Clinical features and the treatment of children with COVID-19: A case series from Wenzhou, China

To the Editor,

The World Health Organization (WHO) has declared the outbreak of novel coronavirus (COVID-19) a public health emergency of international concern since 30 January 2020.1 Children are a particularly vulnerable population, at high risk of COVID-19 infection due to the characteristics of transmission via the respiratory tract that lend this population to being more vulnerable.2 Despite their vulnerability as a population, to date, most studies have focused on COVID-19 infection in adults. The clinical features and treatment of children with COVID-19 is unclear and understudied. Therefore, we provide information and experience with treatment of pediatric cases with confirmed COVID-19 infection.

The data were derived from 136 confirmed cases, which were hospitalized in Wenzhou Sixth People Hospital from 17 January to 11 February 2020. Three children with COVID-19 infection, aged 2 to 12 years, were prospectively followed from the hospital admission to discharge. All cases were diagnosed using a real-time fluorescence polymerase chain reaction assay. Throat swab samples and blood sample were collected and chest radiography and/or computed tomography (CT) were performed as a standard process of admission of hospital.

According to this epidemiological investigation, all children were in close contact and infected from others with confirmed infections of COVID-19. Their onset symptoms were not specific, and varied from persistent fever to cough, but did not include muscle pain, runny nose, or gastrointestinal symptoms such as diarrhea. An unexpected finding was from patient 3, was that they only had an occasional slight cough (Table 1). In addition, patient 1 was found to have a bronchiolitis infection upon admission to the hospital.

Table 1 illustrates that patient 1 had lymphopenia, high LDH reaching 408 U/L, and high AST reaching 48 U/L, while patient 2 had a low PaO2 of 9.3 kPa. Progressive radiographic changes were observed in all the patients, but slight pneumonic changes were only found on the CT of patients 2 and 3. Patient 2 had a typical ground-glass pneumonic change (Figure S1). On admission, all children were treated with interferon α-2b by aerosolization twice a day (Table 1). Interferon α-2b was used since it medicates the immune system and inhibits the progression of the virus. Lopinavir/ritonavir is an antiviral agent that targets the RNA virus and has been used for treatment of human immunodeficiency virus. Some studies suggest that it may work in adult patients. Considering the potential side effects of other antiviral agents in children, we did not use in pediatric patients. Patients 2 and 3 needed oxygen inhalation. After the therapy, the patients’ symptoms were relieved and there were no adverse effects observed. All patients had a complete recovery with no clinical evidence from chest radiographs indicating impact to lung function. Follow-up was continuing every week, with samples taken to measure serum immunoglobulin G and immunoglobulin M and severe acute respiratory syndrome coronavirus-2 in blood, feces, and nasopharyngeal swabs. Of note, no patient had recurrence of positive RNA or postsymptoms at the 4-week follow-up.

The children’s clinical presentation, and prognosis was much milder, and radiological changes were milder and resolved quicker than those of adults. No one was infected by the children because they had been in self-quarantine at home after tracing. No patient presented with diarrhea, which was observed in adult patients. Typically, gastrointestinal symptoms such as diarrhea is a chief complaint for those with infectious viruses.3 However, we did not find this pattern of clinical presentation among the children in this study. The clinical presentation for children with COVID-19 is different than that for SARS where children have two distinct patterns of clinical presentation.5 Although there is no standard treatment protocol for COVID-19, the antiviral therapy combined with interferon α-2b has appeared successful in relieving the symptoms.

The presented case series demonstrates that COVID-19 is more likely to be a milder form and to have a less-aggressive clinical course in children compared to adults. In this study, symptoms resolved quickly after antiviral treatment and interferon α-2b was administered to these children. Our preliminary findings, which are limited by small sample size, suggests that symptoms of COVID-19 in children are nonspecific, but that the long-term prognosis of children infected with COVID-19 infection is favorable. It also indicates that stringent clinical symptoms should not be used to diagnose children as their presentation may differ from adults.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

JC and GH conceptualized and designed the study, collected data, and reviewed and revised the manuscript. WS conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. MG carried out the analyses, critically reviewed the manuscript for important intellectual content, and reviewed and

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| TABLE 1 | The clinical feature, laboratory test, clinical prognosis, and treatment of the children with COVID-19 from Wenzhou |
|---------|------------------------------------------------------------------------------------------------------------------|
| Patient number | 1 | 2 | 3 |
| Age, y | 2.2 | 11 | 10 |
| Sex, M/F | M | M | M |
| BMI | 15.97 | 17.76 | 23.04 |
| Past history | Diagnosed of bronchiolitis 8 d ago |
| Clinical features | | | |
| Fever | No | T (max) 38.5°C | No |
| Cough | No | No | Yes |
| Wheezing attack | No | No | No |
| Diarrhea | No | No | No |
| Vomit | No | No | No |
| Fatigue | No | No | No |
| Runny nose | No | No | No |
| Sore throat | No | No | No |
| Chills/riors | No | No | No |
| Myalgia | No | No | No |
| Headache | No | No | No |
| Other | No | Dizziness | No |
| Contact history | Mother and grandmother | Father | Father and sister |
| Oxygen saturation on room air (%) | 98 | 98 | 98 |
| Respiratory rate | 28 | 20 | 19 |
| Laboratory findings | | | |
| Lowest leukocyte count (×10⁹/L) | 8.4 | 5.51 | 8.8 |
| Lowest lymphocyte count (×10⁹/L) | 3.1 | 1.7 | 2.7 |
| Lowest PaO₂ (kPa) | NA | 9.3 | 30.2 (FiO₂ 33%) |
| Highest serum ALT, U/L | 22 | 13 | 22 |
| Highest serum AST, U/L | 48 | 24 | 20 |
| Highest serum CKP, U/L | 230 | 67 | 65.1 |
| Highest serum LDH, U/L | 408 | 258 | 182 |
| Highest CRP, mg/L | 0.2 | 1.3 | 0.4 |
| Radiological findings of thorax (radiograph/computed tomography) | | | |
| Initial change | Increased bilateral bronchovascular shadows (day 4) | Patchy ground-glass opacities on the left lower lobe with air bronchogram (day 3) | Bilateral clear lung fields with no obvious ground-glass opacities (day 1) |
| Progressive change | Slight ground-glass opacities on the right lower lobe and increased bilateral bronchovascular shadows (day 9) | Scattered ground-glass opacities on left lower lobe (day 10) | Slight stripe fibrosis on right lung (day 4) |
| Treatment and outcome | | | |
| Aerosol therapy with interferon-α-2b (20 μg/kg twice/day) | Yes | Yes | Yes |
| Oral prednisolone | No | No | No |
| Probiotics | No | Yes | Yes |
| Traditional Chinese medicine | No | Yes | Yes |
| Ventilatory support | No | Nasal cannula (day 1) | Nasal cannula (day 1-2) |
| Maximum oxygen requirement | Air 2 L/min | 2 L/min | |
| Outcome of symptoms | No symptom | Relief | Relief |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CKP, creatine kinase; CRP, C-reactive protein; LDH, lactic dehydrogenase.
revised the manuscript. JW carried out the analyses, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT
This study was approved with the written consent by the Ethics Committee of Wenzhou Central Hospital. Written consent was obtained from the parent. Consent for publication was obtained from the parent.

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