Clinical Commentary

Management of Severe Acute Respiratory Syndrome
The Hong Kong University Experience

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Severe acute respiratory syndrome (SARS) is a highly contagious and predominantly pneumonic illness caused by a novel coronavirus now commonly known as SARS-CoV (1, 2). Since its recognition in February 2003, SARS has spread to 30 countries and has affected over 8,000 people, resulting in almost 700 deaths worldwide (3). In Hong Kong, over 25% of the victims are health care workers, and the fear of this disease has created devastating socioeconomic effects in Hong Kong and worldwide. SARS is a severe and potentially progressive disease, and many patients progress to severe pneumonia and some even die with diffuse alveolar damage (4). Although it is increasingly being recognized that the mode of transmission is predominantly via droplets, it is now suspected that SARS could also be transmitted via fomites and contaminated sewage systems (5). Although the outbreak of SARS has triggered tremendous international research collaboration, which has enabled rapid dissemination of newly found knowledge to combat this frightening condition, there is very little published literature illustrating the experience of clinicians in the management of these patients. As the vast majority of cases occurred in Hong Kong, Singapore, Taiwan, the mainland of China, and Toronto, physicians outside these areas have seldom had the opportunity to manage these patients (4, 6, 7).

Although it is commonly agreed that SARS-CoV infection, being a viral illness, does not respond to antibiotic therapy, other treatment modalities are controversial (6, 8–11). In Hong Kong, a combination of corticosteroid and ribavirin, a broad-spectrum antiviral agent, is routinely used. The use of ribavirin has attracted considerable skepticism because it exhibits no *in vitro* efficacy against SARS-CoV and it is associated with considerable toxicities, including hemolytic anemia (10, 12, 13).

Until we have an efficacious vaccine and implementation of effective epidemiologic infection control measures, and in the absence of effective anti-SARS-CoV agents in sight, SARS is likely to remain a major health threat to the world. In this article, we attempt to address the diagnostic and therapeutic experience regarding this new condition, and in doing so we hope our experience will assist clinicians in their encounter with this potentially devastating, poorly understood new disease.

CLINICAL AND INVESTIGATION PROFILES

The vast majority of patients with SARS initially present with fever ($> 38°C$ for over 24 hours) and chills. Over half of the patients also complain of nonproductive cough, dyspnea, malaise, and headache on presentation (4, 7, 11). Very few patients report upper respiratory tract symptoms such as rhinorrhoea, nasal obstruction, sneezing, sore throat, or hoarseness. There is usually an interval of 3–7 days from the onset of fever to experiencing dyspnea (4, 11). Physical examination of the chest will eventually reveal crackles and dullness on percussion in most patients (4). Whereas leukocytosis, leukopenia, and thrombocytopenia are uncommon, lymphopenia ($< 1{,}500$ cells/mm^3) is almost always seen at disease onset (4). Transaminases including aspartate aminotransferase (AST) or alanine aminotransferase (ALT) are elevated slightly in 40–60% of our patients, and these tend to normalize simultaneously with clinical and radiologic recovery (4). Renal function, as reflected by serum creatinine levels, is usually normal (4, 11).

Daily radiographic assessment is essential for monitoring of this potentially rapidly progressive pneumonic illness. Invasive procedures, such as bronchoscopy and associated specimen collection, impose a prohibitory high infection risk to the operators. The primary radiologic appearance of SARS is air–space shadowing, and this is readily demonstrated using high-resolution computed tomography scans to be subpleural focal consolidation with air bronchograms and ground glass opacities (Figure 1). These changes predominantly affect the lower lobes. Initial radiographs, however, might be normal. Rapid progression of ground glass opacification, sometimes even overnight, despite potent antibiotic therapy, is probably the most helpful diagnostic clue. Air–space opacification often progresses within a few days in size, extent, and severity. In some severe cases, diffuse opacification suggestive of acute respiratory distress syndrome develops despite intensive treatment. Very rarely, nodules not dissimilar to those seen in miliary tuberculosis also appear in a background of ground glass opacification, and this necessitates invasive investigations, such as transbronchial biopsies, as milary tuberculosis and fungal infections have to be excluded. This is particularly important at later stages of the disease, when patients might develop secondary infection of the lung after receiving considerable doses of corticosteroids. Radiographically, SARS is closely mimicked by bacterial bronchopneumonia or other viral pneumonias. The appearance of the high-resolution computed tomography scan of SARS could mimic that of other interstitial lung diseases, resulting in subpleural air–space shadowing such as bronchiolitis organizing pneumonia and acute interstitial pneumonia (4, 11, 14–17). Contrary to bronchiolitis organizing pneumonia, there is no lymphadenopathy or pleural effusion in SARS (4, 17). In the later stages, particularly with diffuse involvement of the lungs, the radiographic appearance of SARS is similar to that of acute respiratory distress syndrome.

