Prevention of COVID-19 infection in a pediatric oncology ward in Wuhan

Ai Zhang | Qun Hu | Aiguo Liu | Songmi Wang | Shourui Jin | Yao Wang | Li Wang | Yan Hao

Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Correspondence
Qun Hu, Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 430030 Wuhan, China. Email: qunhu2013@163.com

Funding Information
Huazhong University of Science and Technology Emergency Technology Research Project Response to COVID-19, Grant/Award Number: 2020kyXGYJ020

Abstract
Objective: To assess the screening and isolation measures for preventing coronavirus disease 2019 (COVID-19) infection from newly admitted patients into a pediatric oncology ward.

Methods: We retrospectively analyzed 44 patients with established hematologic malignancies admitted for chemotherapy from January 23 to March 27, 2020 in the Department of Pediatric Hematology of Tongji Hospital, Wuhan. Every patient and their caregivers were well educated on personal protection and put it into effect at home and in hospital. Screening for COVID-19 of all the patients and caregivers before admission was performed. Both clinical features and screening results including chest computerized tomography (CT); nucleic acid testing of nasopharyngeal, oropharyngeal or anal swabs; and quantitative antibodies (IgM and IgG) detecting of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of these patients were described.

Results: The results of nucleic acid and antibodies (IgM and IgG) testing of all the 44 inpatients and their caregivers were negative. Abnormal chest CT images were observed in six symptomatic patients, while chest CT images of their caregivers did not show the changes related to viral pneumonia. These symptomatic patients all recovered after antibacterial combined with antifungal treatment, but without any antiviral agents.

Conclusions: COVID-19 infection could be prevented in pediatric patients with malignancies if proper protective measures were implemented. For patients presenting suspicious symptoms, comprehensive examinations should be carried out.

KEYWORDS
children, coronavirus, COVID-19, malignancy

1 | INTRODUCTION

In December 2019, a new type of coronavirus causing pneumonia was detected in Wuhan, China. This virus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) later on, and the infectious disease was officially named "corona virus disease 2019" (COVID-19) by World Health Organization (WHO) on February 11, 2020. With the ongoing rapid spread of this virus worldwide, COVID-19 was declared a pandemic in March 2020.

The virus is considered to be transmitted by respiratory droplets and contact. In the early days of the COVID-19 infection outbreak, pediatric patients were rather rare, who were thought to be not susceptible to this virus. However, along with the emerging of familial aggregation, the number of children suffering from COVID-19 infection gradually increased. Meanwhile, cancer itself along with its treatment makes cancer patients more susceptible to infections due to weakened immune response to respiratory bacteria and virus. Liang et al were the first to assess the impact of COVID-19 on cancer patients in China. They found that 1% of those infected with COVID-19 had a history of cancer, higher than the incidence of cancer in the Chinese population (0.29%), and the risk of developing...
severe events in COVID-19 disease is statistically significantly higher in patients with cancer, with a hazard ratio of 3.56.

By now, little has been known about the situation of pediatric cancer patients in the current pandemic. Wuhan is the epicenter of the outbreak of COVID-19 pandemic in China. Wuhan is the epicenter of the outbreak of COVID-19 pandemic in China. Herein, we had an investigation on the management of the cancer patients undergoing treatment in the Department of Pediatric Hematology of Tongji Hospital, one of the main treatment centers for childhood cancers in Wuhan and even in Hubei province.

2 | MATERIALS AND METHODS

2.1 | Subjects

As the epicenter of the outbreak in China, intensive travel restrictions were imposed on Wuhan on January 23, 2020, as well as many other cities across Hubei province, to limit the spread of COVID-19 in China. Hence, patients’ mobility into the hospital was negatively impacted, which was reflected in the decline in the number of admitted patients during the lockdown period. In this study, we recruited 44 patients with established hematologic malignancies admitted for chemotherapy in the Department of Pediatric Hematology of Tongji Hospital from January 23 to March 27, 2020. All these cases were in complete remission when admitted. For acute lymphoblastic leukemia patients, they had oral chemotherapeutic agents such as mercaptopurine and methotrexate at home. This study was approved by the ethics committee of Tongji Hospital, and written informed consent was obtained from the patients for the publication of individual data from before enrolment when data were collected retrospectively.

2.2 | Patients’ management

1. For patients at home, prevention of infection in communities was important. We suggested the family members to stay indoors and refrain from going out. The patients were required to remain in a separate room and eat alone. Patients and their family members were advised to keep wearing common masks at home. They were all asked to wash their hands frequently, especially after using the toilet and before cooking or eating. A locational distance of at least 1 m should be kept between each family member.

2. For inpatients, nurses would take the body temperature of everyone as well as their caregivers and dispense surgical masks for them every morning. Additionally, indoor area disinfection, adequate room ventilation, and hand hygiene education were implemented daily by nurses. Social distance was kept to avoid potential exposure.

