Chapter 6

Chest Radiography: Clinical Correlation and Its Role in the Management of Severe Acute Respiratory Syndrome (SARS)

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Introduction

Chest radiography not only plays an important role in the diagnosis of SARS, it is crucial in the management of these patients. During treatment there are variable clinical and radiological responses in different patients and serial chest radiography help in deciding whether escalation to more aggressive treatment is necessary. Based on our preliminary experience, we believe that changes on serial radiographs is also an important prognostic indicator. This chapter aims to examine the correlation between the clinical course and the radiological features, and the role of chest radiography in the management of SARS.

Treatment Protocol

The treatment of SARS patients is discussed in detail in a separate chapter. However, in order to better understand the clinical and radiological correlation one must be familiar with the basic treatment principles. These are therefore discussed briefly in the following paragraph.

Patients were treated for the first 2 days with broad spectrum antibiotics for community-acquired pneumonia according to the American Thoracic Society Guidelines. Our initial treatment consisted of intravenous cefotaxime 1g every 6 hours and oral clarithromycin 500 mg twice daily (or oral levofloxacin 500 mg daily for those who could not tolerate clarithromycin).

Clinical symptoms, arterial blood oxygen saturation and chest radiograph were assessed daily.

If fever persisted, patients were given a combination of ribavirin and “low-dose” corticosteroid therapy commencing on Day 3-4 (oral ribavirin as a loading dose of 2.4 g stat followed by 1.2 g three times daily and prednisolone 0.5-1 mg/kg body weight per day).

Those with dyspnoea at presentation were treated with intravenous ribavirin (400 mg every 8 hours) combined with hydrocortisone (100 mg every 6 hours).

Pulses of high-dose methylprednisolone (0.5 g IVI for three consecutive days) were given as a response to persistent fever, radiographic progression of lung opacity and hypoxemia despite combination therapy. Further pulses of methylprednisolone were given as deemed necessary, up to a total of three grams.
Patients who continued to deteriorate despite these measures were given convalescent plasma. The intention was to continue with the combination of ribavirin and “low-dose” corticosteroid for up to 12 days. Those who became afebrile but with incomplete radiological resolution were given oral ribavirin 600 mg t.i.d. and prednisolone 0.5 mg/kg body weight per day for at least one further week.

**Radiological and Clinical Patterns During Treatment**

Based on our experience treating over 300 SARS patients, there are certain basic radiological and clinical patterns that we have observed:

1. **Radiological Pattern during Treatment** (Figure 1)

   It is clear that serial chest radiographs contribute significantly in the daily management of patients with SARS. Based on the serial chest radiographs from the initial 138 SARS patients, we have observed four radiographic progression patterns during treatment:

   - **Type 1**: High percentage of lung involvement with a peak of >25%.
   - **Type 2**: Moderate progression with a peak of >25%.
   - **Type 3**: Mild progression with a peak of <25%.
   - **Type 4**: Continuous progression without recovery.

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**Figure 1**

Schematic diagram shows four radiographic progression patterns of SARS during treatment in hospital.
Type 1- initial radiographic deterioration to peak level followed by radiographic improvement, with maximum radiographic change > 25% (Figure 2);

**Figure 2**
Type 1 radiographic progression pattern
Serial chest radiographs in a 28-year old man with SARS
(a) frontal chest radiograph at presentation shows ill-defined consolidation in left paracardiac area
(b) follow-up chest radiograph 7 days later shows progressive air-space lesions involving both lower zones
(c) subsequent follow-up chest radiograph another 6 days later shows radiographic improvement
Type 2 - fluctuating radiographic changes, with at least two radiographic peaks and an intervening trough which differed by > 25%;
Type 3 - static radiographic changes, with no discernible radiographic peak or change of involvement area < 25% for more than 10 days; and
Type 4 - progressive radiographic deterioration (Figure 3).

