Chapter 13

Imaging of SARS in North America

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Introduction

Clinical Manifestations of SARS in North America

Radiographic Manifestations of SARS in North America

High Resolution CT Findings of SARS in North America
Introduction

The first diagnosis of SARS in North America was made in Toronto on March 13, 2003. This was the first recognized case of the disease outside of Asia. By June 2, 198 cases of probable SARS were reported in Canada, 30 (15%) of whom had died. In the United States at the same time 66 cases of probable SARS had been reported, none of whom had died.

The first patient with SARS in North America was a 78-year-old woman who returned home to Toronto on February 23, 2003 after a visit to relatives in Hong Kong. Two days later she developed fever, myalgia, a sore throat, and mild nonproductive cough. Five days later she developed increasing cough and dyspnea. She died three days later, on March 5, at home, nine days after the onset of her illness. The diagnosis of SARS was only made in retrospect.

The index patient’s 43-year-old son developed fever and sweating on February 27, two days after his mother first noted symptoms. He subsequently developed nonproductive cough, chest pain, and dyspnea and eventually high fever (temperature, 39.8°C). A chest radiograph revealed bilateral lower lobe consolidation. He was admitted to the hospital with a diagnosis of community-acquired pneumonia. On the second day after admission, he developed respiratory failure, was intubated and received mechanical ventilation. He died on March 13, 2003, 15 days after becoming ill.

On March 8 and 9, because of concern about possible tuberculosis in the family, the remaining five adult family members and their three children, who had all been exposed to the index patient, underwent screening chest radiography. All had fever, cough, or dyspnea, and abnormal chest radiographs, except for the three children and one of the adults. One of the adults met the criteria for suspected SARS, and three met the criteria for probable SARS. All four were admitted to the hospital, three of them to intensive care units; one patient required mechanical ventilation.

Unfortunately, because spread to contacts had already occurred before the first patients presented to hospital the SARS outbreak spread rapidly. By March 31, contact tracing had identified an additional 100 patients as having probable or suspected SARS in the Greater Toronto area. Transmission was limited to close contacts of patients, including household members, health care workers, or other patients who were not protected with contact or respiratory precautions. Furthermore, case-finding measures identified additional individuals
who had developed SARS after returning from travel to areas in Asia where there had been documented transmission of SARS.

The only other cluster of cases in North America occurred in Vancouver. The first patient was a 55-year-old man who presented to the emergency department at Vancouver General Hospital on March 7, 2003 with a history of recent travel from Hong Kong and symptoms of pneumonia. ² He had arrived from Hong Kong on March 6th. He had little contact outside of immediate family. He was provided with a mask within minutes after arriving at the emergency department. Shortly thereafter, he was admitted into full respiratory isolation. Because of these circumstances he did not spread the disease. Subsequently only 3 more cases were observed in Vancouver, two in individuals with recent travel to Asia and one in a health care worker exposed to one of these patients.

**Key Points**

*Initial experience: North America:*
- Case clusters had traceable contact with Hong Kong or Asia

**Clinical manifestations of SARS in North America**

The clinical manifestations of the first 10 patients with SARS in North America, including 9 from Toronto and 1 from Vancouver were described by Poutanem et al. ¹ The patients ranged from 24 to 78 years in age. The main presenting symptoms included fever (in 100 percent of cases), nonproductive cough (in 100 percent) and dyspnea. Commonly seen laboratory findings included lymphopenia (in 89 percent of cases), elevated lactate dehydrogenase levels (in 80 percent), and elevated aspartate aminotransferase levels (in 78 percent). Five of the 10 patients required mechanical ventilation and three died.

Booth et al reviewed the clinical findings and short-term outcomes of 144 patients with a diagnosis of suspected or probable SARS in the Greater Toronto Area. ⁴ The study included patients who had fever, a known exposure to SARS, and respiratory symptoms or parenchymal abnormalities seen on chest radiograph. Patients were excluded if an alternative diagnosis was determined. Of the 144 patients, 111 (77%) were exposed to SARS in the hospital setting. The most common clinical manifestations included fever (99%), nonproductive cough (69%), myalgia (49%), and dyspnea (42%). Common laboratory
features included elevated lactate dehydrogenase (87%), hypocalcemia (60%), and lymphopenia (54%). Twenty-nine patients (20%) were admitted to the ICU with or without mechanical ventilation, and 8 patients died (21-day mortality, 6.5%). Multivariable analysis showed that the presence of diabetes and other co-morbid conditions were independently associated with poor outcome.

