Clinical Infectious Diseases

BRIEF REPORT

A Case Series of Children With 2019 Novel Coronavirus Infection: Clinical and Epidemiological Features

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(See the Editorial Commentary by Fuk-Woo Chan et al, on pages 1552–3.)

We first described the 2019 novel coronavirus infection in 10 children occurring in areas other than Wuhan. The coronavirus diseases in children are usually mild and epidemiological exposure is a key clue to recognize pediatric case. Prolonged virus shedding is observed in respiratory tract and feces at the convalescent stage.

Keyword. 2019 novel coronavirus; coronavirus diseases; children.

A novel coronavirus (2019-nCoV) was identified as the causative agent associated with a cluster of cases of pneumonia detected in Wuhan City by Chinese authorities on 7 January [1]. Since the discovery of 2019-nCoV, the virus has been diagnosed quickly [2, 3]. With the number of people confirmed with 2019-nCoV rising rapidly in Wuhan and increasing outside of Wuhan and China, the World Health Organization declared that the outbreak of 2019-nCoV constitutes a Public Health Emergency of International Concern on 30 January 2020 [4]. By 11 February 2020, 44 672 confirmed cases were reported in China with 8255 (18.5%) severe cases and 1023 (2.3%) deaths, and 395 confirmed cases with 1 death were reported in 24 countries outside of China [5, 6]. Thus far, the notifiable cases were mostly among adults, with pediatric cases rarely reported [7, 8]. The clinical profiles of 2019-nCoV infection in children is unknown. Herein we reported the clinical and epidemiological features in children with coronavirus diseases (COVID) in China.

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METHOD

Between 19 January and 3 February, 2020, a total of 10 children with confirmed 2019-nCoV infection were admitted to the Children's Hospital in Shanghai, Hainan, Hefei in Anhui province, and Qingdao in Shandong province. According to China Centers for Disease Control and Prevention (CDC) protocol for detection of 2019-nCoV, a duplex 1-step real-time reverse transcription polymerase chain reaction was performed to confirm 2019-nCoV infection at the local CDC reference laboratory. If respiratory samples obtained from patients were successfully tested positive by both open reading frame 1ab gene and nucleocapsid protein gene, the specimens were considered as positive and the case was considered to be laboratory-confirmed. A cycle threshold value <35 was defined as a positive test. All pediatric cases were hospitalized for the screening of 2019-nCoV infection when they were considered as suspected cases based on the following 2 criteria: having an epidemiological link to adult cases or an exposure to Wuhan or other epidemic areas in Hubei province and presenting with acute fever and or respiratory symptoms. All patients were admitted to the isolation ward within 2 days after illness onset, and nasopharyngeal and throat swabs were collected immediately for the detection of 2019-nCoV. At the meantime, influenza virus A and B were routinely tested on respiratory swab by colloidal gold assay for all patients.

RESULTS

The detailed information on patients was shown in Table 1. Seven (70%) children were local residents, 2 (20%) were from Wuhan, and 1 (10%) was from Xiaogan (an endemic area 50 kilometers far away from Wuhan). Eight (80%) children had direct contact with adult patients with 2019-nCoV infection who had a history of travel to Wuhan or contact with persons from Wuhan. Exposure setting included household exposure in 7 patients (70%), endemic area exposure in 2 patients (20%), and bus traveling exposure in 1 (10%) patient who had contact with 2 adult travelers from Wuhan who already had mild respiratory symptoms during the bus traveling and were confirmed with COVID after returning to Wuhan. Among 7 children exposed to household adult cases, the number of secondary symptomatic cases including the child ranged from 1 to 4 (mean: 2.43). For the 3-month-old infant (patient 7 in Table 1), her parents developed symptomatic COVID 7 days after they looked after the sick baby without protection measures. The interval between symptom onset and exposure to index symptomatic case ranged from 2 to 10 days (mean: 6.5 days), and the interval between symptom onset and departure from endemic areas was 1 day and 9 days.

