

Coronavirus Pandemic

Symptomatic recurrence of SARS-CoV-2 infection in healthcare workers recovered from COVID-19

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Abstract

There is rising concern that patients who recover from COVID-19 may be at risk of recurrence. Increased rates of infection and recurrence in healthcare workers could cause the healthcare system collapse and a further worsening of the COVID-19 pandemic. Herein, we reported the clinically symptomatic recurrent COVID-19 cases in the two healthcare workers who treated and recovered from symptomatic and laboratory confirmed COVID-19. We discuss important questions in the COVID-19 pandemic waiting to be answered, such as the protection period of the acquired immunity, the severity of recurrence and how long after the first infection occurs. We aimed to emphasize that healthcare workers should continue to pay maximum attention to the measures without compromising.

Key words: COVID-19; healthcare workers; recurrence; SARS-CoV-2.

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Introduction

Since December 2019, the COVID-19 pandemic caused by the SARS-CoV-2 has infected more than 28 million people and nearly one hundred thousand of healthcare workers worldwide [1]. The number of infected healthcare workers was announced as the 7428 by the ministry of health in Turkey. Recently, articles about the recurrence of positive SARS-CoV-2 cases among recovered COVID-19 patients have been published [2-4]. Herein we reported the recurrent COVID-19 cases in two healthcare workers who recovered from COVID-19 and we aimed to emphasize that healthcare workers should continue to pay maximum attention to the measures without compromising.

Case 1

First patient 46-year-old male who is pediatrician without comorbid disease and one of the study author. Diagnosis of COVID-19 was suspected in March 2020 based on a clinical picture like fever, sore throat,

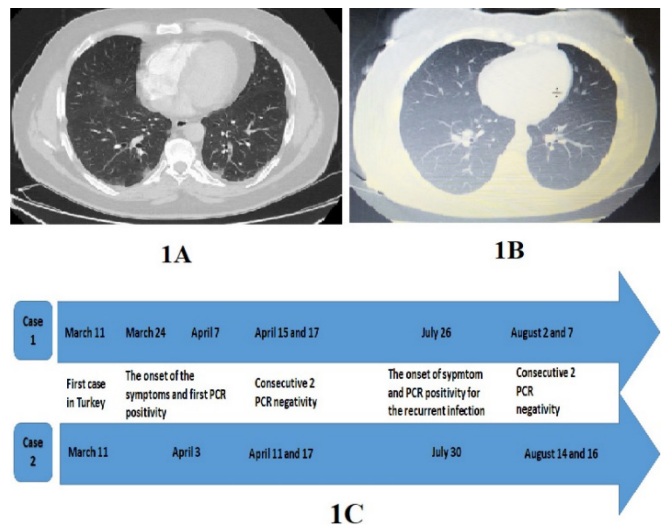
headache, cough, weakness, nausea and diarrhea. The COVID-19 diagnosis was made on the typical chest computed tomography (CT) scan appearance on 24 March 2020, with bilateral ground glass opacities and peribronchial thickening predominating on the right lung (Figure 1A), confirmed by a positive SARS-CoV-2 RT PCR performed on nasopharyngeal sample on 7 April 2020. The influenza A + B test result performed from the nasopharyngeal swab was negative. The patient received hydroxychloroquine (HCQ), azithromycin for five days and ceftriaxone for ten days. SARS-CoV-2 RNA by nasopharyngeal swab results were negative on 15 and 17 April. The patient, whose symptoms resolved, started working in the clinic after completed the 14-day isolation period. On July 26, complaints of sore throat, fever, headache, myalgia, weakness and nausea started again, and the SARS-CoV-2 RT PCR test obtained on the same day was found to be positive. 5 days of favipiravir, azithromycin and ceftriaxone treatment was administered in home quarantine. Clinical improvement started from the

second day of treatment. SARS-CoV-2 RT PCR tests taken on August 2 and 7 were reported as negative. The time interval from the onset of the illness to the last PCR negativity was defined as the diseases duration and the disease durations for this case were determined as 24 and 12 days, respectively.

Case 2

The second patient is a 47-year-old female, working as a nurse in the filiation team, and has frequent contact with COVID-19 patients. On 3 April 2020, myalgia, headache and abdominal pain started without fever and cough. On the same day SARS-CoV-2 RNA test obtained from nasopharyngeal was reported as positive. Palpitations developed in the patient who received HCQ treatment for 5 days. Metoprolol antiarrhythmic therapy was initiated with the diagnosis of arrhythmia as a result of electrocardiogram, echocardiogram and 24 hour holter monitoring of the patient who was evaluated by the cardiology department. There was no pathological finding on chest CT. SARS-CoV-2 RNA by nasopharyngeal swab results have become negative on 11 and 17 April. On 30 July, sore throat, headache and myalgia occurred. There were also fever, cough and mild respiratory symptoms in the re-infection attack. On the same day, ground glass opacities and subpleural nodule on the left lung base (Figure 1B) consistent with COVID-19 were detected on chest CT imagine and the

Figure 1. Chest CT images for the first infection attack of the first case (1A) and re-infection attack of the second case (1B) Timeline of patients SARS-CoV-2 RT PCR results of cases (1C).



diagnosis confirmed with a positive SARS-CoV-2 RT PCR. She received antipyretic and 5-day favipiravir therapy in home quarantine. The complaints improved. On August 14 and 16, SARS-CoV-2 RT PCR tests became negative (Figure 1C). The disease durations in this case were determined as 14 and 18 days, respectively. The demographic and clinical information of the cases were summarized in Table 1.

