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Review

Imaging in Severe Acute Respiratory Syndrome (SARS)

G. E. ANTONIO*, K. T. WONG*, W. C. W. CHU*, D. S. C. HUI†, F. W. T. CHENG‡, E. H. Y. YUEN*, S. S. C. CHUNG§, T. F. FOK‡, J. J. Y. SUNG†, A. T. AHUJA*

*Departments of Diagnostic Radiology and Organ Imaging, †Medicine and Therapeutics, ‡Paediatrics, and §Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR

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Severe acute respiratory syndrome (SARS) is a highly infectious disease caused by a novel coronavirus, and has become pandemic within a short period of time. Imaging plays an important role in the diagnosis, management and follow-up of patients with SARS. The current status of imaging in SARS is presented in this review. Antonio, G. E. *et al.* (2003). *Clinical Radiology* **58**: 825–832.

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INTRODUCTION

An outbreak of atypical pneumonia has wreaked havoc in many Asian countries including Hong Kong since early March 2003. The illness is defined by World Health Organisation (WHO) as severe acute respiratory syndrome (SARS). Within a very short time, the disease became pandemic with new cases appearing in the rest of the world. At the time of writing of this article, there are 7628 cases of probable SARS cases and 587 deaths worldwide [1]. [As of 5 July 2003 the WHO declared that SARS outbreaks have been contained worldwide. Ed.] This novel infection has been associated aetiologically with a novel coronavirus named SARS-associated coronavirus (SARS-CoV) [2,3], which is highly infectious.

The case definition provided by the WHO is updated periodically and SARS is categorized into suspect and probable cases [4] (Table 1). There is no single test that can confidently diagnose this new disease. The diagnosis is currently based on a combination of clinical information and imaging features. The

chest radiograph examination is one of the major diagnostic components according to WHO and CDC guidelines [5,6].

Currently the discharge policy is predominantly based on clinical and epidemiological parameters. The discharge criteria of SARS patients in our institution include: (1) afebrile for at least 96 h after the last dose of steroid; (2) resolving respiratory symptoms and oxygen independence; (3) radiological improvement (based on serial chest radiographs); and (4) improving laboratory parameters.

There have been over 300 cases of SARS treated at our institution over the last 2 months. In our experience, imaging plays an important role in diagnosis and management. Several radiology articles have been published recently, including our initial cohort of SARS patients [7–10]. This review, based on the same initial cohort of patients, is a summary of imaging of SARS with additional information on paediatric cases and early follow-up appearances.

RADIOLOGICAL ASSESSMENT

Plain chest radiography and high-resolution computed tomography (HRCT) of the thorax are the two main imaging techniques we have used for patients with SARS. Chest

Guarantor and correspondent: G. E. Antonio, Department of Diagnostic Radiology and Organ Imaging, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR. Tel: +852-2632-1036; Fax: +852-2648-7269; E-mail: gregantonio@cuhk.edu.hk

Table 1 – World Health Organisation (WHO): case definition of SARS (updated on 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 radiograph
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.

radiography helps in the diagnosis by demonstrating pneumonic changes in lungs and helps in evaluating progress of the disease and response to treatment [7]. HRCT is an important tool for early diagnosis in patients with a high clinical suspicion and a negative initial chest radiograph [8]. In patients with residual symptoms and persistent abnormality on follow-up chest radiograph after discharge, HRCT provides more accurate assessment of the nature and extent of lung changes.

Our imaging protocol for suspected cases of SARS is presented in Fig. 1. Patients with clinical suspicion of SARS are initially investigated with a chest radiograph. If there is a

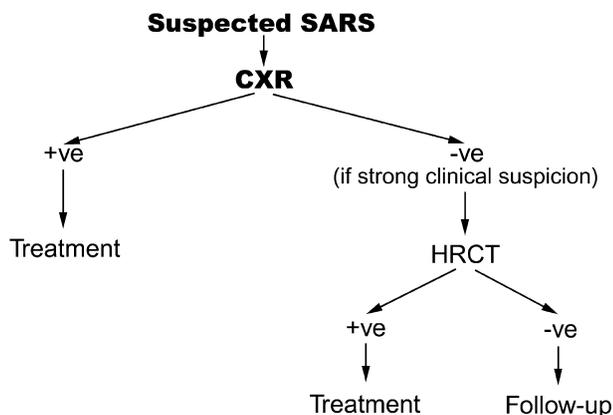


Fig. 1 – Imaging protocol for suspected case of SARS used at our institution.