All 4 patients with proven SARS in Vancouver had temperature greater than 100.4°F (greater than 38°C) and one or more clinical findings of respiratory illness including cough, shortness of breath, difficulty breathing, or hypoxia. All had lymphopenia (absolute lymphocyte count < 1000 per cubic millimeter) and elevated serum liver transaminases (Aspartate aminotransferase and Alanine aminotransferase). One of the 4 patients required mechanical ventilation. All 4 patients survived.

**Key Points**

*Clinical presentation: fever, nonproductive cough, myalgia, dyspnea*

*Laboratory findings: ↑ LDH, hypocalcemia, lymphopenia*

**Radiographic manifestations of SARS in North America**

The radiographic findings of SARS at presentation include unilateral or bilateral areas of consolidation (Figure 1) or poorly defined hazy increased opacities without obscuration of underlying vascular margins (ground glass opacities) (Figure 2) \(^5,6,7\). These findings may involve any or all lung zones and be random in distribution, but tend to involve mainly the lower lung zones and the outer third of the lungs. In a small percentage of symptomatic patients the chest radiograph may be normal at presentation but unilateral or bilateral consolidation is usually evident in these patients on radiographs performed 24 to 48 hours later \(^6,7,8\).

In patients who present with focal consolidation, the consolidation may remain unchanged for several days and then clear \(^8\). More commonly however the consolidation remains focal but increases in extent and then gradually clears. \(^8\). In patients with more severe symptoms the consolidation can progress to multifocal patchy or confluent bilateral consolidation. Patients with multifocal unilateral or bilateral disease at presentation often develop more extensive disease after admission and tend to have a more protracted clinical course (Figure 3) \(^8\).
Figure 1
29-year-old man with SARS
Chest radiograph at presentation demonstrates patchy bilateral areas of consolidation.

Figure 2
29-year-old woman with SARS
a. Chest radiograph on admission shows ill-defined hazy increased density (ground-glass opacity) in right middle lung zone.
b. Chest radiograph 24 hours later shows dense focal consolidation. Form Müller NL et al. AM J Roentgenol 2003;181:July 2003, with permission.
Several groups of investigators have reviewed the radiographic manifestations of SARS seen in Toronto and Vancouver. Grinblat et al. reviewed the radiographic findings in 40 patients with SARS seen at a University of Toronto teaching hospital. The patients ranged from 17 to 73 years of age; 55% were female. Fifty eight per cent (23/40) of patients presented with unilateral or bilateral areas of consolidation and 42% (17/40) presented with a normal chest radiograph. All patients with initially normal radiograph developed focal unilateral (12/17, 71%) or bilateral consolidation (5/17, 29%) within 24 to 48 hours. Overall, the mean duration from the date of exposure to the first abnormal chest radiograph in the 40 patients was 12 days (range 4-26). The mean time period from onset of fever to an abnormal radiograph was 5 days (range 1-19).

Twenty of the forty (50%) patients in the study by Grinblat et al. had focal consolidation and 20 had multifocal or bilateral consolidation (Figure 4). In all cases the consolidation had poorly defined margins. In 26 (52%) patients the consolidation had a predominantly peripheral distribution; in the remaining cases there was no apparent central or peripheral...
predominance. In 70% (28/40) of patients the consolidation involved the middle or lower lung zones, and 30% (12/40) the middle or upper lung zones. Seventy-five per cent of the patients (15/20) with focal consolidation as the initial abnormality did not worsen or cleared completely on subsequent radiographs. The remaining 25% (5/20) of patients with focal consolidation progressed to bilateral disease within a mean of 2.2 days (range 1-4 days) of the initial focal findings (Figure 4). Patients with multifocal unilateral or bilateral disease at presentation often developed more extensive disease after admission and frequently had a protracted clinical course 8. Radiographs in patients with residual disease after several weeks often show a predominantly reticular pattern suggestive of fibrosis (Figure 5).

Nicolaou et al reported the radiographic and CT findings in the first case of SARS seen in Vancouver 9. The patient was a 55-year-old previously healthy man who had traveled to Hong Kong and presented with a 2-week history of fever, headache, malaise, dyspnea, and cough. Bedside computed radiograph demonstrated extensive bilateral ground-glass opacities and dependent areas of consolidation (Figure 6).

