

Original Article

The value of computed tomography in the diagnosis and supervision of infants and children infected with coronavirus 2019 (COVID-19)

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Abstract: Pneumonia associated with COVID-19 had been a concerning and serious public health threat around the world. In this article, we retrospectively explored the value of unenhanced chest CT in the diagnosis and supervision of infants and children infected with COVID-19 from Beijing, China. A total of 25 infants and children who were confirmed to have COVID-19 by reverse transcription polymerase chain reaction (RT-PCR) were included. All cases underwent unenhanced chest CT upon admission day, some cases underwent chest CT during hospitalization and during follow-up after discharge, and the CT imaging characteristics were analyzed. Basic information, treatment and follow-up results were recorded. There were 6 infants and 19 children and the median age was 6.5 (3.1-9.5) years old. There were 18 patients upon admission who had negative CT images, 10 with initial negative images that had secondary negative CT scans and 3 children with initial negative images who had third negative CT scans. There were 16 children who were cured and discharged, 7 that were positive in the pharyngeal swab test of nucleic acids during the follow-up period, and all them had initial negative CT images. Leukocytopenia, lymphocytosis, evaluated T lymphocyte and CD4 T lymphocyte counts were found in some cases. We found that the vast majority of infants and children with confirmed COVID-19 had negative CT scans at the initial presentation and follow-up period and this result might suggest a low need for chest CT, meanwhile, some children seemed to have a higher re-positive test of nucleic acids.

Keywords: Computed tomography, infants and children, COVID-19

Introduction

Among adults, patients with confirmed Coronavirus Disease 2019 (COVID-19) have frequent abnormalities on chest CT including bilateral pulmonary parenchymal ground-glass progressing to organizing pneumonia [1-3]. However, the use of chest CT for infants and children with suspected COVID-19 and follow-up of infants and children with confirmed COVID-19 is not well understood. In this report, we describe chest CT, clinical features and management in 25 infants and children with confirmed COVID-19 in Beijing, China.

Materials and methods

Patients and setting

From January 20 to April 15, 2020, all infants (less than 3 years old) and children (3-14 years old) were included with confirmed COVID-19 and who lived in the same house or had close contact with adults confirmed to have COVID-19 illness. COVID-19 in these infants and children was confirmed by reverse transcription polymerase chain reaction (RT-PCR) test for nucleic acids in respiratory samples (pharyngeal swab or phlegm). Detection of other respiratory pathogens, such as influenza A, influenza

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B virus and bacteria, was also performed. All infants and children upon admission day and some cases in the therapeutic process and during follow-up underwent unenhanced chest CT. General information, routine blood tests, C-reactive protein, T-lymphocyte subsets and early clinical symptoms were recorded, and follow-up visits were carried on during the study period.

The study protocol was approved by the ethical committee. The ethical committee waived the requirement to obtain written informed consent because the study was retrospective.

Chest CT scan evaluation

All infants and children underwent unenhanced chest CT scans (Germany's Siemens AG) in the supine position. Infants were sedated to reduce the impact of involuntary movement. A total of 15 patients underwent a second unenhanced CT scan and 5 patients underwent a third unenhanced CT scan to assess for changes during the study time window.

Two radiologists (10 years of experience) independently reviewed the CT images with any disagreements resolved by consensus. If there was no agreement, a third fellowship-trained radiologist with 20 years of experience made the final decision. Each radiologist was blind to the patient scenario.

Statistical analysis

Parameters were tested for normality using the Shapiro Wilk test. Continuous variables were expressed as a median. Categorical variables were expressed as numbers (%). Statistical analyses were performed using SPSS software (version 19; SPSS Inc, Chicago, IL).

