Clinical Implications of 37 Childhood Cases with 2019-nCoV Infection in Shenzhen, China

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Abstract

Background 2019-nCoV was first identified in December 2019 in samples obtained from a 61 years old man who died of acute respiratory failure in the city of Wuhan, China with a subsequent outbreak in China. Till now, there were rare reports about childhood patients with 2019-nCoV infection.

Methods We report 37 children diagnosed with 2019-nCoV infection admitted in the Third People's hospital of Shenzhen from December 11, 2019 to February 11, 2020.

Results There were 9 mild cases, 20 common cases and 1 severe case and 7 cases with asymptomatic infection. The age ranged from 7 months to 18 years old and the median age was 7 years old. The common clinical features were fever (29.7%, 11/37) and cough (32.4%, 12/37). No death occurred among our patients. 86.5% (32/37) children were infected with 2019-nCoV after their family members (parents or grandparents). 1 child was identified with 2019-nCoV infection after 3 times testing. The majority (78.4%) of cases occurred in those children who travelled to Hubei Province. The percentage of cases in preschool and in schools was 21.6% and 54.1% ($P<0.05$) respectively.

Conclusions Family cluster transmission of 2019-nCoV was suspected in 86.5% of patients. Timely continuous 2019-nCoV pathogen testing is recommended. More attention should be paid to school children.

Background

In December 2019, the 2019-nCoV infection was first reported in Wuhan, China in a 61 years old man with severe pneumonia. The virus causes worldwide infections, as well as family cluster and health-care-associated infections. As of February 15, 2020, 66576 people have been identified as having 2019-nCoV infection, and 1524 have died since the first reported case was detected. Till now, there were rare reports about childhood

patients. Here we report 37 pediatric cases of 2019-nCoV infections. Data was collected including the epidemiological and clinical features, laboratory findings and treatment outcomes in a China outbreak.

Methods

Ethical consideration

This study was approved by the Ethics Committee of the Third People's Hospital of Shenzhen, China, on January 23, 2020. Informed consent was obtained from the patients' guardians.

Clinical and epidemic findings*:* We obtained clinical data and possible exposures to 2019-nCoV by direct interviewing with their guardians. All symptoms, physical examination, laboratory, and image data were obtained from medical records. The patients' inclusion criteria were: (1) below 18 years old, (2) laboratory-confirmed 2019-nCoV infection with PCR (polymerase chain reaction) test of the virus in samples taken from the respiratory tract of the patient, and (3) patients admitted to the Third People's Hospital of Shenzhen from January 11, 2020 to February 11, 2020. The exclusion criteria were suspected cases of 2019-nCoV without a confirmed diagnosis. All acquired data were crosschecked by two physicians to ensure that there was no duplicated data. Clinical classification was recommended according to the diagnostic criteria.

Specimen collection: Nasopharyngeal swabs, sputum, blood and/or tracheal aspiration samples were tested for nucleic acid from each patient at various times. Two sets of nasopharyngeal swab samples were collected at initial diagnosis. Follow-up sets of specimens were collected after symptoms had disappeared.

2019-nCoV laboratory testing: Specimens were tested using a 2019-nCoV real-time reverse transcription PCR (RT-qPCR) method. A licensed kit was recommended by National microbiology Data Center of China for detection of 2019-nCoV. The related laboratory

information shows below.

Target 1 (ORF1ab):

Forward Primer(F)：CCCTGTGGGTTTTACACTTAA

Reverse Primer(R)：ACGATTGTGCATCAGCTGA

Fluorescent probe(P)：5'-FAM-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3'

Target 2(N):

Forward Primer(F)：GGGGAACTTCTCCTGCTAGAAT

Reverse Primer(R))：CAGACATTTTGCTCTCAAGCTG

Fluorescent probe(P)：5'-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3'

C_t value of virus>40 is negative, <37 is positive, between 37 and 40 is susceptive and timely continuous testing is recommended. All PCR procedures were done at Center for Disease Control and Prevention of Shenzhen and the results were reported within 48 hours of collection.

Treatment: According to the guideline, Lopinavir/litonavir (200mg/50mg), the recommended doses: weight 7-15kg, 12mg/3mg/kg; weight 15-40 kg, 10 mg/2.5 mg/kg; weight >40 kg, 400 mg/100 mg as adult each time, twice a day for 1-2 weeks. Interferon-α2b nebulization, 100,000-200,000 IU/kg, twice a day for 5-7 days. No patients received intravenous immunoglobulin (IVIG) and methyl-prednisone.

Data analysis: Basic descriptive analyses were carried out in all patients. A result of p value<0.05 indicated statistically significant. IBM SPSS statistics was used for statistical analyses.

