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Clinical characteristics and radiological features of children infected with the 2019 novel coronavirus

Y. Lu [a], H. Wen [a], D. Rong [b], Z. Zhou [a], H. Liu [a,*]

[a] *Department of Radiology, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, 318 Renmin Middle Road, Guangzhou, 510120, China*

[b] *Department of Radiology, Third Affiliated Hospital of Sun Yat-Sen University, 600 Tianhe Road, Guangzhou, 510630, China*

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AIM: To identify and summarise the common findings from 2019 novel coronavirus (2019-nCoV) infections in children.

MATERIALS AND METHODS: The clinical characteristics and radiological findings (chest radiography and chest computed tomography [CT]) of nine children infected with the 2019-nCoV were reviewed in this retrospective case series.

RESULTS: Among the children, six had fever (including two children with cough), one had only cough, one had a stuffy nose when initially diagnosed, and one was an asymptomatic carrier. Chest radiographs seemed mostly normal in six cases whereas increased and/or disordered bilateral bronchovascular shadows and dense hilar shadows were seen in three cases. Chest CT exhibited no obvious abnormal signs in four cases. Typical CT findings included patchy, peripheral ground-grass opacities, subpleural lamellar dense shadows, and parenchymal bands. Pleural effusions, mediastinal lymphadenopathy, cavitation, and pleural thickening were absent.

CONCLUSION: The clinical manifestations and radiological findings of the 2019-nCoV-infected children were mild and lacked a typical pattern.

Introduction

On 31 December 2019, the Health Commission of Hubei Province, China, first reported a cluster of cases of unexplained pneumonia in people associated with the Huanan Seafood Wholesale Market in Wuhan, Hubei Province, with clinical presentations resembling viral pneumonia and manifesting as fever, cough, dyspnoea, radiographic ground-glass lung changes, and normal or lower than average white blood cell lymphocyte counts.[1] On 7 January 2020, the Chinese Center for Disease Control and Prevention (CDC) identified a novel coronavirus (2019-nCoV) from both a throat swab sample from a patient and a sample from the Huanan Seafood Wholesale Market, confirming that the

* Guarantor and correspondent: H. Liu, Department of Radiology, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, 318 Renmin Middle Road, Guangzhou, 510120, China. Tel.: +86-020-8133-0552; fax: +86-020-8133-0552.
E-mail address: liuhongsheng0708@163.com (H. Liu).

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virus was associated with the initial cluster.[2] With rapid person-to-person transmission, the epidemic has spread throughout all provinces of the country including Tibet. As of 8 February 2020, a total of 37,198 confirmed cases and 28,942 suspected cases, including 6,188 cases of severe illness, 811 deaths cases, and 2,649 cured cases, were reported by the National Health Commission of China.[3] Cases have also been reported in 24 countries outside of China.[4] According to the 5th edition of the *Diagnosis and Treatment Program of Novel Coronavirus Infected Pneumonia* (4 February 2020), respiratory droplets, contact transmission, suspected aerosol transmission, and alimentary tract transmission are the main transmission routes. The 2019-nCoV poses significant threats to international health.

In the early part of January 2020, the reported cases revealed that the elder population was at high risk for the 2019-nCoV, especially for severe cases. On 27 January 2020, the National Health Commission of China distributed the *Diagnosis and Treatment Program of Novel Coronavirus Infected Pneumonia* (edition 4, January 27, 2020) and announced that all populations were susceptible to the 2019-nCoV, including children and infants. On 5 February 2020, a 30-hour-old infant was confirmed as having 2019-nCoV infection in Wuhan, the youngest patient so far, strongly suggesting the possibility of maternal–infant vertical transmission. To date, some studies have revealed the epidemic pattern, clinical symptoms, and radiological features of 2019-nCoV pneumonia.[5–8] These studies mainly involved the adult cluster; however, research focusing on child clusters is still lacking, especially concerning the radiological features of infection in children. Therefore, it is important to understand the clinical pattern of child clusters of 2019-nCoV infection.

