A Young Infant With Severe Acute Respiratory Syndrome

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ABSTRACT. Severe acute respiratory syndrome (SARS), a new contagious respiratory disease associated with a novel coronavirus, has spread worldwide and become a global health concern after its first outbreak in Guangdong Province of the People's Republic of China in November 2002. The clinical presentation and the radiologic, hematologic, biochemical, and microbiologic findings of a 56-day-old male infant with SARS are described. Some clinical and laboratory features are similar to those reported in adult and pediatric patients. However, this infant had a more severe clinical course as compared with the older children. This is the youngest patient with symptomatic SARS reported to date. ***Pediatrics*** **2003;112:e257–e260. URL: http://www.pediatrics.org/cgi/content/full/112/4/e257;** ***SARS, SARS-associated coronavirus, chest radiograph.***

ABBREVIATIONS. SARS, severe acute respiratory syndrome; CXR, chest radiograph; PICU, pediatric intensive care unit; RT-PCR, reverse transcriptase-polymerase chain reaction; CPAP, continuous positive airway pressure; SARS-CoV, SARS-associated coronavirus.

CASE REPORT

A 56-day-old (corrected age: 38 weeks) male premature infant was hospitalized on April 4, 2003, because of a cyanotic attack and shortness of breath on the day of admission. He did not have coryza, vomiting, diarrhea, or fever, but he did have unproductive cough the day before admission. He was born at 30 weeks' gestation by unassisted vaginal delivery, with a birth weight of 1.62 kg. He had several problems related to prematurity during the neonatal period, including transient hypoglycemia, neonatal hyperbilirubinemia, intraventricular hemorrhage (grade 2), apnea of prematurity, and anemia of prematurity. His hemoglobin level was 9.0 g/dL when checked on March 21, 2003. He had no additional apneic attacks on discharge on March 28, 2003. However, he was readmitted 1 week after discharge. There was no history of travel or close contact with a patient suspected of or diagnosed with severe acute respiratory syndrome (SARS). His mother, who solely took care of him after discharge, was asymptomatic all along.

On admission, the infant was hypothermic with a rectal temperature of 35.8°C. He was noticed to have respiratory distress with insucking of chest. The respiratory rate was 66/min, and oxygen saturation in room air was 84%. His blood pressure was normal. The chest was clear on auscultation. Examination of the abdomen and of the cardiovascular and neurologic systems was unremarkable.

The laboratory and microbiologic findings on admission are summarized in Table 1. Initial chest radiograph (CXR) revealed focal consolidation of the right lower zone (Fig 1).

The infant was treated with broad-spectrum antibiotics, including ampicillin, cefotaxime, and erythromycin, to cover the usual pathogens of community-acquired pneumonia. He developed fever up to 38.5°C on day 3 of illness. Oxygen saturation could be maintained at 95% to 100% initially with 1 L/min oxygen via nasal cannula. However, fever persisted, and increasing respiratory distress was noted on day 4 of illness. Oxygen saturation was only 94% while he was administered 3 L/min oxygen, and his respiratory rate increased to 70 to 90/min with severe insucking. In view of the clinical deterioration, he was transferred to the pediatric intensive care unit (PICU) for additional treatment.

On admission to the PICU, diffuse crepitations but no rhonchi were detected on chest examination. Systemic examination also showed mild hepatomegaly (3 cm below costal margin) and anal fissures. Blood tests were repeated, and the results are listed in Table 1. Nasopharyngeal aspirate for reverse transcriptase-polymerase chain reaction (RT-PCR) against a novel coronavirus was also requested 1 day after PICU admission because of an ongoing outbreak of SARS in our region and clinical deterioration despite broad antibiotic coverage. Repeat CXR showed progression of consolidation to involve the left side as well (Fig 2). The infant was then put on nasal continuous positive airway pressure (CPAP) of 5 cm H_2O with fraction of inspired oxygen of 0.4. Packed cell transfusion was given for anemia (hemoglobin level: 8 g/dL). Ventilatory support was discontinued after 16 hours of CPAP, and oxygen requirement was decreased to 1 L/min via the nasal cannula. His temperature normalized soon after admission. There were 2 episodes of blood-stained stool on day 1 in the PICU secondary to anal fissures. The patient was started on tube feeding on day 5 of illness, and full oral feeding was established on day 8 of illness when he was transferred out of the PICU. Supplemental oxygen was subsequently discontinued on day 9 of illness, although repeat CXR still showed bilateral lower zone opacification. RT-PCR for the novel coronavirus associated with SARS (SARS-CoV) turned out to be positive in the nasopharyngeal aspirate. Intravenous ribavirin (20 mg/kg/d) was prescribed on day 8 of illness in view of a positive PCR result, although the infant's clinical condition was improving. Repeated RT-PCR tests for SARS-CoV on day 9 of illness were negative in pernasal swab and urine but positive in stool. Ribavirin was continued for 14 days without any adverse effect, especially hemolytic anemia, during the course of treatment. Antibiotics were continued for a total of 10 days from onset of illness. No corticosteroid was administered. Blood tests, including complete blood count, liver function test, creatine kinase, and lactate dehydrogenase, were normalized on day 13 of illness. CXR repeated on day 21 of illness showed complete resolution of consolidation. The infant was discharged on day 24 of illness at 80 days of life. The paired serum titer for the novel coronavirus as measured by indirect fluorescent antibody increased from <25 to 200 after 7 days of illness.

