J Microbiol Immunol Infect
2003;36:161-168

Severe acute respiratory syndrome in a medical center in Taipei

Hwee-Kheng Lim[1], Chang-Pan Liu[1,4,5], Fu-Yuan Huang[3], Hsu-Tah Kuu[2], Yuh-Cheng Yang[4], Pei-Jan Chen[2], Chun-Ming Lee[1,6], Nan-Chang Chiu[3], Hsiang-Kuang Tseng[1]

Divisions of [1]Infectious Diseases and [2]Chest, Department of Internal Medicine; Departments of [3]Pediatrics and [4]Medical Research, Mackay Memorial Hospital, Taipei; [5]Mackay Junior College of Nursing; and [6]Taipei Medical University, Taipei, Taiwan, ROC

Received: July 2,2003 Revised: July 25, 2003 Accepted: August 5, 2003

From April 18 to May 31, 2003, 46 patients with probable severe acute respiratory syndrome were admitted to the negative-pressure isolation rooms of Mackay Memorial Hospital in Taipei, Taiwan. Their demographic, clinical, laboratory, and radiologic characteristics and clinical outcomes were analyzed. There were 15 males and 31 females, in this cohort, 13 of whom were healthcare workers. The latter included 6 hospital staff and 7 medical personnel transferred from other hospitals. The most common symptoms were fever (100%, 46/46), cough (72%, 33/46), shortness of breath (46%, 21/46), and diarrhea (39%, 18/46). Other common findings were lymphopenia (57%, 26/46), thrombocytopenia (39%, 18/46), elevated lactate dehydrogenase (63%, 29/46), and elevated creatine kinase (24%, 11/46). A total of 7 patients (15%) required mechanical ventilation, and 8 (17%) died. Advanced age was an independent significant risk factor for death. Fever followed by rapidly progressive respiratory compromise led to significant morbidity and mortality in this cohort.

Key words: Advanced age, fever, severe acute respiratory syndrome (SARS)

Severe acute respiratory syndrome (SARS) is a new infectious disease in humans, the earliest cases of which are now known to have occurred in mid-November 2002 in the Guangdong province of China [1-3]. It is an atypical pneumonia characterized by high rate of transmission to healthcare workers, in the local community and worldwide [4-7]. It is important to make early diagnosis as early treatment and infection control will improve response and reduce the spread of the disease. In late April 2003, there was a significant epidemic of SARS in Taiwan. At the time of writing, a total of 8437 SARS cases have been reported to the World Health Organization (WHO) from 32 countries, including 813 deaths [4,5]. There were 670 probable cases and 84 deaths in Taiwan. All known chains of person-to-person transmission of SARS virus have been broken as of July 5, 2003.

We describe here the clinical, laboratory, radiologic features and clinical outcomes of all 46 patients with probable SARS who were admitted to Mackay Memorial Hospital, Taiwan during the outbreak.

Patients and Methods

We retrospectively reviewed all cases of probable SARS managed at Mackay Memorial Hospital from April 18 to May 31, 2003. The demographic data, clinical features, and outcomes were analyzed. On the basis of the modified WHO definition of SARS, our case definition included: fever (temperature >38°C), a chest radiograph showing evidence of air space opacification with or without respiratory symptoms (cough, shortness of breath), and close contact within 10 days before onset of symptoms with a person with a diagnosis of SARS and/or a history of travel within 10 days before onset of symptoms to an area with reported SARS transmission.

Laboratory investigations included complete blood count with a differential count, prothrombin time, activated partial thromboplastin time, and serum biochemical measurements including electrolytes, renal and liver function, creatine kinase (CK), and lactate dehydrogenase (LDH). Chest radiography was performed every other day until clinical or radiological improvement occurred. Throat swabs or sputum samples obtained from all patients in this study were screened for SARS-associated coronavirus RNA by reverse-transcriptase polymerase chain reaction (RT-PCR). Blood cultures were performed in all cases. *Chlamydia* IgM, *Mycoplasma* IgM, and *Legionella* urinary antigen were assessed in 34 patients.