**Figure 4**

44-year-old man with SARS

a. Chest radiograph at hospital admission shows focal consolidation in the region of the right costoprenic sulcus.

b. Chest radiograph three days later demonstrates increased right lower lobe consolidation and patchy areas of consolidation in the left upper and lower lobes.
Figure 5
62-year-old man with SARS
a. Chest radiograph performed six days after hospital admission shows extensive bilateral consolidation.
b. Chest radiograph performed seven weeks after hospital admission demonstrates coarse reticular opacities involving mainly the middle and upper lung zones. A tracheostomy tube is in place.
Müller et al reviewed the radiographic findings in 12 patients with SARS, including 5 from Vancouver and 7 from Hong Kong. The main radiographic findings at presentation consisted of unilateral or bilateral ground glass opacities (n=5), focal unilateral or bilateral areas of consolidation (n=5), and diffuse small nodular opacities (n=1) (Figs 2 and 3). In one patient the admission chest radiograph was normal. In one other patient the chest radiograph had been prospectively interpreted as negative, although in retrospect subtle bilateral ground glass opacities could be seen. Ground glass opacities were bilateral, extensive and fairly symmetric in three patients, limited to one lung in two patients, limited to the lower lobes in one patient, and bilateral and asymmetric in one patient. The areas of consolidation involved mainly the upper lung zones in two patients, the lower zones in two patients and the middle lung zones in one patient. Eight of the 10 patients who were hospitalized and had follow-up chest radiographs performed within 24 hours of presentation demonstrated progression of disease. In these eight patients follow-up radiographs
demonstrated extensive unilateral (n=2) or bilateral areas of consolidation (n=6) regardless of the initial radiographic pattern ⁷.

**Key Points**

**Chest Radiograph manifestations:**
May be initially normal in a small number of patients

**Opacities:**
- unilateral of bilateral areas of consolidation OR
- poorly defined haze increased opacities without obscuration of underlying vascular margins (ground glass opacities)

**Location of lesions:**
- random involvement
- mainly the lower lung zones and the outer third of the lungs

**Key Points**

**Radiographic Progression:**

**Focal consolidation at presentation:**
- consolidation increases in extent and then gradually clears.
- patients with more severe symptoms, may progress to multifocal patchy or confluent bilateral consolidation.

**Multifocal disease at presentation:**
- often develop more extensive disease after admission and tend to have a more protracted clinical course

**High resolution CT of SARS in North America**

The high resolution CT manifestations of SARS consist of unilateral or bilateral ground glass opacities and/or unilateral or bilateral areas of consolidation (Figure 7) ⁷, ¹¹, ¹². Smooth thickening of interlobular septa and smooth intralobular lines are often present superimposed on areas of ground glass attenuation. The parenchymal abnormalities tend to involve mainly the lower lobes. The findings can be diffuse or random in distribution but tend to involve mainly the outer third of the lungs ¹¹, ¹². In all cases reported so far high resolution CT
has been abnormal at initial presentation even when concurrent radiographs are normal or show only questionable abnormalities (Figures 7, 8) \(^7,11,12\). Furthermore, in the majority of patients high resolution CT shows more extensive disease than apparent on the radiograph \(^12\).

Müller et al reviewed the initial CT findings seen at presentation in 5 patients from Vancouver and 7 from Hong Kong \(^7\). One of the patients had normal chest radiograph, one had radiograph prospectively interpreted as normal but in retrospect demonstrated bilateral ground glass opacities, two had bilateral ground glass opacities and one had focal consolidation seen on the radiograph. High resolution CT in the one patient with normal chest radiograph showed patchy bilateral areas of ground glass attenuation and focal consolidation in the superior segment of the left lower lobe. High resolution CT in the three patients with ground glass opacities on the radiograph demonstrated extensive bilateral areas of ground glass attenuation (n=3) and small focal areas of consolidation (n=2) (Figure 9). The areas of consolidation involved mainly the dorsal lung regions. High resolution CT in the remaining patient showed focal consolidation in the right lower lobe.

![Figure 7](image)

**Figure 7**
30-year-old woman with SARS

a. Chest radiograph shows haziness (ground glass opacity) over the lateral aspect of the right lung base with some loss of definition of the right hemidiaphragm.

b. High-resolution CT demonstrates bilateral focal areas of consolidation.
Figure 8
66-year-old woman with SARS
a. Chest radiograph was interpreted by the emergency room physician as being normal. The radiologist reviewing the radiograph the following morning noted a vague opacity overlying the anterior right second rib and recommended high-resolution CT for further evaluation.
b & c. High-resolution CT images of the right upper lobe demonstrate focal area of consolidation, ground-glass opacities, mild septal thickening and smooth intralobular lines.
In a subsequent study, Müller et al reviewed the high-resolution CT findings in 29 patients with SARS, including 4 from Vancouver and 25 from Hong Kong. The patients included 16 men and 13 women ranging from 25 to 82 years of age. Twelve of the 29 patients had CT performed at presentation or within 12 hours after hospital admission. All patients had parenchymal abnormalities on initial high-resolution CT, including 8 patients who had normal concurrent chest radiographs. The predominant high-resolution findings at
presentation consisted of unilateral (n=6) or bilateral (n=2) ground glass opacities or focal unilateral (n=2) or bilateral (n=2) areas of consolidation. Four of the 12 (33%) patients had associated mild thickening of the interlobular septa within the areas of ground glass attenuation or adjacent to areas of consolidation. The abnormalities involved predominately or exclusively the lower lung zones in five patients, the middle lung zones in five patients, and upper lung zones in two patients. A predominantly subpleural distribution was evident on high-resolution CT in eight patients, a patchy random distribution in three, and diffuse abnormalities in one patient. None of the patients had had evidence of hilar or mediastinal lymphadenopathy or pleural effusion at presentation.