ESTABLISHMENT OF DIAGNOSIS

Despite the availability of several reverse transcriptase–polymerase chain reaction (RT-PCR) techniques, these remain to

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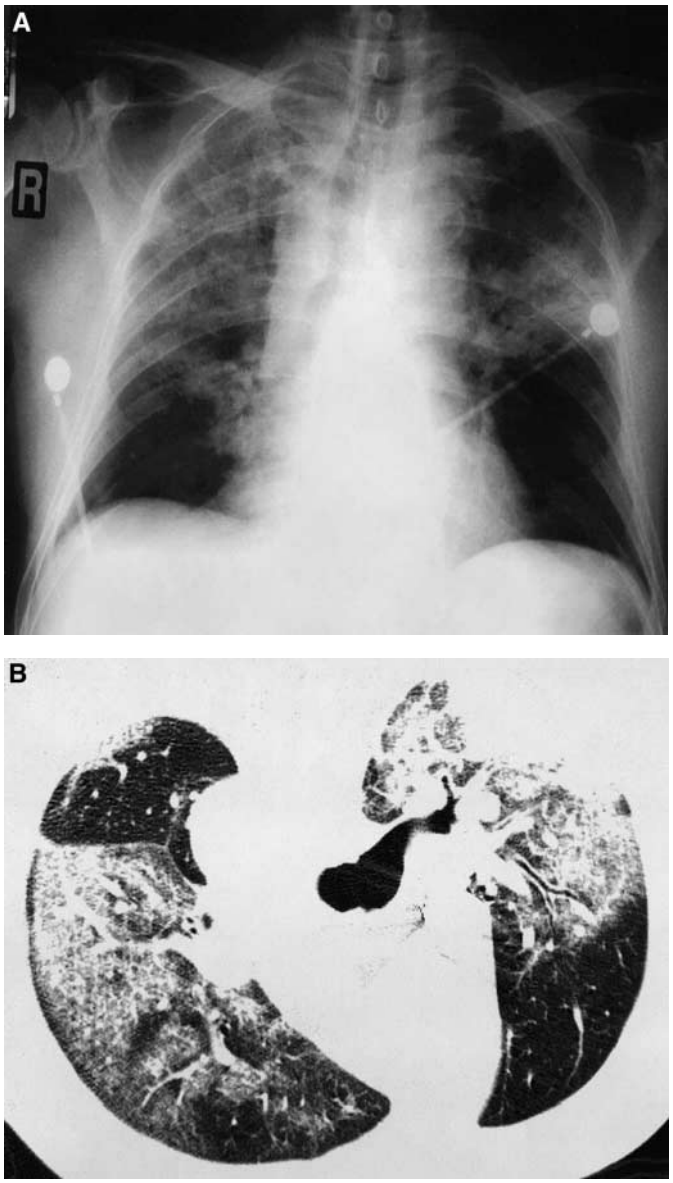

Figure 1. (*A*) Chest radiograph and (*B*) high-resolution computed tomography scan of a patient with severe acute respiratory syndrome showing upper- and mid-zone ground glass appearances, which is more florid in distribution and severity when examined by the high-resolution computed tomography.

be validated and currently have the disadvantages of relatively low sensitivity and specificity (18, 19). Serologic testing on the detection of specific IgG against SARS-CoV is very specific, but it takes 30 days for just over 90% of patients to show a significant rise in titer (20). Even the pathologic findings of SARS, readily recognizable on autopsy and open-lung biopsies as diffuse alveolar damage, are still regarded as nonspecific (4). Established diagnostic criteria for a probable case of SARS, therefore, do not necessarily require laboratory proof of SARS-CoV infection (RT-PCR detection of SARS-CoV, serologic proof of a significant rise in specific antibody titer, or positive viral culture yielding SARS-CoV) (18, 19, 21). The diagnosis of SARS therefore remains a clinical decision that can be made only by an experienced physician, on the basis of the clinical features, radiologic findings, and hematologic and biochemical profiles of a patient. More importantly, the diagnosis should be made only after considerable efforts are made to exclude background pneumonia, especially that caused by atypical organisms (e.g., *Mycoplasma pneumoniae*, *Chylamdia pneumoniae,* and *Legionella pneumophilia*), and other mimicking diseases (especially bronchiolitis organizing pneumonia).

In our unit, there are four prerequisites for diagnosis of SARS. These include the presence of radiologic evidence of consolidation, failure to demonstrate a clinical or radiologic response to potent antibiotic therapy, history of contact with suspected or confirmed patients with SARS or traveling history to at-risk areas, and otherwise unexplained and persistently abnormal lymphopenia and raised AST and ALT. In an effort to rapidly diagnose SARS clinically, we routinely conduct four daily clinical rounds, two by senior residents who are supervised by accredited pulmonologists, followed by those conducted by two senior pulmonologists of consultant grade. The management plan at our institute is shown in Figure 2. Briefly, all patients with community-acquired pneumonia and fever are admitted to the isolation wards.