3. Before admission, all the patients and caregivers had to complete examinations including nonenhanced chest computed tomography (CT) scan, nucleic acid testing of nasopharyngeal, oropharyngeal or anal swabs, and quantitative antibodies (IgM and IgG) detection of SARS-CoV-2 to exclude COVID-19 infection. Complete blood count is not included in these examinations because the results of postchemotherapy patients are mostly abnormal. It would take 6 h for the results of nucleic acid testing, 3 h for antibody detection, and 1 h for chest CT scan. And the patients had to wait in the hospital in the meantime.

4. Patients with positive screening results were sent to designated hospital for COVID-19 treatment. For those who did not meet the case definition for probable COVID-19, every one of them was arranged in a separate room in isolated ward to be observed for 7 days before being transferred to nonisolated ward. In the nonisolated ward, only two beds were placed in each room to reduce the risk of cross-infection. Both in the isolated and nonisolated wards, patients and caregivers were required to keep staying in the room and visit to the ward was forbidden. One assigned nurse was in charge of their daily life such as distributing meals and drinking water every day.

5. Because of strict thorough COVID-19 screening before admission, chemotherapy was deemed as safe to be given to those with adequate neutrophil counts and normal organ function. To reduce the risk of infection, intravenous immunoglobin (IVIG) was administered in patients with neutropenia (blood neutrophils < 0.5 x 10⁹/L) after chemotherapy at a dose of 100-200 mg/kg per day for 2-3 days.

6. For patients with suspicious symptoms like fever, cough, or dyspnea, virus nucleic acid testing was performed twice with an interval of 24 h, if tested negative. The swabbing samples were taken from different sites such as pharynx or anus to lower the false-negative rate.

2.3 | Data collection

Demographic information and clinical characteristics including exposure history, signs and symptoms, chest CT scan results, treatments, clinical outcomes, and laboratory findings of each patient were obtained from the electronic medical record system of Tongji Hospital. SARS-CoV-2 RNA in pharyngeal or anal swab samples was identified by a reverse transcription PCR. The level of SARS-CoV-2 antibodies in the serum was detected by chemiluminescence assay.

3 | RESULTS

The clinical features of patients in our investigation are displayed in Table 1. In this study, we reviewed 44 cases (27 males and 17 females) with medium age of 6 years old (ranging from 1 year 7 months to 15 years old). Their types of malignancies were as follows: acute lymphoblastic leukemia (39/44, 88.6%), lymphoma (4/44, 9.1%), and acute myeloid leukemia (1/44, 2.3%). All the 44 cases and their caregivers denied the history of contact with confirmed or suspected COVID-19 patients.

Examinations for COVID-19 including nonenhanced chest CT, nucleic acid testing, and antibody detection of SARS-CoV-2 were carried out in all these cases together with their caregivers. The results...
of COVID-19 screening of the patients on admission are shown in Table 2. In general, most of the patients did not present with suspected symptoms (86.4%) on admission, only few (13.6%) had fever, cough, or tachypnea. As the results of SARS-CoV-2 nucleic acid testing could be false negative, the samples for testing were taken twice with an interval of 24 h from different sites (nasopharynx, oropharynx, or anus) for the six symptomatic cases. Nucleic acid testing and antibodies detection (IgM and IgG) of SARS-CoV-2 of the 44 cases and their caregivers were all negative. Chest CT images of the 38 routine screened cases as well as caregivers of the 44 cases all came out to be normal. Abnormal imaging manifestations of chest CTs were observed in the six symptomatic cases, including ground-glass opacities (1/6), consolidation (1/6), patchy shadows (2/6), and segmental atelectasis (2/6). All their symptoms and chest CT images improved by antibacterial combined with antifungal treatment, but without antiviral agents.

### 4.1 Measures for personal protection

As SARS-CoV-2 is spread by droplets and close contact, wearing face masks and hand hygiene are quite important approaches to protect from infection. For patients staying at home, we suggested the family members to stay indoors. The patients were required to remain in a separate room and eat alone. Patients and their family members were advised to keep wearing common masks at home. They were all asked to wash their hands frequently, especially after using the toilet and before cooking or eating. A locational distance of at least 1 m should be kept between each family member. For inpatients, we provided masks for every child and their caregivers. Health education on hand hygiene was promoted in the ward. Body temperature of the patients and caregivers was recorded daily in the morning. Social distance was kept to avoid potential exposure. The number of beds in each room was cut down to keep a distance of 3 m between two patients. Patients and caregivers were required to keep staying in their room and visit to the ward was forbidden to minimize cross-infection. The value of IVIG at
neutropenia period is uncertain, but in some cases, it is considered to be beneficial in the treatment of viral infection for immunocompromised patients. In our study, IVIG was administered in patients with chemotherapy-induced neutropenia at a dose of 100-200 mg/kg per day for 2-3 days.

