

Radiographic Features of a Case of Severe Acute Respiratory Syndrome with Fatal Outcome

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Abstract

Introduction: Severe acute respiratory syndrome (SARS) is a new form of atypical pneumonia caused by a coronavirus. We present the clinical course and chest radiographic findings of a case of SARS with fatal outcome. **Clinical Picture:** A 39-year-old Chinese male presented with fever, sore throat and non-productive cough. During his illness, serial chest radiographs showed increasingly severe air-space shadowing in both lungs. **Treatment and Outcome:** The patient was treated with supplemental oxygen, levofloxacin, oseltamivir, ribavirin and methylprednisolone. As his condition worsened, he required ventilatory and inotropic support. He later developed a myocardial infarct and coagulopathy, and succumbed to his illness. **Conclusion:** The reported case mortality of SARS is about 9% worldwide. In Singapore, the mortality is 15.5%. Acute respiratory distress syndrome (ARDS) is believed to be a contributory factor to our patient's demise. We report this case to show the radiographic changes of ARDS in a patient with SARS.

Ann Acad Med Singapore 2003; 32:542-6

Key words: Acute respiratory distress syndrome, Air-space shadowing, Atypical pneumonia, Coronavirus, Thoracic radiography

Introduction

Severe acute respiratory syndrome (SARS) is an atypical pneumonia that was first reported in early 2003.^{1,2} Reports of outbreaks of cases rapidly appeared in Hong Kong, Vietnam, China and Singapore. A cumulative total of 8437 cases of SARS and 813 deaths were reported from 32 countries³ as of 11 July 2003. In Singapore, 206 cases and 32 fatalities have been reported.⁴ The causative organism is believed to be a coronavirus⁵ and the mode of transmission is likely to be contact with infected droplets.

The diagnosis of SARS is made based on a combination of clinical criteria and chest radiographic findings (Table I).⁶ Early diagnosis, isolation of the patient and implementation of barrier nursing are essential in preventing further spread of infection. We present the findings in one of the first cases of SARS in Singapore with complications and a fatal outcome.

Case Report

The patient was a 39-year-old Chinese male with a medical history of childhood asthma. He had visited a patient in hospital who was later diagnosed to have SARS. The patient he visited subsequently recovered. Two days later, he developed a fever with a temperature of 39.8°C, chills and rigours, sore throat, non-productive cough and slight shortness of breath on lying down. The onset of symptoms is designated as day zero of his illness.

The patient was admitted to the hospital on day 6 of his illness. His temperature was initially 37.6°C, but that evening it rose to 40.2°C. The clinical parameters, on admission, were as follows: heart rate 95/min, respiratory rate 25/min and blood pressure 114/77 mm Hg. Auscultation of the lungs revealed occasional late inspiratory crepitations. The patient was conscious and alert, but tachypnoeic.

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TABLE I: CASE DEFINITIONS FOR SURVEILLANCE OF SEVERE ACUTE RESPIRATORY SYNDROME (SARS) – Last Revised 1 May 2003

Suspect Case	
1.	A person presenting after 1 November 2002 with history of : · high fever ($>38^{\circ}\text{C}$) - AND · cough or breathing difficulty - AND one or more of the following exposures during the 10 days prior to onset of symptoms: · close contact with a person who is a suspect or probable case of SARS · history of travel to an area with recent local transmission of SARS · residing in an area with recent local transmission of SARS
2.	A person with an unexplained acute respiratory illness resulting in death after 1 November 2002, but on whom no autopsy has been performed AND one or more of the following exposures during the 10 days prior to onset of symptoms: · close contact with a person who is a suspect or probable case of SARS · history of travel to an area with recent local transmission of SARS · residing in an area with recent local transmission of SARS
Probable Case	
1.	A suspect case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray
2.	A suspect case of SARS that is positive for SARS coronavirus by one or more assays
3.	A suspect case with autopsy findings consistent with the pathology of RDS without an identifiable cause
Exclusion criteria: A case should be excluded if an alternative diagnosis can fully explain their illness	
Definitions:	
1) Close contact: having cared for, lived with, or had direct contact with respiratory secretions or body fluids of a suspect or probable case of SARS	
2) Local transmission* has occurred when one or more reported probable cases of SARS have most likely acquired their infection locally regardless of the setting in which this may have occurred.	
3) If no new locally acquired cases are identified 20 days after the last reported locally acquired probable case died or was appropriately isolated, the area will be removed from the list of affected areas.	
*World Health Organisation. Areas with recent local transmission of SARS. Available from: URL: http://www.who.int/csr/sars/areas/2003_06_04/en/ . Accessed on June 5, 2003.	

