

# SARS in children: clinical image and differentiation

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**Background:** SARS is an acute infectious pulmonary disease caused by a so-called coronavirus. The aim of this study was to assess the characteristics of clinical images of severe acute respiratory syndrome (SARS) in children for further understanding of the disease.

**Methods:** Clinical data and radiographic findings in 38 patients with clinically confirmed SARS in the period of January 2003-April 2003 were retrospectively analyzed. Chest radiography was performed in all the patients, and additional chest HRCT was given in a few of these patients.

**Results:** The radiological features of SARS in these patients were divided into three patterns: 1) massive consolidation ( $n = 27$ , 71.1%) marked by patchy and segment air-space consolidations; 2) pulmonary interstitial infiltration ( $n = 8$ , 21.0%) shown by coarse lung markings, and enhanced or inordinately reticular and drop shadows; 3) mixed pattern ( $n = 3$ , 7.9%) characterized by marked lung markings with patchy opacity and reticular shadows. Radiographically the foci of lesions appeared early, progressed rapidly and were absorbed slowly. They could be grouped into early, progressive and convalescent stages, in which the median days were 4, 6 and 9 respectively.

**Conclusions:** The lung lesions of pediatric SARS patients appear early, and present bilateral or unilateral single or multiple patchy shadows predominantly. It is necessary to differentiate SARS from other pulmonary diseases through combined use of clinical and laboratory examinations.

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**Key words:** children; radiography; severe acute respiratory syndrome; pneumonia; X-ray; CT

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## Introduction

Severe acute respiratory syndrome (SARS) is a new communicable respiratory disease, which is also known as infective atypical pneumonia in China. It is critical to diagnose the disease in its earlier period while prescribing isolation therapy. Image examination as one of the diagnostic choices is extremely important to verify image characteristics of the disease. In the period of January to April 2003, we studied clinical images of 38 pediatric patients with SARS who were treated at our hospital.

## Methods

### Patients

Of the 38 patients, 20 were boys and 18 girls, aged from 3 months to 13 years (mean 7.3 years). On examination, all the patients had a high fever with armpit temperature of  $> 38^{\circ}\text{C}$ . Thirty-five patients showed cough, and 3 diarrhea. Coarse breath sounds and dry or wet rales were found in most of the patients.

### Laboratory examination

The count of leukocytes in peripheral blood was less than  $5.0 \times 10^9/\text{L}$  in 22 patients (57.9%), and between  $5.0 \times 10^9/\text{L}$  and  $9.0 \times 10^9/\text{L}$  in 16 (42.1%). It was predominantly lower in 20 patients.

### Diagnostic criteria

According to the Criteria for the Clinical Diagnosis of SARS issued by the Public Health Ministry of China, five specialists from Guangdong Province discussed the conditions of the patients. The criteria are as follows:

1. Epidemiologic evidence: Close contact with infected individuals in the past two weeks, or with evidence of infecting other people.

2. Symptoms and signs: The disease develops quickly with fever (always over  $38^{\circ}\text{C}$ ). The patient may have cough, mostly nonproductive cough with little sputum; some serious patients may have tachypnea, which even develops to acute respiratory depressive syndrome. The signs of the lung may not be obvious, and signs of consolidation may present.

3. Laboratory examination: Total white blood cell count in peripheral blood almost does not increase, and even may decrease.

4. X-ray or CT examination of the lung: On one side or both sides, nonsymmetrical focal patchy infiltrates are noted.

5. No obvious effects after antibiotic therapy.

Suspicious diagnostic criteria: They accord with items 1 + 2 + 3 or 2 + 3 + 4.

Clinical diagnostic criteria: They accord with items 1 + 2 + 3 + 4 or 2 + 3 + 4 + 5.

### Radiological data

Frontal chest radiographs were taken when the 38 patients received medical treatment for the first time. Once massive consolidation was found in some patients, they were subjected to lateral chest radiography. During the treatment, all the patients were followed up by chest radiography using a mobile X-ray machine to observe the dynamic changes till the disappearance of lung lesions. Follow-up radiographs were taken in all

the patients every one to three days at the acute stage of the disease, and reviewed every three to five days when the clinical symptoms diminished markedly. High resolution CT was performed in a few patients for the assessment of their recovery from the 7th to the 10th day after that they had been discharged from the hospital.

