Received: 30 March 2021 | Accepted: 28 April 2021

DOI: 10.1002/jmv.27055

SHORT COMMUNICATION

JOURNAL OF MEDICAL VIROLOGY WILEY

The breadth of concomitant virological features in a family cluster outbreak of COVID-19 pneumonia

Guanglin Lei[1] | Fanping Meng[1] | Cheng Wang[2] | Jin Yan[1] | Fang Sun[1] | Lei Shi[1] | Wengang Li[1] | Junqing Luan[1] | Siyu Wang[1] | Penghui Yang[1]

[1]Department of Hepatobiliary Surgery, Fifth Medical Center of Chinese PLA General Hospital, National Clinical Research Center for Infectious Diseases, Beijing, P. R. China

[2]Department of Orthopedics, First Medical Center, Chinese PLA General Hospital, Beijing, China

Correspondence

Penghui Yang, Department of Hepatobiliary Surgery, Fifth Medical Center of Chinese PLA General Hospital, National Clinical Research Center for Infectious Diseases, 100039 Beijing, P. R. China.
Email: ypenghuiamms@hotmail.com

Funding information

National Natural Science Foundation of China, Grant/Award Number: 81971564

Abstract

An outbreak of a novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had emerged in 2019 and rapidly posed a global epidemic. Here, we report the breadth of concomitant virological features of a family cluster with COVID-19. The period of virus shedding is significantly different between upper respiratory and feces samples. Even the SARS-CoV-2 virus titers were undetectable in feces, it could be positive again soon and likely related to fluctuated inflammation levels (interleukin-6, etc.) and lowered immune responses (CD4 + T lymphocyte, etc.). Our findings expand the novel understanding of the breadth of concomitant virological features during a non-severe family cluster of COVID-19.

KEYWORDS

coronavirus, epidemiology, fecal contaminant, immune responses, T cell, virus classification

A novel coronavirus (coronavirus disease 2019 [COVID-19]) epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been reported since the end of 2019. At present, the virus is still widely spread worldwide and poses a great threat to people's health. COVID-19 spread so rapidly that the World Health Organization declared a global emergency in this pandemic and named it coronavirus disease 2019 (COVID-19), and this new 2019-nCov was renamed SARS CoV-2. Most COVID-19 patients have mild to severe symptoms, such as severe fever, cough, respiratory discomfort, and influenza.[1–3] Family clusters of infected individuals have been reported, and cause a serious threat to public health.[4] In a previously reported family cluster, most infected individuals had clinical symptoms or they are asymptomatic cases.[1,5] However, clinical temporary progression and viral shedding of each family member was still elusive. Here, we report the virological features concerning clinical characteristics and immune response of a family cluster with mild-to-moderate COVID-19 that required hospitalization. On January 27, 2020, a family cluster of three, returned from Wuhan to Beijing, was diagnosed with the SARS-CoV-2 virus by the Beijing Center for Disease Control and Prevention. The three patients made a relatively slow recovery and were discharged on February 15, 2020.

In this family of three, one 41-year-old woman (Patient 1) first had clinical symptoms, a normal lymphocyte count, chest computed tomography (CT) images, and a positive polymerase chain reaction (PCR) result on January 27, 2020. By contrast, the other two family members—a 45-year-old man (Patient 2) and a 13-year-old boy (Patient 3)—had almost simultaneous clinical symptoms with increased C-reactive protein and lactate and positive PCR results on the same day. Notably, Patient 2 had abnormal lymphocyte counts and the chest CT images at that time.

On January 18, 2020, Patient 1 traveled from Beijing to Wuhan (Hubei, China) with her husband (Patient 2) and son (Patient 3) by high-speed rail, came back to Beijing on January 27 by self-driving. They had no history of contact with animals, visits to markets including the

Guanglin Lei and Fanping Meng contributed equally to this study.