Table 1. Epidemiological and Clinical Features Among 2019-nCoV Infected Children

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Basic information										
Admission date	19 Jan	25 Jan	31 Jan	1 Feb	3 Feb	30 Jan	26 Jan	1 Feb	27 Jan	27 Jan
City	Shanghai	Shanghai	Shanghai	Shanghai	Shanghai	Qingdao	Haikou	Sanya	Sanya	Hefei
Age (month)	84	131	131	108	7	72	3	48	96	60
Sex	Male	Female	Female	Male	Female	Female	Female	Female	Male	Male
Epidemiological history										
Exposure setting	Household	Household	Epidemic area	Bus traveling[a]	Household	Household	Epidemic area	Household	Household	Household
Contact with index case directly	Yes	Yes	Unknown	Yes	Yes	Yes	Unknown	**Yes**	**Yes**	**Yes**
Index case	Father	Adult sister	Unknown	Wuhan travelers	Grandfather	Grandmother	Unknown	Friends	Mother	Grand-mother
The interval between symptom onset and exposure to index case (days)	8	7	Unknown	8	7	3	Unknown	10	2	7
Number of secondary symptomatic cases including the child[b]	1	1	1	1	3	4	3	3	3	2
Clinical characteristics										
Peak of fever (°C)	38·0	38.4	37.7	39.2	Afebrile	38.5	38.2	afebrile	38.6	38.5
Duration of fever (days)	1	1	1	1		1	1			1
Cough	Yes		Yes	Yes	Yes			**Yes**		**Yes**
Sneezing				Yes	Yes					
Stuffy nose		Yes	Yes		Yes					
Rhinorrhea				Yes	Yes					
Sore throat		Yes	Yes	Yes					**Yes**	
Dyspnea										
Diarrhea										
Treatment										
Symptomatic treatment	Yes	Yes	Yes	Yes	Yes	Yes	Yes	**Yes**	**Yes**	**Yes**
Antibiotic						Yes	Yes	**Yes**	**Yes**	**Yes**
Radiographic findings										
Chest X-ray	Normal	Normal	Retrocardiac opacity on the left	Opacities in the right lung	Opacities in the right lung	Normal	Normal	Opacities in the right lung	Normal	Normal
Laboratory findings										
White blood cell count ($\times 10^9$/L); (normal range 3.9–9.9)	16.0↑	5.9	6.7	3.2↓	8.0	6.0	9.7	5.4	11.9↑	12.5↑
Hemoglobin (g/dL); (normal range 11–16)	12.8	14.2	13	15.2	11.3	13	12.3	13.1	12.1	14.4
Neutrophil count ($\times 10^9$/L); (normal range 2·0–7·0)	11.2↑	3.4	3.2	1.1↓	2.0	1.6↓	4.2	1.3↓	8.07	7.4

Table 1. Continued

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Lymphocyte count (×10^9/L); (normal range 1·2–4.0)	3.2	1.7	1.2	1.7	5.1	3.7	4.2↑	3.6	2.1	3.3
Platelet count (×10^9/L); (normal range 162–341)	138	184	211	312	188	186	494↑	311	357↑	266
C-reactive protein (mg/L); (normal range 0.0–8·0)	15.0↑	8.0	16.0↑	35.0↑	8.0	7.0	5.6	0.5	3.1	4.8
Procalcitonin (ng/dL);(normal range 0.0–0.5)	0.07	0.03	0.08	0.07	0.12	0.03	0.07	0.02	0.05	0.09
Creatine kinase-MB (U/L);(normal range <25)	29.0↑	14.9	42.3↑	12.3	33.0↑	13	12	27.0↑	31.0↑	19
Alanine aminotransferase (U/L); (normal range 9·0–50·0)	17.0	7.7	19.8	26.2	100↑	13.6	40.0	19.0	18.0	14.0
Aspartate aminotransferase (U/L); (normal range15·0–40·0)	33.0	21.4	27.5	19.7	142↑	24.5	51.0↑	28.0	20.0	34.0
Urea (mmol/L); (normal range 2·8–7.6)	3.7	4.1	3.2	3.2	1.9↓	3.8	0.5↓	2.6↓	3.0	3.0
Creatinine (μmol/L);(normal range 21–65)	29.0	54.0	54.0	48.0	13.0↓	58.9	16.0↓	23.0	38.0	33.0
Lactate dehydrogenase (U/L); (normal range 110–290)	394↑	161	228	189	368↑	194	280	Normal	Normal	304↑
D-dimer (μg/mL); (normal range 0.0–0.5)	0.6↑		0.3	0.6↑		0.2	Normal			
Detection of 2019-nCoV RNA										
Nasopharyngeal/ throat swabs	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Duration of virus shedding in respiratory swabs (days)	12	22	8	8	6	15	8	12	14	15
Stool	Positive	Negative	Positive	Positive	Positive	Not tested[c]	Positive	Not tested[c]	Not tested[c]	Not tested[c]
Duration of virus shedding in stool (days)	>30	10	>20	>19	>18	Not tested[c]	>23	Not tested[c]	Not tested[c]	Not tested[c]
Urine	Negative	Negative	Negative	Negative	Negative	Not tested[c]	Negative	Not tested[c]	Not tested[c]	Not tested[c]
Serum	Negative	Negative	Negative	Negative	Negative	Not tested[c]	Negative	Not tested[c]	Not tested[c]	Not tested[c]

Abbreviation: nCoV, novel coronavirus.

[a]Patient 4 contacted 2 adult travellers from Wuhan who already had mild respiratory symptoms during the bus travelling and were confirmed with COVID after returning to Wuhan.

[b]The number of symptomatic secondary cases included the sum of the affected child in this case series and his/her family members who were exposed a common index case and developed symptoms.

[c]Not tested means the patient's sample not being tested for 2019-nCoV RNA.