It is beyond the scope of this article to describe the details of infection control measures practiced in our institute. Very briefly, we have designated wards for "confirmed SARS," "suspected SARS," "triage" (i.e., all initial admissions), and "step down" (i.e., non-SARS). These are open or "Nightingale-style" wards with cubicles usually accommodating four to six beds, and each bed is separated from the next by 6 ft. An air exchange rate of 12 times per hour and a temperature of 20°C are maintained in these wards. Patients are required to wear a surgical mask at all times except during meals, and no visiting by family or friends is permitted. All staff entering these wards are required to follow strict and stepwise "gowning" and "degowning" procedures, under the supervision of designated patrol nurses. Standard personal protection equipment includes a disposable surgical paper cap, N95 mask, reusable eye goggles, reusable cotton neck-to-heel surgical gown that tie at the back, and reusable surgical boots. Gloves and clear plastic face shields are donned for patient care or specimen collection procedures and disposed afterward. Staff are trained to wash hands properly (or rub with alcohol-containing gel) after contact with patients or with potentially contaminated materials or surfaces. Diluted bleach (1 in 49 dilution of 5.25% sodium hypochlorite solution) is used to wipe all work surfaces and the floor every hour or after any potential contamination. As nebulizer therapy was alleged to be the cause of a major hospital outbreak in Hong Kong, this mode of therapy is forbidden for patients with suspected or probable SARS in Hong Kong (11). Similarly, the vast majority of patients with suspected or probable SARS do not receive noninvasive nasal ventilation or continuous positive airway pressure in Hong Kong because aerosolization of respiratory secretions could theoretically occur, although anecdotal experience from mainland China suggests that these treatment modalities are not associated with increased cross-infection.

The initial treatment includes a combination of intravenous cefepime (2 g three times a day) and oral clarithromycin (500 mg two times a day). In the presence of penicillin allergy, intravenous levofloxacin (500 mg/day) is used in place of cefepime and levofloxacin. Most patients with non-SARS community-acquired pneumonia would have resolution, even if partial, of fever and radiographically. Diagnosis of SARS in these patients could effectively be excluded, although they would continue to be monitored for at least 10 more days. For a typical case of SARS, high fever, lymphopenia, and AST/ALT abnormalities usually persist, together with radiographic deterioration, with or without high-resolution computed tomography evidence of more widespread changes. These patients would then be considered for specific

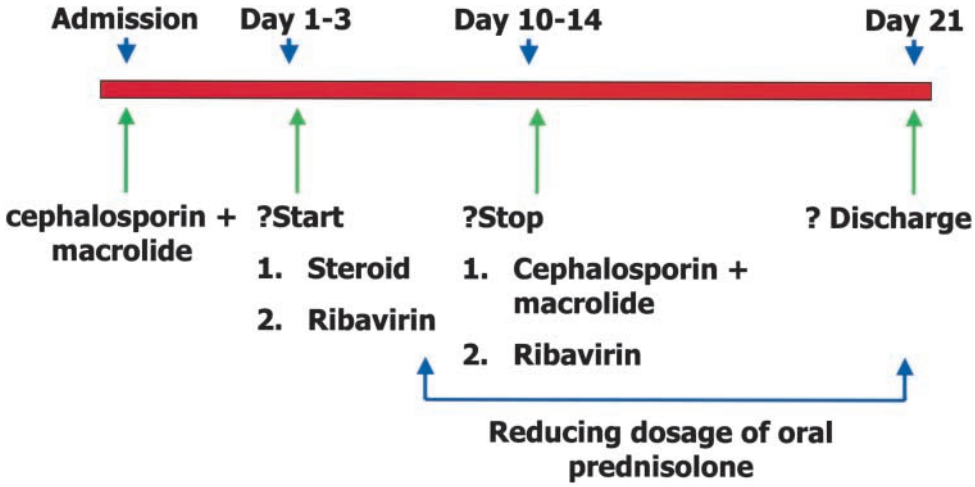

Figure 2. A schematic sketch of the treatment protocol for a "typical" patient with severe acute respiratory syndrome at Queen Mary Hospital of the University of Hong Kong.

anti-SARS therapy (Figure 2), which is usually administered on Days 2 and 3, although it could take 2–11 days before a patient could be diagnosed as clinically suffering from SARS or otherwise. Often, there is difficulty for the more indolent cases that neither progress nor improve clinically or radiographically within the first few days after admission, particularly if the epidemiologic link is not explicit. Because the use of RT-PCR, even on multiple specimens including those tested on nasopharyngeal aspirate, saliva, urine, and stool remains to be validated, we generally place more value on the results of serum anti–SARS-CoV IgG, which could be positive as early as Day 10 (20). A negative serum anti–SARS-CoV IgG, however, has little diagnostic value before Day 30 (20).

Although physicians could make a clinical diagnosis of probable SARS without much difficulty on the basis of World Health Organization and Centers for Disease Control and Prevention criteria (18, 19), they should also be aware of mimicking conditions, rather than SARS-CoV infection, which could be the actual cause of this syndrome for any individual patient. The latter problematic condition, or "non–SARS-CoV SARS," is the result of a lack of reliable, rapid diagnostic tests for SARS-CoV infection, as negative microbiologic results on SARS-CoV serology and RT-PCR only become available later. In our institute, 98% of patients diagnosed with clinical probable SARS develop a significant rise in anti–SARS-CoV IgG on Day 21 of symptom onset (unpublished data).