definite abnormality on the initial chest radiograph, further imaging is not required for diagnosis and the patient will receive treatment. If the chest radiograph is normal and clinical features are strongly suspicious, HRCT of the thorax helps to detect early disease. If HRCT is positive for lung parenchymal abnormality, the patient will receive treatment. If HRCT is negative, the patient is followed up in a review clinic on an out-patient basis.

CHEST RADIOGRAPHY

Chest radiography is the most commonly employed imaging investigation for patients with SARS.

Diagnosis (Figs 2 and 3)

Our initial experience of chest radiography findings in patients with SARS [7] showed that:

- (1) the majority (108/138, 78%) of patients had air-space opacification of various extent on the chest radiograph at presentation,
- (2) the right lung was more affected than the left (82/108, 76% versus 67/108, 62%),
- (3) the lower zone (70/108, 65%) and peripheral lung fields (81/108, 75%) were commonly involved,
- (4) unifocal involvement (59/108, 55%) was more common at presentation,

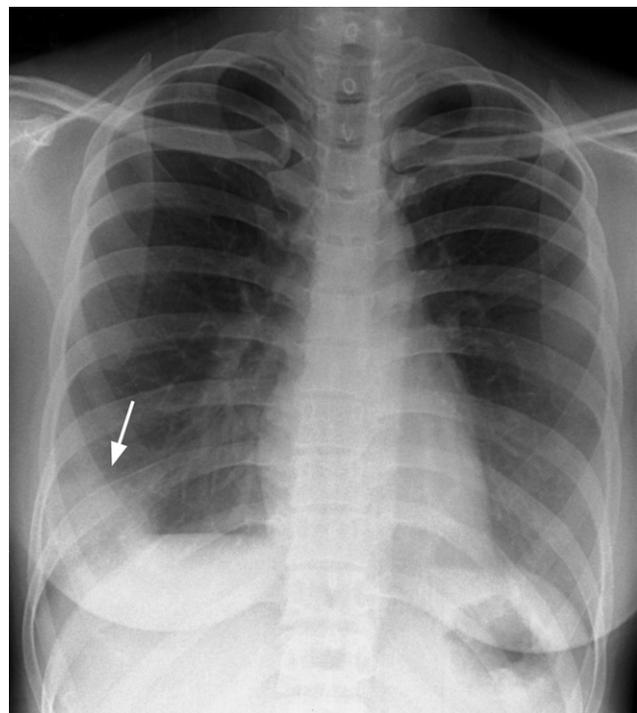


Fig. 2 – A 26-year-old woman with SARS. Frontal chest radiograph at presentation shows focal ill-defined air-space opacity in periphery of right lower zone (arrow). Note the absence of cavitation, lymphadenopathy and pleural effusion.



Fig. 3 – A 26-year-old woman with SARS. Frontal chest radiograph at presentation shows multifocal ill-defined air-space opacities in both lower zones.

(5) cavitation, lymphadenopathy and pleural effusion were not present.

In 22% of patients (30 out of 138) with SARS in our series, the initial chest radiograph was normal [7]. These patients had clinical signs and symptoms highly suspicious of SARS and HRCT was performed, which detected early lung changes (Fig. 4). Subsequent follow-up radiographs in all these patients showed air-space opacification.