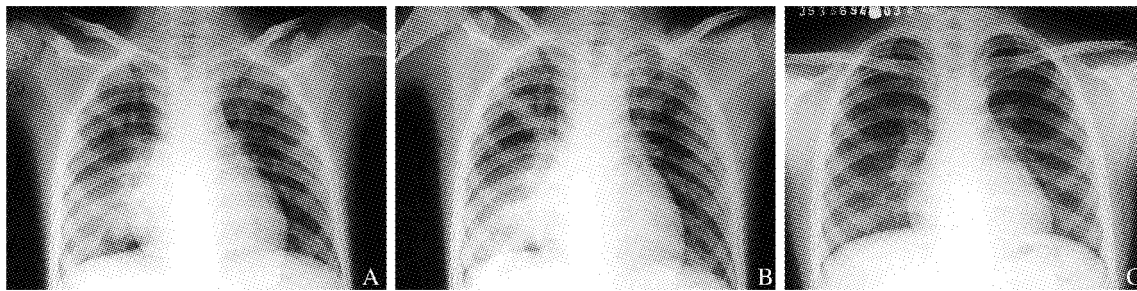
## Results

### Image findings

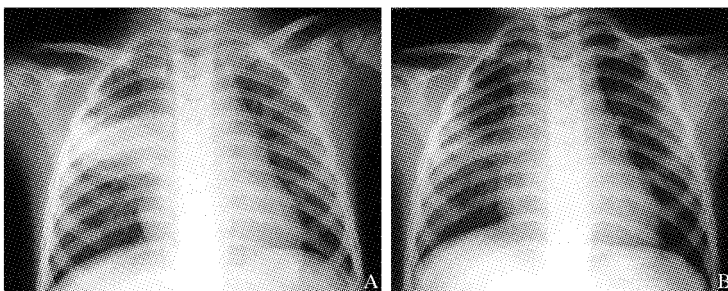
The lesions of the patients were categorized into the following three types.

#### *Massive consolidation*

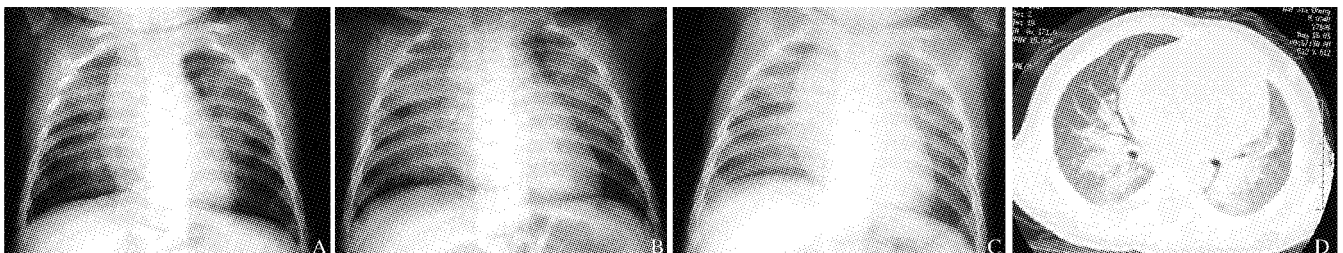
Predominant pulmonary consolidation associated with enlarged hilum of the lung was seen in 27 patients (71.1%). Patchy or segment opacity appeared with clouding margin in the unilateral lung in 21 (Figs. 1, 2) and in both lungs in 6 (Fig. 3).



**Fig. 1.** Frontal chest X-ray film of a 9-year-old boy with SARS. **A:** Radiography on the 4th day after the onset of the disease shows patchy air-space consolidation in the right lower lung lobe. **B:** Frontal chest radiograph on the 6th day shows the enlarged focus of the lesion and enhanced density. **C:** Follow-up chest radiograph on the 16th day shows the focus of the lesion disappeared.



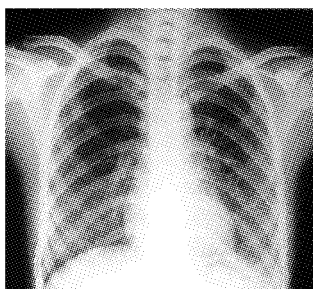
**Fig. 2.** Frontal chest radiograph of a 3-year-old girl with SARS. **A:** Radiograph on the 1st day shows patchy opacity in the right upper lung lobe involving the right lung hilum. **B:** Seven days later, obvious progression of the focus of the lesion. **C:** Fourteen days later, the opacity disappeared.