TREATMENT OPTIONS

It is vitally important to appreciate that SARS presents in a highly individualized fashion, both in terms of acuity and severity. It is likely, from general principles, that there is a viral replication phase in the initial stages of the illness, which could precede the pneumonia phase, during which we speculate that self-perpetuating destructive immune response occurs. It is also likely that many patients proceed to develop parenchymal fibrosis. It would theoretically be most sound to develop an effective anti–SARS-CoV agent(s) to stop further pathogenic sequelae. Despite the intensive efforts and tremendous enthusiasm, there is still no known effective agent(s) that could be used either singly or in combination and has *in vitro* or *in vivo* efficacy against SARS-CoV. The role of ribavirin in the treatment of SARS, which was originally administered to the two earliest index cases in Hong Kong, who were clinically suffering from fulminant "viral pneumonia syndrome," remains controversial (6, 8, 10–13, 22). The efficacy of other possible anti–SARS-CoV agents such as antiproteases like Kaletra (Ritonavir and Lopinavir), and convalescence serum remains to be evaluated. Although there are no controlled-trial data available, it is generally believed in our locality that corticosteroid therapy is effective in clearing the radiologic consolidative changes in SARS (4, 9, 11). However, the use of steroids is of concern in the presence of an overwhelming infection, and further immunosuppression could be detrimental to the host by encouraging secondary sepsis. In our experience, the latter is seldom encountered among unintubated patients.

In Hong Kong, there are variations among different specialist units in the use of steroids, although the use of ribavirin is more uniform (8 mg/kg intravenously, three times a day, for the first 5 days, followed by 1,200 mg orally, three times a day, for a total of 10–14 days). The following steroid regimens are used as initial treatment: hydrocortisone, 2 mg/kg four times a day or 4 mg/kg three times a day, intravenously; methylprednisolone, 2 mg/kg four times a day or 4 mg/kg three times a day intravenously; and pulse methylprednisolone, 500 mg/day for 5 days intravenously, followed by maintenance on oral prednisolone, 50 mg two times a day, reducing to 20–30 mg/day on Day 21 (4, 11, 23). It is our practice to use pulse methylprednisolone therapy for most patients, except for very indolent cases with minimal symptoms and radiologically nonprogressive disease, in whom we would commence oral administration of prednisolone, 50 mg/day, and ribavirin, 1,200 mg three times a day.

The timing of commencement of the corticosteroid and ribavirin therapy is difficult to determine and varies from patient to patient, and in our unit, for each case, the consensus of the two consultant pulmonologists is required. Generally, this entails the presence of continued clinical instability or deterioration (oxygenation, fever, worsening of cough, and development of dyspnea); progressive radiographic or high-resolution computed tomography deterioration or lack of improvement; explicit contact history with a probable patient with SARS; persistent lymphopenia and rise in AST/ALT; and confident exclusion of other mimicking conditions. Identification of SARS-CoV from saliva, urine, or stool by RT-PCR and serologic evidence of SARS-CoV infection are actively sought to help us diagnose the disease in the patient, although the condition of some patients deteriorates quickly, thereby disallowing any waiting for the results of these studies.

TREATMENT RESPONSES

Clearly, there is a spectrum of clinical response even to the same treatment regimen. Our unit is increasingly inclined to

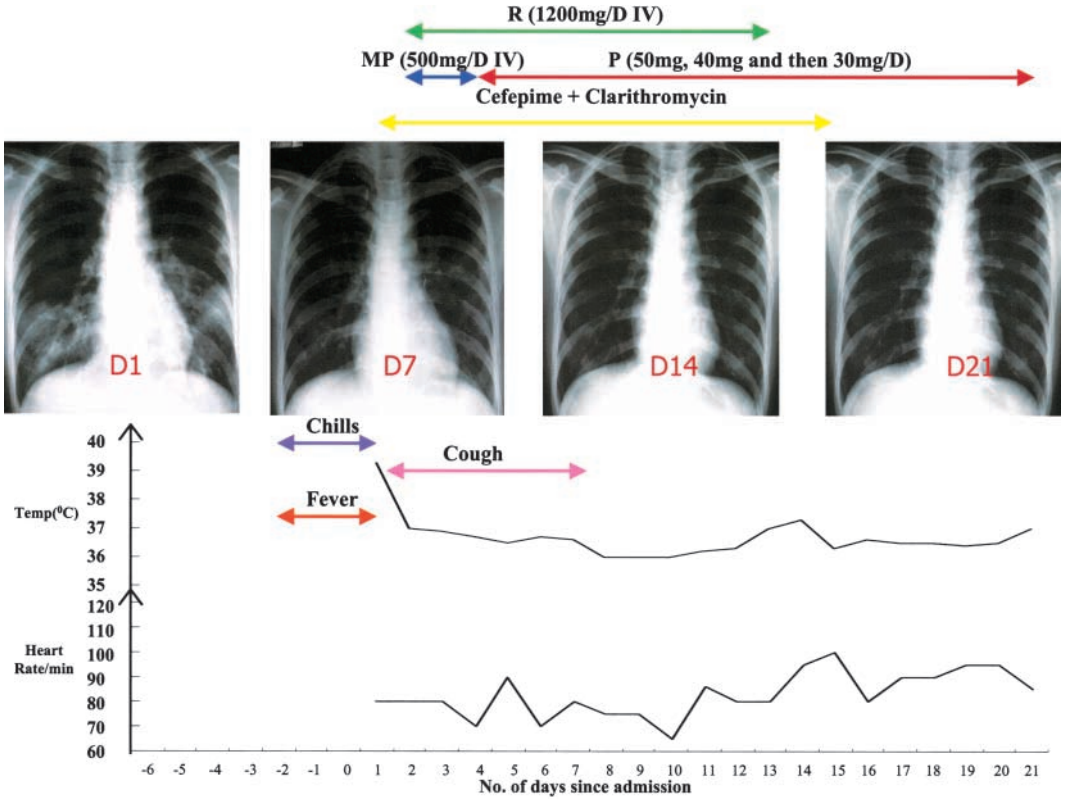

Figure 3. The clinical and radiologic course for case 1 (29-year-old woman) with severe acute respiratory syndrome showing an initial good response that persisted after treatment with combined pulse methylprednisolone (MP) and ribavirin (R), and later prednisolone (P).