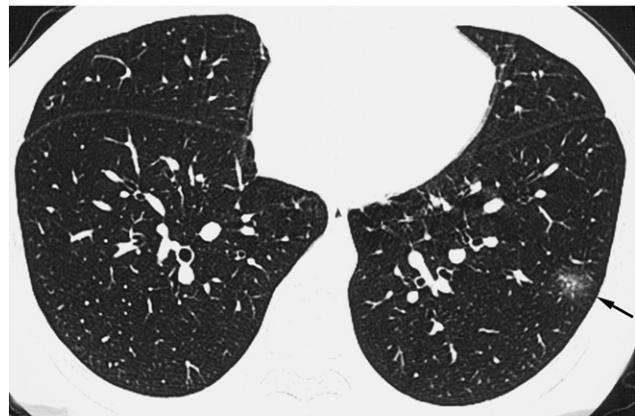
The radiographic appearances of SARS are indistinguishable from other causes of atypical pneumonia such as mycoplasma, chlamydia and legionella [11,12]. There is also overlap with other types of viral pneumonia in adults [13]. As imaging alone cannot differentiate SARS from other atypical pneumonias, clinical information [including presence of high fever ($>38^{\circ}\text{C}$), chills, rigor, myalgia and laboratory findings such as leucopenia and thrombocytopenia] are indispensable for accurate diagnosis [14].

Monitoring Progress and Treatment Response

Patients with a confirmed diagnosis of SARS in our institution are treated with a combination of ribavirin and corticosteroid [14]. For patients not responsive to first-line treatment, other forms of therapy such as pulsed intravenous methylprednisolone and convalescent serum were used. Serial chest radiographs play an important role in patient management during the treatment period as obvious radiographic deterioration would require escalation to more aggressive treatment such as pulsed intravenous methylprednisolone. During the treatment period we observed four different types of radiographic progression [7] (Table 2; Figs 5 and 6); type 4 patients



(a)



(b)

Fig. 4 – A 36-year-old healthcare worker with SARS. (a) Frontal chest radiograph at presentation is unremarkable. (b) HRCT of the lungs on the same day shows small area of ground-glass opacification in periphery of lateral basal segment of left lower lobe (arrow). HRCT was performed in view of the high clinical index of suspicion and a negative chest radiograph. Subsequent radiographs showed obvious air-space opacification at this site.

had the worst prognosis in terms of mortality and intensive care requirement.

Paediatric Patients

The number of children infected by SARS is far less than the adult population. Up to mid May 2003, children constituted less than 5% of the infected population in Hong Kong. In our first cohort of the initial 10 children admitted to the hospital [15], we found that the clinical course and radiological changes of

Table 2 – Pattern of radiographic progression of SARS during treatment

Progression pattern	Description	Number of patients (%)	Number of death
Type 1	Radiographic progression followed by improvement	97 (70.3%)	0
Type 2	Fluctuating with at least two radiographic peaks	24 (17.4%)	2
Type 3	Static with no obvious peak	10 (7.3%)	0
Type 4	Progressive radiographic deterioration	7 (5%)	6

children were generally much milder and the duration for resolution was also shorter. Most children (90%) have radiographic abnormalities on presentation to the hospital. The primary radiographic finding in paediatric patients with SARS was air-space opacification, which can be focal or multiple. Children of younger age usually present with focal segmental consolidation. A few teenage patients, who presented with a more severe disease and required oxygen therapy, had bilateral lung involvement and multi-focal consolidation [15] (Fig. 7). In general, the consolidative changes on chest radiography in children are less extensive than adults. The majority of children showed slight radiographic deterioration on serial chest radiographs with a mean peak on day 6 after the onset of fever. Lymphadenopathy, pleural effusion and cavitation are not features of paediatric SARS, in contrast to the more common paediatric chest infections such as tuberculosis [16] and pneumococcal pneumonia [17]. At the time of writing of this review, all the patients in our initial cohort have recovered with complete resolution of radiographic changes.

HRCT

During the early phase of the outbreak, as we had no literature to refer to for this new disease, both conventional CT and HRCT were performed in patients with high clinical index of suspicion but a normal chest radiograph. With increasing experience of the CT features of SARS, especially lack of lymphadenopathy or pleural abnormality, we now perform only HRCT for diagnosis and follow-up. Our CT protocol was: 1 mm collimation, 6 mm interval, patient supine and inspiration, 1 s acquisition time, 120 kV, 140 mA.