**Fig. 3.** Frontal chest radiograph of a 3-month-old boy. **A:** Radiograph on the 3rd day shows multifocal bilateral air-space opacities in both lungs. **B:** On the 5th day, further progression of the consolidation. **C:** On the 41st day, the lesions persisted with patchy opacities at the right lung. **D:** On the 43rd day, HRCT scanning showing patchy opacities bilaterally in both lower lungs with streaky shadows surrounded, suggesting fibrosis tissue proliferation.

### ***Pulmonary interstitial infiltration***

The lesions involved pulmonary interstitial tissue in 8 patients (21.1%). Reticular and drop shadows in the pulmonary medial zone were complicated by increased lung markings in 6 patients (Fig. 4), of whom 2 suffered from minor emphysema. Enhanced lung marking was observed in 2 patients, one of them was associated with enlarged hilum.



**Fig. 4.** Frontal chest radiograph of a 12-year-old girl with SARS showed lung markings enhanced with reticular shadows.

### ***Mixed pattern***

The lesions involved with the interstitial tissue and parenchyma in 3 patients (7.9%). They were characterized by mixed patchy or reticular shadows, uneven density, and enhanced lung marking in the unilateral lung in 1 patient and in both lungs in 2.

### **Dynamic changes of clinical image**

The lung lesions on films were divided into three stages.

#### ***Early stage***

The lesions presented radiographically 1-6 days after onset of the illness (median 3 days). The lesions were seen 1-3 days after onset of the disease in 20 patients (Fig. 2A), and 4-6 days in the remaining patients. At this stage, the lesions were localized with a low density and unclear margin. Coarse markings penetrated indistinctly into the lesions in some patients. Lightly changed lung markings were easily neglected.

#### ***Progressive stage***

On X-ray, the lesions progressed for 4-11 days after onset of the disease (median 6 days). Peak of progression appeared on days 5-7 in 20 patients (Fig. 2B) and exceeded 10 days only in 2 patients. The lesions expanded rapidly at this stage, and their adjacent patchy consolidation inoculated with enhanced density. Some lesions were found in the opposite lung lobe in a few patients. Though old lesions were absorbed, new ones appeared elsewhere in a few patients.

### ***Convalescent stage***

The lesions diminished gradually or lightened in density 5-15 days after onset of the illness (median 9 days). The lesions disappeared 5-7 days after illness in 12 patients, 8-10 days in 18, 10-13 days in 7, and 15 days in 1. The lesions were absorbed mostly or completely within 15 days in 24 patients (Fig. 2C), and in over 15 days in 14 (36.8%) (Fig. 1C). The lesions in one patient remained on day 73. Radiography on day 41 demonstrated multi-patchy opacity in both lungs (Fig. 3C) and HRCT on day 43 showed patchy consolidation together with fibrous streak, suggesting possible pulmonary fibrosis (Fig. 3D). The localized lesions were absorbed promptly, whereas the extensive ones slowly.

### **Prognosis**

All the patients recovered fully without use of alexipyretiss. Their body temperature was normal for over 7 days. The symptoms of the respiratory system were ameliorated and 30% of the abnormalities disappeared on chest radiography. Laboratory examination showed leucocytes in peripheral blood or other variables nothing abnormal. The time for absorption of lesions was positively correlated with their extent. It was shorter for simple and interstitial lesions, but longer for the multiple lesions. For example, the lesions did not disappear in one patient after 43 days of treatment. Moreover, the absorption of lesions was slower than the improvement of clinical symptoms. The films taken after discharge of the patients from the hospital demonstrated the lesions were absorbed basically with less lingering effects in most patients.

## **Discussion**

### **Characteristics of clinical manifestations**

SARS is an acute infectious pulmonary disease caused by a so-called coronavirus.<sup>[1-4]</sup> It is thought to transmit by means of droplet infection in a short distance, secretion of the respiratory tract, and close contact with the patient.<sup>[3-5]</sup> Children with SARS are rare, and their symptoms are less evident than those of adult patients.<sup>[6-9]</sup> In our study, high fever (temperature > 38°C) and cough (dry cough and few sputum) were common in most patients. Digestive symptoms and physical signs in the chest including rales were observed in a few patients. The count of leucocytes was normal or decreased in all the patients. Since SARS is characterized by rapid onset and strong infection in crowds, and there is no patent medicine for treatment, it is extremely important to have pediatric patients diagnosed and treated early.