Initial blood tests showed a total white cell count of $8.1 \times 10^9/\text{L}$, haemoglobin of 12.4 g/dL and platelet count of $187 \times 10^9/\text{L}$.

On admission, the chest radiograph showed small areas of patchy ground-glass opacities in the left mid and lower zones and periphery of the right lower zone (Fig. 1). A diagnosis of atypical pneumonia was made using the World Health Organisation's (WHO) case definition (Table I). He was placed in an isolation room. Treatment was started with intravenous levofloxacin 500 mg OM and the antiviral agent oseltamivir 75 mg bid orally.

From days 7 to 9, the patient continued to have a high fever which rose to 40°C . He was more lethargic and breathless, but not in distress. Auscultation revealed bilateral basal lung crepitations. He was given supplemental oxygen, with oxygen saturation remaining satisfactory ($>95\%$). Serology for dengue, respiratory syncytial virus, adenovirus, influenza, parainfluenza, mycoplasma and legionella were all reported as negative. A peripheral blood film for malaria parasite was also negative. On day 9, the chest radiograph showed progression of air-space shadowing, with diffuse ground-glass opacities affecting all zones of the left lung and additional patchy consolidation in the left mid and lower zones. More prominent patchy ground-glass opacities were seen at the periphery of the right mid and lower zones (Fig. 2).

On day 10, the patient deteriorated. He became very tachypnoeic, with a respiratory rate of 58/min. He was also tachycardic (100/min) and his blood pressure was 178/80 mm Hg. Oxygen saturation was 89% on 100% oxygen; it declined further to 60%. Bilateral basal crepitations were auscultated in the lungs. The patient was transferred to the medical intensive care unit and intubated for mechanical ventilation.

The diagnosis at this time was acute respiratory distress syndrome (ARDS) secondary to SARS. The post-intubation chest radiograph on day 10 showed almost confluent consolidation of the left lung with air bronchograms. The right lung showed diffuse ground-glass opacities and more extensive consolidation in the mid and lower zones (Fig. 3). Later that night (day 10), the patient became hypotensive (blood pressure, 72/51 mm Hg) and required inotropic support (dopamine and dobutamine).

The patient remained critically ill for the next week and was maintained on ventilatory support and inotropic agents. His temperature fluctuated between 37°C and 38.5°C , with a peak of 40.3°C on day 11. Ribavirin and steroid were added to his medication. His condition deteriorated on day 18, with development of an inferior myocardial infarct and supraventricular tachycardia. He also had a coagulopathy and passed melaenic stools. The platelet count plunged to $39 \times 10^9/\text{L}$ and the white cell count soared to $34.8 \times 10^9/\text{L}$.

A chest radiograph taken on the evening of day 18 (Fig. 4) showed persistent bilateral consolidation, but this appeared less opaque compared with the radiograph done on day 10 (Fig. 3). This was likely due to better pulmonary inflation after intubation and ventilatory support. On day 19, a temperature of 40.3°C was recorded, the highest in a week. This raised the suspicion of superimposed nosocomial bacterial infection. The patient's cardiac status progressively worsened, with development of complete heart block and bradycardia. His blood pressure continued to fall despite maximum dosage of inotropes.



Fig. 1. Chest radiograph on day 6 shows small areas of ground-glass opacities in both lower zones, left more than the right.

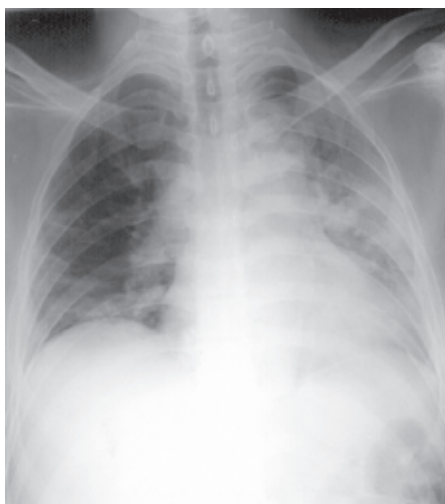


Fig. 2. Chest radiograph on day 9 shows progression of air-space shadowing.