DISCUSSION

An outbreak of atypical pneumonia, subsequently termed SARS, has occurred in Guangdong Province, People's Republic of China, since mid-November

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TABLE 1. Summary of Presenting Features and Investigation Results

Presenting Features	Hematologic and Biochemical Findings			
		Initial	At the Time of PICU Admission	Normal Range
Fever	WBC	23.1×10^9/L	25.8×10^9/L	$6.0–17.5 \times 10^9$/L
Dyspnea	ANC	11.8×10^9/L*	17.5×10^9/L	$1.0–8.5 \times 10^9$/L
Unproductive cough	Lym	9.4×10^9/L	7.3×10^9/L	$4.0–13.5 \times 10^9$/L
Cyanotic attack	Hb	7.6 g/dL	8.6 g/dL	10.0–20.5 g/dL
	Platelet	580×10^9/L	519×10^9/L	$210–650 \times 10^9$/L
	CRP	24.6 mg/L		<8.0 mg/L
	AST		245 IU/L	<77 IU/L
	ALT	80 IU/L	312 IU/L	<56 IU/L
	CK		380 IU/L	<295 IU/L
	LDH		1143 IU/L	170–450 IU/L
	D-dimer		>0.2 mg/L	<0.2 mg/L

Microbiologic Findings	
Blood culture	No bacterial growth
NPA for IF (Influenza A & B, Adenovirus, Parainfluenza types 1, 2 & 3, RSV)	−ve
Serology (Influenza A & B, Adenovirus, Parainfluenza types 1, 2 & 3, *Mycoplasma, Chlamydia*)	No rising titer in convalescent serum
NPA for SARS-CoV RT-PCR	+ve [day 5]
Stool for SARS-CoV RT-PCR	+ve [day 9]
Pernasal swab and urine for SARS-CoV RT-PCR	−ve [day 9]
NPA, stool and urine for viral culture	−ve
Serology for SARS-CoV (IFA)	1:<25 (day 3) 1:200 (day 9)

WBC indicates total white blood cells; ANC, Absolute neutrophil count; Lym, Lymphocyte; Hb, Hemoglobin; CRP, C-reactive protein; AST, asparate aminotransferase; ALT, alanine aminotransferease; LDH, lactate dehydrogenase; CK, creatine kinase; NPA, nasopharyngeal aspirate; IF, immunofluorescence; RSV, respiratory syncytial virus; IFA, indirect fluorescent antibody.
* Left shift of neutropils present.

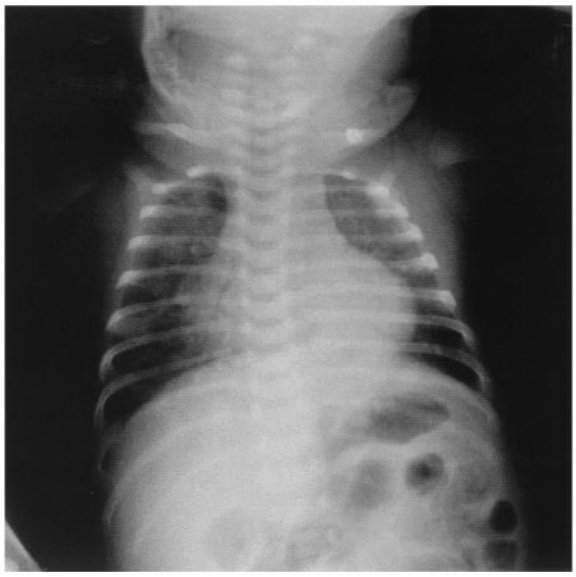

Fig 1. CXR at presentation showing focal consolidation in right lung.

2002. As of May 5, 2003, >6500 people in 27 countries have been affected worldwide.[1] Several case series on SARS have been published, only 1 of which was pediatric, with age of the patients ranging from 1.5 to 16.4 years.[2–5] There is evidence that a previously unrecognized novel coronavirus is associated with SARS.[6–8] Our report describes the youngest patient so far, with the corrected age of only 38 weeks, who fulfills the surveillance case definition of SARS as defined by the World Health Organization and the Centers for Disease Control and Prevention.[9,10]

In several adult series,[2–4] the most common symptoms at presentation were fever, chills, rigor, myalgia, unproductive cough, dyspnea, headache, and dizziness. Teenagers were noticed to have similar clinical presentation to that of adults, whereas younger children presented more commonly with cough and runny nose.[5] During the onset of the disease, our patients had dry cough, dyspnea, and hypothermia progressing later to fever. However, the fever was only short lasting (present only on days 3–4 of illness). Several hematologic and biochemical abnormalities described in the adult and pediatric series were also present in our patient.[2] These included leukocytosis and elevated D-dimer, alanine aminotransferase, creatine kinase, and lactate dehydrogenase levels. However, the commonly observed lymphopenia was not seen in our patient. Among all these, a high peak lactate dehydrogenase level and raised absolute neutrophil count were found to be associated with ICU admission and death.[2] Our patient, who had these 2 risk factors, deteriorated on day 4 of illness with increased respiratory distress and oxygen desaturation. Subsequently, he required ventilatory support for 16 hours.

