



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Case Report

# A SARS-CoV-2 familial cluster infection reveals asymptomatic transmission to children



Ming Chen<sup>a,b,1</sup>, Panpan Fan<sup>b,1</sup>, Zhi Liu<sup>b</sup>, Rui Pan<sup>a</sup>, Shaowu Huang<sup>a</sup>, Junhua Li<sup>a,\*</sup>, Dongchi Zhao<sup>b,\*</sup>

<sup>a</sup> Xiangyang Central Hospital, Affiliated Hospital Of Hubei University of Arts and Science, Xiangyang, 441100, China

<sup>b</sup> Department of Pediatrics, Children's Digital Health and Data Center, Zhongnan Hospital of Wuhan University, Wuhan, 430071, China

## ARTICLE INFO

### Article history:

Received 12 April 2020

Received in revised form 18 May 2020

Accepted 20 May 2020

### Keywords:

COVID-19

SARS-CoV-2

Children

Asymptomatic infections

Transmission

## ABSTRACT

Information on SARS-CoV-2 asymptomatic infection and infectivity in children is limited. In this study, we aimed to report the epidemiological and clinical characteristics of a familial cluster infection including children with SARS-CoV-2. On February 1, 2020, two children (case 1 and case 2), an 8-year-old girl and a 9-year-old boy, were admitted to the isolation ward in Xiangyang Central Hospital, Hubei province, China, with the diagnosis of COVID-19. Before admission, they had been staying at home with their father and never contacted with any confirmed patients except their mother (case 3) who returned from Wuhan on January 22. Both case 1 and case 2 got mild symptoms. Case 3 didn't develop any symptoms until February 6, 2020, with an asymptomatic period of 15 days. She was transferred to ICU and administered multiple treatment according to the disease progression and chest CT manifestations. Her nucleic acid test turned positive until Feb 21, 2020, 15 days after symptoms onset, 30 days after her return from Wuhan. Our data showed that patients with SARS-CoV-2 may have the ability to transmit during their asymptomatic period even with the negative of viral nucleic acid in pharyngeal swabs.

© 2020 The Author(s). Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

The transmission of SARS-CoV-2 through asymptomatic carriers via person-to-person contact was observed in many reports, while all those asymptomatic carriers were confirmed with positive SARS-CoV-2 nucleic acid [1,2]. Available reports to date show that COVID-19 seems to be uncommon in children [3,4], and pediatric cases are mainly family cluster cases that have epidemiological links to adult patients [5]. In this study, we report a SARS-CoV-2

familial cluster consisting of two children infected by their asymptomatic and viral nucleic acid negative mother.