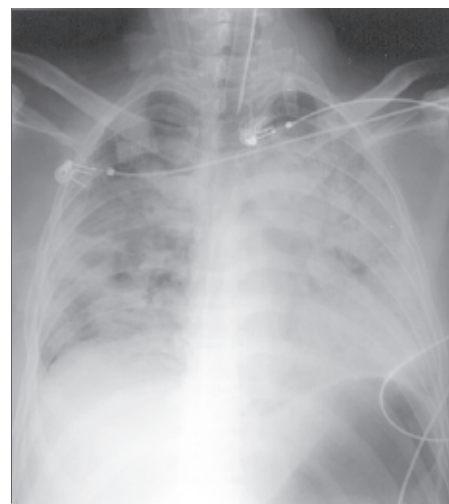


Fig. 3. Chest radiograph on day 10 shows findings consistent with acute respiratory distress syndrome. The patient was intubated.

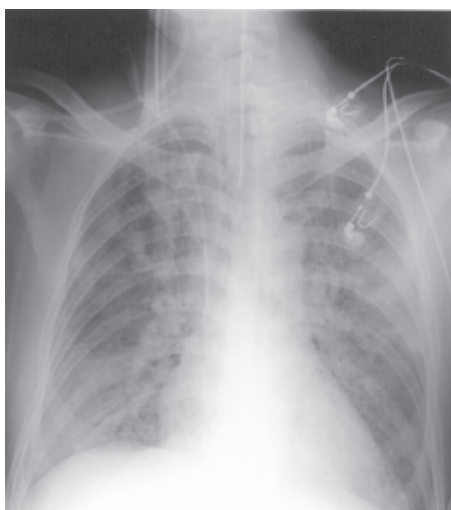


Fig. 4. Chest radiograph on day 18 shows better lung inflation, but persistent bilateral consolidation. Endotracheal tube and central venous line in-situ.



Fig. 5. Chest radiograph on day 19 shows increased air-space shadowing in the right lung. A Swan-Ganz catheter was inserted.

The final chest radiograph taken on day 19 (Fig. 5) showed new diffuse air-space shadowing in the right lung. There was some improvement in consolidation in the left lung. On the evening of day 19, the patient passed away from multiorgan failure. Subsequently, methicillin-resistant *Staphylococcus aureus* was isolated from his blood cultures.

Discussion

Viral infections in healthy adults rarely cause serious pneumonia. Examples include influenza A or B, parainfluenza, respiratory syncytial virus and adenoviruses. However, these organisms, as well as herpes simplex, varicella zoster, cytomegalovirus and measles viruses, may

cause significant opportunistic infections in immunocompromised patients. Parainfluenzae and respiratory syncytial viruses were the most common isolates in one series of lung transplant recipients.⁷ In certain populations of immunocompetent persons, where there is overcrowding, poor ventilation and poor hygiene, there may be increased incidence of these pneumonias. For example, recently enlisted military recruits had a high adenovirus pneumonia infection rate until a vaccine was introduced.⁸

The imaging findings in viral pneumonia are not specific to a particular organism.⁹ Most viral organisms affect the epithelium and adjacent interstitial tissue in the lung. Infection initially results in degeneration and desquamation

of the epithelial cells, with early radiographic findings of patchy areas of peribronchial ground-glass opacities, bronchial wall thickening or small (4 to 8 mm), poorly defined nodules. If unchecked, progression to parenchymal involvement occurs, particularly in an immunocompromised state. Widespread alveolar damage, pulmonary haemorrhage, oedema and fibrin formation are seen in an advanced stage.

The chest radiographic findings in our patient with SARS are similar to some findings in other viral pneumonias⁷ and are consistent with other reports.^{5,10} Air-space shadowing consisting of ground-glass opacities, focal or patchy consolidation was reported on the initial chest radiographs in the series from Hong Kong, which increased in size, extent and severity within the first 10 days after admission.¹⁰ The series of the first 10 cases of SARS in Canada showed bilateral changes which were predominantly in the basal lung zones.⁵

In this patient, the initial chest radiographic findings of patchy ground-glass opacities are not specific. Although each component of the case definition, like the radiographic findings, is not specific, the constellation of a relevant contact history, symptoms and chest radiographic findings define the patient as a probable case. The role of other investigations is to exclude other causes of atypical pneumonia.