Diagnosis

In our experience the majority of patients with SARS had an abnormal chest radiograph on presentation, further imaging was therefore not necessary for diagnosis. We found HRCT of the thorax particularly important in patients with a high clinical index of suspicion and a negative chest radiograph. All patients in this selected group showed abnormality on HRCT examination [8]. The importance of strong clinical correlation should be emphasized, as HRCT was invariably negative in patients with minor symptoms and low index of clinical suspicion [8]. These CT examinations were performed as most of the “patients” were staff in the hospital and there was generally a high state of anxiety among the staff at the time of the outbreak.

The commonest features on HRCT found in patients with SARS included [8,9] (Fig. 8; Table 3):

– ground-glass opacification which was present in 102 of 149

(68.4%) lung segments with abnormalities; pure consolidation in 25/149 (16.8%) and mixed ground-glass opacification and consolidation in 22/149 (14.8%);

- lower lobe predilection (30/40 patients, 75%);
- peripheral/subpleural location (107/149 lung segments with lesions, 71.8%);
- multifocal or bilateral (17/40, 42.5%) involvement;
- thickening of the intralobular interstitium (48/149, 32.3% lung segments with abnormalities) or interlobular septa (36/149, 24.2%) within areas of ground-glass opacification. In florid cases, a “crazy-paving” pattern was seen;
- no cavitation, calcification, lymphadenopathy or pleural effusion in any patient

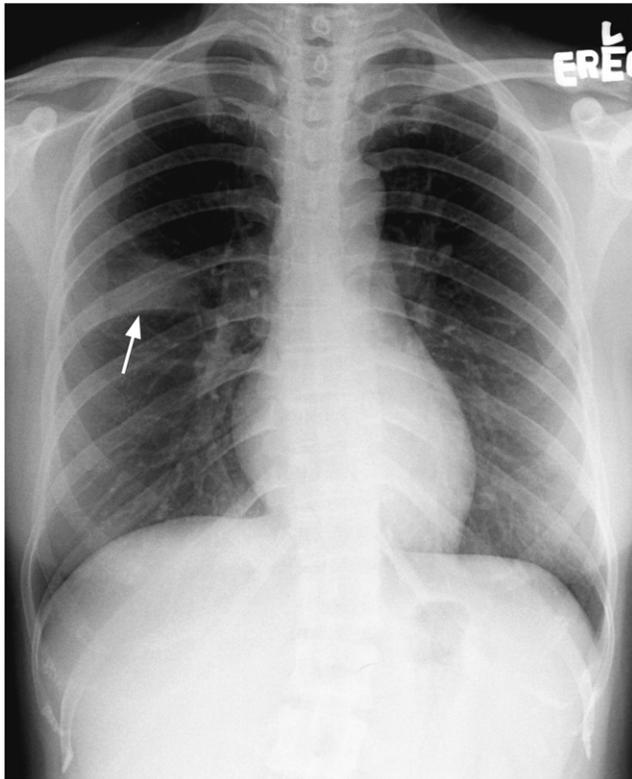
Follow-up

HRCT is usually not required to monitor progress and response to treatment as chest radiography alone is often enough for these purposes. In patients with prolonged illness unresponsive to standard treatment, HRCT may help to assess the pulmonary parenchymal abnormality to differentiate whether the predominant component is ground-glass opacification (which is considered to be reversible and amenable to medical treatment) or fibrosis (which is considered to represent irreversible lung damage).