Results

A total of 271 patients with RT-PCR confirmed COVID-19 were evaluated over the study period. Of these, 25 (9.2%) cases were infants and children. There were 6 infants and 19 children, 9 males and 16 females, and the median age was 3.8 (2.2-6.5) years old. One child (3 years and 10 months) suffered from acute lymphoblastic leukemia and had undergone 8 cycles of chemotherapy, and was in remission for a long time. Others had no underlying diseases

(e.g., diabetes, hypertension, cardiovascular disease). The families of 22 patients cases had at least 1 infected family member, 3 cases children had recent travel to Wuhan (**Table 1**). Another 16 children cases had been discharged from the hospital and 8 patients remained on the mend, in the hospital at the time of analysis.

Three children (12.5%) had no definite symptoms. In 22 children with symptoms, the median time was 2.0 (1.5-5.0) days from symptom onset to hospital admission. Initial symptoms were fever (36.0%), cough (24.0%), pharyngeal malaise (12.0%), diarrhea (4.0%), fatigue (4.0%), headache (4.0%) and runny nose (4.0%). In the meantime, one infant (9 months) was infected with influenza A virus and the child with acute lymphoblastic leukemia suffered from bacterial pneumonia on admission day. The blood counts results of the infants and children upon admission (the child who suffered from acute lymphoblastic leukemia was excluded) showed that the median level of Leukocytes and Lymphocytes was $5.7 (4.7-8.3) \times 10^9/L$ and $2.9 (1.8-3.8) \times 10^9/L$, and 9 (36.0%) children showed leukocytopenia (less than age-related reference values), and 4 infants and 1 child (20.0%) showed lymphocytosis (more than age-related reference values). The median values of c-reactive protein (CRP) were 0.9 (0.1-1.8) mg/ml. T-lymphocyte subset was tested in 16 cases on admission, the median T lymphocyte amount and CD4 T lymphocyte count were 1852.5 (1403.5-2375.5) cells/u and 1013.5 (662.8-1262) cells/u, which were close to the upper limit of normal, and they increased significantly in 1 infant and 5 children (37.5%). More details were shown in **Table 1**.

Chest CT, with 45 sessions, were performed in all 25 cases, with 15 cases having 2 CT scans and 5 cases having 3 CT scans. The median time interval was 14 (8-26) days and 11 (7.5-27) days between the first and second CT scan and between the second and third CT scan. A total of 5 infants and 13 children (72.0%) had negative images, 1 infant and 6 children (28.0%) had positive images (**Table 2**). Among the infants and children with negative images, all 10 cases with second CT scans and 3 cases with third CT scans were still negative, while 5 (27.8%) children showed leukocytopenia and there were 5 cases (27.8%) with lymphocytosis,

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Table 1. Baseline characteristics of infants and children included in the study (n=25)

Parameter	Number (percent)
Age group	
Infant (<3 years old)	6 (24)
Child (3-14 years old)	19 (76)
Sex	
Female	16 (64)
Male	9 (36)
Age (y)	
Median	3.8
Interquartile Range	2.2-6.5
Exposure history	
Recent travel to Wuhan	3 (12)
Exposure to infected family member (Including 10 imported cases)	22 (88)
Symptoms	
Time from symptom onset to admission (d)	2.0 (1.5-5.0)
Fever	9 (36)
Time of pre-hospital fever(d)	2.0 (1.0-4.8)
Temperature (°C)	38.2 (37.5-38.7)
Cough	6 (24)
Pharyngeal malaise	3 (12)
Diarrhea	1 (4)
Fatigue	1 (4)
Headache	1 (4)
Runny nose	1 (4)
No obvious symptoms	3 (12)
Co-infection	
Virus infection	1 (4)
Bacterial infection	1 (4)
Underling diseases (Acute lymphoblastic leukemia)	1 (4)
Blood routine test (n=24*)	
Leukocytes count (× 10 ⁹ /L)	5.7 (4.7-8.3)
Lymphocyte count (× 10 ⁹ /L)	2.9 (1.8-3.8)
C-reactive protein (mg/ml)	0.9 (0.1-1.8)
T-lymphocyte subsets (n=15)	
T-lymphocyte amounts (cells/ul)	1852.5 (1403.5-2375.5)
CD4 T lymphocyte count (cells/ul)	1013.5 (662.8-1262.0)