Guangzhou Women and Children's Medical Center is the largest children's hospital in southern China and shoulders the responsibility of admission and management for 2019-nCoV-infected children in Guangzhou Province, mainly in Guangzhou City. The present study systematically reports data on 2019-nCoV-infected children in Guangzhou Women and Children's Medical Center. The clinical characteristics including general patient information, clinical symptoms, epidemiological history, and 2019-nCoV nucleic acid tests of secretions, and the radiological appearances were examined in detail, with emphasis on identifying and characterising the most common features of child clusters.

Materials and Methods

Patients and basic data

Written informed consent was waived by the institutional ethics committee review board for this retrospective case series. To avoid any potential risk to patients, identifying information was deleted. Patients and the researchers were double-blind.

From 22 January 2020 to 9 February 2020, nine children were admitted to Guangzhou Women and Children's Medical Center with confirmed 2019-nCoV infection. None of the nine children had an underlying disease. All children were positive for 2019-nCoV via laboratory testing of respiratory secretions obtained by oropharyngeal swabs, and reconfirmed by the local CDC. Fever was classified as follows (axillary body temperature, °C): low fever for 37.3–38, moderate fever 38.1–39, and high fever for 39.1–41. The normal range for white blood cell (WBC) counts is $5–12\times10^9$/l; the normal range for lymphocyte counts is $1.55–4.88\times10^9$/l.

Radiological imaging

All bedside chest radiographs were obtained with a mobile DR machine (MUX-100DJ, Shimadzu Corporation, Japan) in the supine position.

Chest volume computed tomography (CT) was performed using a 64-section spiral CT system (Aquilion TSX-101A, Toshiba Medical System, Japan). The scanning range was from the superior aperture of the thorax to the costophrenic angle. The parameters were as follows: 120 kV tube voltage, 50–70 mA tube current 0.5 s/rot bulb rotation speed, and 0.2 mm slice thickness. All examinations were performed with the child in the supine position during end-inspiration without intravenous contrast medium. Palliative administration of oral 10% chloral hydrate at a concentration of 0.5 ml/kg body weight was performed when the children were too young or uncooperative.

Imaging review

All chest radiographs and CT images were reviewed independently by two fellowship-trained cardiothoracic radiologists each with >10 years of experience, blinded to the other reviewer's results. A third well-trained radiologist with >15 years of experience adjudicated the final decision when disagreement occurred between the two primary radiologists.

For each of the nine children, the initial CT images were evaluated with the following features: presence, location, number, size, shape, density, severity, border, and findings such as ground-glass opacities, shadows, nodules, thoracic lymphadenopathy (defined as a lymph node size of >10 mm), and the presence of pleural effusion. Other abnormalities were noted.

Results

Five male and four female patients were included (age: 7.8±5.3 years, range: 2 months to 15 years). When initially diagnosed, four children (44.4%) had only fever, including two with a low fever and two with a moderate fever, two children (22.2%) had a fever and simultaneous cough (one with a moderate and one with a high fever), one child (11.1%) had only a cough, and one child (11.1%) had a stuffy nose and rhinorrhoea. Notably, one child (11.1%) was an asymptomatic carrier. All nine children had exposure to the epidemic area (Hubei Province, China) or a history of close contact with confirmed or suspected 2019-nCoV-infected patients within 2 weeks of onset, and all had familial aggregations of the infection. In terms of laboratory examinations, WBC counts were normal in all nine children, and lymphocytes decreased in two children, increased in two children, and remained normal in five children. The 2019-nCoV nucleic acid real-time polymerase chain reaction (PCR) test results for secretions from cloacal swabs were positive in four of nine children (44.4%). The nucleic acid test result for urine was also positive in one child. The details of all nine children infected with 2019-nCoV are shown in Table 1.

Bedside chest radiography features

Among the chest radiographs of the nine children, four (44.4%) showed increased and/or disordered bilateral bronchovascular shadows and dense hilar shadows. The other five cases (55.6%) showed no obvious abnormality (Fig 1). The detailed radiographic features for each child are listed in Table 2.