In viral pneumonia, worsening infection is manifest radiographically as confluence of the early peribronchial ground-glass opacities to form homogeneous or patchy air-space consolidation, which may be unilateral or bilateral. Involvement of multiple lobes is usual, as compared to lobar pneumonia which is more likely to be bacterial in origin.⁷ The serial chest radiographs of our patient are consistent with this description. Pleural effusion and hilar adenopathy are not prominent features in viral pneumonia and SARS.

The deterioration of the patient on day 10 and corresponding chest radiographic findings are consistent with the development of ARDS. This is a non-cardiogenic form of pulmonary oedema associated with a high mortality rate of 40% to 60%.¹¹ It is due to increased pulmonary vascular permeability and can develop in response to a large variety of insults, such as bacterial sepsis, pneumonia, aspiration of gastric contents, circulatory shock, trauma, burns and drug overdose. In ARDS, the findings on chest radiograph are bilateral widespread, ill-defined air-space shadowing usually without cardiomegaly, upper lobe blood diversion or pleural effusion. The air-space shadowing can progress in severity to produce confluent consolidation, the distribution of which is variable, but usually all lung zones are involved centrally and peripherally, and air bronchograms may be a prominent feature.¹²

In the penultimate days, the new chest radiographic findings in the right lung could have been due to worsening respiratory distress or a secondary infection. The sudden rise in temperature and white cell count could point to an infection. The patient was relatively young and had no previous history of cardiac disease. There were no clinical or radiographic features of cardiac failure.

The utility of imaging in viral pneumonia lies more in the assessment of progression and prognosis, rather than in the diagnosis of a specific organism. New findings on chest radiographs in patients with isolated respiratory viral pneumonia may herald more severe infection. However, other causes of new findings must be considered, such as pulmonary oedema, superimposed bacterial or fungal infection and the onset of ARDS, which are associated with poorer clinical outcomes.⁷

The current outbreak of SARS began in East Asia and is rapidly spreading to the rest of the world. Prompt collection and dissemination of information by both the WHO and the Centers for Disease Control and Prevention (CDC) in the United States relies on the establishment of case definitions. They allow standardised reporting within countries and between different countries. The case definitions issued by the WHO and CDC previously differed with regard to radiographic changes of pneumonia.⁶ The WHO's case definition classifies a suspect case as a probable case if there are chest radiographic findings of pneumonia. The CDC's case definition previously included all cases regardless of the radiographic findings. However, this has since been updated to be similar to the WHO's case definition.¹³

In terms of the causative virus, a new coronavirus has been isolated from respiratory specimens of suspected cases.⁵ Peiris et al¹⁴ have provided evidence that a virus in the coronavirus family is the causal agent of SARS. Coronaviruses were first grown in-vitro in 1965,¹⁵ and they are named for their corona-like (halo) appearance in electron micrographs. The corona is due to an array of surface projections on the viral envelope. They are positive-sense ribonucleic acid viruses, which undergo recombination at high frequency. Classically, coronaviruses are associated with about 15% of common cold infections and are, therefore, spread from person to person through droplets, close contact, hand contamination and even fomites.¹⁶ It has also been shown that coronaviruses are able to survive in the environment for up to 3 hours.¹⁷ Respiratory infections with coronavirus usually result in a mild, self-limiting disease, with a higher incidence in winter. Repeat infections appear to occur throughout life, implying the presence of several serotypes. To date, no vaccine has been developed against coronaviruses because they have previously been associated only with the common

cold, and also because of multiple serotypes.

The new coronavirus implicated in SARS appears to target lung tissue with alarming virulence. The exact number of human isolates, number of serotypes and extent of antigenic variation are not known as these are difficult to grow in culture.

This case report highlights the radiographic pattern of progression in a fatal case of previously undescribed viral pneumonia. With this disease showing particular virulence and ease of transmission, as well as the utilisation of chest radiographs in the identification of probable SARS cases, it is important that medical professionals are familiar with these radiographic features of SARS.

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