Initial treatment included ceftriaxone (or cefepime), and a new quinolone (levofloxacin or moxifloxacin) or clarithromycin to target common

Corresponding author: Dr. Chun-Ming Lee, Division of Infectious Diseases, Department of Internal Medicine, Mackay Memorial Hospital, 92, Section 2, Chung Shan North Road, Taipei, 104, Taiwan, ROC. E mail: leecm@ms2.mmh.org.tw

pathogens causing community-acquired pneumonia. Oral ribavirin, loading dose 2000 mg orally once followed by 600 mg twice a day was given to 45 patients. If fever persisted after 48 h, methyl prednisolone 2 mg/kg/day was started and then tapered gradually according to the clinical condition. For patients with persistent fever or progressive clinical or radiological worsening, pulse intravenous methylprednisolone 500 mg every 12 h for 3 days and intravenous immuno-globulin (IVIG) 1 g/kg/day continuous infusion were administered for 2 to 4 days.

Patients with hypoxemia were given oxygen through a nasal cannula or a non-rebreathing mask according to the extent of arterial oxygen saturation. If respiratory failure developed, patients were intubated after adequate sedation and mechanically ventilated. Patients were discharged if they had no fever for 5 days, resolution of cough, improving chest radiographs, and laboratory abnormalities returning toward normal.

On May 4, 2003, 4 medical staffs in the emergency department of our hospital were infected due to exposure to patient 1, who was subsequently found to meet the criteria for probable SARS.

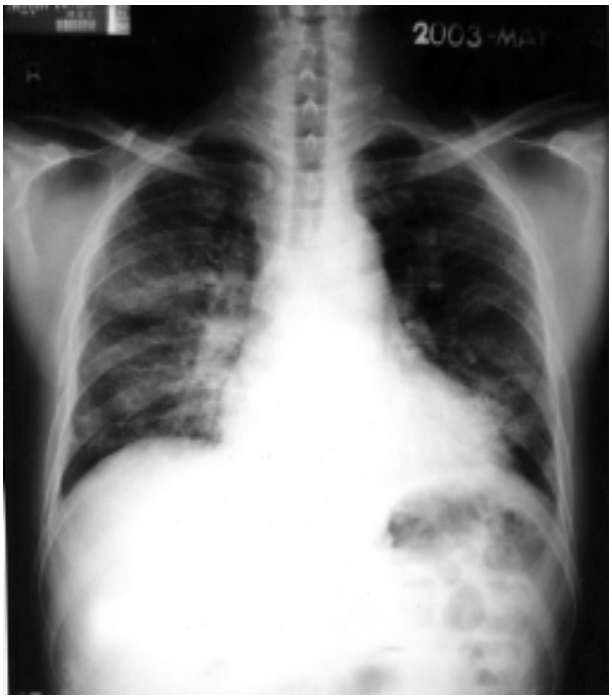

Fig. 1 Chest radiograph of Case 1 on admission to the emergency department shows multifocal bilateral air-space opacities.

Case Descriptions

Case 1

This 49-year-old man had high fever with chills for about 1 week. He visited several local medical clinics and was treated without improvement. He came to our emergency department on May 4, 2003, complaining of dry cough, sore throat, and dyspnea. He had no recent travel history, known contact with SARS patients, or visits to areas in Taipei where a significant incidence of SARS had been reported. He had no underlying disease. Blood pressure was 117/72 mm Hg, respiratory rate 26 /min, pulse rate 123 /min, and temperature 40.6°C. Hemoglobin was 15.9 mg/dL, white blood cell count 5900/μL, neutrophils 76%, lymphocytes 17%, platelets 152 000/μL, alanine aminotransferase (ALT) 108 U/L, LDH 608 U/L, and C-reactive protein (CRP) 15.9 mg/dL. Blood and sputum were collected for culture, and intravenous ceftriaxone and oral levofloxacin were started. Chest radiograph showed irregular multifocal opacities in both lung fields (Fig. 1). On May 5, 2003, he was intubated due to worsening respiratory failure consistent with acute respiratory distress syndrome. However, his condition continued to deteriorate, with progressive multiorgan dysfunction. Cardiac arrest occurred and, despite cardiopulmonary resuscitation, he died on May 5, 2003. Ribavirin and methylprednisolone were not given because he died within 24 h of arrival to the emergency department. Blood cultures and sputum cultures for bacteria had no growth, and RT-PCR for SARS virus was positive. No autopsy was performed.