Huanan Seafood Market in Wuhan. The family stayed in the same room throughout their travel. After they arrived in Wuhan on January 18, Patient 1 developed a cough, without a sore throat, arthralgia, myalgia, chills, fever, or headache. Six days later, when they returned to Beijing, Patient 2 developed a fever of 38.4°C with cough, fatigue, muscle soreness. Chest CT scans at the clinic showed bronchopneumonia. On the same day, Patient 3 also developed a fever of 38.4°C with bronchopneumonia symptoms by Chest CT scans. They were admitted

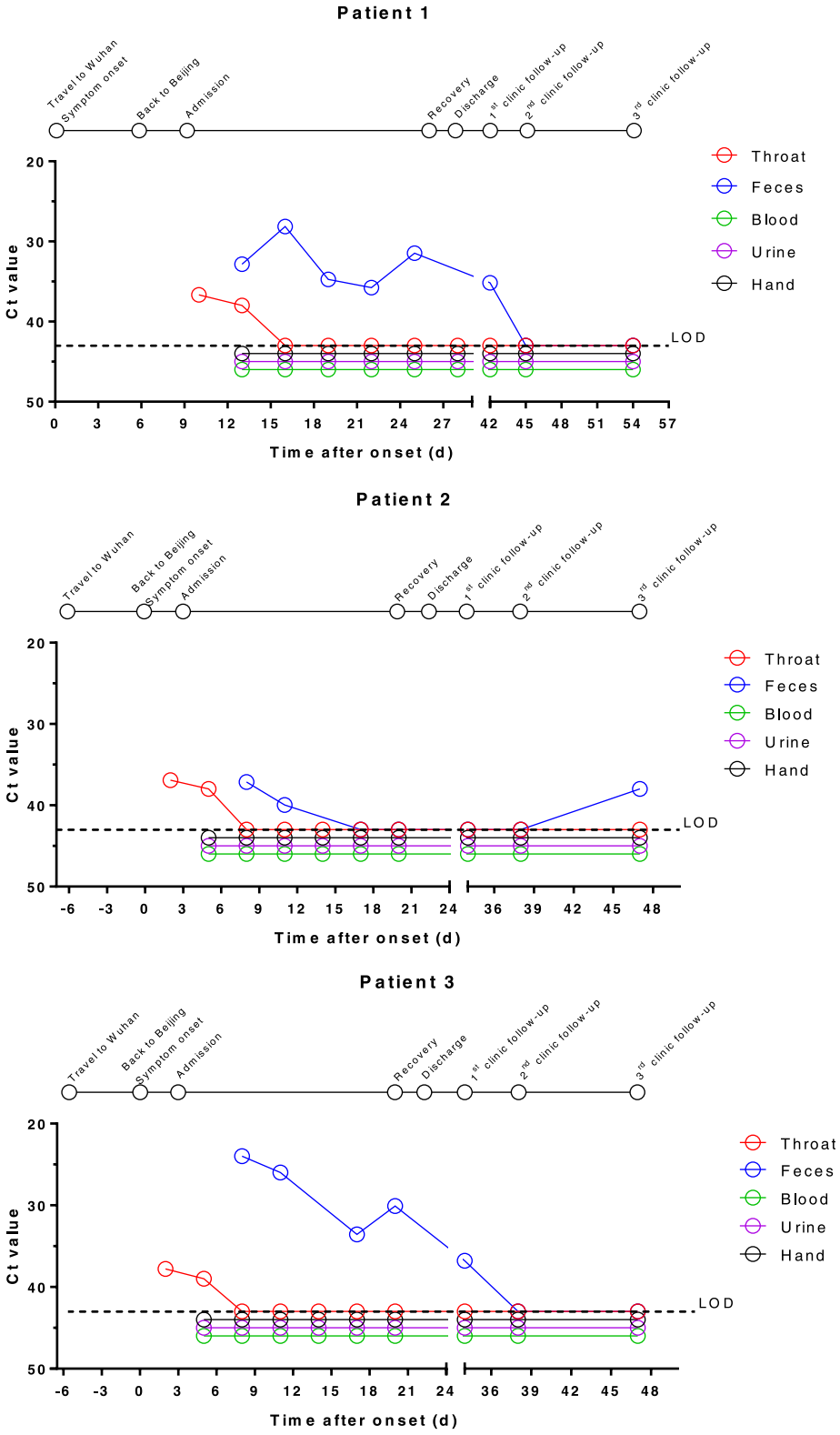

FIGURE 1 Virus shedding in the throat, feces, blood, urine, and hand samples of a Beijing family clusterinfected with SARS-CoV-2 infection at different time points. LOD, lower of detection; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

to the Fifth Medical Center of PLA General Hospital together on January 27, due to persistent symptoms.

The three patients had normal or lower than average total white plasma cell counts. Substantially increased C-reactive protein, aspartate aminotransferase, lactate dehydrogenase levels (Table S1). Patient 2 showed multifocal patchy ground-glass opacities, especially around the peripheral parts of the lungs on CT scans, which were compatible with changes seen in viral pneumonia. With the antiviral treatment, the pulmonary symptoms significantly improved by lung CT scanning (Figure S1). On the contrary, the other two patients did not have obvious pulmonary symptoms (Figure S2).