## Case presentation

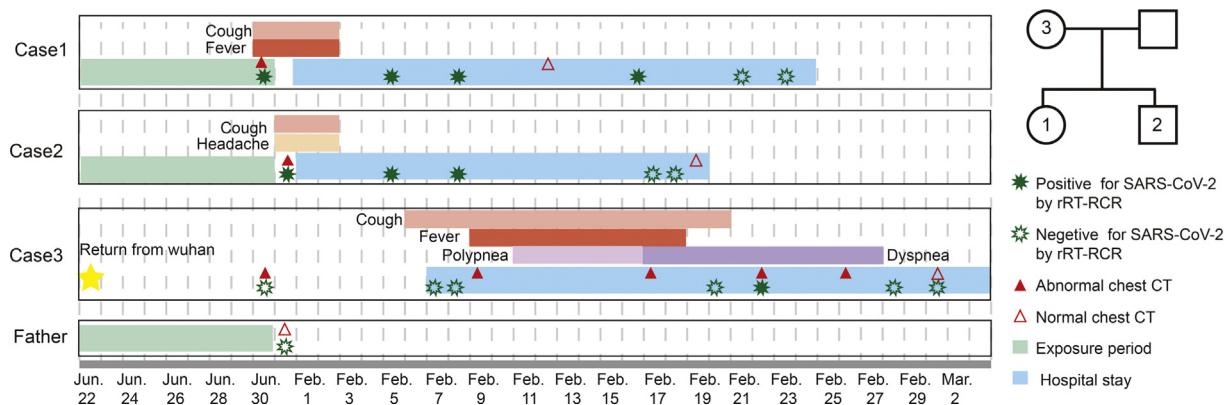
### Case 1

The first patient, an 8 years girl, got a fever of 38.6 °C with a mild cough on January 30, 2020. She had not been to Wuhan recently or in close contact with anyone suffering from fever or cough, and she lived with her brother and father who had not been to Wuhan neither, but her mother (case 3) returned from Wuhan on January 22, 2020. Her chest CT showed subpleural ground-glass opacities (GGO) in the left lower lobe and nucleic acid of SARS-CoV-2 on the next day was positive, so she was immediately admitted in isolation ward.

\* Corresponding authors.

E-mail addresses: [chenming830427@yahoo.com](mailto:chenming830427@yahoo.com) (M. Chen), [fan10.29@hotmail.com](mailto:fan10.29@hotmail.com) (P. Fan), [83972576@qq.com](mailto:83972576@qq.com) (Z. Liu), [pc79926com@163.com](mailto:pc79926com@163.com) (R. Pan), [swhuang718@126.com](mailto:swhuang718@126.com) (S. Huang), [m13797631535@163.com](mailto:m13797631535@163.com) (J. Li), [zhao.wh2004@hotmail.com](mailto:zhao.wh2004@hotmail.com) (D. Zhao).

<sup>1</sup> Co-first authors contributed equally to this study.



**Fig. 1.** Timeline of COVID-19 cases within a familial cluster in Xiangyang, Hubei Province, China. The mother returned to Xiangyang from Wuhan on Jun.22 and then lived with her family. In the following month, the younger sister, brother, and mother developed COVID-19. The course of symptoms and hospitalization are shown in different colors. RT-PCR, real-time reverse transcription PCR; ICU, intensive care unit. The white box is father, ①,② ③ are cases.

After admission, laboratory investigations showed a white blood cell (WBC) count of  $3.36 \times 10^9/L$  and an absolute lymphocyte count value of  $1.78 \times 10^9/L$ . Her symptoms disappeared one day after admission although the nucleic acid tests turned negative 22 days later. The course of disease is shown in Fig. 1.

#### Case 2

A 9 years boy, elderly brother of case1, got a fever of  $38.6^{\circ}\text{C}$  accompanied with mild headache on January 31, 2020. His chest CT images showed a small piece of GGO accompanied by consolidation in the right lower lobe and nucleic acid was also positive. After admission, his laboratory results showed a WBC count of  $2.32 \times 10^9/L$  without lymphopenia. His symptoms lasted for two days, however the nucleic acid tests turned negative 17 days later.

#### Case 3

The initial patient, a 34-year-old women, mother of case 1 and 2, had spent a couple of days in Wuhan and returned to Xiangyang on January 22, 2020. Although having no symptoms, she performed a routine examination on January 30, 2020. Her chest CT image showed GGO in the right lower lobe, while the nucleic acid test was negative. So, she was diagnosed with suspected case according to the diagnostic criteria at that time [6], and was in quarantine until she developed a cough and expectoration on February 6, 2020, 15 days after returning from Wuhan. On February 9, 2020, she developed a fever, which lasted for 10 days. On February 11, 2020, she developed shortness of breath. On February 17, 2020, she was transferred to intensive care unit (ICU) since dyspnea onset with CT imaging demonstrated a large consolidation with GGO in the right lower lobe (Fig. 2). On February 27, after 11 days in ICU, her conditions improved significantly. She was discharged on March 3, 2020.

On February 8, her laboratory results showed a normal WBC count of  $6.87 \times 10^9/L$  and lymphocyte count of  $1.12 \times 10^9/L$ . On February 18, the next day she was transferred to ICU, the WBC count was  $6.70 \times 10^9/L$  and lymphopenia  $0.99 \times 10^9/L$ . And on February 19, the results showed a WBC count of  $9.37 \times 10^9/L$  and lymphocytes was  $0.55 \times 10^9/L$ . The viral nucleic acid in pharyngeal swabs

kept negative even when her condition progressed, while it turned positive on February 21, 2020, 16 days later after symptoms onset, and turned negative 6 days later.

