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Case Report

Apparent and occult infections of medical staff in a COVID-19 designated hospital

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A B S T R A C T

Since the outbreak of novel coronavirus (SARS-CoV-2)-infected pneumonia (COVID-19), numerous medical staff are fighting on the frontline. However, the possibility of occult infection in medical staff is ignored in many recent studies. Herein, we collected data in a COVID-19 designated hospital from January 22, 2020 to March 10, 2020. A total of 33 medical staff had at least one nucleic acid test of throat swab, immunoglobulin G (IgG) or IgM serum antibody test, and chest computed tomography (CT), were enrolled. Finally, we identified 25 cases (75.8\%) were isolated for hospitalized treatment after positive virus detection. In addition, 4 cases who were all negative for nucleic acid test detection with no clinical symptoms, and none of their chest CT were abnormal. However, the results of serum IgG or IgM antibody test in these 4 cases were positive, suggesting the presence of occult infection. In conclusion, data from our single center indicated that SARS-CoV-2 had a high medical infection rate (29/33 = 87.9\%) and might have a potential risk of occult infection.

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Introduction

Since December 2020, novel coronavirus (SARS-CoV-2)-infected pneumonia (COVID-19) occurred in Wuhan, and rapidly spread throughout China [1,2]. Recently studies mainly focused on infections in patients, while little attention has been paid to the apparent and occult infections in medical staff.

Methods

Since the outbreak of COVID-19, Wuhan Red Cross Hospital was designated as the hospital for fever and COVID-19 on January 22, 2020. As of March 10, 2020, 33 staff had at least one nucleic acid test of throat swab for SARS-CoV-2, IgG-IgM combined serum antibody test for SARS-CoV-2, and chest computed tomography (CT) to screen potential infections.

The swab virus nucleic acid was detected by the RT-PCR assay method according to the manufacturer’s protocol (Shanghai BioGerm Medical Technology Co.,Ltd) [3]. The blood antibody was detected by the point-of-care lateral flow immunoassay method according to the manufacturer’s protocol (Shenzhen Yahuilong Biological Technology Co.,Ltd) [4]. The antibody test was reported with a reliable sensitivity of 88.66\% and specificity of 90.63\% [4].

This study was approved by the ethics committee of Wuhan Red Cross Hospital, and written informed consents were obtained.

Results

Table 1 showed the basic information of the included subjects. In brief, all medical staff worked in different departments, whereas they shared the same access to and from work. The 33 medical staff had an average age of 38.1 years (range: 25–56) and an average work duration of 13.9 days (range: 1–40) in the isolation ward (Fig. 1). Among these staff, 25 people (75.8\%) were isolated for hospitalized treatment after positive virus detection.
Table 1
The basic information of 33 subjects.

| Patients | Age | Gender | Department                                      | Position |
|----------|-----|--------|-------------------------------------------------|----------|
| 1        | 45  | Male   | Orthopedics (turned into fever ward)            | Doctor   |
| 2        | 38  | Female | Geriatrics (turned into fever ward)             | Doctor   |
| 3        | 37  | Female | Emergency                                       | Nurse    |
| 4        | 42  | Female | Color Doppler Ultrasound Room                   | Doctor   |
| 5        | 29  | Female | Orthopedics (turned into fever ward)            | Nurse    |
| 6        | 25  | Female | Intensive care unit                             | Nurse    |
| 7        | 47  | Female | Obstetrics and Gynecology (turned into fever ward) | Doctor   |
| 8        | 30  | Female | Emergency                                       | Nurse    |
| 9        | 30  | Female | Gastroenterology (turned into fever ward)       | Doctor   |
| 10       | 28  | Female | General Surgery (turned into fever ward)        | Nurse    |
| 11       | 26  | Female | General Surgery (turned into fever ward)        | Nurse    |
| 12       | 53  | Male   | Cardiology (turned into fever ward)             | Doctor   |
| 13       | 45  | Female | Intensive care unit                             | Nurse    |
| 14       | 46  | Female | Logistics                                       | Logistics|
| 15       | 37  | Female | Logistics                                       | Logistics|
| 16       | 33  | Female | Pediatrics (turned into fever ward)             | Doctor   |
| 17       | 36  | Female | Logistics                                       | Logistics|
| 18       | 46  | Male   | Pharmacy                                        | Pharmacist|
| 19       | 42  | Male   | Neurology (turned into fever ward)              | Nurse    |
| 20       | 26  | Female | Pharmacy                                        | Pharmacist|
| 21       | 57  | Male   | Pediatrics (turned into fever ward)             | Doctor   |
| 22       | 38  | Male   | Breast surgery (turned into fever ward)         | Nurse    |
| 23       | 28  | Female | Orthopedics (turned into fever ward)            | Nurse    |
| 24       | 30  | Female | Oncology (turned into fever ward)               | Doctor   |
| 25       | 43  | Female | Endocrinology (turned into fever ward)          | Nurse    |
| 26       | 46  | Female | Registration                                    | Registration|
| 27       | 48  | Female | Oncology (turned into fever ward)               | Doctor   |
| 28       | 55  | Female | Outpatient                                      | Nurse    |
| 29       | 33  | Female | Radiology (turned into fever ward)              | Doctor   |
| 30       | 56  | Male   | Pediatrics (turned into fever ward)             | Nurse    |
| 31       | 35  | Female | Oncology (turned into fever ward)               | Nurse    |
| 32       | 24  | Female | Oncology (turned into fever ward)               | Nurse    |
| 33       | 48  | Female | Registration                                    | Nurse    |

Among the 8 staff with negative virus detection, 4 subjects were hospitalized for fever or respiratory symptoms. Other 4 subjects were asymptomatic, and chest CT scan showed no abnormalities.