In this family cluster, we collected the throat, urine, plasma, hand, and feces samples at different time-point during their stay in the hospital. The respiratory samples of all individuals were positive for the N gene by real-time reverse transcription-PCR when they were admitted to the hospital together on January 28. However, virus titers in the throat of three patients rapidly changed negatively after consecutively ralproveravir/ritonavir antiviral therapy. Meanwhile, we determined virus shedding in urine, blood, hand, and feces samples of each family member. Surprisingly, Patient 1 had significantly higher virus titers in feces than throat samples from 13 to 42 days after onset. Peaks achieved at 16 days. Whereas, there was no virus titers could be detected in throat samples of Patients 2 and 3 from 8 to 47 days after onset. Viral titers in feces of Patient 2 declined to negative on 17 days after onset. Patient 3 had higher viral titers in feces during the disease course. Furthermore, virus titers in Patient 1 and 3 could be observed in the feces and lasted until after 2 weeks discharged. Subsequently, all samples of three family members were negative in the second follow-up test. Of note, a feces sample of Patient 2 was positive again on 47 days after onset. Besides, all patients' urine, hand, and blood samples were negative for this SARS-CoV-2 virus (Figure 1). Meanwhile, we analyzed the kinetics of inflammatory markers (interleukin-6 [IL-6], C-reactive protein, platelets, serum ferritin) and immune cell response (CD4, CD8, NK) while they were in the hospital. Results showed that levels of inflammatory markers of Patient 2 fluctuate greatly and $CD4^+$, $CD8^+$ T, and NK lymphocyte counts were significantly lower than other family members (Figure S3), suggesting that fluctuated inflammatory marker levels and lower immune responses were likely related to SARS-CoV-2 virus-positive again. Thus, any of the three individuals could have been the first one to become infected and thus transmitted the virus to the other two family members by feces or respiratory tract, because viral titers in feces were higher and last longer than that of in throat in some family members.

Collectively, our study provides novel contributions to the understanding of the breadth of concomitant virological features during a non-severe family cluster of COVID-19. To prevent and control this highly infectious disease as early as possible, people with family members with SARS-CoV-2 infection should be closely monitored and examined to rule out infection. It is necessary to detect the virus in the feces when the patient is discharged because the virus in feces may also be a potential source of infection. And the detection of feces virus load could sever as an essential auxiliary method for the monitoring of latent or asymptomatic people with negative virus loading in the throat. In the case of this family, since the time of discovery and investigations of SARS-CoV-2 infection was short, more studies, including how long the virus lasts in the feces, the homology of each virus isolate, etc. are needed to explore symptoms and test results of infected individuals in greater detail. Furthermore, our study speculated SARS-CoV-2 virus-positive again was likely related to fluctuated inflammation levels (IL-6, etc.) and lowered immune responses ($CD4^+$ T lymphocyte, etc.), and warrants validation in a much large cohort population.

ACKNOWLEDGMENT

This work was supported by the National Natural Science Foundation of China (81971564).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

The study was approved by the Ethics Committee of the Fifth Medical Center of PLA General Hospital.

CONSENT TO PUBLISH

Written informed consent for publication of their clinical details and clinical images was obtained from all included patients and guardians of the patient. Consent to publish has been obtained.

ORCID

Penghui Yang http://orcid.org/0000-0001-6519-5927

REFERENCES

1. Pan X, Chen D, Xia Y, et al. Asymptomatic cases in a family cluster with SARS-CoV-2 infection. *Lancet Infect Dis*. 2020;20(4):410-411.
2. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents*. 2020;55(3)105924.
3. Singhal T. A review of coronavirus disease-2019 (COVID-19). *Indian J Pediatr*. 2020;87(4):281-286.
4. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020;395(10223):514-523.
5. Huang R, Xia J, Chen Y, Shan C, Wu C. A family cluster of SARS-CoV-2 infection involving 11 patients in Nanjing, China. *Lancet Infect Dis*. 2020;20(5):534-535.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Lei G, Meng F, Wang C, et al. The breadth of concomitant virological features in a family cluster outbreak of COVID-19 pneumonia. *J Med Virol*. 2021;93:5635-5637. https://doi.org/10.1002/jmv.27055