Note: Except where indicated, the data in parentheses is percentages. Normal reference values: Leukocytes count, (5-12) × 10⁹/L; Lymphocyte count, (1-5) × 10⁹/L; C-reactive protein <10 mg/mL; T-lymphocyte amounts, (1027-2086) cells/ul; CD4 T lymphocyte count (706-1125) cells/ul; *The child suffered from acute lymphoblastic leukemia was excluded.

and 5 (1 infant and 4 children) of 6 cases (27.8%), had increased T lymphocyte amounts and CD4 T lymphocyte counts. Among the infants and children with positive images, a total of 29 lesions were found at the first CT scan, while most lesions occurred in the peripheral area, there was unilateral involvement in 2 cases (28.6%) and bilateral involvement in 5 cases (71.4%), the median diameter was 11.0 (8-14) mm; the common CT images were mixed

ground glass opacity (GGO) and consolidation (4 cases, 57.1%), pure GGO (1 cases, 14.3%), complete consolidation (1 case, 14.3%) and patchy and streaky shadows (1 case, 14.3%) (**Figure 1**).

After appropriate treatment according to the guidelines of COVID-19 (Trial Version 7) [4], patients were discharged if they met all of the following criteria: body temperature returned to

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Table 2. Chest CT imaging characteristics of infants and children during management

CT imaging	First (n=25)	Second (n=15)	Third (n=5)
Negative images	18 (72.0)	10 (66.7)	3 (60)
Positive images	7 (28.0)	5 (33.3)	2 (40)
Lesion number	29	8	3
Maximum diameter (mm)	11.0 (8.0-15.5)	7.6 (6.3-13.8)	5.2 (4.6-5.9)

Note: Except where indicated, the data in parentheses is percentages.

normal for more than 3 days; respiratory symptoms improved; inflammation of the lungs showed obvious signs of absorption; and pharyngeal swab or phlegm nucleic acid was negative for two consecutive times (one-day sampling time interval at least).

In the following CT scans, 8 lesions were found in 5 cases at the second CT scan and the median diameter was 7.6 (6.3-13.8) mm; 3 lesions were found in 2 cases at the third CT scan and the median diameter was 5.2 (4.6-5.9) mm (**Table 2; Figure 2**). During the follow-up period, 7 cases turned positive in the pharyngeal swab test of nucleic acids, and all of them had initial negative CT images; of these, 3 cases who underwent CT scans still had negative images. All cases that turned positive in nucleic acid testing were asymptomatic and did not require any treatment.

Three asymptomatic children did not obtain any medical treatment but received regular pharyngeal swab nucleic acid tests. Treatment for 6 symptomatic cases included antipyretics, cough-suppression and phlegm-dissipating, such as liquorice tablets (Beijing Double Crane Pharmaceutical Company Limited, Beijing, China), paracetamol (Johnson & Johnson Pharmaceuticals Ltd, Shanghai, China), acetylcysteine solution (Hainan Star Pharmaceutical Co., Ltd, Qionghai, China). Four children received antibacterial [azithromycin (Pfizer Inc, Shanghai, China) or cefmetazole sodium (Sichuan Hexin Pharmaceutical Co., Ltd, Chengdu, China)] combined with antiviral [α -interferon atomization inhalation (Kawin Technology Share-Holding Co., Ltd, Beijing, China) or oseltamivir (Yichang HEC Changjiang Pharmaceutical Co., Ltd, Yichang, China) or peramivir (ranbaxy Guangzhou, Guangzhou, China)] therapy. Seven children received traditional Chinese medicine combined with antiviral [α -interferon

atomization inhalation (Kawin Technology Share-Holding Co., Ltd, Beijing, China)] therapy. Four children received antiviral [α -interferon atomization inhalation (Kawin Technology Share-Holding Co., Ltd, Beijing, China)] therapy only and one child received only antiinfection [ceftriaxone sodium (Roche pharmaceuticals Ltd, Shanghai, China)] therapy. Details are shown in **Table 3**.

