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CASE REPORT

PEDIATRIC PULMONOLOGY WILEY

Insight into COVID-2019 for pediatricians

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Abstract

Since December 2019, patients with unexplained pneumonia have been found in Wuhan City, Hubei Province, China. The pathogen in these cases is a new type of coronavirus. The World Health Organization confirmed this diagnosis and named the pathogen SARSCoV-2. The disease caused by SARSCoV-2 is called Corona Virus Disease (COVID-2019). The virus is highly infectious and pathogenic, causing human-to-human transmission. At present, SARSCoV-2 is still rampant in the world. Zhengzhou City in Henan Province serves as an example, 102 people have been confirmed to be infected with SARSCoV-2 (at 24:00 on February 5th, 2020), including three children, the youngest is 4 years old. From the perspective of clinical pediatricians as the first line fighting the epidemic, this paper will discuss the clinical characteristics, prevention and control measures, outcomes, diagnosis, and treatment of pediatric cases.

KEYWORDS

COVID-2019, pediatric infection, SARSCoV-2

1 | CLINICAL DATA

1.1 | Case 1

A 4-year-old male was admitted to the hospital with the main complaint of "cough and runny nose for 3 days."[1] The patient had good spirits, normal temperature, no wheezing, dyspnea, and so forth. Before admission, the child had contact with his grandfather and grandmother who had returned from the epidemic area of Wuhan, and both of them and the child's parents were diagnosed with COVID-2019. Laboratory examination results showed white blood cells (WBC): 5.87×10^9/L, neutrophil: 32.8%, lymphogranulocyte: 53.4%, monocyte: 12.7%, neutrophil: 1.93×10^9/L, lymphocyte: 3.13×10^9/L, and C-reactive protein (CRP): 11.2 mg/L; blood biochemistry results showed a total protein: 70 g/L, albumin: 42.1 g/L, alanine aminotransferase (ALT): 10 U/L, aspartate aminotransferase (AST): 31 U/L, total bilirubin: 4.3 μmol/L, direct bilirubin: 0.8 μmol/L, indirect bilirubin: 31 μmol/L, total bile acid: 8.6 μmol/L, urea: 4.6 mmol/L, creatinine: 34 μmol/L, and uric acid: 212 μmol/L; and there were no obvious abnormalities in six blood coagulation parameters or the myocardial enzyme range. A chest computed tomography (CT) showed spots in the two upper lobes, right lower lobes, and left lower lobes that were considered to result from an infectious disease. Real-time fluorescence reverse-transcription polymerase chain reaction (RT-PCR) detection of SARSCoV-2 nucleic acid in respiratory tract samples of the child was positive. He is still under active treatment and has not been discharged (Figure 1).

1.2 | Case 2

Additionally, a 4-year-old female was admitted to the hospital with the main complaint of "10 days of contact with a confirmed case of COVID-2019." The girl is the cousin of the abovementioned child with the same epidemiological history, and the girl's grandparents and parents have a confirmed diagnosis of novel coronavirus pneumonia, all of which are thus in the hospital for treatment. The laboratory examination results showed WBC: 6.68×10^9/L, neutrophil: 49.5%, lymphogranulocyte: 42.3%, monocyte: 6.3%, neutrophil: 3.31×10^9/L,

Yuanzhe Li and FeiFei Guo contributed equally to this work.

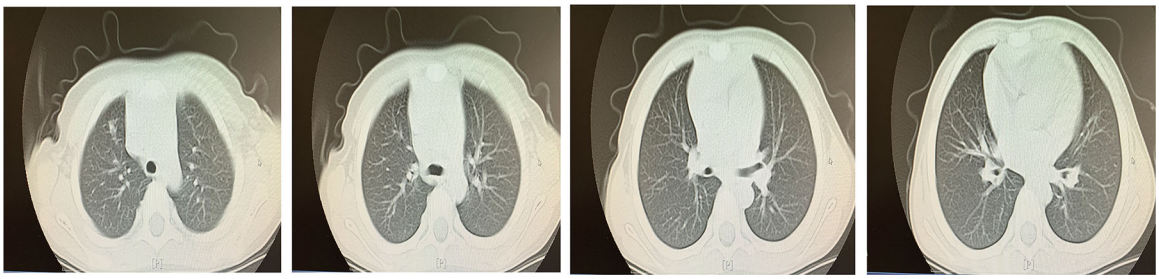

FIGURE 1 The chest computed tomography of case 1 [Color figure can be viewed at wileyonlinelibrary.com]