### X-ray images and pathological basis

X-ray images of pediatric SARS patients present a variety of characteristics. Pulmonary lesions involve predominantly the parenchyma of the unilateral lung, but less the initial tissue or both the parenchyma and interstitial tissue. Consolidation presents massive and segmental high density in the pulmonary lobe and segment and in one side of the lung. Interstitial infiltration appears to be increased by lung markings with reticular and drop-like clouding shadows in the medial pulmonary zone. The mixed type presents patchy and reticular shadows with asymmetrical density by reinforced lung markings. Lesions appear early, progress rapidly, and peak earlier (median 7 days), but they are slowly absorbed. Pulmonary emphysema and changes of the hilum are rarely found as well as lung abscess and pleural changes. Prognosis is good. Lesions absorb promptly after therapy without side-effects like fibrosis shown by radiography. X-ray findings are consistent with clinical symptoms but not with physical signs. Radiographic changes of the lesions can be substantially delayed behind the resolution of signs and symptoms.

Reports<sup>[10-13]</sup> have shown pathological changes of SARS patients including pulmonary lesions, immune organ injuries, systemic vasculitis and generalized toxic reaction. Of them, lung injuries are predominant. Gross findings in lung tissue include dark red and tenacious lesions. Sections of lung lobe show diffused lesions with exudative consolidation. Dilated blood vessels are hyperemic with spotted bleeding and infarct on lung surface. Histologically, the alveolar wall is thickened obviously because of edema and infiltration of lymphocytes and monocytes. Pink exudates from alveoli and cellulose, erythrocytes, macrophages and epithelial cells could be noted. Structures like viral inclusion bodies and multinuclear giant cells are found in some alveoli apart from hyaline membrane. In addition, capillary extension, thrombosis in small vessels, and infiltration of monocytes and lymphocytes are seen at the interlobular septum, with necrosis of the microbronchus wall. Pulmonary vascular engorgement, edema and inflammatory exudation present thin patchy or ground-glass opacity on radiological films in early stage. Alveolitis desquamativum and formation of hyaline membrane take place with inflammatory absorption and proliferation of some fibrous tissue in convalescent stage.

### Diagnosis and differential diagnosis

The diagnosis of SARS in pediatric patients can be made on the basis of epidemiological history; age of over 5 years; rapid onset of the disease with fever, dry cough, indistinct pulmonary signs and decreased or

normal leucocytes in peripheral blood; early appearance and rapid development of big lesions in the unilateral lung; rare development of pulmonary emphysema and disorders of the hilum without abscess and pleural abnormality; slow absorption of the lesion; lesions being not consistent with physical signs but no scar of the lesion left over after recovery.

From the point view of image, SARS should be different from pneumonia.

### *Mycoplasma pneumoniae*

It happens in school age children with symptoms of fever and cough. Radiographic abnormalities include massive foci in 30% -40% patients who need to be differentiated from SARS patients. Slow episode, persistent on intensive cough, changed lung markings radiating from the hilum to the outside, and rapid absorption of lesions are encountered together with asymmetrically disordered or enlarged hilum in most of such patients.<sup>[14-16]</sup>

### *Adenovirus pneumoniae*

The onset of the disease is rapid with hyperpyrexia, cough and leukopenia in most patients. Being similar to the consolidation type of SARS, the disease is manifested by massive necrosis, obstructive emphysema and slow absorption of lesions, which give risk to such sequelae as irreversible pulmonary fibrosis, chronic bronchitis and bronchiectasis.<sup>[16,17]</sup> Radiographic findings and clinical symptoms are coincident with the progression of the disease. Hence the disease can be differentiated easily from SARS.

### *Bacterial pneumoniae*

Lobar pneumonia and segmental pneumonia are easy to be confused with the consolidation type of SARS, except for obvious symptoms and physical signs and increased count of leucocytes, to which antibiotics are effective. Radiographically, highly dense pulmonary lesions are seen at one segment or one lobe, which are consistent with anatomic locations.<sup>[16-18]</sup> In contrast, SARS patients usually have few physical signs, normal or decreased count of leucocytes, and antibiotics are ineffective.