Case 2

This previously healthy 27-year-old man, a resident doctor of our emergency department, was on duty on May 4, 2003 when Case 1 was in the emergency department. He did not directly care for that patient and was unaware that Case 1 was later found to have SARS. He felt well when he left for vacation in Japan on May 8, 2003, but shortly after arrival, developed a high fever with chills and headache. There were no respiratory symptoms at the time. Fever persisted from May 9 to May 13, although it subsided for 1 to 2 h after he took antipyretic drugs. He returned to Taiwan on May 13 and came to our emergency department on May 14 complaining of diarrhea, myalgia, and fever. His temperature was 39.2°C. Hemoglobin was 14.1 g/dL, white blood cell count 2900/μL, neutrophils 63.5%, lymphocytes 25.3%, platelets 126 000/μL, ALT 40 U/L, LDH 308 U/L, CK182 U/L, and CRP 2.19 mg/dL. Chest radiograph showed right upper and lower lung field air space opacities. He was admitted to a negative pressure isolation room in the intensive care unit and started on intravenous cefepime and oral levofloxacin and ribavirin on May 14. Ribavirin was started with a 2

g oral bolus, then 600 mg twice a day for 10 days. methylprednisolone (2 mg/kg/day) were started on May 16. The fever improved within 24 h after steroids were used, but a mild fever was still noted. On May 17, he complained of dyspnea, and chest radiography revealed multifocal pneumonic infiltrates bilaterally. Therefore, IVIG 1 g/kg/day was started on May 18 and continued for 4 days. Dyspnea significantly improved with resolution of the pneumonic infiltrates on May 19, 2003. Fever totally subsided on May 21, the day after the IVIG regimen was completed. Spontaneous pneumomediastinum with subcutaneous emphysema (Fig. 2) was noted on May 23, but it did not cause significant clinical symptoms. His condition improved and he was transferred to a regular isolation ward on May 31. Blood cultures for bacteria had no growth, but RT-PCR of a throat swab specimen was positive for SARS virus. He was discharged on June 10, 2003.

Statistical analysis

All data were analyzed by SPSS version 8.0 (Arlington, VA, US). We compared risk factors associated with death by Fisher's exact test or chi-square test for categorical variables and unpaired Student *t* test for continuous variables. Significant risk factors identified on univariate analysis were further analyzed by multiple logistic regression to identify independent risk factors associated with death. A p value of <0.05 was considered to indicate significance.

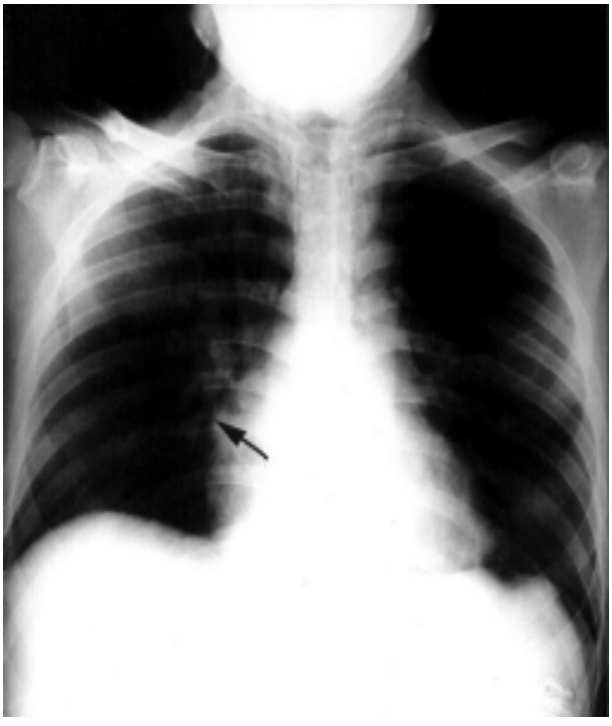

Fig. 2 Chest radiograph of Case 2 on 10 days after admission showing subcutaneous emphysema and pneumomediastinum (arrow) with resolution of pneumonic infiltrates.

Results

Between April 18 and May 31, 2003, a total of 46 patients with probable SARS were admitted. They included 15 males and 31 females, 3 of whom were children (a 4-year-10-month-old boy, a 7-year-3-month-old girl, and a 14-year-old boy). Excluding the 3 children, the patients' mean age was 41 ± 16.1 years. Twelve patients had underlying diseases: diabetes mellitus, hypertension, and chronic renal insufficiency in 4; chronic obstructive pulmonary disease in 3; a history of intracranial hemorrhage in 1; seizure disorder in 1; rheumatoid arthritis in 1; depression in 1; and gastric ulcer in 1.