lymphocyte: 2.63×10^9/L, and CRP: 0.56 mg/L; blood biochemistry results showed total protein: 64.3 g/L, albumin: 42.0 g/L, ALT: 13 U/L, AST: 27 U/L, total bilirubin: 4.6 μmol/L, direct bilirubin: 0.7 μmol/L, indirect bilirubin: 3.9 μmol/L, total bile acid: 5.4 μmol/L, urea: 4.6 mmol/L, creatinine: 35 μmol/L, and uric acid: 318 μmol/L; and there were no obvious abnormalities in six blood coagulation parameters or the myocardial enzyme range. A chest CT showed increased and slightly disordered bronchovascular bundles on both sides (Figure 2). Real-time fluorescence RT-PCR detection of SARSCoV-2 nucleic acid in respiratory tract samples was initially negative but positive after 1 day,[2] but the signs were still mild. After admission, supportive treatment and oxygen therapy were strengthened. At present, the patient's vital signs are stable. She is still under active treatment and has not been discharged. The family genealy of the two kids see (Figure 3).

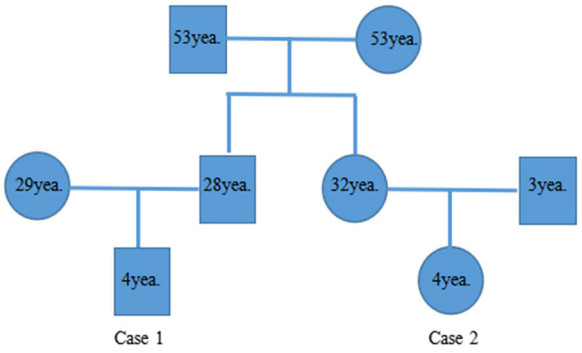

FIGURE 3 The family genealy of the two kids [Color figure can be viewed at wileyonlinelibrary.com]

2 | DISCUSSION

In response to the epidemic, China has launched the first-level response to major public health emergencies. As of 24:00 on February 5th, the National Health Commission has received a total of 28 018 confirmed cases reported. The number of confirmed cases is far more than the total number of confirmed cases of a severe acute respiratory syndrome (SARS) worldwide, which indicates that the infectivity of SARSCoV-2 is higher than that of SARS coronavirus. There have been 3859 severe cases, 563 fatal cases, and more than 110 confirmed cases in children. The disease is still in progress.[3] SARSCoV-2 is the seventh coronavirus that can infect humans and belongs to the β-coronavirus group. Current research shows that SARSCoV-2 may come from wild animals, but its specific source needs further study. SARSCoV-2 is a new β-coronavirus, and its gene sequence is most similar to that of viruses isolated from bats, but there is likely an unknown intermediate host. At present, it has been found that patients with SARSCoV-2 infection are the main source of infection, and the transmission effect of asymptomatic patients should not be underestimated. According to the current data, the main routes of transmission are respiratory droplet transmission and contact transmission. Close contact with patients with SARSCoV-2 infection and asymptomatic infection is the main way to cause children's infection. It has also been reported that SARSCoV-2 can also be transmitted through aerosols, the fecal-oral route, and suspected mother-to-infant transmission.

The incubation period of SARSCoV-2 infection in children is 1 to 14 days, generally 3 to 7 days. The clinical manifestations are asymptomatic or include fever, fatigue, and dry cough; a few patients have upper respiratory tract symptoms, such as nasal obstruction, runny nose, and sore throat; and a few patients have gastrointestinal symptoms, such as abdominal discomfort, nausea, vomiting, stomachache, and diarrhea.