Figure 3
Type 4 radiographic progression pattern
Serial chest radiographs in a 74-year old woman with SARS (a) frontal chest radiograph at presentation shows ill-defined consolidation in right lower zone (b) follow-up chest radiograph after 3 days shows radiographic progression with more extensive involvement of right upper and middle zones. New finding of ill-defined air-space opacification involving left upper and middle zones is noted. (c) follow-up chest radiograph after another 3 days shows progressive radiographic deterioration. The patient succumbed on the day after the last radiograph.
Key Points

Four radiographic progression pattern during treatment
(1) initial deterioration followed by improvement (commonest) (70.3%)
(2) fluctuating radiographic changes (17.4%)
(3) static radiographic changes (7.2%)
(4) progressive deterioration (least common, poor clinical outcome) (5.1%)

(2) Clinical Pattern during Treatment
The clinical course of SARS appears to follow a triphasic pattern:
- Phase 1 (viral replication) is associated with increasing viral load and clinically characterized by fever, myalgia, and other systemic symptoms that generally improve after a few days.
- Phase 2 (immunopathological damage) is characterized by recurrence of fever, oxygen desaturation, radiological progression of pneumonia with a fall in viral load. The majority of patients will respond to treatment with a combination of ribavirin and intravenous steroid whereas 20% of patients may progress into
- Phase 3, characterized by acute respiratory distress syndrome (ARDS) necessitating ventilatory support.

Among these 138 cases, 36 (26.1%) were admitted to the ICU because of respiratory failure. In the first 4 weeks of this outbreak, there were 8 mortalities (crude mortality rate = 5.8%). All 8 cases were originally admitted for major medical conditions. Two patients suffered from myelodysplastic syndrome, four with cardiac diseases (1 with congestive heart failure, 2 with ischemic heart disease, and 1 with rheumatic heart disease), one with alcoholic liver cirrhosis, and one with hepatitis B reactivation.

Key Points
- Triphasic clinical pattern of SARS during treatment
  (1) Viral replication phase
  (2) Immunopathological damage
  (3) Acute respiratory syndrome
- Over 25% of patients develop respiratory failure requiring intensive care.
(3) Radiographic changes and correlation with clinical course

a) Phase 1: The initial chest radiograph was performed on average 2.5 days after onset of fever (range 0 to 10 days). On presentation, the majority (78.3%) of our patients with SARS had evidence of air space consolidation on their chest radiographs. One must note that based on a single chest radiograph, the radiographic appearances of SARS cannot be distinguished from other causes of pneumonia. The initial chest radiography may appear normal up to 25% of cases but serial CXR invariably demonstrates abnormal air space disease after 1 to 7 days (median 3 days). The opacities occupy a peripheral or mixed peripheral and axial location in 88% of patients. The rapid radiographic progression, predominant involvement of lung periphery and the lower zone, in addition to the absence of cavitation, hilar lymphadenopathy or pleural effusion, are the more distinctive radiographic features of SARS.

b) Phase 2: Radiographic progression from unilateral focal air-space opacity to either multi-focal or bilateral involvement occurs during the second week of the disease. Fifty-nine patients (54.6%) had focal unilateral opacity while 49 (45.4%) had unilateral multi-focal or bilateral involvement. Radiographic progression of consolidation occurred at a peak of mean 8.6 days ± 3.1 days from fever onset in about 80% of our patients, at almost the same time as clinical deterioration with recurrence of fever and respiratory failure. Even when there is only 10% of pneumonic changes noted in the lung field, approximately 40% of patients would require supplementary oxygen to maintain satisfactory oxygenation. Of the patterns of radiographic progression, type 1 was the most common (70.3%) followed by type 2 (17.4%), type 3 (7.2%) and type 4 (5.1%) pattern. Radiographic improvement following pulse steroid treatment is commonly encountered towards the end of phase 2.

c) Phase 3: The significant morbidity of SARS was reflected by the wide spectrum of clinical symptoms followed by progression of consolidation leading to respiratory failure, intensive care admission, ARDS and death in some cases. In addition, there appears to be a high incidence of pneumo-mediastinum/ pneumothorax (Figures 4 and 5) causing worsening of hypoxaemia, which may occur either spontaneously or be related to barotrauma in SARS. These complications are probably due to poor lung compliance.
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Figure 4
Frontal chest radiograph in a 46-year old man with SARS show presence of pneumothorax and loculated pleural effusion during in-patient treatment. A chest drain and pigtail catheter have been inserted for drainage.

Figure 5
Frontal chest radiograph in a 33-year old man with SARS shows complication of pneumomediastinum and surgical emphysema.

