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Case Series

Co-Occurrence of SARS-CoV-2 Infection and Inactivated SARS-CoV-2 Vaccination among Healthcare Workers

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The presented cases describe the concurrent SARS-CoV-2 infection and inactivated SARS-CoV-2 vaccination among eight healthcare workers (HCWs). These cases highlighted the importance of broad hospital screening during the COVID-19 vaccination campaign. Further study regarding the durability of antibody response induced by infection and first-dose vaccination is required to determine the appropriate time for giving a second dose of inactivated SARS-CoV-2 vaccine among these cases.

1. Introduction

Since the first coronavirus disease 2019 (COVID-19) case caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected in China in December 2019, the disease has spread rapidly worldwide. Indonesia is one of the Southeast Asian countries with a high number of confirmed and active COVID-19 cases [1]. Although preventive measures such as physical distancing, quarantine, and isolation effectively reduced the number of people becoming infected, the risk of SARS-CoV-2 infection persisted in the population without immunity against SARS-CoV-2. Therefore, the availability of the COVID-19 vaccine is essential to induce immunity and protect the population from SARS-CoV-2 infection.

In Indonesia, the COVID-19 vaccination campaign using inactivated SARS-CoV-2 vaccine (CoronaVac, Sinovac Life Sciences) started at the end of January 2021, initially prioritizing healthcare workers (HCWs). As CoronaVac is an inactivated vaccine containing a whole virus structure [2], vaccinated individuals would be expected to elicit antibodies against many SARS-CoV-2 antigens, such as antispike (anti-S) and antinucleocapsid (anti-N). The remarkable increase of neutralizing antibodies, spike-specific immunoglobulin G (IgG), and receptor-binding domain- (RBD-) specific IgG occurred on day 14 after the second dose of vaccination [3]. Although the most common adverse reaction was injection site pain, systemic reactions such as fever, fatigue, cough, myalgia, and headache have been reported after each injection [3, 4].

The following presented cases, showing the co-occurrence of the first time use of CoronaVac with positive SARS-CoV-2 RNA among HCWs, are important due to it raising several considerations related to (1) the possibility for misinterpretation of COVID-19 symptoms with the systemic adverse reaction of vaccine, (2) the possibility of a false-positive RT-PCR result caused by the vaccine, and (3) the safety and the durability of the immune response during the coincidental events of vaccination and SARS-CoV-2 infection.

2. Case Presentation

This is an eight-case series of HCWs who received the first dose of inactivated SARS-CoV-2 vaccine (CoronaVac) at the Siloam Teaching Hospital (Indonesia) on January 26, 2021. The time elapsed between the first dose of vaccination and the onset of symptoms ranged from 4 to 9 days (median time 6 days). HCWs were confirmed for SARS-CoV-2 detection

Table 1: COVID-19 cases among first-dose vaccinated healthcare workers (HCWs) at Siloam Teaching Hospital, Indonesia, January 26–February 9, 2021.

No.	Age	Sex	Occupation	Probable source of contamination	Symptoms	Comorbidities	Date of the 1st vaccine	Date of RT-PCR (+)	Date of symptoms	Indication for testing	Day of symptom onset[a]	Number of days from symptom onset to testing	Ct values target 1 (N)	Ct values target 2 (ORF1ab)	Hospitalization	Death
1	25	F	Nurse	Community	Fever, headache	None	01 February 2021	14 February 2021	10 February 2021	Symptoms	9	4	25.3	22.1	No	No
2	26	F	Staff	Community	Fever	None	29 January 2021	08 February 2021	02 February 2021	Symptoms	4	6	Neg	33.7	No	No
3	40	F	Nurse	Community	Fever, headache	None	04 February 2021	12 February 2021	10 February 2021	Symptoms	6	2	31.1	31.1	No	No
4	29	F	Nurse	Healthcare setting	Fever, cough	None	03 February 2021	17 February 2021	10 February 2021	Symptoms	7	7	16.1	16.5	No	No
5	31	M	Housekeeper	Community	Fever	None	05 February 2021	14 February 2021	10 February 2021	Symptoms	5	4	18.3	18.5	No	No
6	34	M	Staff	Healthcare setting	NA	None	01 February 2021	03 February 2021	Asymp	Exposure	NA	NA	31	31.5	No	No
7	41	F	Nurse	Healthcare setting	Fever, cough	Diabetes	01 February 2021	09 February 2021	07 February 2021	Symptoms	6	2	32.7	35.5	No	No
8	23	M	Nurse	Community	NA	None	02 February 2021	09 February 2021	Asymp	Exposure	NA	NA	18.1	18.5	No	No