Discussion

Infected children and infants with COVID-19 are reported to have mild symptoms and better outcomes than adults [2, 4, 5]. According to COVID-19 guidelines (China National Health Commission), diagnosis and treatment of pneumonia caused by new coronavirus-Trial Version 7), the infants and children in this study had mild and moderate classification of disease. Our study is consistent with those prior results and reveals that most infants and children had negative chest CT scans.

Most studies regarding the use of chest CT for evaluation of pneumonia in COVID-19 are based on data collected from infected adults [6-8]. Even in asymptomatic individuals, positive chest CT findings occur in 88%-100% of cases, including some patients with RT-PCR results [9-11]. Previous research in adults showed intensive care unit admission and fatality rates ranged from 26.1% to 32% and from 4.3% to 15% [12, 13], CT scanning was helpful for diagnosing and monitoring disease and implementing timely treatment [13-15]. The characteristics of clinical and laboratory testing in infants and children were significantly different from adults with COVID-19 infection, such as family clustering (the second or third generation cases with low acute toxicity), timely identification and treatment (early in the course of illness), higher circulating lymphocyte counts, T-lymphocyte and CD4 T lymphocyte count levels (probably resulting from previous high rates of viral infection and vaccination and boosting immune function) in some cases [16], which might have resulted in enhanced immune function and viral clearance, as with the severity being much milder and the clinical progression much less aggressive in young children suffering from severe acute respiratory syndrome

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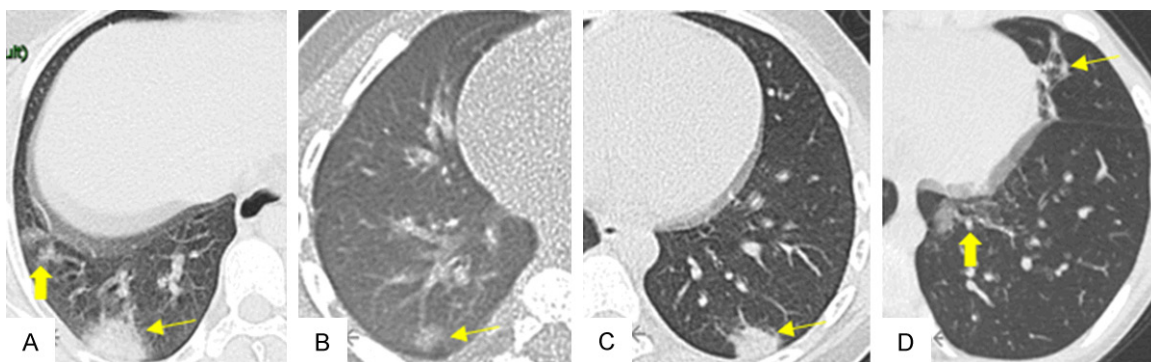


Figure 1. Chest CT findings of infants and children with COVID-19 infection. A: Mixed GGO (thick arrow) and consolidation (thin arrow). B: GGO (thin arrow). C: Consolidation (thin arrow). D: Patchy (thick arrow) and streaky (thin arrow) shadows.