Results

Gender and age distribution of 2019-nCoV infection

A total of 37 patients, including 19 boys and 18 girls, met the eligible criteria. There were 9 mild cases, 20 common cases, 1 severe case and 7 cases with asymptomatic infection. The male had relatively higher opportunity to be infected by 2019-nCoV than female, but the difference did not show significantly (P>0.05) (table 1). The age ranged from 7 months to 18 years old and the median age was 7 years old. The percentage of cases in preschool and in schools was 21.6% and 54.1% (P<0.05) respectively (table 2).

Clinical manifestations, radiological and laboratory findings of the cases

The onset clinical characteristics included fever (29.7%, 11/37) and cough (32.4%, 12/37. The temperature ranged from 38.0℃ to 39.0℃. Table 3 showed the clinical manifestations, radiological and laboratory findings of the cases. The majority of thoracic physical examination was normal but thoracic Computed Tomography (CT) showed multiple small ground-glass appearance on lower lobe of both lungs (figure 1). Only 1 case had wheezes and hypoxia and there was no critical case. 29 cases (78.4%) had travelled to Hubei Province and 33 (89.2%) were infected with 2019-nCoV after their family members (parents or grandparents). 1 child’s specimen was tested 2019-nCoV RT-qPCR for three times within two weeks and was identified with 2019-nCoV infection eventually.

Discussion

In this report, 86.5% people among the close contacts acquired the infection, the finding indicated that the family cluster transmission of 2019-nCoV was the main mode of transmission among children. The median incubation duration for secondary cases associated with human to human transmission is about 14 days. Only one patient had no epidemiologic exposure history. The median time from illness onset to diagnosis was 2 days.

7 patients had asymptomatic infection but showed pneumonia upon thoracic CT. The lack of prominent symptoms often delayed diagnosis. The thoracic CT findings of 2019-nCoV

infection may present bilateral patchy densities, interstitial infiltrates, or opacities, consolidation, and pleural effusions in adults'. However, our pediatric pneumonia typically infected the lower lobes. So those cases of lower-lobe pneumonia that occur during 2019-nCoV outbreak and had epidemiology history of exposure should be considered the possibility of 2019-nCoV infection.

It was reported that fever, sore throat, cough, myalgia, lymphopenia usually occurred among adult patients. However, only one third of our patients presented fever. The respiratory symptoms such as cough and sputum were not prominent during the onset of the disease. Mildly increased C-reactive protein (CRP), Lactate dehydrogenase (LDH) and white blood cells (WBC) level occurred in 5 patients respectively. Only 1 patient presented neutropenia which was frequently observed in adult patients. Previous study indicatedthat age, viral load and blood biochemistry indexes such as, CRP and LDH may be predictors of disease severity. It was evident that childhood patients' laboratory features were not similar to adults'.

We noticed that school children predominance of 2019-nCoV infection was observed in our study. Till now, the reason for the difference is still unknown and may attribute to the school children's activity.

In this report, the positive rate of 2019-nCoV was 89.2% at admission. 3 patients were identified with 2019-nCoV infection two days later and 1 child was confirmed infected case the third time ten days later. So those children who had a history of exposure to 2019-nCoV infected patients are recommended for timely continuous 2019-nCoV pathogen testing in order to effectively diagnose the patients and promptly to isolate the source of infection. An extensive public awareness campaign may play an important role in preventing the spread of infection.

Previously Lopinavir/ritonavir and INF-a2b nebulization were used during the SARS

epidemic of 2003 and MERS of 2014[7]. These drugs kill viruses at high doses individually, whereas a combination of Lopinavir/ritonavir and IFN-a2b had a synergistic affection at much lower doses with possible lower toxicity. 2019-nCoV is similar to the 2 CoVs, so therapy with Lopinavir/ritonavir and IFN-a2b may be a potential treatment for 2019-nCoV. Further study should be carried out to better understand the therapeutic effect of antiviral treatment.

Conclusions

This report suggests that family cluster transmission of 2019-nCoV was suspected in 86.5% of patients. Timely continuous 2019-nCoV pathogen testing is recommended. A high degree of attention should be paid to school children.

Abbreviations

2019-new coronavirus (2019-nCoV)

Interferon-α2b (IFN-a2b)

Center for Disease Control and Prevention (CDC)

PCR (polymerase chain reaction)

Real-time reverse transcription PCR (RT-qPCR)

Computed Tomography (CT)

C-reactive protein (CRP)

Lactate dehydrogenase (LDH)

White blood cell (WBC)

Declarations

Ethics approval and consent to participate: The study was approved by the Ethics Committees of the Third People' Hospital of Shenzhen. Informed consent was obtained from parents or guardian for participants under 16 years old.

Consent for publication

Consent for publication obtained from guardians

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions Y Y and XW: data collection and clinical diagnosis of patients; Y L and LL: Study design; YW: data analysis and writing. All authors read and approved the final manuscript.

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Tables

Table 1 Gender-Specific proportion of cases infected with 2019-nCov

Gender	Asymptomatic infection	Mild patients	Common patients	Severe patients
Male	2(28.6)	5(55.6)	13(65.0)	0(0)
Female	5(71.4)	4(44.4)	7(35)	1(100.0)
total	7(100.0)	9(100.0)	20(100.0)	1(100.0)

Data in brackets refer to percentage of total cases in the corresponding clinical type.