All microbiologic investigations for common bac-

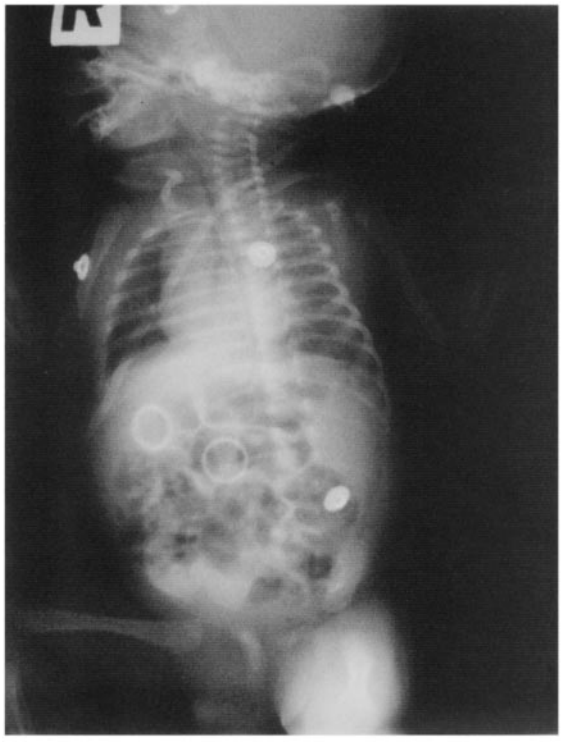

Fig 2. CXR showing progression of consolidation to involve the left side.

terial and viral respiratory pathogens were uninformative. These results speak against the possibility of a common microorganism as the cause of illness, although it could not be totally excluded. Both nasopharyngeal and fecal samples were positive for a novel SARS-CoV. RT-PCR for the coronavirus was associated with a high specificity, although the sensitivity was only 50% to 55%.[8] The above evidence strongly suggests that a novel coronavirus was the cause of SARS in our patient. This is further supported by a rise in convalescent serum titer against the coronavirus. The RT-PCR for SARS-CoV, which was repeated on day 9 of disease, was negative in the pernasal swab but positive in stool. This may suggest persistent shedding of coronavirus in stool, although the virus may be defective. The duration of virus shedding in children needs to be investigated further.

Most of the adult and pediatric patients had abnormal CXRs at presentation with either unilateral or bilateral air space consolidation as the usual finding.[2,5] All severe cases had progression of initial pulmonary infiltrates to involve multiple areas of bilateral lung fields during clinical deterioration. In our case, focal consolidation of the right lower zone was evident at presentation, and there was subsequent involvement of the left lung as the disease progressed.

This infant had been an inpatient in the nursery when other pediatric SARS patients were being treated in the same hospital. He might have been exposed inadvertently to the highly contagious coronavirus during his hospitalization. However, the infant had been exposed to the community on several occasions after discharge from the hospital. Although the onset of the clinical symptoms within 6 days after discharge from the nursery is consistent with the incubation period of 2 to 16 days as reported in the published series, the possibility of community-acquired SARS cannot be excluded entirely.[2–4]

In one large adult series, administering albuterol through a jet nebulizer was postulated as aggravating the spread of the virus by aerosol and resulting in an outbreak of SARS in the hospital.[2] The use of CPAP and other forms of noninvasive ventilation was considered to be associated with similar risk of aerosolization.[11] As the diagnosis of SARS was not suspected when our patient was initially admitted to the PICU, nasal CPAP without a viral and bacterial filter was used in our patient for 1 day, and during that day, there were 4 patients in the surrounding area (with beds at least 3 feet apart) and multiple health care workers exposed. All staff in the PICU had been wearing protective gowns, N95 masks, eye shields, caps, and gloves when handling the patients because of the outbreak of SARS in our region. Fortunately, none of the health care worker or patients came down with SARS on subsequent follow-up.

Most of the adult patients and some pediatric patients were treated empirically with a combination of ribavirin and systemic steroid in addition to broad-spectrum antibiotic coverage.[2,3,5,11] However, our patient showed clinical improvement even before commencement of antiviral therapy. Although ribavirin was subsequently given, it did not seem to have altered the clinical course. It seems that this infant had a more aggressive clinical course than the older children, except adolescent, included in an earlier report.[5] The SARS-CoV may cause more severe disease in premature infants similar to other viral respiratory infections, such as respiratory syncytial virus. However, this issue cannot be addressed with a single case. The wide spectrum of disease manifestation and severity for SARS in children of different ages will be better understood when large series of pediatric patients are reported. The prognosis of the condition in different age groups remains to be determined. Apart from good supportive care, the need for definitive antiviral therapy remains controversial.

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