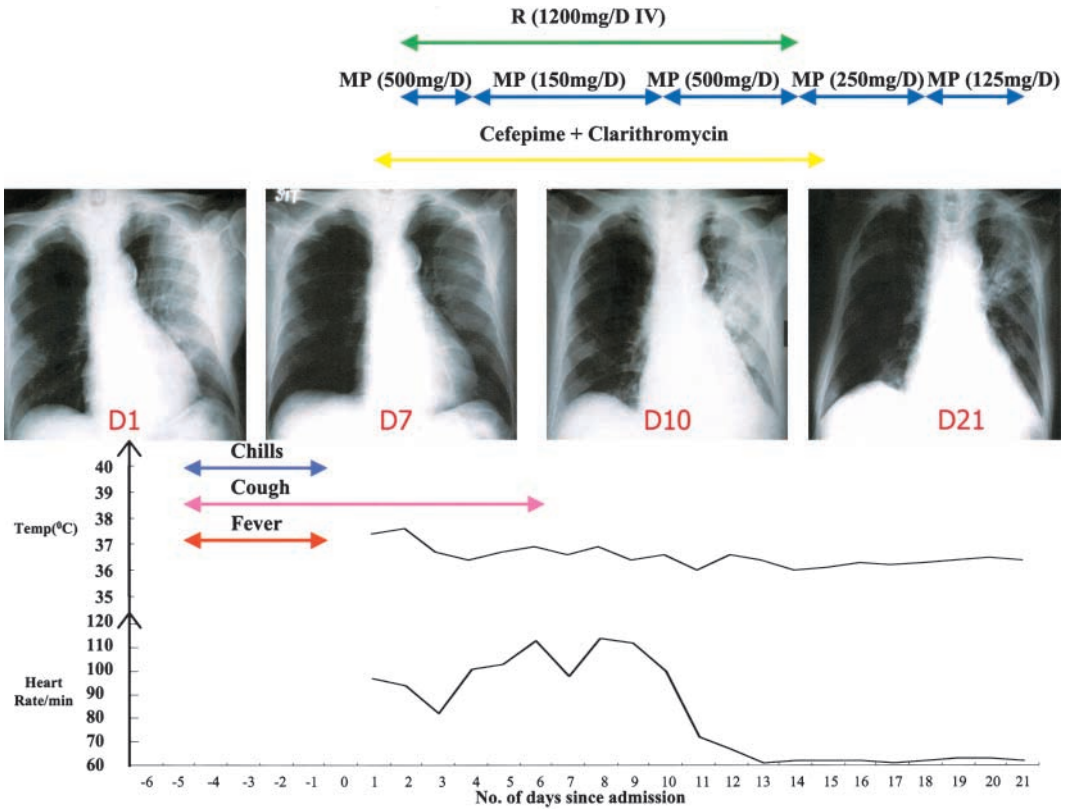

Figure 4. The clinical and radiologic course for case 2 (82-year-old man) with severe acute respiratory syndrome showing his initial good response to combined pulse methylprednisolone (MP) and ribavirin (R) and then recurrence of disease.

commence patients on pulse methylprednisolone regimen. It would be helpful to describe the treatment responses, which clinically can be divided into four patient stereotypes.

Case 1—A Good Responder

A 34-year-old, otherwise healthy, nonsmoking female executive was admitted to Queen Mary Hospital on March 24, 2003 with a 3-day history of fever and chills 7 days after sharing a room with an undiagnosed patient with SARS in a private hospital where the former was admitted with sore throat after tonsillectomy in mid-February 2003. On admission, chest radiograph showed bilateral lower lobe ground glass opacification, and there were bilateral lower lobe crackles on auscultation of the chest. Her clinical course and radiographic progress are shown in Figure 3. The patient was started on pulse methylprednisolone and ribavirin on Day 2 after admission, in view of the strong epidemiologic link, typical blood pictures (total leukocyte count 4.2×10^9/L [$4–11 \times 10^9$/L], lymphopenia 0.7×10^9/L [$1.5–4 \times 10^9$/L], raised AST/ALT 39/59 U/L [13–33 and 6–53 U/L, respectively]), and progressive radiographic deterioration. The patient responded rapidly and had complete resolution of fever overnight, and all her respiratory symptoms disappeared over the next 3–5 days. She was started on oral prednisolone, 50 mg/day, and this was reduced every 5 days to a final dosage of 30 mg/day when she was discharged with no respiratory symptoms and a completely normal chest radiograph. Her blood indices normalized within 10 days of commencement of treatment. The nasopharyngeal aspirate SARS-CoV RT-PCR of our patient returned positive 6 days after admission, and the anti–SARS-CoV IgG titer taken 14 days after admission was also positive at 1/160. This patient has been attending our SARS clinic every week since her discharge on Day 21, and has had no recurrence of symptoms. Her current medication includes only prednisolone at a dosage of 5 mg/day.