4.2 Procedures for admission

In our study, strict admission procedures were applied to minimize the possibility of nosocomial transmission. This decision could be justified in the context of facing an unknown disease with unexpectedly large outbreak in the epicenter, with the admission of particularly vulnerable patient cohort. It has been found that a proportion of asymptomatic patients with COVID-19 exists. Asymptomatic carrier may not have RNA positive, but they can be infectious to other patients. Chest CT examination is of great value in diagnosis because it is conducive to the early detection of asymptomatic infections. Therefore, for all the patients and caregivers, whether symptomatic or not, examinations for screening including nonenhanced chest CT scan, nucleic acid testing, and quantitative antibodies (IgG and IgM) detection of SARS-CoV-2 were implemented before admission. After admission, every patient had to stay in a separate room in isolated ward to be observed for 7 days before being transferred to nonisolated ward.

4.3 Strategies for suspected cases

According to the diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus, symptoms such as fever, fatigue, and dry cough can be presented in child with COVID-19. All the patients in our study were considered to have the residence history of the endemic areas due to the location of our hospital. Therefore, strict inspections must be implemented for patients presented with symptoms such as fever, cough, or tachypnea, which are also very common in non-COVID-19 pneumonia of children with cancer after chemotherapy.

The conventional diagnostic criteria might not always be suitable for pediatric patients with hematologic malignancies. Leukopenia and lymphopenia that are characteristics in the diagnosis of COVID-19 in ordinary pediatric patients may result from chemotherapy in children with malignancies. The specific chest CT images that are fairly important for the diagnosis of COVID-19 could also appear in other infections such as fungi for patients with malignancies. Hence, nucleic acid testing together with antibody detection of this virus was of great significance to exclude infection of COVID-19. Since the results of virus nucleic acid testing could be false negative, repeated and multisite sampling is essential to improve accuracy of diagnosis. The often-used methods for sampling were nasopharyngeal, oropharyngeal, and anal swabs, which were easy to handle. However, nasopharyngeal swabs should be avoided for cancer patients with thrombocytopenia or coagulating disorder to prevent bleeding. Given that SARS-CoV-2 could be detected in stool specimens of the patients, whether gastrointestinal symptoms occurred or not, anal swab samples could be an option to assist with diagnosis. Having said this, nasopharyngeal and oropharyngeal swabs were preferred due to its comparatively better accuracy as per WHO guideline.

In our study, six patients got the above symptoms, so examinations containing chest CT scan, nucleic acid testing, and antibody testing of SARS-CoV-2 were carried out subsequently. The chest CT images were abnormal in all the six patients, showing as ground-glass opacities, consolidation, patchy shadows, or segmental atelectasis. The nucleic acid and antibodies (IgM and IgG) testing of SARS-CoV-2 of these symptomatic patients all came out to be negative. And chest CT images of their caregivers did not show the changes related to viral pneumonia. Moreover, the six patients with symptoms and abnormal chest CT images all had improvement after antibacterial combined with antifungal treatment, but without any antiviral agents, which could be another proof of exclusion of COVID-19 infection.

In conclusion, strict screening including viral tests and CT scan might be effective measure to identify SARS-COV-2-infected patients or caregivers. The strict measures could prevent spread of COVID-19 infection into pediatric oncology ward and spared the other inpatients at risk of cross-infection. As the changes of chest CT images are not specific in cancer patients, nucleic acid and antibody testing should be performed repeatedly to get accurate results.

ACKNOWLEDGMENTS

This work was partially supported by the Huazhong University of Science and Technology emergency technology research project response to COVID-19, 2020kfyXGYJ020.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ORCID

Ai Zhang https://orcid.org/0000-0002-5122-4296

REFERENCES

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
2. 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.
3. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020;21(3):335-337.
4. Shen K, Yang Y. Diagnosis and treatment of 2019 novel coronavirus infection in children: a pressing issue. World J Pediatr. 2020. https://doi.org/10.1007/s12519-020-00344-6.
5. Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatrics patients with 2019 coronavirus disease in China. Pediatrics. 2020. https://doi.org/10.1542/peds.2020-0702.
6. Ogimi C, Englund JA, Bradford MC, Qin X, Boeckx M, Waghmare A. Characteristics and outcomes of coronavirus infection in children: the role of viral factors and an immunocompromised state. J Pediatric Infect Dis Soc. 2019;8:21-28.
7. Shachor-Meyouhas Y, Ben-Barak A, Kassis I. Treatment with oral ribavirin and IVIG of severe human metapneumovirus pneumonia (HMPV) in immune compromised child. Pediatr Blood Cancer. 2011;57(2):350-351.

8. An P, Song P, Wang Y, Liu B. Asymptomatic patients with novel coronavirus disease (COVID-19). Balkan Med J. 2020. https://doi.org/10.4274/balkanmedj.galenos.2020.2020.4.

9. Chen Z, Fu J, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World J Pediatr. 2020. https://doi.org/10.1007/s12519-020-00345-5.

10. Chen Y, Chen L, Deng Q, et al. The presence of SARS-CoV-2 RNA in feces of COVID-19 patients. J Med Virol. 2020. https://doi.org/10.1002/jmv.25825.

How to cite this article: Zhang A, Hu Q, Liu A, et al. Prevention of COVID-19 infection in a pediatric oncology ward in Wuhan. Pediatr Blood Cancer. 2020;67:e28424. https://doi.org/10.1002/pbc.28424