Twenty-five patients in the study by Müller et al had high-resolution CT scans performed 2-27 days after hospital admission (median 9 days) \(^{12}\). The predominant high-resolution CT findings in hospitalized patients consisted of unilateral (n=2) or bilateral ground glass opacities (n= 13) or unilateral (n= 2) or bilateral consolidation (n= 5), or a mixed bilateral pattern of ground glass attenuation, consolidation, and reticulation (n=3). Common findings seen in association with ground glass opacities included mild smooth thickening of interlobular septa and smooth intralobular lines. Reticulation with associated irregular interfaces, architectural distortion and mild traction bronchiectasis was present in 8 patients (32%). Other findings seen on follow-up high-resolution CT included pneumothorax (n=2), pneumomediastinum (n=3), and small pleural effusions (n=2)).

The unilateral and bilateral areas of consolidation seen on high resolution CT in patients with SARS are similar to those seen in a variety of bacterial, fungal, and viral pneumonias \(^{11}\). The findings in patients with SARS differ, however, from those described in other viral pneumonias, by the absence of centrilobular nodular opacities. Centrilobular nodules and branching centrilobular opacities resulting in a “tree-in-bud” pattern are commonly seen in patients with bacterial, viral, and mycoplasma pneumonia \(^{13, 14, 15}\). Reittner reviewed the high-resolution CT findings in 114 patients with different types of pneumonia \(^{13}\). In their study 7 of 9 (78%) patients with viral pneumonia had centrilobular nodules. Septal thickening was seen at presentation in 3 (33%) patients with viral pneumonia in the study by Reittner et al. and in 3 of 12 (25%) patients with SARS in the current study.

In patients with a protracted clinical course a reticular pattern is commonly seen on the radiograph and high resolution CT two weeks or more after hospital admission (Figure 10) \(^{6, 8, 11, 12}\). On high resolution CT the reticular pattern is often associated with irregular interfaces and mild traction bronchiectasis. These findings suggest the presence of fibrosis \(^{16}\). However, long term follow-up will be required to determine whether these changes resolve over time or whether they represent irreversible fibrosis.
Figure 10

48-year old woman with SARS. The admission chest radiograph was normal. The radiographs remained normal until 4 days after admission when minimal consolidation was evident. The consolidation progressed rapidly; the patient developed respiratory failure and required intubation and mechanical ventilation.

a. Chest radiograph performed 7 days after hospital admission shows extensive bilateral consolidation.

b. Chest radiograph performed 1 month after hospital admission shows small foci of consolidation and extensive bilateral coarse reticular pattern.

c. High resolution CT at the level of the left main bronchus demonstrates bilateral ground glass opacities, irregular linear opacities and distortion of architecture.

d. High resolution CT at the level of the right inferior pulmonary vein demonstrates predominantly right sided abnormalities.
Key Points

HRCT manifestations:

Location of lesions:
- unilateral or bilateral distribution
- lower lobe predominance
- diffuse or random in distribution
- mainly the outer third of the lungs

Lesion appearance:
- ground glass opacities and/or consolidation
- smooth thickening of interlobular septa and smooth intralobular lines, often present superimposed on ground glass opacities
- absence of centrilobular nodular opacities or a “tree-in-bud” pattern
- No hilar or mediastinal lymphadenopathy or pleural at presentation

Follow up HRCT findings:
- Reticulation with irregular interfaces, architectural distortion and mild traction bronchiectasis (32%)
- Pneumothorax
- Pneumomediastinum
- Small pleural effusion

Sensitivity of HRCT:
- Abnormal on patients with normal initial radiograph
- Showed more extensive disease than apparent on the radiograph
References

12. Müller NL, Ooi GC, Khong PL, Nicolaou S. Severe Acute Respiratory Syndrome: High-resolution CT findings at presentation and after admission. Submitted for publication.