[a]Considering the day of the first vaccination as day 0. NA, not applicable; Ct, cycle threshold; Asymp, asymptomatic; RT-PCR, reverse-transcriptase polymerase chain reaction; Neg, negative.

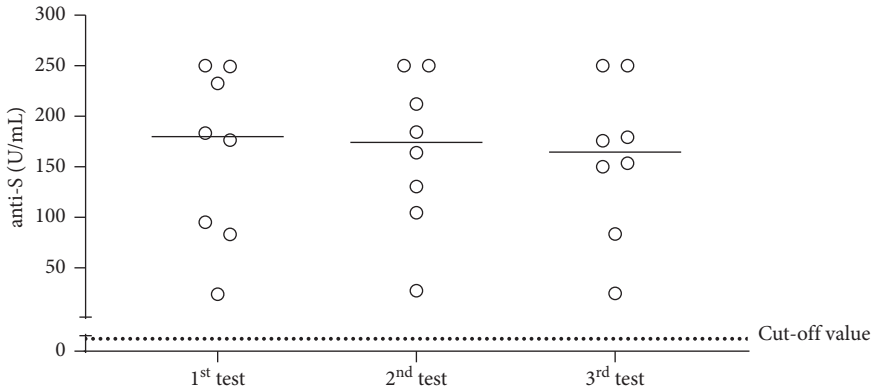

Figure 1: Serial measurement of anti-S antibodies' response among infected HCWs after acquiring the first-dose inactivated SARS-CoV-2 vaccination. Antibodies against RBD of the S protein (anti-S) concentration among eight HCWs who get SARS-CoV-2 infection after receiving the first dose of the inactivated SARS-CoV-2 vaccination are shown. The anti-S antibody concentration was measured on days 30, 60, and 90 after the RT-PCR positive result. The black dotted horizontal line represents the cutoff value (0.8) suggested by the manufacturer for positive interpretation of antibodies to SARS-CoV-2.

by RT-PCR in nasopharyngeal swab samples collected between 2 and 7 days after the onset of the symptoms (Table 1).

The mean age of vaccinated HCWs diagnosed with COVID-19 was 31.1 years (±6.8 years), and 3 (37%) were male. Most of the vaccinated and infected HCWs work as a nurse (63%). Five (63%) HCWs were infected in the community setting, and three (37%) were from a healthcare setting, who might have acquired it through contact with SARS-CoV-2-positive patients or coworkers.

Among these 8 HCWs, 6 (75%) were tested because they had COVID-19 symptoms. The most common COVID-19 symptoms were fever (75%), cough (25%), and headache (25%). Two (25%) asymptomatic COVID-19 HCWs were identified as a part of postexposure and regular hospital screening. Only one subject (HCW7) had preexisting medical conditions. The mean cycle threshold (Ct) values of the N gene and ORF1ab gene were 24.7 (±7.1) and 25.9 (±7.8), respectively. The total antibodies against S1-RBD protein (anti-S) were measured using Elecys anti-SARS-CoV-2 S assay and analyzed on the Cobas e601 platform (Roche Diagnostics, Switzerland). According to manufacturer's guidelines, sample values ≥ 0.8 U/mL were interpreted as positive for anti-S antibodies. The antibody measurement was performed at three time points: on days 30, 60, and 90 after the positive RT-PCR test (Figure 1). The result showed the seroconversion observed in all HCWs on day 30 after the positive RT-PCR test, and the anti-S antibody concentration continued to be stably detected until day 90. No significant difference of anti-S antibody concentration on days 30, 60, and 90 after the RT-PCR positive test was observed ($p > 0.05$, Figure 1). The clinical outcomes of vaccinated HCWs with COVID-19 were favourable in all cases, with no hospitalization and no mortality observed among study cases.