Clinical features

The most common symptoms at presentation were fever (46/46, 100%) with between 39% and 72% of patients reporting cough, shortness of breath, or diarrhea. Less common symptoms included malaise, myalgia, sputum production, sore throat, headache, chills, nausea and vomiting (Table 1). Fever was noted in all patients on admission (median 38.6°C, range 38°C-40.5°C). Findings on auscultation of the lungs were variable, with clear breathing sounds or crackles. No patients in this series had rash or lymphadenopathy on presentation. The median incubation period was 4.8 ± 3.5 days.

Hematologic and biochemical findings

Leukopenia on the initial blood count (total white cell count $<4 \times 10^3/\mu L$) was found in 26% (12/46) of patients. Although the neutrophil count was normal in most cases, 57% (26/46) of patients had lymphopenia (absolute lymphocyte count <1000 /mm^3). Thro-

Table 1. Prevalence of symptoms in probable SARS cases at Mackay Memorial Hospital

Symptom/sign	No of patients (%)
Fever	46 (100)
Cough	33 (72)
Shortness of breath	21 (46)
Diarrhea	18 (39)
Malaise	11 (24)
Myalgia	10 (22)
Sputum	9 (20)
Sore throat	8 (17)
Headache	7 (15)
Chills	7 (15)
Nausea, vomiting	3 (7)

mbocytopenia (platelet count <150 000 /mm^3) was found at initial presentation in 39% (18/46) of patients. Lymphocyte count continued to drop in the first week of hospitalization. Prolonged activated partial thromboplastin time (>38 sec) was noted in 24% (11/46) of patients, whereas the prothrombin time remained normal in most cases.

Renal function was normal in 94% (43/46) of patients. Serum ALT levels were elevated (>45 U/L) in 13% (6/46) of patients. LDH and CK levels were elevated in 63% (29/46) and 24% (11/46), respectively. Hyponatremia (<134 meq/L) was present in 13% (6/46) and hypokalemia (<3.5 meq/L) in 15% (7/46). The laboratory results on day 1 and day 7 of hospitalization are listed in Table 2.

Microbiologic and virologic findings

None of the blood cultures were positive for bacteria. *Mycoplasma* IgM, *Chlamydia* IgM, and *Legionella* urinary antigens were negative in all 34 patients in whom they were tested. RT-PCR of throat swab and sputum specimens were positive in 26/43 patients (60%) and negative in 17 (40%). Three patients transferred from other hospitals did not have specimens collected and sent to the Center for Disease Control of Taiwan, therefore, they had no RT-PCR data available.

Chest radiographic findings

Chest radiographs obtained at presentation were normal in 5 patients (11%) and abnormal in 41 (89%). In all 41 patients, the radiographic pattern was air-space opacities with ill defined margins. None of the radiographs showed a reticular or nodular pattern or a mass. The right lung was involved more frequently with unilateral infiltrates than the left (17 vs 6), while bilateral involvement was seen in 18 of 41 (44%). Unifocal involvement (22/41, 54%) was slightly more common than multifocal involvement (19/41, 41%). There was a predilection for involvement of lower lung regions (24/41, 59%). There was no evidence of cavitation, hilar lymphadenopathy, or pleural effusion. Two patients developed spontaneous pneumomediastinum and one patient developed pneumothorax while on a mechanical ventilator. Among patients with clinical deterioration, serial chest radiographs showed progression of pulmonary infiltrates approximately 4 days after admission. A successful response to therapy was considered demonstrated by serial chest radiographs showing resolution of the lung opacities.

Infection control measures

Four emergency department personnels including Case 2 were apparently infected by Case 1. Based on an epidemiologic analysis of these four cases, strict infection control measures were instituted, including droplet and contact precautions. Healthcare workers used recommended personal protective equipment (N95 masks and double layers of head covers, goggles, gowns, and gloves) and followed strict hand hygiene procedures. Patients were cared for in negative-pressure isolation rooms. Appropriate terminal disinfection of potentially contaminated rooms and equipment was carried out using hypochlorite solution (1000 ppm).