Our preliminary experience suggests that about two thirds of patients with SARS treated with pulse methylprednisolone regimen described previously appear to be good responders. In addition, there appears to be no significant difference in the age, gender, and pretreatment parameters (chest radiograph pattern or severity, oxygen saturation measured by digital oximetry [Sa_{O_2}], AST/ALT levels, and total leukocyte and lymphocyte counts) between patients with good response and their counterparts.

Case 2—A Good Responder with Early Relapse

An 82-year-old, nonsmoking, retired male clerk was admitted to Queen Mary Hospital on April 8, 2003 with a 5-day history of fever, chills, and dry cough. His daughter, who was in the same household, had contracted SARS after visiting Hospital W, and was admitted to Hospital P 3 days before the onset of his symptoms. Chest radiograph on admission showed left upper and mid-zone ground glass opacification. His clinical course and radiographic progress are shown in Figure 4. The patient was commenced on pulse methylprednisolone and ribavirin on Day 2 after admission, in view of the strong epidemiologic link, typical blood pictures (total leukocyte count 4.7×10^9/L; lymphopenia 0.6×10^9/L; raised AST, 61 U/L, but normal ALT, 39 U/L), and progressive radiographic deterioration. The patient responded rapidly and had complete resolution of fever overnight, and all respiratory symptoms disappeared over the next 24 hours. His chest radiograph became virtually normal on Day 3 of methylprednisolone therapy, and the dosage was reduced to 150 mg/day on Day 3, at which level it was maintained until Day 7. However, he developed dyspnea at rest and required 50% oxygen therapy on Day 10, and there was overnight deterioration in the patients' condition, as observed from a chest radiograph, which showed extensive left lung consolidation. This was treated with resumption of intravenous methylprednisolone, 500 mg/day and the patient responded both clinically and radiographically. However, on Day 21, a few residual shadows were observed in the left upper lobe, consistent with scarring. His blood indices all normalized within 7 days of commencement of treatment, except that he had persistent lymphopenia (Day 21, 0.2×10^9/L). The nasopharyngeal aspirate, urine, and stool SARS-CoV RT-PCR of our patient returned negative, although the anti–SARS-CoV IgG titre taken 14 days after admission was positive at 1/160. The patient recovered well and was maintained on prednisolone, 10 mg/day. On Day 28, the day before his planned discharge, the patient suffered from unprovoked asystole leading to cardiorespiratory arrest and did not respond to resuscitation measures. Autopsy of the patient showed mild lung scarring but no evidence of acute myocardial infarction, pulmonary embolism, or cerebrovascular accident.

A proportion of good responders appear to have recurrence of disease during Week 2 of their illness. This often coincides with the reduction in the dosage of methylprednisolone and appears to be less frequent since we increased the duration of pulse therapy to 5 days from our initial practice of 3 days. In our experience, it appears that patients with such recurrence of pneumonic illness could become very ill with fever, respiratory failure, lymphopenia, raised AST/ALT, and more extensive radiographic disease compared with the original presentation. The vast majority of such patients respond to the second pulse methylprednisolone therapy.

Case 3—A Fair Responder

A 47-year-old, otherwise healthy, nonsmoking housewife was initially admitted to Hospital P on April 4, 2003, after having visited a patient with SARS at Hospital W that had major outbreaks of the disease among staff and patient. SARS was diagnosed in her two brothers and one sister-in-law, and all required active treatment at hospital P, to which she was also admitted. Her clinical and radiographic progress is shown in Figure 5. On initial presentation to Hospital P, she had a 2-day complaint of fever, dry cough, and chills. On admission, her blood test showed total leukocyte count of 4.6×10^9/L, lymphopenia 0.9×10^9/L but normal AST/ALT (33/29 U/L). Her chest radiograph showed left upper lobe peripheral ground glass opacification and consolidation. This was initially treated with prednisolone, 50 mg/day, and oral ribavirin (1.2 g three times a day) for 2 days, which was changed to hydrocortisone, 200 mg three times a day, and intravenous ribavirin when she continued to have radiographic deterioration. Despite a 3-day treatment with hydrocortisone, methylprednisolone at a dosage of 1,000 mg/day for 3 days was commenced in view of increasing dyspnea at rest, increasing oxygen requirement (8 L/minute via nasal cannulae to maintain an Sa_{O_2} of 97%), and development of bilateral ground glass opacification over both lung fields. She improved clinically and radiographically, and was switched to intravenous hydrocortisone, 200 mg three times a day, for 2 days, when she again showed clinical and radiographic deterioration. She was therefore transferred to our unit for further management, when she was commenced on a further 6-day course of methylprednisolone, 500 mg/day. This resulted in resolution of the ground glass appearance, and she was switched to prednisolone, 50 mg two times a day, daily for 5 days before it was reduced gradually over 10 days to 30 mg/day, when she was discharged on Day 31. On discharge from our care, her blood indices showed total leukocyte count of 11.7×10^9/L, lymphopenia 0.44×10^9/L, normal AST/ALT, and her Sa_{O_2} on breathing room air was 98%. The nasopharyngeal aspirate SARS-CoV RT-PCR of our patient returned negative 5 days after admission, but the anti–SARS-

