

Coronavirus Pandemic

Three elderly asymptomatic SARS-CoV-2 infected patients in ICU

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Abstract

Previous studies on asymptomatic COVID-19 carriers indicated that asymptomatic infections always occurred in people in community or patients in general wards, prone to be young and middle aged people. Limited data are available for asymptomatic infections in critically ill patients in intensive care unit or elderly people. Here we reported three elderly asymptomatic SARS-CoV-2 infected patients in intensive care unit. These three elderly patients had negative CT images and 14 consecutive negative RT-PCR test results, with dynamic changes in IgG-IgM antibody levels without any clinical symptoms, which might be related to their weakened immune responses due to elder age (over 85 years old) and the history of hypertension. Therefore, combining nucleic acid RT-PCR and the IgM-IgG antibody test can provide more accurate SARS-CoV-2 infection diagnosis, especially for elderly asymptomatic patients.

Key words: asymptomatic; COVID-19; elder age; ICU; IgG.

J Infect Dev Ctries 2022; 16(2):265-267. doi:10.3855/jidc.13405

(Received 06 July 2020 – Accepted 11 March 2021)

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Introduction

Previous studies on asymptomatic COVID-19 carriers indicated that asymptomatic infections always occurred in people in community or patients in general wards, prone to be young (< 15 years old) [1] and middle aged people (30 to 49 years old) [2]. Limited data are available for asymptomatic infections in critically ill patients in intensive care unit (ICU) or elderly people. Here we reported three elderly asymptomatic SARS-CoV-2 infected patients in ICU.

Methodology

Three hospitalized patients were treated in ICU at Zhongnan Hospital of Wuhan University, Wuhan, China from Feb 12 to March 25, 2020. The ICU they stayed is a non-isolated ward. Clinical records, laboratory parameters and radiological findings were collected from electronic medical records.

Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test, SARS-CoV-2 IgG-IgM antibody and chest CT scans were performed every 3-5 days. The RT-PCR tests were performed on throat swabs or sputum specimens following a previously described method [3]. The RT-PCR test kits were recommended by the Chinese Center for Disease Control and Prevention (BioGerm, Shanghai, China).

Venous blood was drawn to test SARS-CoV-2 IgG-IgM antibody (Medomics, Nanjing, China). All samples were processed at the Department of Clinical Laboratory of Zhongnan Hospital.

This study was approved by the Medical Ethical Committee of Zhongnan Hospital of Wuhan University. Written informed consent was obtained from each patient.

Results

Patient 1, 85 years old, underwent cardiopulmonary resuscitation because of a sudden cardiac arrest. Patient 2, 91 years old, were admitted to ICU with esophageal fistula after extraction of esophageal foreign bodies. Patient 3, 95 years old, required kidney replacement therapy due to acute cardiogenic pulmonary edema.

All three patients were male and the age range was 85 to 95 years. None of them reported a history of epidemiological exposure to COVID-19 before they admitted to ICU. No family members were infected. All patients had the underlying comorbidity of hypertension and denied the history of diabetes, COPD, malignancy or other chronic illnesses.

Patient 1 and patient 2 developed fever without chills, with body temperature fluctuating from 36.5 to 38 °C, but none presented high fever (body temperature

greater than 39), which were discussed by clinical expert panel and considered as an infusion of intravenous albumin, esophageal fistula infection respectively and were therefore not grouped as cases with symptoms caused by COVID-19. Patient 3 presented no fever. None of them had cough, expectoration, dyspnea or digestive tract symptom.

Normal white cell count and lymphopenia ($< 1.0 \times 10^9/L$ cells per L), elevated concentration of C-reactive protein and D-dimmer were observed in three patients. Prothrombin time, creatine kinase-MB, hypersensitive troponin I, lactate dehydrogenase and total bilirubin of these three patients were not abnormal. All tests for influenza A and B viruses were negative. Chest CT of patient 1 showed bilateral pleural effusion caused by hypoproteinemia. CT imaging of patient 3 showed bilateral precipitation pneumonia. CT imaging of all three showed no ground-glass opacification or consolidation.

The RT-PCR test were repeated every three to four days from Feb 12 to March 25, 2020 and all were negative. An additional RT-PCR test was performed on sputum using a kit from a different manufacturer and the results were also negative for all patients. IgG-IgM were repeated every four days from March 4 to March 25, 2020. IgG was 4 times greater than normal for the first time, then decreased gradually, and normal after the third time. All IgM were negative in the course of the disease (Table 1).

As of Mar 30, patient 1 remained in ICU, patient 2 was discharged and patient 3 was transferred to the general ward.

Discussion

These three elderly patients had negative CT images and 14 consecutive negative RT-PCR test results, with dynamic changes in IgG-IgM antibody levels without any clinical symptoms. They were diagnosed as asymptomatic SARS-CoV-2 infected patients according to the 7th Guidelines for COVID-19 published by the National Health Commission of the People's Republic of China (NHC) [4].

The ICU they stayed is a non-isolated area. We attributed the infections to contact with an infected but potentially presymptomatic nursing staff working in ICU, while other patients in the ICU were not infected with COVID-19. These might be related to their weakened immune responses due to elder age. On the other hand, all three patients had the history of hypertension, which might increase the possibility of infection [5].

Previous studies reported that IgG antibody of SARS could persist for more than 3 months [6,7]. Since SARS-CoV-2 shares a 79% nucleotide identity with the sequence of SARS-CoV [8], its antibody duration is assumed to be similar. In these series, IgG antibody showed positive results, IgM remained negative, indicating these three patients were infected some time ago. However, IgG-positive results lasted only 14 days, and soon became negative. These might due to low levels of virus loads-NA test results remained persistent negative or limitation to a small number of patients. Further study on large number of cohort needs to be done.

In addition, some evidence suggested that age may be risk factor for poor outcome [9]. As of Mar 30, all the three patients were alive. These might because of their no underlying disease except hypertension. What is more, patient 1 and patient 3 were survivors of the China's War of Liberation, indicating they were in better health than ordinary people.

For asymptomatic patients over 85 years of age, there may be differences in NA test results, dynamic changes in IgG antibody and outcome compared to patients of other age ranges. Considering asymptomatic carriers transmission of COVID-19, combining NA RT-PCR and the IgM-IgG antibody test can provide more accurate SARS-CoV2 infection diagnosis, especially for elderly asymptomatic patients.

Acknowledgements

We are grateful to all the front-line medical staff for their dedication in face of this outbreak. We are very thankful to Jiarui Zhou for his excellent assistance during the data collection.

Table 1. Dynamic profile of IgG-IgM antibody levels in three elderly asymptomatic patients in ICU (Normal range: < 0.9 AU/mL).

Date	Patient 1		Patient 2		Patient 3	
	IgG	IgM	IgG	IgM	IgG	IgM
March 4	4.977	0.721	4.497	0.666	4.452	0.443
March 8	2.429	0.081	2.391	0.105	1.663	0.128
March 12	2.232	0.238	2.556	0.332	1.815	0.158
March 16	0.148	0.060	0.174	0.043	0.696	0.032
March 20	0.387	0.102	0.435	0.089	0.489	0.024
March 25	0.209	0.045	0.135	0.012	0.278	0.063

Authors' contributions

FZ, YZ and XG contributed to the literature search. FZ, YL and ML were in charge of the manuscript draft. XG, YZ and ML contributed to data collection. YZ conceived and designed the study and made substantial revisions to the manuscript.

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Conflict of interests: No conflict of interests is declared.