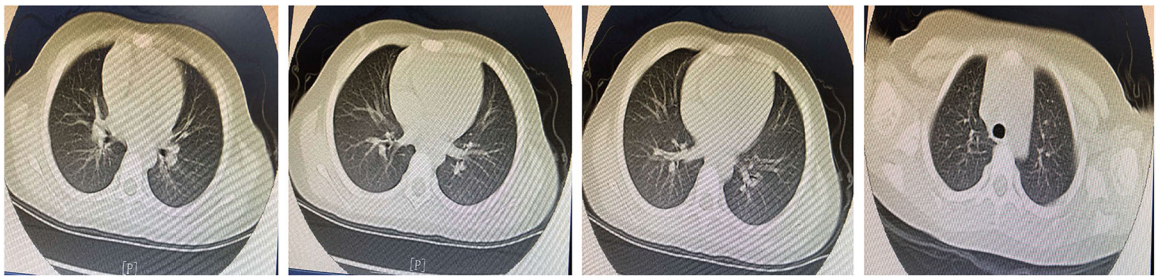

FIGURE 2 The chest computed tomography of case 2 [Color figure can be viewed at wileyonlinelibrary.com]

From the current situation of pediatric cases, most of the clinical manifestations are relatively mild, with no fever or pneumonia, and have a good prognosis. Most children have recovered within 1 to 2 weeks, but some pediatric cases may progress to lower respiratory tract infection. The clinical classification of COVID-2019 is divided into four types. (a) Asymptomatic infection (recessive infection): the SARSCoV-2 etiology test is positive, but there are no corresponding clinical symptoms, and imaging examination is normal. (b) Acute upper respiratory tract infection: only fever, cough, pharyngeal pain, nasal obstruction, fatigue, headache, myalgia, or discomfort are observed. There is no pneumonia manifestation on imaging examination or pyemia. (c) Mild pneumonia: with or without fever and accompanied by respiratory symptoms such as cough; chest imaging examination shows pneumonia manifestations but does not reach the threshold of severe pneumonia. (d) Severe pneumonia: any of the following: (i) respiratory rate increase: RR ≥ 70 times/min under 1-year old or RR ≥ 50 times/min over 1-year old, excluding the effects of fever and crying; (ii) oxygen saturation <92%; (iii) manifestations of anoxia: auxiliary respiration (moaning, nasal flaring, and trireTraction sign is positive), cyanosis, and intermittent apnea; (iv) disturbance of consciousness: drowsiness, coma, and convulsion; and (v) food refusal or feeding difficulty and dehydration signs. (e) Critically ill children: those who meet one of the following conditions and need ICU monitoring and treatment: (i) respiratory failure with mechanical ventilation; (ii) shock; and (iii) combination with other organ failures.[4]

Compared with the clinical characteristics of adult cases, the obvious phase of symptoms lasts for 1 to 2 weeks after the disease, and the detoxification period can lasts for 3 to 4 weeks or longer. The condition of children is obviously milder, recovery faster, and have a better prognosis.[5] We observed that the SARSCoV-2 infection in the two children was characterized by familial aggregation, which further proved that SARSCoV-2 had the characteristics of human-to-human transmission. And the conditions of the two cases were relatively mild, while the six adults who were in close contact with them all had symptoms such as high fever and dyspnea. Case 1 with SARSCoV-2 infection had only mild respiratory tract infection symptoms, the chest CT indicated pulmonary infection, and case 2 had no clinical manifestations of infection. The laboratory examination, including the blood test, CRP, liver, and kidney function and myocardial zymogram, and so forth of the two infected children were not significantly abnormal, which was different from the SARSCoV-2 infection in an adult. In addition to the symptoms of severe respiratory tract infection, most of the adult patients with different degrees of abnormal liver function. At present, there were no obvious manifestations of abnormal liver function among the children infected with infection in domestic reports.[6-8] Among the confirmed cases of the SARS, there were only 135 cases of infection in children, and there were no deaths in children under 12 years old. The MERS caused 2143 people infected and 750 fatal cases, while 11 children been confirmed to be infected with MERS, the symptoms were mild. The symptoms of children infected with SARSCoV-2 are mild or even asymptomatic, which may be its characteristic. With the wide application of pathogen detection, whether the number of cases in children will increase needs to be observed with more clinical data.