Chest CT features

Among the nine children's CT images, the images from four cases (44.4%) showed no significant abnormal signs. The CT images of four children (44.4%) showed multiple fan-shaped/oval ground-glass opacities mainly located in the subpleural area of both lungs, with a central thickened vascular shadow and slightly thickened interlobular septa in one case (Fig 2). These ground-glass opacities were usually infiltrating several lobes but not the whole lung, with blurred edges and some "halo signs" (Fig 3a). There were also some parenchymal bands (Fig 4). Other abnormalities, such as mediastinal lymphadenopathy, pleural effusions, pleural thickening, cavitation, calcification, and bronchiectasis, were absent in the above cases. Two children had follow-up chest CT imaging during the study period. As shown in Fig 3b, the lesions resolved, with a density reduction in the central area, in the same location in the inferior lobe in the right lung 4 days after the last scan. The detailed CT image features for each child are listed in Table 2.

Discussion

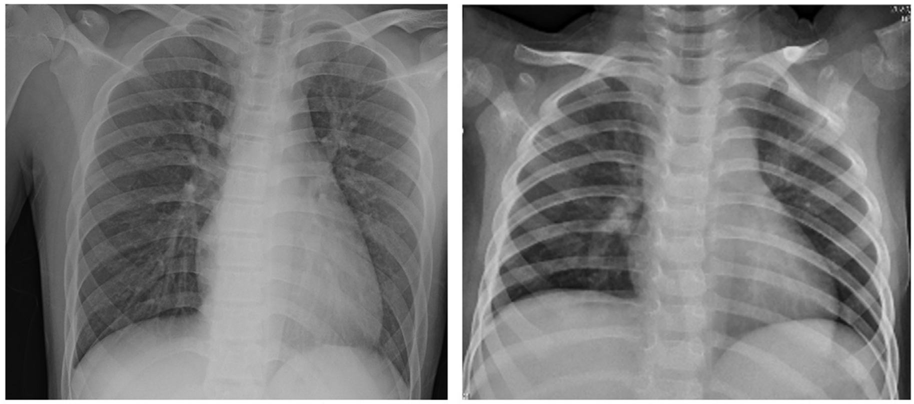
The present study describes the epidemiology, clinical characteristics, and radiological features of 2019-nCoV infection data for nine children who were transferred to the children's hospital from other hospitals across Guangzhou Province, mainly Guangzhou city. Generally, the clinical symptoms were mild in all nine children compared to the clinical symptoms of the adult cluster.[9] No child was admitted to the intensive care unit (ICU). The radiography and CT image features were also atypical. There were few significant diagnostic findings on the radiographs. CT image features varied, and included ground-glass opacities (4/9, 44.4%) and parenchymal bands (1/9, 11.1%). Although chest volume CT is a key component of the diagnostic work-up for patients with suspected infection, CT images showed no diagnostic features in four of the nine children in the present study. Therefore, epidemic area (Hubei Province, China) exposure and/or a confirmed or suspected history of close contact with a 2019-nCoV-infected patient were important clues for diagnosis in this child cluster.

In the present study, the mean age of the children was 7.8 years and the youngest infected child was 2-months old. The children's symptoms included fever (6/9, 66.7%), cough (3/9, 33.3%), stuffy nose (1/9, 11.1%), and rhinorrhoea (1/9,

Table 1
Clinical characteristic of nine children infected with 2019-nCoV.

Case no.	Sex	Age (year)	Initial diagnosis		Epidemiology history				WBC count ($\times 10^9$/l)	Lymphocyte count ($\times 10^9$/l)	2019-nCov nucleic acid real-time PCR test		
			Temp (°C)	Symptoms	Exposure history[a]	Close contact history	Familial cluster	Incubation period (day)			Oropharyngeal swab	Cloacal swab	Urine
1	Male	13	36.8°	None	-	+	+	-[b]	5.9	2.03	+	-	-
2	Female	7	38.7°	Fever	+	-/+	+	2–14[c]	5.7	2.34	+	+	+
3	Male	1	37.8°	Fever	+	+	+	9	7.8	6.19	+	+	-
4	Female	12	38°	Fever	+	-	+	4–10[d]	3.8	1.26	+	-	-
5	Male	6	39.1°	Fever/cough	+	-	+	2–8[e]	12	1.35	+	+	-
7	Male	3	36°	Stuffy nose/post-nasal drip	-	+	+	9	8.8	4.73	+	+	-
7	Female	15	38.5°	Fever	+	-	+	12	4.0	1.66	+	-	-
8	Male	13	38.5°	Fever/cough	+	-	+	9	7.8	1.75	+	-	-
9	Female	0.17	36.8°	Cough	+	+	+	>8[f]	10.8	9.05	+	-	-