The 10 patients were aged 3–131 months (mean: 74 months), and the ratio of male to female was 1:1.5. Eight (80%) patients had fever, 6 (60%) had cough, 4 (40%) had sore throat, 3 (30%) had stuffy nose, and 2 (20%) had sneezing and rhinorrhea. None of patients had diarrhea or dyspnea during the course of illness. Fever resolved 24 hours after fever onset with the peak of fever ranging from 37.7°C to 39.2°C. Chest radiograph revealed unilateral patchy infiltrate in 4 (40%) of 10 patients. The laboratory findings showed (median): white blood cell count 7.35×10^9/L, C-reactive protein 7.5 mg/L, procalcitonin 0.07 ng/dL, creatine kinase-MB 23 U/L, alanine aminotransferase 18.5 U/L, aspartate aminotransferase 27.7 U/L, urea 3.1 mmol/L, creatinine 35.5 μmol/L, lactate dehydrogenase 25 U/L, and D-dimer 0.45 μg/mL; influenza virus A and B were all negative. All patients received symptomatic treatment with no need of oxygen therapy, and a few of the patients with pneumonia received empirical antibiotic therapy. As of 19 February, all patients had been discharged when they recovered uneventfully with 2 consecutive respiratory samples tested negative for 2019-nCoV RNA.

2019-nCoV RNA was detected in nasopharyngeal and throat swabs from all patients within 4–48 hours after symptom onset. 2019-nCoV RNA in nasopharyngeal/throat swabs was undetectable within 6–22 days (mean: 12 days) after illness onset. Six patients had fecal samples tested for 2019-nCoV RNA within 3–13 days after illness onset, and 5 (83.3%) showed positivity (of note, fecal sample from patient 2 was obtained on day 10 after illness onset and showed negativity). As of 19 February, these 5 patients still have 2019-nCoV RNA detected in feces within 18–30 days after illness onset and are under close follow-up. Five patients had urine and serum samples tested for 2019-nCoV RNA within 2–3 days after illness onset, and all showed negativity.

DISCUSSION

This is the first case series report on 2019-nCoV infection in children. Our preliminary clinical findings showed that children with COVID usually presented with mild respiratory infections, as compared with adult cases [9]. For pediatric patients, fever and mild cough are common symptoms at disease onset. For mild cases, fever is brief and resolved rapidly. A few of the patients presenting with/without cough also showed radiographic evidence of patchy infiltrate at symptom onset. In one study of a family cluster, an asymptomatic 10-year-old child infected with 2019-nCoV due to household exposure had radiological ground-glass lung opacities [7]. Radiographic evidence of pneumonia was a characteristics of 2019-nCoV infection at the earliest stage of infection; thus, close observation is very necessary for a child with either mild symptomatic or asymptomatic infection. We d not recommend use of antiviral agents for the treatment of self-limited nonsevere COVID because no evidence has shown the effectiveness of antiviral agents currently available. Influenza virus screening is necessary to rule out the possible coinfection considering the seasonal overlap between influenza and COVID. Empirical antibiotic initiation is not recommended for treatment of nonsevere 2019-nCoV-associated pneumonia without evidence of superbacterial infection. By 22 January 2020, all notifiable COVID cases and severe cases were aged ≧ 15 years old in Wuhan [9, 10]. In theory, children are also susceptible to 2019-nCoV and mild or atypical cases were largely underdiagnosed according to the initial screening criteria, which focused on suspected pneumonia cases [2].

The epidemiological evidence has demonstrated that COVID can be transmitted from person to person, and the basic reproductive number was estimated to be 2.2 [10]. We observed the mean number of secondary symptomatic cases in household exposure settings was 2.43. Our findings highly support the evidence of human-to-human transmission of COVID. All pediatric patients had an epidemiological link directly or indirectly to Wuhan or other endemic area of Hubei, where the outbreak of COVID originated and is ongoing. Most of the pediatric cases occurring outside of Wuhan were secondary cases after exposure to adult cases through household contact or travel contact. However, we cannot neglect the potential risk of transmission from the infected child to adult contacts, as shown in patient 7. Thus, personal medical protection is crucial when care providers look after the infected child. The major pattern of transmission was intrafamily transmission. The general transmission pattern of COVID is similar to that of SARS and MERS in children [11, 12]. Based on our field investigation, the mean incubation period between household exposure to a symptomatic adult case and symptom onset was 6.5 days, longer than 5.4 days observed in adult cases [10]. This difference could be suggestive of longer incubation period for 2019-nCoV infection in children. Currently, these epidemiological features are a key clue to help early recognition of 2019-nCoV infection in children outside of Wuhan and take infection prevention control interventions in time.

Virus shedding in respiratory specimens is longer in children with mild COVID, which will impose a challenge for infection control. 2019-nCoV RNA was not detected in serum samples in our study. Viremia could be related to the severity of disease because 2019-nCoV RNA was detected in blood samples obtained from 15% of adult patients with pneumonia [9]. Surprisingly, we also noted a high frequency (83.3%) of 2019-nCoV RNA detection in feces in mild patients and prolonged virus RNA shedding in feces for at least 2 weeks and even more than 1 month, which raises a question concerning whether the gastrointestinal tract may be another site of viral replication. The impact on 2019-nCoV shedding in feces on transmission model and infection prevention and control should be further assessed.

The COVID epidemic is now spreading globally. Further research and surveillance are crucial to help us understand the clinical characteristics and natural history of 2019-nCoV infection in children.

Notes

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Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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