



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Case Report

A patient presenting with ARDS after COVID-19 vaccination: A COVID-19 case report



Ayşe Sahin Tutak^{a,*}, Fatih Söylemez^b, Hazal B. Konuk^b, Erkan Çakmak^b,
Bülent Karakaya^b, Ali Doğan^b, Hakan S. Sayiner^c, Selçuk Aksöz^c, Mehtap Alev^c

^a Department of Internal Medicine, Adiyaman University School of Medicine, Adiyaman, Turkey

^b Department of Internal Medicine, Adiyaman University of Training Hospital, Adiyaman, Turkey

^c Department of Infectious Disease, Adiyaman University School of Medicine, Adiyaman, Turkey

ARTICLE INFO

Article history:

Received 4 May 2021

Received in revised form 27 May 2021

Accepted 29 May 2021

Keywords:

COVID-19

SARS-CoV IgG/M

ARDS (Acute Respiratory Distress Syndrome)

ABSTRACT

COVID-19 is a disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The introduction of vaccines against COVID-19 caused great enthusiasm around the world as immunization might end the pandemic. However, it was previously stated that COVID-19 cases would rarely continue to occur despite immunization. Fourteen days after the second dose of the vaccine, a 66-year-old male patient with a negative COVID-19 PCR test result and high levels of IgG and low levels of IgM-A against SARS-CoV-2 was admitted to our intensive care unit (ICU) due to the clinical picture of Acute Respiratory Distress Syndrome (ARDS). We aimed to stress the need for continuing preventive measures in vaccinated individuals, too, by presenting the clinical findings of the patient, who was considered to have developed ARDS due to COVID-19, as high levels of IgG and IgM-A against SARS-CoV-2 were detected on day 8 during ICU admission.

© 2021 The Authors. Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Introduction

COVID-19 is a disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2). The incubation period of the disease varies from 2 to 14 days (median 5 days). Although the disease is asymptomatic in some patients, it may progress to pneumonia, respiratory failure, and even death at the end of the first week in some cases [1].

Since vaccines against COVID-19 have become available in recent months, it is too early to know the length of the protection period against COVID-19 after vaccination. Studies are ongoing to answer this question. Even though the available data are encouraging by showing that most survivors of COVID-19 have developed an immune response that enabled protection against reinfection for at least some time, the efficacy and the length of such protection and protective levels of SARS-CoV-2 IgG antibodies still need to be established.

In this study, we aimed to present the clinical findings of a patient, who was treated for acute respiratory distress syndrome (ARDS) in the intensive care unit (ICU) despite the presence of high

levels of SARS-CoV-2 IgG antibodies developing after vaccination, and thus, to stress the need for continuing preventive measures.

Case report

A 66-year-old male patient was admitted to the emergency department with shortness of breath. The medical history of the patient informed that he had had fatigue for three days and developed shortness of breath a day ago. The patient was dyspneic and hypoxic and had oxygen saturation levels ranging from 85 to 90 under oxygen therapy that was administered at a rate of 15–20 l/min through a nasal cannula and an oxygen reservoir bag in the emergency department. The result of the PCR test for COVID-19 was negative (it has been worked on the PCR ROCHE BIO-RAD Kiagen device, RTA kit). In the thoracic CT sections, the patient had ground-glass densities diffusely. On the posterior-anterior chest X-ray (PA-CXR), diffuse infiltration was observed bilaterally (Fig. 1a, c, d). The patient was admitted to ICU due to the diagnosis of COVID-19 pneumonia. The patient had received the second dose of the COVID-19 vaccine 14 days ago. The patient did not have comorbidity. Despite the administration of a combination of high-flow oxygen (HFO) therapy and delivery of oxygen via a reservoir mask (RMO), non-invasive CPAP treatment was initiated when the oxygen saturation levels of the patient dropped to levels of 78–80.

* Corresponding author.

E-mail address: aysesahintutak@hotmail.com (A. Sahin Tutak).

Table 1
Change in the laboratory test results of the patient on days 1 and 8.

	Day 1 of hospitalization	Day 8 of hospitalization
SARS-CoV-2 IgM-A	6.17	14 (normal: ≥ 8)
SARS-CoV-2 IgG	30.5	48.8 (normal: ≥ 6)
COVID-19 PCR	Negative	Negative
D-dimer	3980	2340
Procalcitonin	2.8	8.2
CRP	18.8	8
Ferritin	1106	1218
Fibrinogen	739	459
WBC	11,200	16,700
Lymphocyte	312	178
PaO ₂	45 (without oxygen)	58 (under mechanical ventilation, FiO ₂ 100%)
Albumin	3.1	2.1
pH	7.37	7.26
Creatinine	0.9	3.71