[a] Clear history of exposure to epidemic area including Wuhan (three cases), Suizhou (one case), Jingzhou (two cases), Enshi (one case) cities, Hubei Province, China.
[b] Patient had no symptoms but was living in Wuhan and visited Guangzhou with his grandfather on 20 January 2020. He was tested for 2019-nCoV by the CDC because his grandfather had confirmed 2019-nCoV infection.
[c] Between 12–24 January 2020, the patient visited the epidemic area of Suizhou, but did not have a history of contact with suspected 2019-nCoV-infected patients. Once back in Guangzhou, the patient was exposed to a suspected infected person on a train on 24 January 2020, and had fever on 26 January 2020.
[d] Patient was visiting the epidemic area of Jingzhou from 16–22 January 2020, and had fever on 26 January 2020.
[e] Patient was visiting the epidemic area of Wuhan from 14–20 January 2020, and had fever and cough on 22 January 2020.
[f] The incubation period (>8 days) of this 2-month-old patient is unclear, but was living in Wuhan, Hubei Province, and visited Guangdong Province on 25 January 2020. The patient's father had cough, weakness, and sore throat, and the patient then developed the disease as the final member of this family on 2 February 2020.



(a) (b)

Figure 1 (a) A 13-year-old asymptomatic male patient infected with the 2019-nCoV, with a history of close contact with confirmed 2019-nCoV-infected patients. The bedside radiograph indicated no obvious abnormality. (b) A 3-year-old male patient, presented with a stuffy nose and rhinorrhoea, with a history of close contact with confirmed 2019-nCoV-infected patients. Bedside radiographs indicated increased and/or disordered bilateral bronchovascular shadows and dense hilar shadows.

11.1%), with no shortness of breath, myalgia, fatigue, confusion, chest pain, headache, or sore throat. Case 1 (a 13-year-old boy) had no symptoms. According to their exposure and/or close contact history, all nine children underwent the 2019-nCoV nucleic acid test using the secretions from cloacal swabs and were confirmed to have 2019-nCoV infection. For the laboratory blood examinations, the WBC count results were all normal, and the lymphocyte ratio was decreased (2/9, 22.2%), increased (2/9, 22.2%), or remained normal (5/9, 55.5%). According to the *Diagnosis and Treatment Program of Novel Coronavirus Infected Pneumonia* (5th edition, 4 February 2020), the WBC count usually remains normal or decreases, and the lymphocyte count decreases. The present data were somewhat different from this guideline and also showed that positive 2019-nCoV nucleic acid occurred in the cloacal swab (4/9, 44.4%) and urine sample (1/9, 11.1%), indicating a new potential transmission route. Therefore, 2019-nCoV patients' excrements should be well disposed to stop the suspected transmission routes.

The present results showed that there were few diagnostic findings on radiography images, which showed insignificant findings such as disordered bilateral bronchovascular shadows and dense hilar shadows. The significant CT features included ground-glass opacities (4/9, 44.9%) and parenchymal bands (1/9, 11.1%). Ground-glass opacities were the most common CT features, with a ratio of 14–77% in published studies.[5,8,9] Patchy, high-density shadows were the most common CT findings in five of the nine children with abnormalities. These CT findings were mainly located in the subpleural or peripheral part of the lungs. Consolidation lesions were absent. These features may be related to the fact that the pathophysiological change of the 2019-nCoV is relatively small and the transitionary process is relatively fast in children.

Table 2
Chest radiography and CT image features of infected children.