#### Discussion

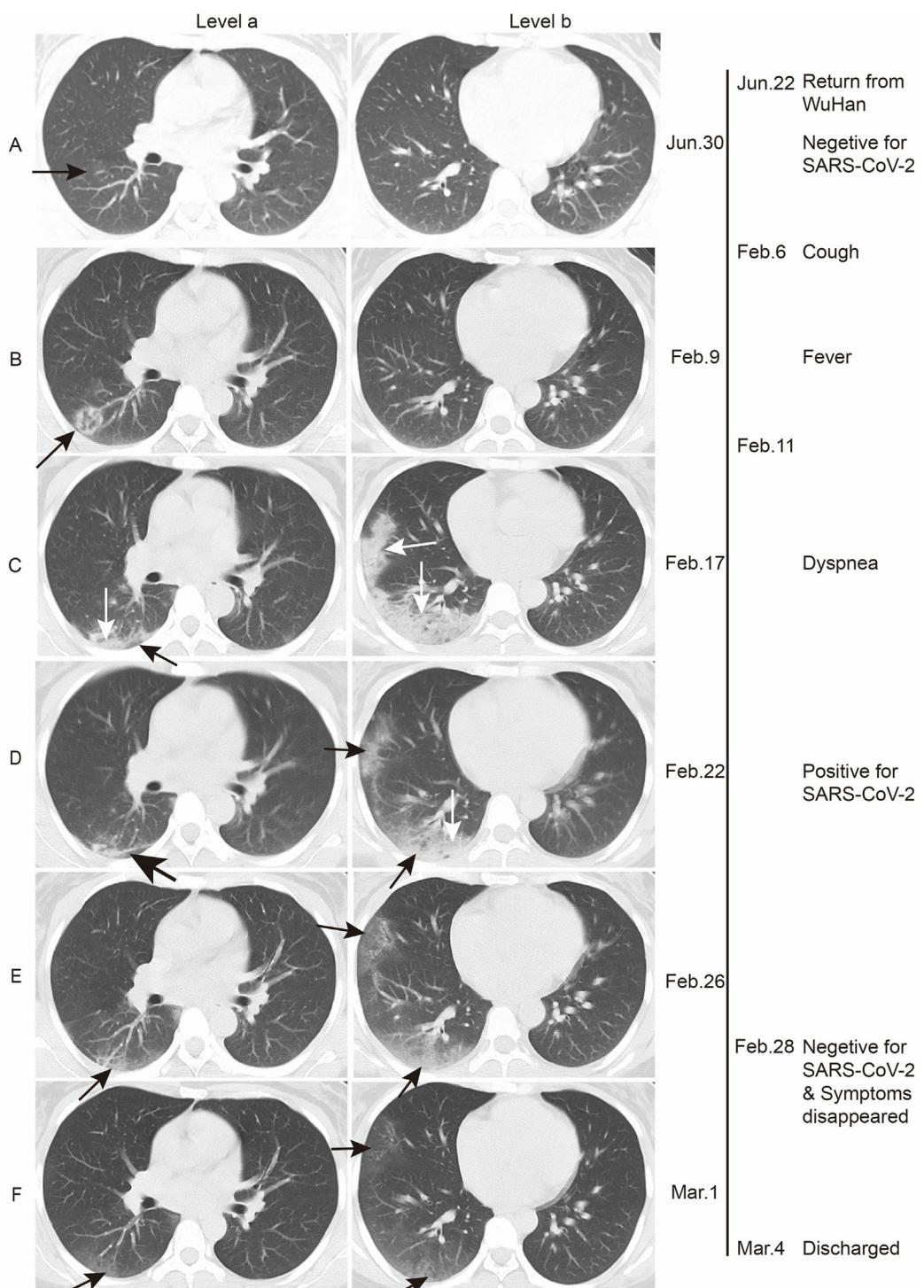
Currently, SARS-CoV-2 is increasingly being reported to be transmitted by droplets from asymptomatic or oligo-symptomatic patients during incubation period [1,7–9]. In our study, case 3 showed a more than 14 days incubation period or asymptomatic period. And the nucleic acid of SARS-CoV-2 kept negative even when the symptoms got exacerbated, and turned positive on the 16th day since symptoms onset.