### *Respiratory syncytial virus pneumoniae*

It is one of the most common causes of infection of the respiratory tract in pediatric patients and characterized predominately by interstitial infiltration. It is necessary to be differentiated from the interstitial infiltration type of SARS. The disease is frequently seen in less than one-year-old infants, presenting early dyspnea, strengthened and inordinate lung markings, and emphysema.<sup>[17-19]</sup>

**Influenza pneumonia**

As one of the infectious diseases caused by influenza virus, this pneumonia is characterized by rapid onset, hyperpyrexia, cough and abnormal shadows in the lung. It is commonly seen in infants in winter and spring. Pulmonary images show enhanced and blurred lung markings in bilateral lungs with highly dense shadows and emphysema but rare massive confluent foci.<sup>[17-20]</sup>

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**Competing interest:** None declared.

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**References**

- Marra MA, Jones SJ, Astell CR, Holt RA, Brooks-Wilson A, Butterfield YS, et al. The genome sequence of the SARS-associated coronavirus. *Science* 2003;300:1399-1404.
- Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, et al. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1953-1966.
- Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan-Yeung M, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;348:1977-1985.
- Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, et al; SARS Working Group. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1953-1966.
- Seto WH, Tsang D, Yung R, Ching TY, Ng TK, Ho M, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003;361:1519-1520.
- Nicolaou S, Al-Nakshabandi NA, Muller NL. SARS; imaging of severe acute respiratory syndrome. *AJR Am J Roentgenol* 2003;180:1247-1249.
- Grinblat L, Shulman H, Glickman A, Matukas L, Paul N. Severe acute respiratory syndrome: radiographic review of 40 probable cases in Toronto, Canada. *Radiology* 2003;228:802-809.
- Wong KT, Antonio GE, Hui DS, Lee N, Yuen EH, Wu A, et al. Severe acute respiratory syndrome: radiographic appearances and pattern of progression in 138 patients. *Radiology* 2003;228:401-406.
- Liu JX, Jiang SF, Chen BH, Zhang LG, Huang DY, Huang WZ, et al. Image appearances of severe acute respiratory syndrome (a preliminary study of 260 cases). *Chin J Med Imaging Technol* 2003;19:790.
- Tse GM, To KF, Chan PK, Lo AW, Ng KC, Wu A, et al. Pulmonary pathological features in coronavirus associated severe acute respiratory syndrome (SARS). *J Clin Pathol* 2004;57:260-265.
- To KF, Tong JH, Chan PK, Au FW, Chim SS, Chan KC, et al. Tissue and cellular tropism of the coronavirus associated with severe acute respiratory syndrome: an in-situ hybridization study of fatal cases. *J Pathol* 2004;202:157-163.
- Lang ZW, Zhang LJ, Zhang SJ, Meng X, Li JQ, Song CZ, et al. A clinicopathological study of three cases of severe acute respiratory syndrome (SARS). *Pathology* 2003;35:526-531.
- Nicholls JM, Poon LL, Lee KC, Ng WF, Lai ST, Leung CY, et al. Lung pathology of fatal severe acute respiratory syndrome. *Lancet* 2003;361:1773-1778.
- Reittner P, Muller NL, Heyneman L, Johkoh T, Park JS, Lee KS, et al. Mycoplasma pneumoniae: radiographic and high-resolution CT features in 28 patients. *AJR Am J Roentgenol* 2000;174:37-41.
- Qiu HX. Clinical and radiological analysis of mycoplasma pneumoniae pneumonia in children. *J Practical Radiol* 2002;18:951-953.
- He ML, Lai H, Yang YJ. Radiological analysis of non-bacterial infectious pneumonia in children. *J practical radiol* 2002;18:1037-1039.
- Xu SY. Practical radiological diagnosis in pediatrics. Beijing: Beijing Press, 1999:309-311.
- Virkki R, Juven T, Rikalainen H, Svedstrom E, Mertsola J, Ruuskanen O. Differentiation of bacterial and viral pneumonia in children. *Thorax* 2002;57:438-441.
- Liu LW, Sun WC. Clinical X-ray imaging of respiratory syncytial virus pneumonia in infant. *J Chin Practical Pediatr* 1991;6:44-46.
- Redding G, Singleton R, Lewis T, Martinez P, Butler J, Stamey D, et al. Early radiographic and clinical features associated with bronchiectasis in children. *Pediatr Pulmonol* 2004;37:297-304.

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