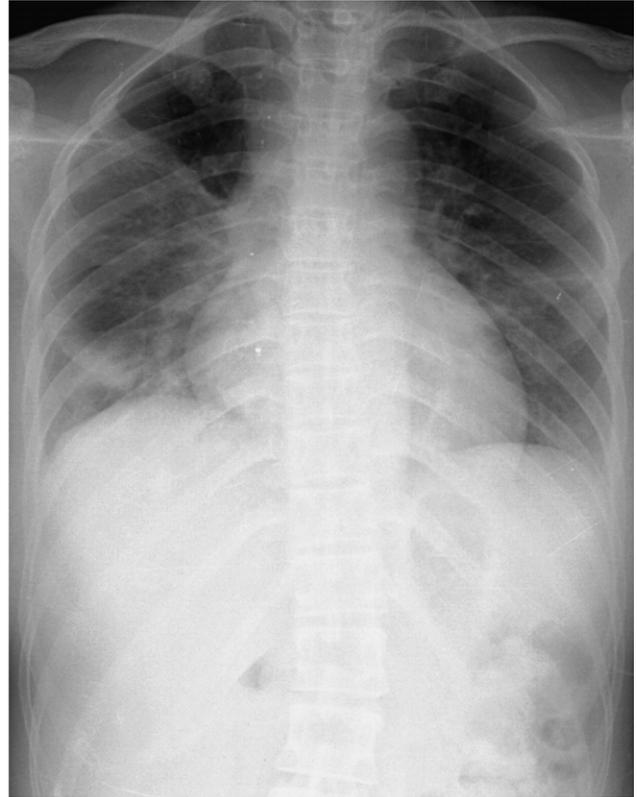
After discharge some of our patients complained of exertional dyspnoea and reduced exercise tolerance. As we were looking for residual disease or lung damage we performed HRCT in addition to chest radiography in these individuals. Our preliminary observation (on a small series of patients) showed that about 60% (15 of 24 patients) of these patients had evidence of fibrosis (presence of parenchymal band, irregular surface and traction bronchiectasis) on follow-up HRCT after discharge [10] (Fig. 9). Patients with evidence of fibrosis at follow-up were older and had more severe disease during the period of treatment [higher intensive admission rate, more steroid dosage required, higher peak lactate dehydrogenase (LDH) level and more severe peak radiographic changes] than those without fibrosis. Although the HRCT at discharge does

Table 3 – Radiological features of SARS on high-resolution computed tomography (HRCT)

Ground-glass opacification +/- consolidation
Lower lobe predilection
Peripheral/subpleural location of lesions
Commonly multi-focal or bilateral involvement
Thickening of the intralobular interstitium or interlobular septa within areas of ground-glass opacification
No cavitation, calcification, lymphadenopathy or pleural effusion



(a)



(b)



(c)

Fig. 5 – A 45-year-old woman with SARS. (a) Frontal chest radiograph at presentation shows focal segmental air-space opacity in right upper lobe outlining part of horizontal fissure (arrow). (b) Follow-up radiograph 6 days later shows radiographic progression to involve most of right lung and left lower zone. (c) Follow-up radiograph after another 8 days shows near complete resolution of bilateral lung infiltrates after successful therapy.