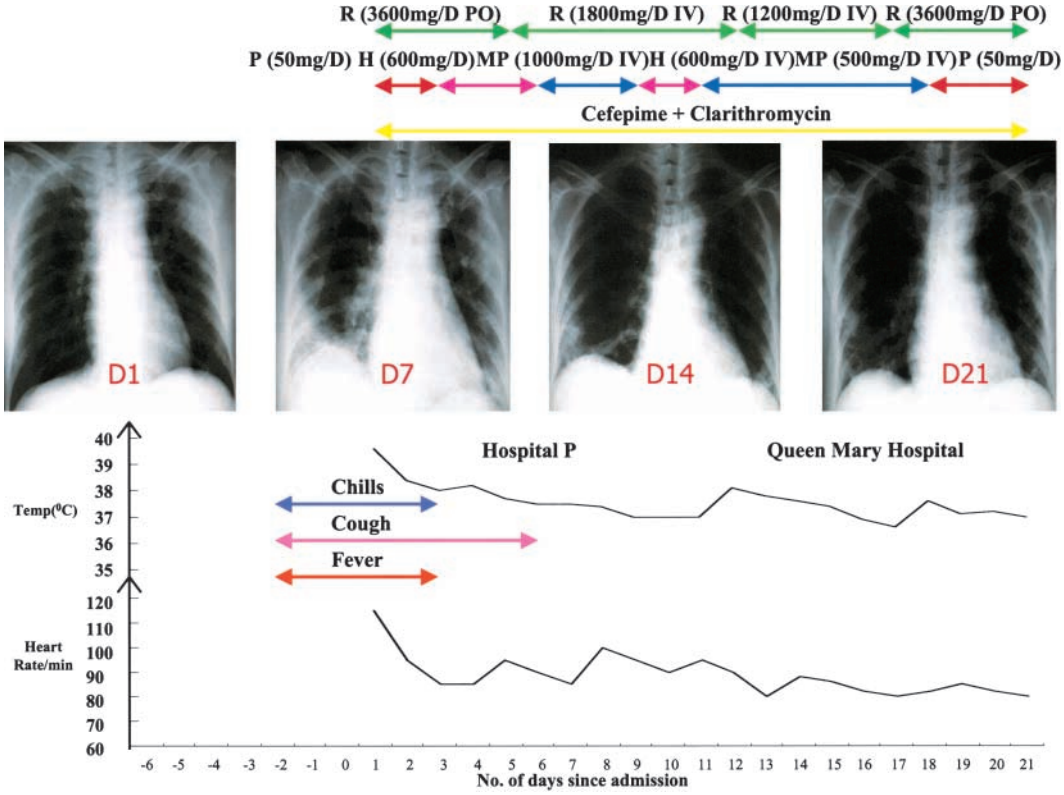

Figure 5. The clinical and radiologic course for case 3 (47-year-old woman) with severe acute respiratory syndrome showing her fair response to combined pulse methylprednisolone (MP) and ribavirin (R), prednisolone (P) and hydrocortisone (H), and resolution of disease.

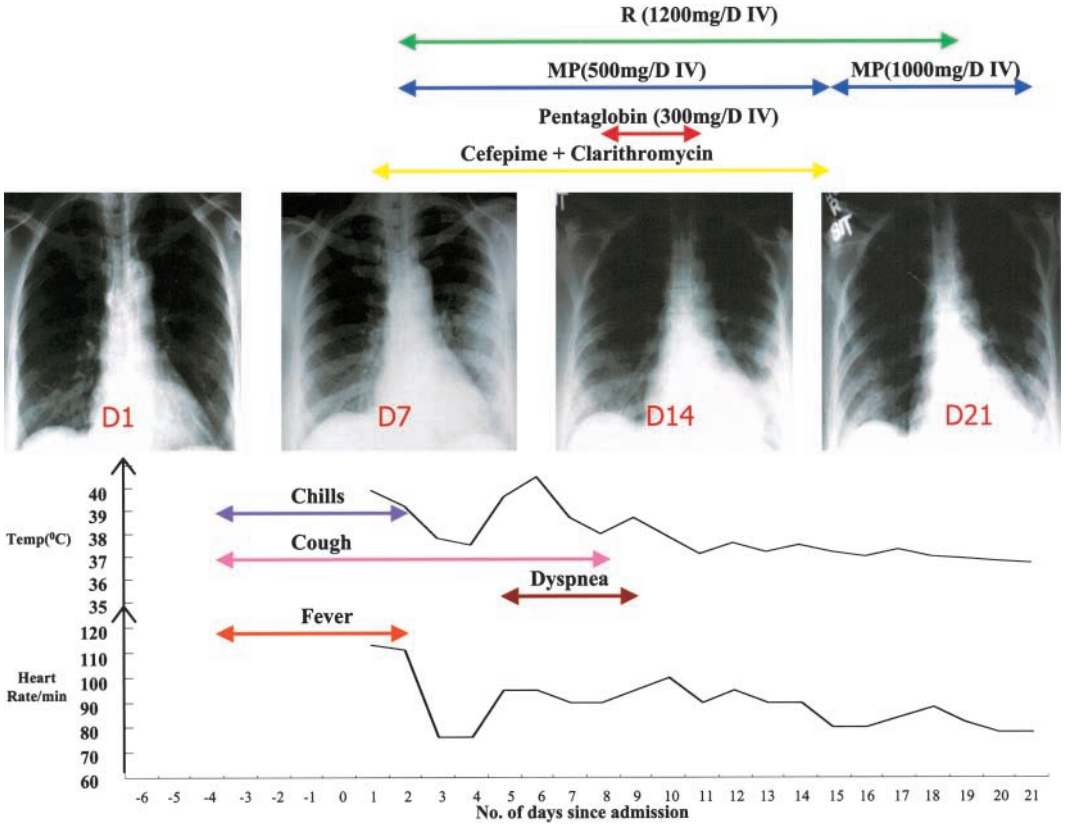

Figure 6. The clinical and radiologic course for case 4 (46-year-old woman) with severe acute respiratory syndrome showing poor response to prolonged pulse methylprednisolone (MP) and ribavirin (R).