Clinical outcome

Of the 46 patients, 7 (15%) required mechanical ventilation for acute respiratory failure. Eight patients died (crude mortality, 17%) including a nurse transferred from Ho Ping hospital. The other 12 healthcare workers were all discharged by May 31, 2003 and were stable at last follow-up. Four of the 8 patients who died had major underlying medical conditions

Table 2. Laboratory results for 46 patients with SARS on day 1 and 7 of hospitalization

Laboratory result	Day 1	Day 7
Hemoglobin (g/dL)	12.6 ± 2.1	12.2 ± 1.9
White cells count (x10^{-9}/L)	5.6 ± 2.3	12.4 ± 6.5
Neutrophils (x10^{-9}/L)	4.2 ± 2.1	11.0 ± 6.5
Lymphocytes (x10^{-9}/L)	0.8 ± 0.4	0.8 ± 8.2
Platelets(x10^{-9}/L)	177 ± 81.1	272.1 ± 94.8
Creatine kinase (U/L)	295.1 ± 800.4	78.6 ± 102.8
Lactate dehydrogenase (U/L)	309.9 ± 188.6	292.0 ± 139.1
BUN (mg/dL)	15.1 ± 21.1	24.8 ± 36.8
Creatinine (mg/dL)	1.1 ± 1.1	1.4 ± 2.7
Sodium (meq/L)	136.1 ± 5.9	137.3 ± 4.5
Potassium (meq/L)	4.0 ± 0.5	4.3 ± 0.6
Aspartate aminotransferase (U/L)	43.7 ± 32.1	42.7 ± 32.1
Alanine aminotransferase (U/L)	42.8 ± 50.1	53.8 ± 37.3

Note: Values reported as mean ± standard deviation

(chronic obstructive airway disease and liver cirrhosis; chronic obstructive airway disease, chronic renal failure, and hypertension; diabetes mellitus and end-stage renal disease on hemodialysis; a history of intracranial hemorrhage). As of May 31, 2003, 37 patients (80.4%) had been discharged and one was still hospitalized in an ordinary isolation room and was improving clinically.

Factors predictive of death

On univariate analysis, advanced age, a low platelet count, and a low ALT were significant predictors of death (Table 3). The latter finding, however, may be spurious as ALT data on patients who died in the emergency department was incomplete, since it was not routinely measured. The presence of underlying disease did not appear to be associated with a worse clinical outcome (p=0.18). In the multivariate analysis, advanced age (odds ratio for every 10 years of age, 2. 4; 95 percent confidence interval, 1.2 to 4.9; p=0.01) was the only significant risk factor.

Discussion

Severe acute respiratory syndrome was first recognized as a global health hazard in March 2003. Originating in the Gunagdong province of China, the disease rapidly spread to Hong Kong and then as people who were infected traveled by air to other parts of Asia and Canada. In view of the threat posed by this disease, the WHO issued a global alert for the first time in more than a decade. This highly infectious disease is caused by a novel coronavirus transmitted by means of droplets and, possibly, fomites. Therefore, both respiratory and contact infection control precautions are important for healthcare workers, as recommended by the Centers for Disease Control and Prevention [1-4].

Severe acute respiratory syndrome usually presents with a high fever (temperature >38ºC for more than 24 h) with or without chills, followed by a dry cough, which may in some cases proceed rapidly to respiratory failure, accompanied by radiographic evidence of air-space-disease [5-8]. In this series, we have identified several cardinal symptoms of SARS. Besides fever, present in 100% of cases, cough was present in 72%, diarrhea in 39%, and shortness of breath in 46%. In addition, lymphopenia, thrombocytopenia, a prolonged activated partial thromboplastin time, and elevated LDH, CK, and ALT levels were prevalent in the early phase of illness in this series. Although these symptoms and laboratory findings are nonspecific, the constellation of these features should raise suspicion of the possibility of SARS.

The radiographic appearance of peripheral air-space opacities in SARS is indistinguishable from other causes of atypical pneumonia, such as *Mycoplasma*, *Chlamydia*, *Legionella*, and other types of viral pneumonia in adults [9]. Since imaging alone cannot help differentiate SARS from other atypical pneumonia, awareness of the clinical manifestations is indispensable. The presence of characteristic clinical features, laboratory findings and exposure history are very suggestive of SARS, and further weight is given to the likelihood of SARS if typical radiographic features are present.

