first admission	Flavipiravir and levocitirazine	Flavipiravir and levocitirazine and Vitamin C	Vitamin C Levocetirizine
Treatment received after relapse of symptoms	Ramdesivir and Dexamethasone	Dexamethasone	Ramdesivir Dexamethasone
Follow-up (6 months)	Stable	Stable	Stable

Table 2 Tabular representation of the case details .

	Symptoms	Treatment
Mild	Without evidence of breathlessness and hypoxemia.	Symptomatic treatment Flavipiravir Vitamin C antihistamines.
Moderate	With evidence of breathlessness and hypoxia SpO_2 <94% (90-94%).	Anticoagulation with low molecular heparin 40 IU, sc. Dexamethasone 6 mg, IV, OD Awake proning.
Severe	Clinical signs of pneumonia plus one of the following tachypnea >30 breaths/min, and hypoxemia SpO_2 <90%.	Anticoagulation with low molecular heparin 40 IU, sc. Ramdesivir 400 mg stat f/b 200 mg, OD Dexamethasone 6 mg, IV, OD High Flow Nasal Oxygen Mechanical ventilation.

Discussion

The three cases were treated between July 2020 to September 2020 with symptomatology mentioned above and were enrolled after obtaining ethical clearance from Institutional Ethical Committee of IMS & SUM Hospital, SOA University and informed consent was obtained from the clients. All these cases were admitted with mild symptoms (Table 1), and we had a severity based standard treatment protocol (Table 2).[3] Home quarantine was provided as per patient preference with regular teleconsultations. Our treatment protocol incorporated dexamethasone as a part in moderate to severe categories five along with Ramdesivir (Table 2).

SARS COV-2 virus belongs to the beta coronavirus group with a highly contagious nature comparing to another beta virus-like MERS, with a median incubation period of 2-14 days. Virus spike protein attaches to the Angiotensin-converting enzyme-2 (ACE), leading to increased Angiotensin II levels, ultimately with exaggerated host immune response leading to cytokine storm (Kawasaki like syndrome) with the hypercoagulable response from host.[4,5,6] The primary mode of transmission of SARSCOV-2 is the direct person to person respiratory transmission; when an infected person coughs or sneezes, the virus shredded in respiratory secretions might infect another person if he inhales or if it comes in direct contact with the mucous membranes.[7] The other mode of transmission where patient secretions might contaminate the surfaces like cots, lift bells, doors by touching the contaminated surfaces one's hands might get contaminated and takes a systemic root by rubbing eyes and touching mucous membranes.[8] The later cause has less potential to become an infection source in the general public, but this has its mark of incidence among health care workers, which might probably cause reinfection. Interesting, even though all three cases had no comorbidities matched, case 1 & 2 are healthcare workers who resumed back to work after normalizing the symptoms and both the cases had the step-up symptomatology after resuming back to work. Case-3 was a case of thalassemia, which incidentally detected to be positive. We have not given a blood transfusion to avoid transfusion-related immunological complications during this ongoing hyperimmune response condition, and later she visited the hospital for blood transfusion.

In *The Lancet*, Christian Holm Hansen and colleagues conducted a population-level observational study in Denmark.[9] Among eligible RT-PCR positive individuals from the first surge of the epidemic, 72 (0.65%) tested positive again during the second surge compared with 16 819 (3.27%) of 514 271 who tested negative during the first surge and found that protection against repeat infection was 80·5% among the patients who were previously infected with COVID-19 and 47.1% among subjects more than 65 years. This study concluded only based on RT-PCR, where the chances of false positivity are high, especially among naturally infected and immunized subjects. Considering this 20% chance of reinfection, which can be more commonly seen in geriatric patients than authors, they can also occur in health care workers who have a high chance of exposure to high viral load. The protective immunity obtained by natural infection to the reinfection remained unanswered. The new variants with altered phenotype unlikely to be covered under the immunological natural T cell-mediated immunity. Rosemary J Boyton supported the chances of reinfection after natural infection.[10] In an early report by Wang D et al., from China, it was estimated that among the incidence of COVID-19, 43% were hospital-acquired.[11,12] The study extended to evaluate incidence among the USA residents, which showed near identical results to the previous study conducted by Wang D colleagues proving health care individuals are more prone to infection even with less common modes of transmissions like fomites, fecal shedding.

In all our three subjects RT-PCR was negative on the 14th day of illness and discharged from hospital. A few days later all of them were presented with increase in severity of symptoms (clinical) and a rise in CTSI score after a brief asymptomatic period. The study could not conform the reinfection at genomic level analysis due lack of development of specific marker against the new strains of Corona Virus. This cannot be considered as "long COVID syndrome" as the symptoms regressed, after a certain period the clinical symptoms reappeared with increase in severity.[13] However, this cases series can only act as a driving tool for future RCTs (Randomised Controlled Trail). A statistically significant and adequately powered sample size would give better evidence with detailed mapping of immune parameters.

Consent

Consent has been obtained from the patients and the study was approved by IRB of IMS & SUM Hospital (DMR/IMS/SH/SOA/22/338).

Conflict of interest

The authors disclose that they have no conflicts of interest among them.

Funding Source

Nil.

Acknowledgements

The authors are highly grateful to the chairman of Siksha O Anusandhan (Deemed to be) University, Prof. Manoj Ranjan Nayak for providing the support during the study. The authors are also thankful to the Dean, IMS and Sum Hospital, Siksha O Anusandhan (Deemed to be) University, Prof. Gangadhar Sahoo for encouraging and supporting.

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