(χ^2=20.405，P value=0.622)

Table 2 Age distribution of 2019-nCov cases

Age (y)	Asymptomatic infection	Mild patients	Common patients	Severe patients
<6	3	6	9	0
>6	4	3	11	1

(χ^2=20.405，P value=0.027)

Table 3. Clinical manifestations, radiological and laboratory findings of the patients

Item	Result
Median age	7y(7m-18y)
Median incubation duration	14d(1-20d)
Median time from illness onset to diagnosis	2d(0.5–10 d)
Fever	
Yes	11
No	26
Cough	
Yes	12
No	25
diarrhea/vomit	
Yes	1
No	36
CT/DR	
Positive	20
Negative	17
Leukocyte	
<4*109/L	1
4-10*109/L	31
>10*109/L	5
Lymphocyte	
$<1.5*10^9$/L	1
Normal	36
CRP	
<10mg/L	32
>10mg/L	5
LDH	
Normal	32
≥250U/L	5

Figures

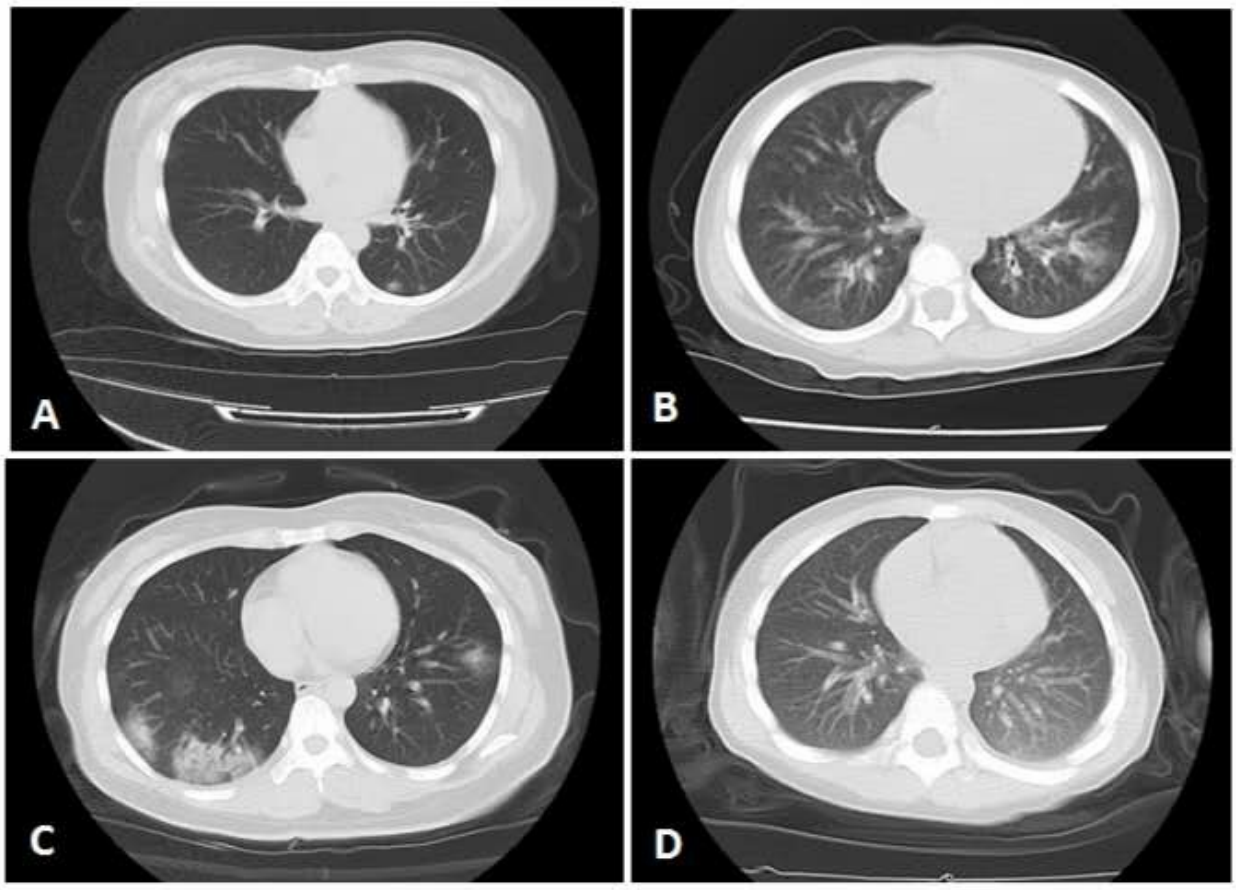

Figure 1

Representative images of the thoracic CT scans in the lungs of patients, A: mild case; Band D:common case; C: severe case