Absence of neutralizing activity in serum 1 year after successful treatment with antivirals and recovery from MERS in South Korea

We evaluated the neutralizing activity in serum from three patients >1 year after recovery from Middle East respiratory syndrome (MERS) associated with mild pneumonia treated with antivirals during the MERS outbreak in South Korea at 2015. The neutralizing activity in serum was measured by pseudovirus inhibition assays. Three-fold diluted serum of subjects showed only 9.7%, 10.3%, and 2.2% reductions in relative light units. So, significant neutralizing activity was not demonstrated in any sera of three patients with mild pneumonia >1 year after being successfully treated with antiviral agents and recovering from MERS coronavirus infection.

Keywords: Middle East respiratory syndrome coronavirus, Neutralizing antibodies, Serum
the patient was treated with a combination of interferon-

mild dyspnea commencing 4 days before diagnosis. Chest

fever, myalgia, sore throat, cough, sputum production, and

where MERS-CoV infections were diagnosed in a multi-bed

MERS-CoV between 25 and 29 May 2015 at another hospital,

Subject 2 was a 33-year-old woman diagnosed with MERS-

without any complications, and a blood sample was collected

15-24 June 2015. Repeated MERS-CoV PCR tests showed neg

lopinavir/ritonavir (400 mg/100 mg orally every 12 hours) from

13 June 2015 showed pneumonic consolidation on the right

respiratory symptoms, but chest radiography performed on

did not have a cough, sputum production, dyspnea, or other

ver, myalgia, and headache appeared after 10 June 2015. He

ing patient transfer on 5-6 June 2015. Symptoms including fe

CoV infection by real time polymerase chain reaction (PCR)

Subject 1 was a 38-year-old man diagnosed with MERS-

presented as percentage inhibition of relative light units (RLU).

Control serum was collected from a healthy volunteer.

Subject 1 was a 38-year-old man diagnosed with MERS-

infection by real time polymerase chain reaction (PCR)
of nasopharyngeal aspirate on 13 June 2015. He was an am

ambulance driver exposed to a MERS-CoV infected patient dur

during patient transfer on 5-6 June 2015. Symptoms including fe

ver, myalgia, and headache appeared after 10 June 2015. He

did not have a cough, sputum production, dyspnea, or other respi

atory symptoms, but chest radiography performed on 13 June 2015 showed pneumonic consolidation on the right lower lung field. He was treated with combination of interferon-α2a, ribavirin, and lopinavir/ritonavir from 16-28 June 2015. Two consecutive negative results of MERS-CoV PCR were confirmed on 27 and 28 June 2015. The fever subsided 3 days after initiation of treatment associated with improvement on chest radiography. Full recovery was achieved without any complications, and a blood sample was collected on 29 September 2016.

All subjects had no underlying comorbidities.

A Western blot to identify the incorporation of MERS-CoV S protein in the packaged MERS-CoV pseudovirus showed a clear band corresponding to the MERS-CoV S protein.

As shown in Fig. 1, three-fold diluted serum of subjects 1 and 2 showed only 9.7% and 10.3% reductions in RLU, respectively, while that of subject 3 showed only a 2.2% reduction.

![Fig. 1. Inhibitory activity of patients’ sera against Middle East respiratory syndrome coronavirus pseudovirus infection. Three-fold diluted serum of subjects 1 and 2 showed only 9.7% and 10.3% reductions in relative light unit (RLU), respectively, while that of subject 3 showed only a 2.2% reduction. Control serum was collected from a healthy volunteer.](https://doi.org/10.7774/cevr.2019.8.1.86)
The findings of this study are inconsistent with previous observations. A previous study on severe acute respiratory syndrome coronavirus (SARS-CoV) infection found that 93.88% and 89.58% of patients were IgG positive at 1- and 2-year post-symptom onset, respectively [6]. However, 3 years later, only 53.57% of the population had SARS-CoV specific IgG. A study on antibodies against MERS-CoV, including neutralizing antibodies, showed antibody persistence in six of seven individuals (86%), 34 months after the 2012 MERS-CoV outbreak in Jordan [7]. All seven subjects had respiratory symptoms and few underlying diseases, and five had substantial pneumonia. Mild or asymptomatic MERS-CoV infections could potentially be associated with development of lower levels of MERS-CoV neutralizing antibodies over time [8]. Patients from the above study might not have been treated with antivirals. Subjects in our study were also young and healthy, with mild pneumonic consolidations at admission. Moreover, all patients in our study were treated with interferon-α, ribavirin, and lopinavir/ritonavir. Antiviral treatment for MERS associated with mild pneumonia might decrease viral replication and reduce antibody responses in the early stages of the diseases, resulting in the identified low-level neutralizing activity within convalescent serum.

The small number of subjects is an important limitation of this study. Furthermore, we could not evaluate paired sera comparing the early stage of illness and 1-year post-recovery. The viral load at early infection time may be associated with the neutralizing antibody and the disease outcome, but we could not collect data on the viral load of subjects. In addition, we could not validate the pseudovirus inhibition assay with positive control, and subjects without treatment could not be enrolled for comparisons.

In conclusion, neutralizing activity was not demonstrated in any sera of three patients with mild pneumonia >1 year after being successfully treated with antiviral agents and recovering from MERS-CoV infection.

ORCID

Jun Yong Choi  https://orcid.org/0000-0002-2775-3315

Jin Ok Oh  http://orcid.org/0000-0002-2086-1751
Jin Young Ahn  https://orcid.org/0000-0002-3740-2826
Heun Choi  https://orcid.org/0000-0002-9622-9381
Jung Ho Kim  https://orcid.org/0000-0002-5033-3482
Hye Seong  https://orcid.org/0000-0002-5633-7214
Hu Jin Jeong  https://orcid.org/0000-0003-4025-4542
Nam Su Ku  https://orcid.org/0000-0002-9717-4327
Joon-Sup Yeom  https://orcid.org/0000-0001-8940-7170
Jae-Phil Choi  https://orcid.org/0000-0003-4805-7930

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