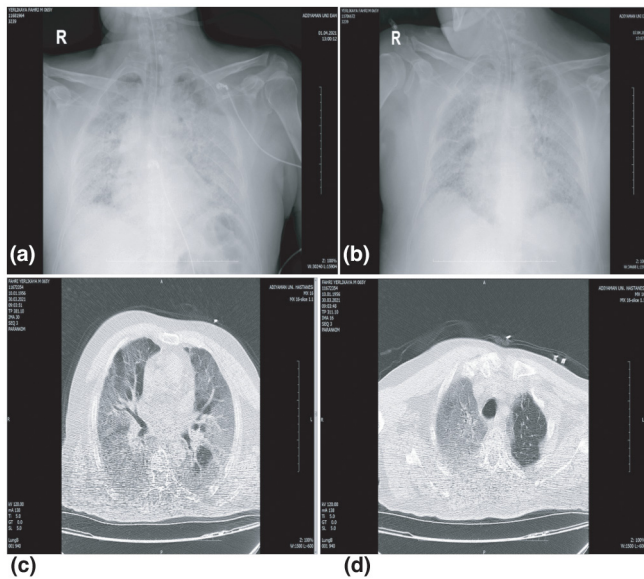


Fig. 1. xxx.

Despite the treatment, the patient with a respiratory rate of >30 and a PaO₂/FiO₂ ratio of ≤ 100 (PEEP ≥ 5 cmH₂O) was considered to have severe ARDS and was intubated electively on the first day of admission. There was no reproduction ETA cultures. Tested Adenovirus, influenza, parainfluenza, respiratory syncytial virus, mycoplasma and legionella negative. In addition to broad-spectrum antibiotherapy (Ceftriaxone and levofloxacin were added to the treatment while the patient was admitted to the ICU. Antibiotics were stopped at the 48th hour of hospitalization due to the lack of growth in the cultures and poor general condition, and the treatment was changed to vancomycin + imipenem. Colimicin was added to the treatment when acinetobacter growth occurred in sputum culture), methylprednisolone therapy was started at a dose of 250 mg/day. Favipiravir, low molecular weight heparin (LMWH), and high-dose ascorbic acid intravenously were added to the treatment because of the suspicion of COVID-19 causing ARDS. The patient had high procalcitonin levels, therefore, he was not considered suitable for receiving tocilizumab therapy. The PCR test for COVID-19 on the endotracheal aspiration fluid, which was collected after intubating the patient, was reported as negative. The antibody tests using the ELISA method (ELISA GRIFOLS branded TIRITURUS model has been studied) at the time of the second PCR test showed SARS-CoV-2 IgG and IgM-A levels of 30.5 (≥ 6) and 6.17 (≥ 8), respectively. The patient was placed in the prone and supine positions alternately. Saturation levels measured every 12–16 h showed a decreasing

trend. PA-CXR findings progressed in time (Fig. 1b). The repeated COVID-19 PCR test on day 8 of hospitalization was negative and the levels of IgG and IgM-A to SARS-CoV-2 were 48.80 (≥ 6) and 14 (8), respectively (Table 1). The patient died on day 9 of hospitalization.

Discussion

Studies using serological tests have reported that positive SARS-CoV-2 IgM and IgG antibody levels are detected after median periods of five and four days, respectively, following a positive COVID-19 PCR result [12]. When we admitted our patient to ICU, IgG was positive and IgM was negative. Despite the high IgG level, the diagnosis of ARDS due to COVID-19 was confirmed because IgM became positive on day 8 of admission. Although the COVID-19 vaccines in use have been shown to be highly effective, the efficacy of none of them will be 100%. After receiving a single dose of vaccine, immunity will usually develop after two weeks following vaccination. In double-dose vaccination regimens, the administration of both doses is necessary to achieve optimum immunization. It is estimated that vaccines against COVID-19 will enable immunization at least to a certain extent against new virus variants and be effective in preventing severe cases and death.

The imaging test findings (Fig. 1) and the clinical picture of the case presented in this study were compatible with COVID-19 pneumonia but the PCR test results on days 1 and 8 of the patient's ICU admission were reported as negative. Although the nucleic acid amplification test using RT-PCR is the general standard diagnostic test for COVID-19, the rate of false-negatives is as high as 20% [2]. Previous studies reported that potential causes of false-negative results included faulty laboratory techniques, insufficient viral loads in the samples, inappropriate transport of specimens, and inadequate sample collection methods [3,4].

Our patient was admitted to ICU on day 14 after receiving the second dose of the vaccine, due to the diagnosis of severe ARDS (PaO₂/FiO₂ ≤ 100) [5] and underwent elective intubation. At the time of ICU admission, the patient's IgG level to SARS-CoV-2 was high and IgM-A level was low (Table 1). On day 8 of ICU admission, his IgM-A level increased confirming the definite diagnosis of ARDS due to active COVID-19. In a study using ELISA test, SARS-CoV-2 IgG antibodies were detected in less than 60% of the samples on days 6 and 10 following the onset of the disease [6,7]. In our patient, the initial high level of IgG was associated with the vaccination.