The 4 medical staff are still working in the frontline because they do not meet the present diagnostic criteria [5]. As of March 10, they all had 48 days' work experience in the isolation ward. Case 1 was a 34-year-old nurse who had a positive detection for IgG, whereas a negative detection for IgM. Case 2 was a 45-year-old doctor. Case 3 was a 39-year-old doctor. Case 4 was a 48-year-old support staff. These 3 cases had a positive detection for IgM, whereas a negative detection for IgG.

Discussion

Viral infection could be divided into apparent and occult infection according to the degree of infection symptoms. Occult infections usually had no or insignificant clinical symptoms and biochemical changes, which could only be detected by immunological testing.

In this study, although all cases undergo protection training before taking up their posts, our data indicate that COVID-19 is a highly contagious disease. There may be two reasons. First, due to a lack of understanding of the epidemiology of SARS-CoV-2 in January, several medical staff might be infected due to insufficient protection and in an incubation period before the hospital was converted into the COVID-19 designated hospital. Second, the hospital itself was a comprehensive hospital, and its transformation into a designated hospital might not completely meet the requirements of hospital for infectious disease. Therefore, even with strictly protective equipment, the apparent infection rate of medical staff reached 75.8%.

Moreover, we identified 4 cases who were all negative for nucleic acid test detection with no clinical symptoms, and none of their chest CT were abnormal. In addition, the serum antibody results showed that 3 cases had a positive detection for IgM, whereas a negative detection for IgG. The IgM positive indicated that patients tend to be in the acute phase of COVID-19 infection. Although a false negative result might be occurred in the nucleic acid test [6], positive results of nucleic acid tests were found in 3
times in case 2 and 2 times in case 3 and case 4. These findings suggested 3 cases with IgM-positive might be COVID-19 patients with occult infection. The remaining case 1 showed a negative result for IgM detection and a positive result for IgG detection, suggesting past exposure to SARS-CoV-2.

In previously SARS-CoV infection, occult infection was found in Heyuan, Guangdong, China [7]. Wang et al. indicated that 29 of the 1129 medical staff tested positive for coronavirus antibodies [8]. Therefore, we could reasonably speculate that occult infection also existed in COVID-19 patients. The proportion of occult infection was also higher in SARS-CoV-2 than SARS-CoV because of the higher infectiousness. However, the infectivity of these occult infections requires further study.

The study is limited to a small number of medical staff and cannot determine which types of work are more likely to develop occult infection. A larger cohort will help us understand the characteristics of occult infection of COVID-19. Additionally, nucleic acid test is not performed on several frequently touched sites in the working environment outside the isolation ward, such as computers, phones, or hand sanitizer buttons, to determine whether occult infection is a potential source of infection in clean office areas. Finally, more studies are needed to confirm that occult infection caused by SARS-CoV-2 are potential carriers of the virus.

Conclusion

In summary, data from our single center indicated that SARS-CoV-2 had a high medical infection rate (29/33 = 87.9%) and might have a potential risk of occult infection.

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Competing interests

None declared.

Ethical approval

Not required.

Author contribution

GZL, CYH, JL and QH collected the data. GZL, NX and HZW prepared and revised the manuscript. GZL, NX and HZW were responsible for summarizing all data related to this study.

References

[1] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He XJ, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20.
[2] Porcheddu R, Serra C, Kelvin D, Kolvin N, Rubino S. Similarity in case fatality rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. J Infect Dev Ctries 2020;14. http://dx.doi.org/10.3855/jidc.12600. PMID: 32146445.
[3] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061–9.
[4] Li Z, Yi Y, Luo X, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. J Med Virol 2020, http://dx.doi.org/10.1002/jmv.25727. PMID: 32104917.
[5] National Health Commission of the People’s Republic of China, Chinese. Available from: Diagnosis and Treatment Protocols of the Novel Coronavirus Pneumonia (trial version 7). Beijing: National Health Commission of the People’s Republic of China; 2020. http://www.nhc.gov.cn/yzwj/202003/46c029a4f4e4ce4f80dc75f912eb1989/files/ ce3e0458133e438ee41350ac0ce964.pdf.
[6] Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. Radiology 2020;200343. http://dx.doi.org/10.1148/radiol.2020200343. PMID: 32049601.
[7] China news, 30 May Available from: Occult Infection of SARS was Found in Heyuan, Guangdong; 2003. http://www.chinanews.com.cn/2003-05-30/26/308779.html.
[8] Wang ZH, Nong Y, Lin JT, Cai Z, Zhou TL, Zhang L, et al. Covert infection of severe acute respiratory syndrome in health-care professionals and its relation to the workload and the type of work. Chin J Tubere Respir Dis 2004;27, http://dx.doi.org/10.3760/j.issn:1001-0939.2004.03.003.