In this series, radiographic progression to mulitfocal unilateral or bilateral involvement occurred in 16 patients who had a focal unilateral infiltrate on the initial radiograph. This progression occurred while the patients

Table 3. Univariate analysis of clinical and laboratory variables associated with death

Variable	Survived	Died	*p*
Age (yr)	37.7 ± 13.1	55.6 ± 20.6	0.04
Hemoglobin (g/dL)	12.6 ± 1.6	12.4 ± 3.5	0.8
White cells count (x10^{-9}/L)	5.4 ± 31.6	6.3 ± 79	0.4
Neutrophils (x10^{-9}/L)	4.1 ± 62.6	5.3 ± 85.6	0.3
Lymphocytes (x10^{-9}/L)	0.8 ± 16.2	0.9 ± 31.6	0.4
Platelets (x10^{-9}/L)	182.9 ± 8 5.7	145.1 ± 26.8	0.04
Creatine kinase (U/L)	320 ± 871.7	167 ± 170.5	0.3
Lactate dehydrogenase (U/L)	282 ± 165.2	454 ± 250.1	0.12
BUN (mg/dL)	14 ± 21.4	20.5 ± 20.1	0.4
Creatinine(mg/dL)	0.9 ± 0.7	1.9 ± 2.1	0. 2
Sodium (meq/L)	135 ± 6.1	137 ± 4.5	0.3
Potassium (meq/ L)	4.0 ± 0.5	4.0 ± 0.4	0.8
APTT	38.7 ± 9.4	42.9 ± 4.9	0.3
Alanine aminotransferase (U/L)	46.0 ± 53.2	22.6 ± 10.4	0.03

Abbreviations: BUN = blood urea nitrogen; APTT = activated partial thromboplastin time
Values are reported as mean ± standard deviation

were being treated with ribavirin and corticosteroids. Progressive radiographic deterioration despite medical treatment seemed to be associated with poor prognosis.

In previous reports, lack of response to initial broad-spectrum antimicrobial treatment led to suspicion that antibiotics alone did not have any clinical benefit [1, 6]. In this study, broad-spectrum antibiotics were given to almost all patients at admission but no significant clinical improvement was noted. Ribavirin (1-β-D-ribafuranosyl-1,2,4-triazole-3-carboximide) is an antiviral agent previously shown to be effective for respiratory syncytial virus, influenza A and B, measles, parainfluenza, and Lassa fever. It is a synthetic nucleoside analog that prevents viral replication. After administration, the drug is phosphorylated to the highly active metabolite ribavirin triphosphate and subsequently catabolized to Triazole carboximide. This inactive metabolite is excreted in urine. Carcinogenic effects have occurred in rats chronically fed with high doses of ribavirin, whereas teratogenicity is only seen when administered during the first trimester of pregnancy. Orally administered ribavirin may also inhibit red cell production [10,11]. Although its effect in SARS patients remains unclear, we used it in all our patients (except for one who died within 24 h of admission) because of its broad antiviral effects. Short-term use of the drug was well tolerated. We encountered no major adverse effects such as severe hemolytic anemia, and the fever subsided after 2 to 3 days of ribavirin use in 71% (32/45) of patients. It is unclear, however, whether this clinical improvement was due to ribavirin alone, to other agents used concomitantly, to synergistic effects of the therapy, or simply because of the natural course of the disease. Whether ribavirin and/or corticosteroids reduce respiratory morbidity secondary to SARS remains unclear.

In a study from Hong Kong, RT-PCR of lung tissue obtained at autopsy from 6 patients who died of SARS, including one patient who had had an antemortem open lung biopsy, was positive for coronavirus in 4 of the 6 cases, and all 6 showed diffuse alveolar damage. Giant cells were present in 4 cases, and in 3 of these, the cells were positive for CD68, a marker of macrophages [12]. These findings led to the hypothesis that there is an early, marked response of cytokines such as tumor necrosis factor, interleukin 1, and interleukin 6 that mediate lung injury in SARS, unleashing a cytokine storm. This is our rationale for using corticosteroids, hoping to suppress the cytokine storm and stop the progression of pulmonary disease [13,14]. Fever subsided within 48 h of beginning steroids in our study in 73% (30/41) of patients. If fever still persisted or there was clinical and radiological deterioration, pulse steroids and IVIG were added. Clinical improvement and resolution of lung infiltrates were noted within 48 h of these treatments in 69% (16/23) of patients. Successful response to IVIG has been reported in West Nile virus encephalitis and parvovirus B19-associated chronic fatigue syndrome [15,16]. Administration of IVIG in respiratory syncytial virus (RSV) infection results in significant reduction of viral titers in pulmonary tissue and clearance of detectable virus in most animals studied [10]. Other studies, however, have not confirmed the efficacy of IVIG in RSV infection. While we saw clinical and radiological improvement within 48 h in 69% (16/23) of our patients treated with IVIG, further controlled studies are needed to determine if IVIG is truly beneficial in treating this novel coronavirus.