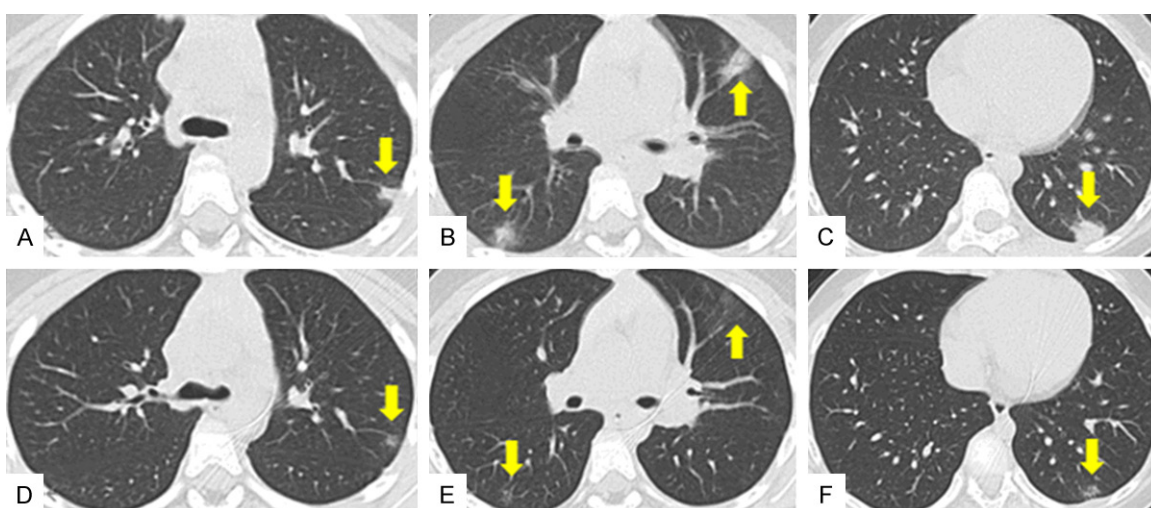


Figure 2. Chest CT image in a child of 6 years and 6 months with history of recent travel to Wuhan who presented with a 2-day fever before admission, the highest temperature is 37.7 °C. A-C: At admission, CT images show scattered subpleural GGO and consolidation in both lungs (thick arrow). D-F: 7 days after admission, CT images show all lesions in both lungs are obviously absorbed (thick arrow).

Table 3. The information about treatment

Measures	Value
No drugs	3 (12.0)
Liquorice tablets, paracetamol, acetylcystein	6 (24.0)
Azithromycin or cephalosporins combining with α -interferon atomization inhalation or oseltamivir or peramivir	4 (16.0)
Traditional Chinese medicine combining with α -interferon atomization inhalation	4 (16.0)
α -interferon atomization inhalation	7 (28.0)
Cephalosporins	1 (4)
Hospital stay times (days)	15 (14.0-18.8)

Note: Except where indicated, the data in parentheses is percentages.

(SARS) [16]. Some studies have shown that young adult patients show significantly less frequency of lesions on CT images compared with middle and older age groups [17, 18], where CT

has little utility in evaluating clinical recovery for children [19]. Therefore, lower positive rates for CT images, mild symptom and favorable outcomes were very common in infants and chil-

dren. At the repeated CT scans, no new lesions were found in the cases with initial negative CT scans. Even among the cases with positive CT images, all lesions were absorbed and significantly reduced or disappeared at the first CT follow-up, and no cases had disease progression, which can be found in some adult patients [14].

A consensus has emerged that CT scans are radioactive, and the risks of future malignancy due to CT scans has been confirmed in childhood, especially in infants [20]. For these reasons, we suggested that performing CT in infants and children should be performed very cautiously for uncomplicated diseases, and that a chest radiography is probably enough. With growing knowledge of COVID-19, further development of diagnostic techniques and incorporation of new technologies, all of which might provide more accurate and faster diagnostic tools in infants and children [21].

Specifically, infected infants and children with initial negative CT images seemed to have higher recurrence rates of positive test of nucleic acids. To some extent, this might predict the negative CT images that didn't represent the complete elimination of COVID-19 from the body, as it could be present in the human body for a longer period and not cause any symptoms.

There are some limitations of this report including a small number of infants and children and lack of long-term follow-up data.

Conclusion

In conclusion, for infants and children with mild symptoms and good prognosis related to COVID-19, chest CT was negative in the most of cases. To avoid unneeded radiation exposure, chest CT scanning should be used judiciously for patients in this age range, meanwhile, a higher recurrence rate of positive test of nucleic acids in this group needs further research.

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Disclosure of conflict of interest

None.

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