According to the current epidemiological data, the infection rate of SARSCoV-2 to children is low. Studies have demonstrated that SARSCoV-2 has a similar binding receptor and binding properties to SARS-CoV, namely the S protein of coronavirus, which is mainly responsible for binding to the receptor protein of the infected host, enabling the virus to invade and infect host cells. Studies have shown that angiotensin-converting-enzyme-2 (ACE2) is the receptor protein of S protein, which provides evidence for human infection of SARSCoV-2.[9,10] The study[11] analyzed the mononuclear RNA sequencing data of more than 430 000 human lung cells (non-SARSCoV-2 infection), and found that more than 80% of the ACE2 in the lung was distributed on the surface of type II alveolar epithelial cells (AT2). ACE2 is necessary for SARSCoV-2 to enter into cells and may be one of the receptors of SARSCoV-2. The reason for the low susceptibility of children to SARSCoV-2 may be related to the imperfect development and function of ACE2 protein, or the intracellular response induced by ACE2 in alveolar epithelial cells of children is lower than that of adults. In addition, it may also be related to the imperfect innate immune development of children, and the subsequent low level of adaptive immune response.[5] The symptoms of COVID-2019 in children are mild which may be related to a reduce inflammatory response because the immune system in children is less well developed. Epidemiological studies show that 43 of 99 adults infected with SARSCoV-2 have different degrees of abnormal liver function. Further studies showed that the abnormal liver function of the patients infected with SARSCoV-2 may be caused by bile duct cell dysfunction and other reasons, but not related to the direct damage of hepatocytes.[12,13] In addition, children are susceptible to a variety of viruses, such as influenza viruses, parainfluenza viruses, adenoviruses, respiratory syncytial viruses, and rhinoviruses. Antibodies produced after infection may cross-react with the coronaviruses to provide some protection. Further studies are needed to confirm whether these manifestations lead to differences in the clinical manifestations of children and adults were infected, whether there are still unexplored mechanisms.

In view of the fact that SARSCoV-2 infection has caused serious social harm and adverse effects, seriously affected people's normal life, therefore, early detection, diagnosis, and timely treatment is an urgent task at present.

The viral nucleic acid detection is still the only gold standard, but clinicians will cross verify according to clinical manifestations and CT images to improve the accuracy. Viral nucleic acid testing is high specificity, but low sensitivity and high technical requirements and the disease changes of pathogen carriers may limit the timeliness of nucleic acid testing. Studies have shown that infection can be limited to the lower respiratory tract. Diagnostic swab samples, which are obtained from the upper respiratory tract, can be negative in the context of typical chest CT findings. In addition, false-negative results can be caused by the wrong collection method and the long storage time (degradation of viral nucleic acid). Early CT scanning may detect significant changes. The suspected diagnosis of children infected

with SARSCoV-2 requires a clear epidemiological, including (a) travel or living history of Wuhan and surrounding areas, or other communities with the patients within 14 days before the onset of the disease; (b) contact history with SARSCoV-2-infected people (nucleic acid test is positive) within 14 days before the onset of the disease; (c) contacted the patients with fever or respiratory symptoms from Wuhan and surrounding areas, or from the community with the case report, have been within 14 days before the onset of the disease; (d) clustering occurrence. And two of the following three clinical manifestations can be diagnosed. The clinical manifestation: (a) fever and/or respiratory symptoms; (b) early chest imaging examination showed multiple small patch shadows and interstitial changes, which were obvious in the peripheral lung, and then developed into multiple ground glass shadows and/or infiltrating shadows in both lungs. Lung consolidation and pleural effusion were rare in severe cases; (c) the total number of WBC in the early stage of the disease was normal or decreased, or the lymphocyte count was decreased. Confirmed cases need to have met one of the two conditions: (a) nucleic acid of SARSCoV-2 test in respiratory or blood samples is positive; (b) the viral gene sequencing of respiratory or blood samples is highly homologous with the SARSCoV-2.[4] This change clarifies the diagnosis of SARSCoV-2 infections in children, although a small number of cases need to be further assessed based on clinical dynamics.

In terms of treatment: the SARSCoV-2 vaccine is still under development, and there is no specific drug at present. It is mainly targeted at symptomatic and supportive treatment. Keep internal environment stable and and respiratory frequency of patient. Oxygen therapy according to the condition. Some antiviral drugs (such as interferon) can be effective, if combined with a bacterial infection, can be treated with appropriate antibiotics.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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