

# Glucocorticoid therapy delays the clearance of SARS-CoV-2 RNA in an asymptomatic COVID-19 patient

To the Editor,

Since December 2019, the outbreak of severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) started in Wuhan China, has quickly spread to all continents except Antarctica and become a global health concern.<sup>1</sup> However, there are still no specific antiviral medicines or vaccines recommended for SARS-CoV-2 infection. Meanwhile, more and more controversial treatments emerged including antiviral therapy (remdesivir, ribavirin, and chloroquine), glucocorticoid therapy, and extracorporeal support.<sup>2</sup>

Systematic corticosteroids treatment was recommended to be an adjuvant therapy according to the 7th trial version of Diagnosis and treatment Scheme for Pneumonitis with 2019-nCoV infection released by the China's National Health Commission.<sup>3</sup> Moreover, suspected advises against the use of corticosteroids were presented according the current interim guidance from WHO on clinical management of SARS-CoV-2 infection,<sup>4</sup> although corticosteroids were widely used in the patients with SARS-CoV or Middle East respiratory syndrome (MERS)-CoV. Recent report showed that a 47-year-old woman with long-term use of glucocorticoids showed atypical infections and was eventually confirmed by tested positive of antibody on day 40 after she left Wuhan.<sup>5</sup> Therefore, more attention must be paid to the COVID-19 patients receiving glucocorticoid therapy.

At present, twice successively negative detections of SARS-CoV-2 remain important index for discharged COVID-19 patients, and the median hospital stay is 10 days.<sup>6</sup> Here, we reported an asymptomatic COVID-19 patient with persistent positive detection of SARS-CoV-2 RNA for 3 weeks, and proposed that glucocorticoid therapy might not only cause atypical infections, but also delay the clearance of SARS-CoV-2 RNA.

On 24 January, a 48-year-old man with fever for 4 days was admitted to the hospital, and he had a history of short stay in Wuhan. Moreover, he had a 10-year history of asthma, and persistently received the inhaled glucocorticoids (salmeterol/fluticasone) at a dose of 50/250  $\mu$ g twice daily. On admission, he developed low-grade fever and cough. Computed tomography images showed the increase of ground-glass opacity in the bilateral superior lobe. Nasopharyngeal swab sample was collected with the standard process as previously described.<sup>7</sup> RNA was extracted with the protease K-magnetic beads (BioPerfectus Technologies, China). Reverse transcriptase-polymerase chain reaction (RT-PCR) assay was performed on 7500 Thermal Cycler (ABI) and the sequences of SARS-CoV-2 were amplified by targeting three genes (*ORF1ab*, *N*, *E* genes) (Liferiver Bio-Tech, China). Eventually, this

patient was diagnosed with mild COVID-19 combined with the positive result of SARS-CoV-2 RNA.

From 25 to 28 January, he received efficient antiviral treatment, including oseltamivir, lopinavir/ritonavir, and IFN $\alpha$ -2b. Considering the asthma attack, the patient felt chest tightness to receive the atomization budesonide and terbutaline from 25 January. From 28 January, he was treated with methylprednisolone to prevent the exacerbation. On 31 January, he had the obvious improvement in respiratory symptoms. From 1 February, he developed a wheeze and paroxysmal cough, and was administered with budesonide and terbutaline to reduce the airway hyper-responsiveness. On 10 February, he fully recovered, and was only required to take regular treatment with the inhaled salmeterol/fluticasone. SARS-CoV-2 RNA detection was negative in nasopharyngeal swab sample, while positive in the sputum sample obtained by nebulization. Same results were successively obtained in the subsequent SARS-CoV-2 RNA detections on 16, 19, and 22 February. Until 1 March, no SARS-CoV-2 RNA was detected in the nasopharyngeal swab and sputum samples.