Patient no.	Radiography features	CT features[a]
1	No clear abnormality	No overt abnormality
2	Disordered bilateral bronchovascular shadows	No overt abnormality
3	No overt abnormality	No overt abnormality
4	No overt abnormality	Parenchymal bands
5	Increased bilateral bronchovascular shadows	No overt abnormality
6	Increased and disordered bilateral bronchovascular shadows, dense hilar shadows	Multiple scattered patchy ground-glass opacities with slightly thickened vascular shadow in the centre, blurred border and “halo sign”
6: follow-up	—	The lesions are well absorbed and shrank, with density reduction in the central area
7	No overt abnormality	Subpleural scattered striped ground-glass opacities with clear edge
8	No overt abnormality	Patchy mild ground-glass opacities in the upper lobe of left lung, small patchy ground-glass opacity with clear edge in the inferior lobe of right lung
9	Increased and disordered bilateral bronchovascular shadows, Dense hilar shadows, a suspected small patchy blurred shadow	Multiple scattered patchy ground-glass opacities in the subpleural or peripheral of both lungs
9: follow-up	-	The patchy shadows are absorbed and shrank, with density reduction

[a] Ground-glass opacity: slightly high-density shadow, like ground glass; parenchymal band: a linear opacity, usually 1–3 mm thick and >2 cm in length (up to 5 cm) that usually extends to the visceral pleura (which is often thickened and may be retracted at the site of contact).

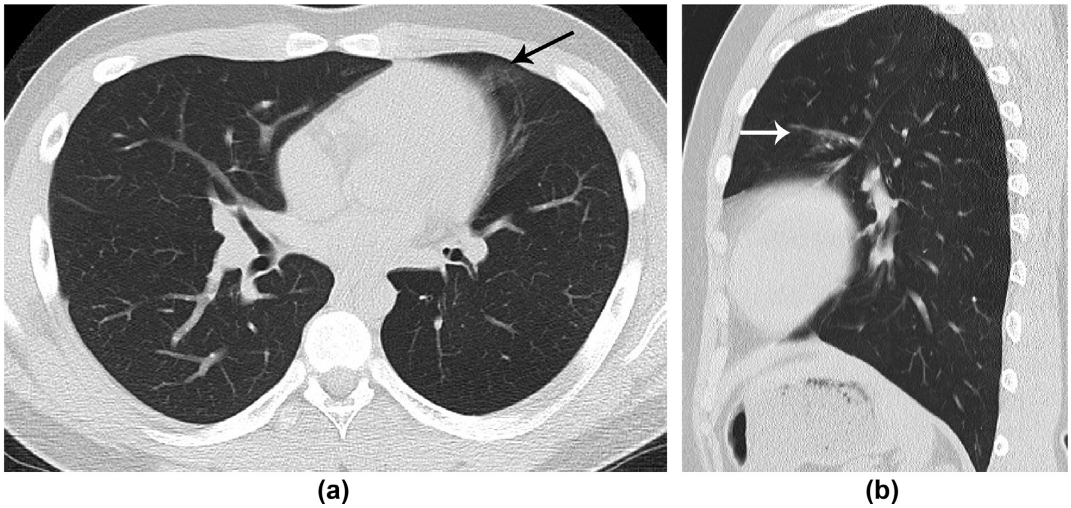


Figure 2 A 13-year-old male patient with a clear exposure history to the epidemic area (Hubei Province, China) who presented with fever and cough received treatment for symptoms in the isolation unit. (a) Axial thin-section unenhanced CT image shows slight ground-glass opacity (black arrow) in the subpleural area of the left upper lobe. (b) Sagittal image shows a patchy ground-glass opacity (white arrow).

These clinical features and CT findings in 2019-nCoV-infected children may overlap with those infected with other corona viruses: Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). MERS and SARS are the result of human–animal interactions, with the capability of person-to-person spread. The preliminary pattern of 2019-nCoV suggests a zoonotic origin,[10] but the exact origin and intermediate hosts have yet to be determined. Ground-glass opacities involving the peripheral lungs are the primary findings on CT. They were quite common findings on CT images; however, the consolidation sign, which was suggested as a marker of disease progression or more severe disease, was hardly shown in the CT images of 2019-nCoV-infected children.[9] The mortality of SARS-CoV has been reported as >10% and that of MERS-CoV at >35%.[11,12] To date, the mortality of 2019-nCoV is reported at approximately 2.18% in mainland China.