CoV IgG titer taken 15 days after admission was positive at 1/640. She continues to be followed up weekly at our SARS clinic and has had no recurrence of any symptoms. At the time of writing of this article, she is on prednisolone only, 15 mg/day.

Our anecdotal experience suggests that fair responders like case 2 often respond to higher dose and prolonged high-dose methylprednisolone therapy. They also tend to make good recovery from their SARS symptoms and in exercise tolerance, although they appear to be less likely to have a completely normal chest radiograph on discharge, contrary to the good responders. It is possible that the patient might have had a less stormy course of illness had she been given a more prolonged pulse methylprednisolone therapy initially. Studies are therefore currently being conducted in our center on the effects of different corticosteroid regimens on the clinical outcome of SARS.

Case 4—A Poor Responder

A 46-year-old, nonsmoking housewife with previous history of treated thyrotoxicosis was admitted to Queen Mary Hospital on April 1, 2003 with a 3-day history of fever, chills, and dry cough. Both the patient and her husband had spent 3 hours at the clinic of a dentist at Amoy Garden, a highly densely populated private housing estate, where a major outbreak of SARS had occurred. Her husband was admitted to our hospital 1 day earlier with typical SARS and his treatment commenced on his Day 2 as inpatient, when the patient presented to our Accident and Emergency Department with the above symptoms and a fever of 40°C. Her clinical and radiographic course of illness is shown in Figure 6. On admission, chest radiograph showed bilateral lower lobe ground glass opacification, and there were bilateral lower lobe crackles on auscultation of the chest. In view of the strong epidemiologic evidence of contact and also the typical blood pictures (total leukocyte count 5.3×10^9/L; lymphopenia 1.0×10^9/L; raised AST/ALT, 36/30 U/L) and progressive radiographic deterioration, she was commenced on pulse methylprednisolone (500 mg/day intravenously) and ribavirin on Day 2. Despite 6 days of intravenously methylprednisolone, the patient continued to have low grade fever and showed progressive deterioration in radiographic ground glass consolidation, worsening dyspnea at rest, and increasing oxygen requirement (from breathing room air at admission to 8 L/minute via nasal cannulae achieving only 95% Sa_{O_2}). She was, therefore, commenced on intravenous pentaglobin (composed of human IgM 12, IgA 12, and IgG 76%; Biotest Pharma GmbH, Dreieich, Germany) at 300 mg/day from Day 8 to Day 10, whereas methylprednisolone was continued until Day 14. The use of pentaglobin was followed by resolution of fever and some radiologic resolution. However, consolidation and ground glass appearance were still persistent in both lower zones, and thus the patient was stepped up to methylprednisolone 1 g/day for 4 days. This was followed by gradual resolution of the radiologic abnormalities and oxygen dependence on Day 21 (2 L/minute achieving an Sa_{O_2} of 98%). After this, the patient was put on oral prednisolone at 50 mg two times a day (2 mg/kg) for 5 days and then on a gradually reducing course over 2 weeks. The patient was discharged on Day 46, being completely asymptomatic, and required no further oxygen therapy. On discharge, her blood indices showed total leukocyte count of 8.7×10^9/L, lymphopenia 0.43×10^9/L, and a raised ALT, 114 U/L. The nasopharyngeal aspirate, stool, and mid-stream urine SARS-CoV RT-PCR of our patient 2, 6, and 9 days, respectively, after admission returned positive, and the anti–SARS-CoV IgG titer taken 14 days after admission was positive at 1/160. This lady has been attending our SARS Clinic every week since her discharge and has had no recurrence of symptoms. Her current medication includes only prednisolone at a dosage of 25 mg/day.

The vast majority of poor responders, who probably constitute less than 10% of all cases, require very intensive therapy. The main concern in dealing with these patients is a potential failure to detect secondary sepsis, as anecdotal experience strongly suggests that some of these cases, especially those who require mechanical ventilation, deteriorate later and succumb to opportunistic fungal pneumonias (Professor NS Zhong, Guangzhou, People's Republic of China, personal communication).

In summary, SARS is a highly contagious and predominantly pneumonic illness caused by a novel coronavirus now commonly known as SARS-CoV. We have described the key diagnostic clinical features, radiologic features, and investigation profiles of these patients. We outline our treatment regimens, specifying as to when we commence corticosteroid and ribavirin therapy. SARS is a highly variable disease, as exemplified by the four cases we have presented. We hope our preliminary experience will assist clinicians when they encounter a patient suspected of having SARS, and help them manage this potentially devastating disease.

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