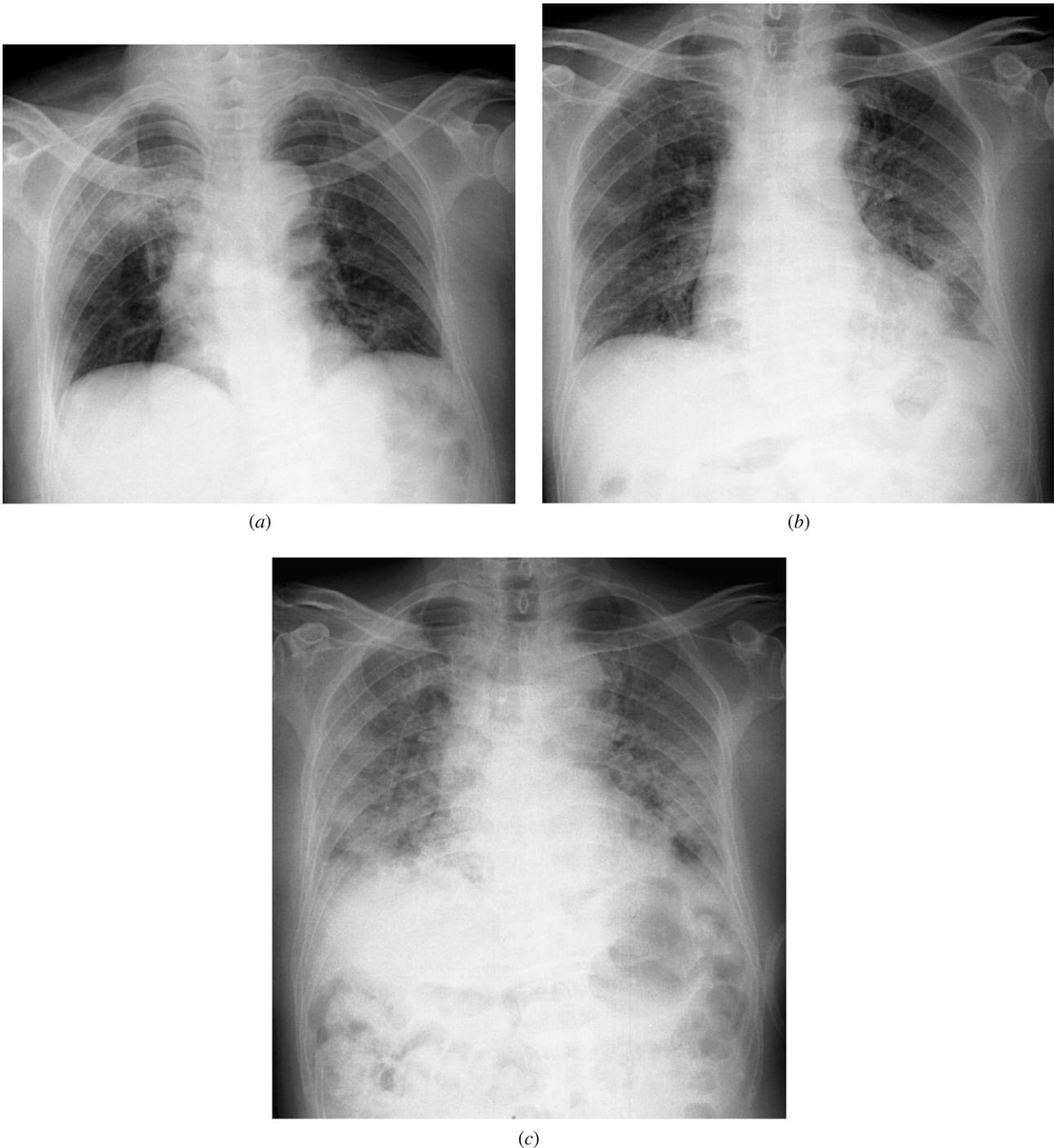


Fig. 6 – Serial chest radiographs in a 75-year-old man with SARS received medical treatment. (a) Frontal chest radiograph at presentation shows multi-focal ill-defined air-space opacities in right upper zone and to a less extent the left lower zone. (b) Follow-up radiograph 6 days later shows progression of lung infiltrates to the rest of both lungs. (c) Follow-up radiograph after another 4 days shows further radiographic progression to confluent bilateral air-space opacifications simulating acute respiratory distress syndrome (ARDS).

show evidence of residual disease and fibrotic changes, we believe it is too early to estimate the true extent of fibrosis. A follow-up HRCT at 6 months combined with clinical features (including lung function test) would be more accurate in reflecting lung damage and its implication on the patients' daily activities and exercise tolerance.

Paediatric Patients

Chest CT is usually not required for the initial diagnosis of paediatric SARS because majority of the patients show radiographic abnormality at presentation. HRCT of the thorax is reserved for children with high clinical index of



Fig. 7 – An 8-year-old male patient with SARS. Frontal chest radiograph shows multi-focal ill-defined air-space opacities in left lower zone (obscuring part of left heart border) and periphery of right mid zone (arrow).

suspicion (contact with infected adults) and a negative chest radiograph.

The use of fast CT scanners has made HRCT a practical proposition in most children without the need for sedation. In order to reduce the radiation dose to children, a lower current technique (50–80 mA) is adopted without significantly compromising the diagnostic value of the scan [18].