The first and most likely scenario of transmission is that she was infected during her stay in Wuhan, and then transmitted the virus to her two children during her asymptomatic and nucleic acid negative period. And the scenario shows that asymptomatic patients have the ability to transmit the virus even with the negative SARS-CoV-2 nucleic acid of pharyngeal swabs. Indeed, according to existing reports, false-negative results may be particularly common in real-time polymerase chain reaction (RT-PCR) tests for SARS-CoV-2, probably due to insufficient viral specimens and thermal inactivation procedures before testing [10]. Another explanation for the low viral load of the upper respiratory tract is that the virus tends to target the lower respiratory tract, where there are high level-expressed ACE2 on type II alveolar cells which can mediate SARS-CoV-2 entry to the host [11].

Adults represent the population with the highest infection rate, however, children can also be easily infected by SARS-CoV-2 once in closely contact [12]. One possible reason for lower morbidity may be the fewer outdoor activities which making them less likely to contract the virus. In our study, except for two children, the father who was likewise a close contact was not infected, indicating that children may be especially susceptible to COVID-19.

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Fig. 2.** Dynamic changes of case 3 lung CT imaging. Two different scanning layers are displayed at each time point. (A) 8 days after returning from Wuhan: only a small pure GGO (black arrow) in the right lower lobe. (B) 18 days after returning from Wuhan and 3 days after the onset of initial symptoms: more severe lesions with GGO in the dorsal segment of right lower lobe (black arrow). (C) 11 days after the onset of initial symptoms: the predominant pattern of abnormality was consolidation (white arrow), accompanied by a small GGO (black arrow) in the right lower lobes. (D-E) 16 to 20 days after the onset of initial symptoms: the extent of the lesions was reduced with consolidation (white arrow), linear opacities (thick black arrow) and GGO (thin black arrow) in the right lower lobe. (F) 2 days after the clinical symptoms disappeared, only residual pure GGO (black arrow).

#### Conflict of interest

The authors have indicated they have no potential conflicts of interest to disclose.

#### Submission declaration and verification

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

## Contributors

Prof. Dongchi Zhao had the idea and designed the study and had full access to all data in the study. Drs. M Chen, and Panpan Fan contributed to data collecting and writing of the article. Drs. Z Liu, R Pan, S Huang and J Li contributed to coordinate and supervise data collection, and critically reviewed the manuscript for important intellectual content.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jiph.2020.05.018>.

## References

- [1] Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020.
- [2] Yu X, Yang R. COVID-19 transmission through asymptomatic carriers is a challenge to containment. *Influenza Other Respir Viruses* 2020.
- [3] 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.
- [4] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506.
- [5] Yang P, Liu P, Li D, Zhao D. Corona virus disease 2019, a growing threat to children? *J Infect* 2020;S0163-4453(20). <http://dx.doi.org/10.1016/j.jinf.2020.02.024>, 30105-5.
- [6] General Office of National Health Commission, General Office of National Administration of Traditional Chinese Medicine. [http://www.gov.cn/zhengce/zhengceku/2020-03/04/content\\_5486705.htm](http://www.gov.cn/zhengce/zhengceku/2020-03/04/content_5486705.htm), 2020 [Z]. 2020.
- [7] Yu P, Zhu J, Zhang Z, et al. A familial cluster of infection associated with the 2019 novel Coronavirus indicating possible person-to-person transmission during the incubation period. *J Infect Dis* 2020.
- [8] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020.
- [9] Zd T, A T, Kf L, et al. Potential presymptomatic transmission of SARS-CoV-2, Zhejiang Province, China, 2020. *Emerging Infect Dis* 2020;26(5).
- [10] Liu P, Zheng J, Yang P, et al. The immunologic status of newborns born to SARS-CoV2-infected mothers in Wuhan, China. *J Allergy Clin Immunol* 2020.
- [11] Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020.
- [12] Lai C, Liu YH, Wang C, et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): facts and myths. *J Microbiol Immunol Infect* 2020.