Corticosteroids are widely used to prevent lung injury caused by severe community-acquired pneumonia due to their excellent pharmacological effects on the suppression of exuberant and dysfunctional systematic inflammation.<sup>8</sup> However, glucocorticoids can exert both stimulating and inhibitory effects on the immune response in the different phases of an infection.<sup>9</sup> Here, we proposed that SARS-CoV-2 RNA clearance would be delayed due to the immunosuppressive effect of higher dose of glucocorticoids. In this research, the COVID-19 patient with asthma was persistently treated with inhaled glucocorticosteroids for 10 years. Other glucocorticosteroids, such as inhaled budesonide/terbutaline and intravenous methylprednisolone, were used to control asthma attack during the hospitalization. We believed glucocorticosteroids inhibited the immune function of this patient, playing a critical role in such delayed clearance of SARS-CoV-2 RNA. Therefore, more attention must be paid to the COVID-19 patients receiving glucocorticoid therapy, and both specimens from upper and lower respiratory tracts must be collected for SARS-CoV-2 RNA detection before hospital discharge.

## ACKNOWLEDGMENT

The study was supported by grants from Key Research and Development Program of Weihai (Weihai Key Laboratory of Medical Microbiology and Immunology, 2017GGH08).

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

Shu-Qing Ma<sup>1</sup>  
Jing Zhang<sup>1,2</sup>  
Yu-Shan Wang<sup>3</sup>  
Jun Xia<sup>4</sup>  
Peng Liu<sup>1</sup>  
Hong Luo<sup>3</sup>  
Ming-Yi Wang<sup>1</sup> 

<sup>1</sup>Department of Central Lab, Weihai Municipal Hospital, Cheeloo College of Medicine, Shandong University, Weihai, Shandong, China

<sup>2</sup>Department of Infectious Diseases, Weihai Municipal Hospital, Cheeloo College of Medicine, Shandong University, Weihai, Shandong, China

<sup>3</sup>School of Laboratory Medicine, Dalian Medical University, Dalian, Liaoning, China

<sup>4</sup>Department of Infectious Diseases, Weihai Chest Hospital, Weihai, Shandong, China

#### Correspondence

Hong Luo, School of Laboratory Medicine, Dalian Medical University, 116044 Dalian, Liaoning, China.

Email: [dmluluo@163.com](mailto:dmluluo@163.com)

Ming-Yi Wang, Department of Central Lab, Weihai Municipal Hospital, Cheeloo College of Medicine, Shandong University, 264200 Weihai, Shandong, China.

Email: [wangmingyi1973@outlook.com](mailto:wangmingyi1973@outlook.com)

#### ORCID

Ming-Yi Wang  <http://orcid.org/0000-0002-7710-4743>

#### REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382:727-733.
2. Zhang C, Huang S, Zheng F, Dai Y. Controversial treatments: an update understanding of the coronavirus disease 2019. *J Med Virol*. 2020. <http://doi.org/10.1002/jmv.25788>
3. New coronavirus pneumonia prevention and control program (7nd ed.) (in Chinese). National Health Commission of the People's Republic of China. March 4, 2020. <http://www.nhc.gov.cn/xcs/zhengcwj/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf>. Accessed March 3, 2020.
4. WHO. World Health Organization; Geneva: Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. January 28, 2020. [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected). Accessed March 13, 2020.
5. Han Y, Jiang M, Xia D, et al. COVID-19 in a patient with long-term use of glucocorticoids: a study of a familial cluster. *Clin Immunol*. 2020; 214:108413.
6. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069.
7. Wu J, Liu J, Li S, et al. Detection and analysis of nucleic acid in various biological samples of COVID-19 patients. *Travel Med Infect Dis*. 2020. <http://doi.org/10.1016/j.tmaid.2020.101673>
8. Jiang S, Liu T, Hu Y, et al. Efficacy and safety of glyco-corticoids in the treatment of severe community-acquired pneumonia: a meta-analysis. *Medicine (Baltimore)*. 2019;98(26):e16239.
9. Isidori AM, Pofi R, Hasenmajer V, Lenzi A, Pivonello R. Use of glucocorticoids in patients with adrenal insufficiency and COVID-19 infection. *Lancet Diabetes Endocrinol*. 2020;8:472-473.