For the patient of this case report, favipiravir with established efficacy was included in the treatment as a loading dose and maintenance doses [8].

ARDS is partially caused by the host's immune response. Although corticosteroids suppress the inflammation in the lungs, they inhibit the immune response along with the clearance of the pathogen at the same time. It has been reported that corticosteroid

use in COVID-19 patients may reduce mortality in moderate-to-severe ARDS [9]. Corticosteroids were included in the treatment of our patient starting from the first day.

Tocilizumab is a recombinant monoclonal IgG1 antibody and an IL-6 antagonist. Studies have shown that the drug reduces the need for mechanical ventilation and mortality in intensive care patients. The major side effect associated with the use of tocilizumab has been reported as the susceptibility to secondary infections [10]. In our patient, as the level of procalcitonin was high and there was a secondary infection, tocilizumab could not be added to the treatment. Empirical treatment with broad-spectrum antibiotics was started by the infectious diseases specialist. LMWH and dipyridamole were also included in the treatment. Our patient was brought to prone and supine positions alternatively because oxygen saturation levels increased in the prone position [11].

Studies using serological tests have reported that positive SARS-CoV-2 IgM and IgG antibody levels are detected after median periods of five and four days, respectively, following a positive COVID-19 PCR result [12]. When we admitted our patient to ICU, IgG was positive and IgM was negative. Despite the high IgG level, the diagnosis of ARDS due to COVID-19 was confirmed because IgM became positive on day 8 of admission. Although the COVID-19 vaccines in use have been shown to be highly effective, the efficacy of none of them will be 100%. After receiving a single dose of vaccine, immunity will usually develop after two weeks following vaccination. In double-dose vaccination regimens, the administration of both doses is necessary to achieve optimum immunization. It is estimated that vaccines against COVID-19 will enable immunization at least to a certain extent against new virus variants and be effective in preventing severe cases and death.

The World Health Organization recommends that anyone should have access to the safe and effective COVID-19 vaccines as soon as possible, with the prioritization of those with the highest risk of severe disease and death. However, considering that our patient died of ARDS despite the high SARS-CoV-2 IgG level, we suggest that protective measures should be continued even after vaccination, until the pandemic is over.

Funding

No funding sources.

Competing interests

None declared.

Ethical approval

Not required.

References

- [1] Singhal T. A review of coronavirus disease-2019 (COVID-19). *Indian J Pediatr* 2020;87(April (4)):281–6.
- [2] Li D, Wang D, Dong J, Wang N, Huang H, Xu H, et al. False-negative results of real-time reverse-transcriptase polymerase chain reaction for severe acute respiratory syndrome coronavirus 2: role of deep-learning-based CT diagnosis and insights from two cases. *Korean J Radiol* 2020;21(4):505–8.
- [3] Li Y, Yao L, Li J, Chen L, Song Y, Cai Z, et al. Stability issues of RT-PCR testing of SARS-CoV-2 for hospitalized patients clinically diagnosed with COVID-19. *J Med Virol* 2020;92(7):903–8.
- [4] Wang Y, Kang H, Liu X, Tong Z. Combination of RT-qPCR testing and clinical features for diagnosis of COVID-19 facilitates management of SARS-CoV-2 outbreak. *J Med Virol* 2020;92(6):538–9.
- [5] Siegel MD, Siemieniuk R, Parsons PE, Guyatt G. Acute respiratory distress syndrome: supportive care and oxygenation in adults. *UptoDate* 2021.
- [6] Liu W, Liu L, Kou G, Zheng Y, Ding Y, Ni W, et al. Evaluation of nucleocapsid and spike protein-based ELISAs for detecting antibodies against SARS-CoV-2. *J Clin Microbiol* 2020;58(6):e0046.
- [7] Mazzini L, Martinuzzi D, Hyseni I, Benincasa L, Molesti E, Casa E, et al. Comparative analyses of SARS-CoV-2 binding (IgG, IgM, IgA) and neutralizing antibodies from human serum samples. *J Immunol Methods* 2020:112937. Epub2020/12/01.
- [8] Dong L, Hu S, Gao J. Discovering drugs to treat coronavirus disease 2019 (COVID-19). *Drug Discov Ther* 2020;14:58–60.
- [9] Villar J, Ferrando C, Martinez D, Ambros A, Munoz T, Soler JA, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomized controlled trial. *Lancet Respir Med* 2020;8:267–76.
- [10] Xu X, Han M, Li T, Sun W, Wang D, Fu B, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci USA* 2020;117, 10970–5,40.
- [11] Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. Covid-19 does not lead to a “typical” acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2020;201:1299–300.
- [12] Suhandynata RT, Hoffman MA, Kelner MJ, McLawhon RW, Reed SL, Fitzgerald RL. Longitudinal monitoring of SARS-CoV-2 IgM and IgG seropositivity to detect COVID-19. *J Appl Lab Med* 2020;5(September (5)):908–20.