Hon *etal* demonstrated that younger children developed a milder form of SARS with a less aggressive clinical course compared with teenagers and adults [17]. The 2 young children and 1 teenager in this study all had abnormal chest radiographs on presentation. The clinical course in the 2 young children was mild and short. One received combined ribavirin and low dose corticosteroids and the other ribavirin alone. Their radiological changes were milder and generally resolved more quickly than those of the teenaged patient. The teenager was a boy who had given mouth-to-mouth resuscitation to his father, who had confirmed SARS. Because of radiological and clinical deterioration with hypoxemia, he was given IVIG and pulse methylprednisolone along with ribavirin, after which he improved. Whether his more severe clinical course compared with the younger children was simply a function of his age, as suggested by the data from Hong Kong, or because of exposure to a large viral load when he resuscitated his father is unknown. Only a larger series would help clarify the clinical course in children.

Three diagnostic tests for SARS are now available, but all have limitations. Enzyme-linked immunosorbent assay (ELISA) detects antibodies reliably only from about day 20 after the onset of symptoms, so it cannot be used to detect cases before potential spread of the infection to others [18]. An immunofluorescence assay detects antibodies reliably after day 10 of infection [18], but this may be too late to prevent spread. RT-PCR has proved helpful but is not sensitive enough. Various versions of real-time and block-based PCR are currently being developed to reduce the number of false negatives [18-21]. In this study, 61% of patients were RT-PCR positive. Other methods of virus detection, including cell culture (where cytopathogenic effects are induced

in Vero cells and fetal rhesus kidney cells), electron microscopy of cell cultures and tissue samples from SARS patients, or immunofluorescent assays with convalescent serum to detect the virus in cell culture [22,23] are all too cumbersome or slow to be useful clinically.

Our knowledge of the natural history, diagnosis, and treatment of SARS have grown at a rapid pace. In retrospect, many of treatments commonly used in the acute management of respiratory disease may have actually facilitated the transmission of the SARS coronavirus [24]. Our Case 1 was treated with nebulized medication before SARS was diagnosed. The use of NIPPV and nebulizers which may produce aerosolization of the virus should be avoided in SARS patients. In addition, rigorous application of respiratory isolation and barrier precautions is an effective means of controlling the spread of this disease in a hospital setting [25,26].

In summary, SARS is a highly infectious and potentially lethal disease for which the medical profession in many countries was unprepared. Although data is inadequate to demonstrate the efficacy of ribavirin, corticosteroids, and IVIG, clinical and radiological improvement did occur in patients treated with these drugs. Control of this epidemic in Taiwan, however, has largely been achieved by government-mandated measures, including vigorous contact tracing, quarantine for those exposed, and prompt isolation of symptomatic individuals. These actions, together with intensive education of the public on personal hygiene, the wearing of masks in public places, and daily measurement of temperatures may have played an important role in the successful control of the SARS epidemic in Taiwan.

Acknowledgment

We are grateful to the members of Infection Control Team of Mackay Memorial Hospital for their assistance in this study.