3. Discussion

Compared to the general population, HCWs have a higher risk of SARS-CoV-2 infection, and the infected HCWs possess a greater risk of transmitting and spreading the infection in hospital and community settings [5]. Therefore, HCWs were prioritized to receive the vaccine in the initial COVID-19 vaccination program in Indonesia. However, in the situation where the vaccination program coincides with the high daily confirmed cases of COVID-19 like in Indonesia, more cases like described above will be expected.

Fever, the most prevalent symptom observed among COVID-19 HCWs in this study, is the common systemic reaction after vaccination with an inactivated COVID-19 vaccine [3, 4]. Consequently, the misdiagnosis of COVID-19 with vaccination side effects is likely to occur. Considering HCWs represent a high-risk group for SARS-CoV-2 exposure, the presence of any symptoms after vaccination cannot be ignored as a vaccination side effect until a further diagnostic test can rule out the COVID-19 diagnosis. In addition, most HCWs acquired the infection through community settings. This result underscores the importance of the high-level awareness of reported symptoms from vaccinated HCWs, particularly in a region where daily confirmed COVID-19 cases are still high. Furthermore, two infected HCWs did not experience any symptoms, which can be a potential transmission source in hospital and community settings [6]. Altogether, these results imply that the hospital needs to be vigilant and introduce regular COVID-19 testing for all HCWs.

Although the false-positive RT-PCR result after vaccination has been reported after administrated intranasal live attenuated influenza vaccine (LAIV) [7, 8], the positive RT-PCR among vaccinated HCWs is possibly not due to the COVID-19 vaccine. The vaccine administration of LAIV and specimen collection for testing were in the same site, resulting in the possibility of positive detection by RT-PCR [7, 8]. In contrast, the COVID-19 vaccine was administrated intramuscularly into deltoid muscle, in which the protein antigen is taken up by antigen-presenting cells (APCs) and then trafficked to the lymph node for adaptive immune cell activation. As a result, it is possibly unlikely to find the trace of the vaccine component in the specimen collection site for RT-PCR.

Furthermore, we observed the favourable clinical outcomes of COVID-19 among vaccinated HCWs, as all of them did not need hospitalization and no one succumbed. This result may indicate that the coincidental inactivated COVID-19 vaccine administration, and SARS-CoV-2 infection seemed to be well tolerated and not causing the overregulation of the immune system. The seroconversion of anti-S was observed in all HCWs after 30 days of the RT-PCR test. Anti-S concentration was heterogeneous among HCWs (range 23.8 to 250, median 179.8), as has been widely described [9, 10]. The antibody was relatively stable until 90 days after the RT-PCR test. Considering that all presented HCW cases in this study were not eligible for acquiring a second dose of the inactivated SARS-CoV-2 vaccine, the longer-term follow-up is required to investigate the durability of observed anti-S antibodies beyond this time point in order to decide the appropriate time for giving a second dose of COVID-19 vaccine among these study cases.

Data Availability

The data used to support the findings of this study are included within the article.

Ethical Approval

This study was approved by the research ethics committee of the Faculty of Medicine of Pelita Harapan University (No: 137/K-LKJ/ETIK/IV/2021).

Consent

No written consent for publication has been obtained from the patients as there are no patient identifiable data included in this case series.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

CC, RW, and NL designed the research study, interpreted the results, and wrote the manuscript , CC acquired data, and CC, RW, NL, and IS analyzed the data.

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