The present study has several limitations. First, the sample size was very small with only nine children from a single institution. Second, there were not enough follow-up CT examinations. Third, there was a lack of severe infection to compare findings between a severely infected child cluster and a mildly infected child cluster. Finally, more detailed patient information was unavailable at the time of analysis.

In a way, this study also has some value. In Guangzhou city, medical resources including hospitals, physicians, numbers of 2019-nCoV nucleic acid detection kits and other supportive conditions, such as medical protective equipment, were relatively sufficient. The ability and speed of the Guangzhou CDC to reconfirm the 2019-nCoV were sufficient. Therefore, suspected 2019-nCoV patients with Hubei exposure or a close contact history could be identified easily in Guangzhou city, especially in the child cluster. In Wuhan city, however, the number of confirmed or suspected 2019-

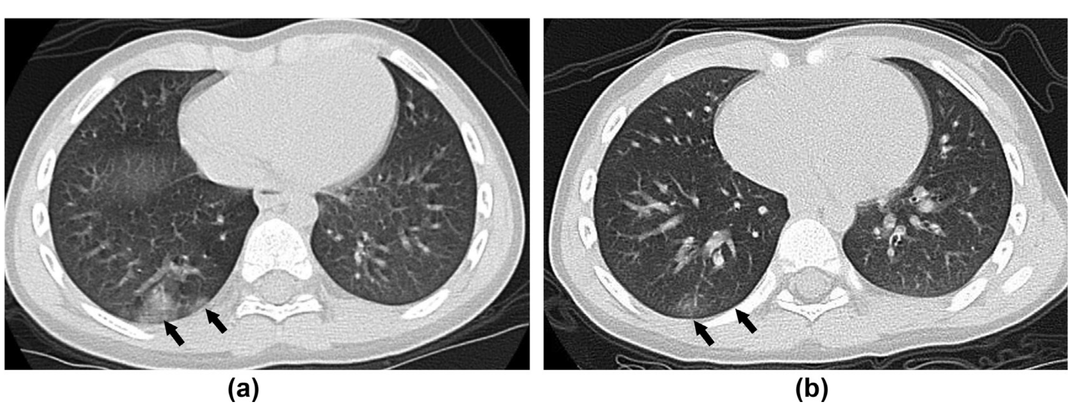


Figure 3 A 3-year-old male patient with a history of close contact with a confirmed 2019-nCoV-infected patient, who presented with a stuffy nose and rhinorrhoea, received interferon-alpha atomising therapy in the isolation unit. (a) Axial unenhanced CT image (scanned on 5 February 2020) shows multiple mixed patchy shadows and ground-glass opacities, with a central thickened vascular shadow and a blurred edge, in the subpleural area of the inferior lobe in the right lung. (b) The CT image (scanned on 9 February 2020) indicates that the lesions resolved, with density reduction in the central area, in the same location in the inferior lobe in the right lung.

Figure 4 A 15-year-old female patient with a history of exposure to the epidemic area, who presented with fever, received treatment for symptoms in the isolation unit. Axial unenhanced CT image shows parenchymal bands.

nCoV infected patients was large enough to restrict the vast majority of medical resources, resulting in many infected patients not being admitted to hospitals. Although there was exposure or a contact history, some mild patients and latent carriers would be missed, which leads to performance bias.

In summary, this work reports an early investigation focusing on a child cluster with confirmed 2019-nCoV infections. The existence of ground-glass opacities, patchy shadows and parenchymal bands could help to identify viral pneumonia. Remarkably, many of the CT images of the 2019-nCoV-infected children showed no abnormalities. CT features alone are not sufficient to diagnose a 2019-nCoV infection, but help to evaluate the severity and process of infection. Clinical characteristics lack a typical pattern. Suspected 2019-nCoV-infected children with fever and/or cough and chest CT features, combined with a history of epidemical exposure/close contact, should not be misdiagnosed, especially when false-negative nucleic acid tests occur at an earlier stage.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

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