Similar to the findings of plain radiography, most paediatric patients present with milder form of the disease with focal segmental air-space disease on HRCT. There is no specific distribution of the disease in children. We have observed an approximately equal involvement of subpleural

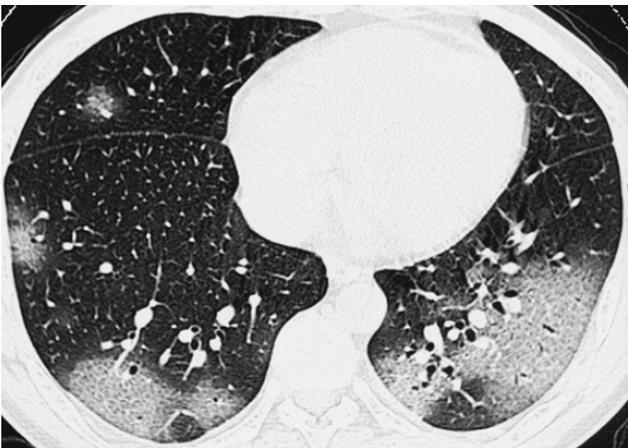


Fig. 8 – A 29-year-old healthcare worker with SARS. HRCT of thorax (3 days after onset of fever) shows multiple, peripheral, subpleural areas of ground-glass opacification involving both lower and right middle lobes.

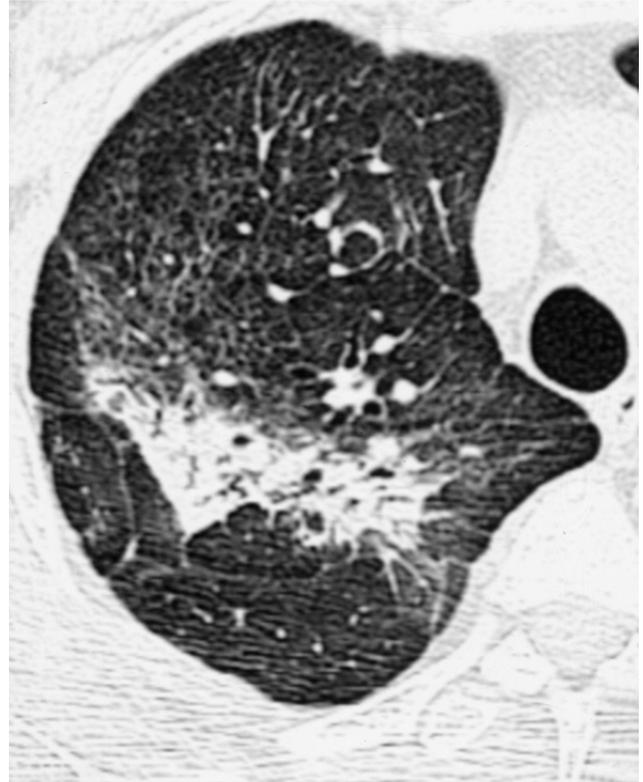


Fig. 9 – A 39-year-old healthcare worker with SARS and discharged after treatment. HRCT of thorax (8 weeks after initial presentation) shows areas of fibrosis with architectural distortion and traction bronchiectasis in posterior segment of right upper lobe. Interstitial thickening and parenchymal band are also noted in the rest of the right upper lobe.

and peribronchial regions in children presenting with either segmental or multifocal disease. Ground-glass opacification and consolidation are the two predominant features on HRCT. Again, the above radiological appearances are non-specific. Both ground-glass opacity and consolidation are common findings in children suffering from infective pneumonia of any aetiology [19]. Cavitation, calcification, lymphadenopathy or pleural effusion is not encountered in paediatric SARS.

FUTURE ROLE OF IMAGING

All that we have learnt about the imaging of SARS has been during the course of the disease with retrospective analysis of the available data. We believe it is therefore necessary to assimilate all available experience and literature and apply it to evaluate the following:

- (1) Can radiographic features seen early in the course of the disease predict clinical response and adverse outcome (intubation and intensive care unit support, death)? This is essential for the medical community to know in case we are faced with a similar situation in the future.
- (2) Treatment of SARS is still evolving as there is currently no widely accepted standard protocol. In the trial of new drugs,

imaging plays a role as one of the parameters to assess response to new treatment.

- (3) The long-term lung damage caused by this new infection is still unknown. Imaging, in particular HRCT, certainly helps to further evaluate the characteristics and extent of lung injury and its functional implications.

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