Table 1. The demographic and clinical summaries of the cases.

Case number	Case 1		Case 2	
	First infection	Recurrent infection	First infection	Recurrent infection
Age/Gender	46/M	46/M	47/F	47/F
Occupation	Pediatrician	Pediatrician	Nurse	Nurse
Chronic Disease	None	None	None	Arrhythmia
Laboratory parameters				
WBC	-	7.6	7.6	5.0
Lymphocyte (10 ⁹ /L)	-	1.2	2.5	1.5
CRP (mg/L)	-	8.3	1.7	2.1
SARS-CoV-2 RT PCR				
Positivity	April 7	July 26	April 3	July 30
First negative	April 15	August 2	April 11	August 14
Second negative	April 17	August 7	April 17	August 16
The time from last negativity to re-positive	-	100 days	-	104 days
The disease durations	24 days	12 days	14 days	18 days
Chest CT	Ground glass opacities and peribronchial thickening	Normal	Normal	Ground glass opacities and subpleural nodule
Treatment	HCQ, azithromycin, ceftriaxone	Favipiravir, azithromycin, ceftriaxone	HCQ	Favipiravir

M: Male; F: Female; WBS: White blood cell; CRP: C-reactive protein; HCQ: Hydroxychloroquine.

Discussion

While the COVID-19 pandemic continues all over the world, recently recurrence of positive SARS-CoV-2 have begun to report. There are important questions in the COVID-19 pandemic waiting to be answered, such as the protection period of the acquired immunity, the severity of recurrence and how long after the first infection occurs. Another key question is how healthcare workers and healthcare systems will be affected by recurrence. Unfortunately, these questions which will discuss in this section, do not have a certain answer today and will become clear with the case series and researches. Although numerous articles on COVID-19 have been published, there is limited data about recurrence of positive SARS-CoV-2 to date. To the best of our knowledge, there is no article presenting re-infections in healthcare workers in the literature.

The protective role of antibodies and their longevity against SARS-CoV-2 remain unclear. In a study published in September 2020, aimed to investigate the duration of protection from seasonal coronavirus re-infections. The re-infection times ranged between 6 and 105 months. They also found that re-infections occurred as early as 6 months (twice with HCoV-229E and once with HCoV-OC43) and 9 months (once with HCoV-NL63), but re-infections were frequently observed at 12 months [5]. Limited studies in the literature have shown that neutralizing SARS-CoV-2 antibody levels decrease within the first 2-3 months after infection, especially after mild COVID-19 [6, 7]. The duration of the neutralizing SARS-CoV-2 antibody protection is understood to be shorter than the seasonal coronaviruses and this results was consistent with our cases. Bruni and *et al.* has published a recent study about persistence of anti-SARS-CoV-2 antibodies in non-hospitalized COVID-19 healthcare workers. They reported that non-hospitalized subjects showed lower antibody titers as compared to patients in intensive care units, irrespective of the antibodies tested. Another notable result from the study was that, in non-severe COVID-19 infections, antibody titers as well as pro-inflammatory cytokines decreased within a month after viral clearance. Thus, rapid decline in antibody titers may be a common feature of non-severe SARS-CoV-2 infection, suggesting that antibody-mediated protection against re-infection with SARS-CoV-2 is of short duration [8]. The lack of data about the SARS-CoV-2 antibodies and the viral load of the cases is the main limitation of our study. The second limitation of the study was that we did not have the opportunity to perform genome analysis of the SARS-CoV-2 strains from infections episodes to confirm that these were

identical. There are different notifications about the clinical severity of re-infection and interval of two episodes. Although some studies report the re-infections as asymptomatic or mild [2,3,9], it can be more serious or even fatal in people at risk groups, especially older patients with comorbid disease [4]. Reported cases from Hong Kong and Nevada describe re-infection occurred 5 months and 48 days after primary infection, respectively [2,9]. In another study involving elderly patients, readmission to hospital was reported for two out of three patients 22 and 41 days after the first attack [4]. In our study, the time from last negativity to re-positive of SARS-CoV-2 PCR tests were 100 and 104 days and both cases were mild (Figure 1C). The cases did not need hospitalization in either infection period. In the first infection attack of the first case, there were findings compatible with COVID-19 in the chest CT, while the CT in the re-infection period was normal. The chest CT findings were the opposite for the second case (Table 1).

Conclusions

In light of the current studies we have examined, we can hypothesize that it is possible for healthcare workers who have intensive and close contact with infected individuals to suffer from COVID-19 disease more than one time. This issue may cause the health system to collapse, especially in countries with poor health infrastructure. In addition to providing adequate personal protective equipment (PPE) and improving working conditions, new and effective strategies are needed to better protect healthcare workers. At the same time, healthcare workers especially those who have had COVID-19, should be aware of this serious issue, and should pay maximum attention to control measures without compromising.

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