Key Points
- The initial chest radiography may appear normal up to 25% of cases
- SARS predominantly involves lung periphery and the lower zone with absence of cavitation, hilar lymphadenopathy of pleural effusion
- Radiographic progression occurs in line with clinical deterioration at approximately the beginning of the second week with a high incidence of spontaneous pneumo-mediastinum and/or pneumothorax.
Clinico-radiological Correlation

Since SARS is a new disease, little is known about its indicators of poor prognosis. We have examined the role of imaging and various biochemical parameters which may predict poor outcome.

(1) Radiographic changes and clinical outcome
   a) The extent of pneumonia on presentation appears to correlate with adverse clinical outcome in SARS. Those who either required ICU care or died had more extensive radiological evidence of pneumonia (%) on the initial CXR (median 3.30, interquartile range 1.70-7.93 vs 1.70, interquartile range 0-3.30, p<0.001) and day 7 CXR from fever onset (median 15.00, interquartile range 6.48-28.73 vs 5.00, interquartile range 2.50-7.50, p<0.001) compared to those survivors not requiring ICU care.
   - Those with consolidation > 1 zone on the initial CXR and day 7 CXR were significantly more associated with ICU admission/death than those with ≤ 1 zone involvement (p<0.001 for both).
   - Patients with bilateral pneumonic changes on the initial CXR were more likely to require ICU care or have a fatal outcome in comparison to those with unilateral pneumonia on admission (p<0.001).
   - Our multivariable analysis has shown that more than one CXR zone involvement on presentation [Odds Ratio = 3.16; 95% C.I. = 1.07-9.32; p=0.037] is an independent predictor of adverse outcome after adjusting for high baseline LDH, advanced age and a high neutrophil count.

b) In addition, the pattern of radiographic progression also appears to correlate well with clinical outcome.
   Among the 97 patients with type 1 pattern on serial CXR, only 17 (17.5%) were either admitted to ICU or dead whereas 21 out of 41 patients (51.2%) with CXR category other than type 1 were either admitted to ICU or dead (p<0.001). Of these 21 patients, 14 had type 2 while 7 had type 4 pattern.
   Thus patients with type 1 pattern (initial radiographic progression followed by improvement) on serial CXR seemed to have a more favourable outcome whereas patients with type 4 pattern (progressive deterioration) had an adverse clinical outcome.
Key Points
Radiological predictors of poor clinical outcome
- more extensive radiographic disease (%) at presentation,
- >1 zone involvement on presentation, and
- type 4 progression pattern.

(2) Radiographic changes and laboratory features
Among all the laboratory parameters, there was a positive correlation between CXR trend and the rate of change of LDH, a marker of tissue damage. The rate of change of LDH (units/day) significantly correlated with the rate of change of CXR % involvement (Spearman $r_s=0.399$, $p=0.014$). We believe that LDH reflects the extent of lung injury in this setting, and both serial chest radiographs and LDH levels are important in the management of SARS.

Key Points
Radiographic progression correlates with LDH, a marker of lung injury.

Role of CXR in Management of SARS
Serial chest radiographs are most useful in guiding treatment of disease progression. Based on evidence of radiographic progression (worsening of pre-existing lung changes by at least 10% or development of new or contralateral lung lesions) and/or hypoxaemia, we initiated treatment with intravenous pulse methylprednisolone to prevent immuno-pathological lung injury, on the rationale that progression of the pulmonary disease may be mediated by the host inflammatory response. The peak of the extent of pneumonic changes has corresponded to the time of commencement of pulse intravenous methylprednisolone treatment. The median time of starting the first pulse of methylprednisolone was 8 days (Interquartile range 6-9 days). Almost 90% of our patients have shown favourable response with deferscence, resolution of radiographic changes by at least 25%, and oxygen independence after steroid treatment. Serial chest radiographs are essential especially in the intensive care setting to detect complications such as pneumothorax and pneumo-mediastinum. In a case series, 12% and 20% of patients developed spontaneous pneumo-mediastinum and evidence of ARDS respectively over a period of 3 weeks.
Key Points
Serial chest radiography is essential in
- monitoring disease progression,
- response to treatment, and
- development of pulmonary complications.

Conclusion
Chest radiography is a useful modality in the diagnosis and management of SARS. More extensive radiographic involvement on presentation is associated with adverse clinical outcome. Serial chest radiographs are essential for guiding appropriate medical treatment, monitoring response to treatment and detecting development of complications such as pneumomediastinum and pneumothorax.
References