References

1. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, Yung MY, Leung CB, To KF, Liu SF, Szeto CC, Chung S, Sung JJY. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348:1986-94.
2. Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K, Tellier R, Draker R, Adachi D, Ayers M, Chan AK, Skowronski DM, Salit I, Simor AE, Slutsky AS, Doyle PW, Krajden M, Petric M, Brunham RC, McGeer AJ. Identification of severe acute respiratory syndrome in Canada. N Engl J Med 2003;348:1995-2005.
3. Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan- Yeung M, Lam WK, Seto WH, Yam LY, Cheung TM, Wong PC, Lam B, Ip MS, Chan J, Yuen KY, Lai KN. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348:1977-85.
4. Severe acute respiratory syndrome and coronavirus testing – United States, 2003. JAMA 2003;289:2203-6.
5. Smith FW. Severe acute respiratory syndrome (SARS): update on a moving target. Cleve Clin J Med 2003;70:413-6.
6. Hsu LY, Lee CC, Green JA, Ang B, Paton NI, Lee L, Villacian JS, Lim PL, Earnest A, Leo YS. Severe acute respiratory syndrome (SARS) in Singapore: clinical features of index patient and initial contacts. Emerg Infect Dis 2003;9:713-7.
7. Wong RSM. Severe acute respiratory syndrome in a doctor working at the Prince of Wales Hospital. Hong Kong Med J 2003;9:202-5.
8. Wu EB, Sung JJY. Haemorrhagic-fever-like changes and normal chest radiograph in a doctor with SARS. Lancet 2003; 361:1520-1.
9. Wong KT, Antonio GE, Hui DSC, Lee N, Yuen EHY, Wu A, Leung CB, Rainer TH, Cameron P, Chung SSC, Sung JJY, Ahuja AT. Severe acute respiratory syndrome: radiologic appearances and pattern of progression in 138 patients. Radiology online 2003; 8 June. Available at: http://radiology.rsnajnls.org/cgi/content/full/2282030593.
10. Kneyber MCJ, Moll HA, Groot RD. Treatment and prevention of respiratory syncytial virus infection. Eur J Pediatr 2000;159: 399-411.
11. Wong VWS, Dai D, Wu AKL, Sung JJY. Treatment of severe acute respiratory syndrome with convalescent plasma. Hong Kong Med J 2003;9:199-201.
12. Nicholls JM, Poon LLM, Lee KC, Ng WF, Tai ST, Leung CY, Chu CM, Hui PK, Mak KL, Lim W, Yan KW, Chan KH, Tsang NC, Guan Y, Yuen KY, Peiris JSM. Lung pathology of fatal severe acute respiratory syndrome. Lancet 2003;361:1773-8.
13. So LKY, Lau ACW, Yam LYC, Chung TM, Poon E, Yung RWH, Yuen KY. Development of a standard treatment protocol for severe acute respiratory syndrome. Lancet 2003;361:1615-7.
14. Chan-Yeung M, Yu WC. Outbreak of severe acute respiratory syndrome in Hong Kong Special Administrative Region: case report. Br Med J 2003;326:850-2.
15. Hamdan A, Green P, Mendelson E, Kramer MR, Pitlik S, Weinberger M. Possible benefit of intravenous immunoglobin therapy in a lung transplant recipient with West Nile virus encephalitis. Transplant Infect Dis 2002;4:160-2.
16. Kerr JR, Cunniffe VS, Kelleher P, Berstein M, Bruce IN. Successful intravenous immunoglobulin therapy in 3 cases of parvovirus B19-associated chronic fatigue syndrome. Chin Infect Dis 2003;36:e100-6.
17. Hon KLE, Leung CW, Cheng WTF, Chan PKS, Chu WCW, Kwan YW, Li AM, Fong NC, Ng PC, Chiu MC, Li CK, Tam JS, Fok TF. Clinical presentation and outcome of severe acute respiratory syndrome in children. Lancet 2003;361:1701-3.
18. A multicentre collaboration to investigate the cause of severe acute respiratory syndrome. Lancet 2003;361:1730-3.
19. Drosten C, Gunther S, Preiser W, Werf SVD, Brodt HR, Becker S, Rabenau H, Panning M, Kolesnikova L, Fouchier RAM, Berger A, Burguiere AM, Cinatl J, Eickmann M, Escriou N, Grywna K, Kramme S, Manuguerra JC, Muller S, Rickerts V, Sturmer M, Vieth S, Klenk HD, Osterhaus ADME, Schmitz H, Doerr HW. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 2003; 348:1967-76.

20. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, Tong S, Urbani C, Comer JA, Lim W, Rollin PE, Dowell SF, Ling AE, Humphrey CD, Shieh WJ, Guarner J, Paddock CD, Rota P, Fields B, DeRisi J, Yang JY, Cox N, Hughes JM, LeDuc JW, Bellini WJ, Anderson LJ. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med 2003;348:1953-66.
21. Peiris JSM, Chu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLM, Law KI, Tang BSF, Hon TYW, Chan CS, Chan KH, Ng JSC, Zheng BJ, Ng WL, Lai RWM, Guan Y, Yuen KY. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet 2003;361:1767-72.
22. Holmes KV. SARS-associated coronavirus. N Engl J Med 2003; 348:1948-51.
23. Ruan YJ, Wei CL, Ee LA, Vega VB, Thoreau H, Yun STS, Chai JM, Ng P, Chiu KP, Lim L, Tao Z, Peng CK, Ean LOL, Lee NM, Sin LY, Ng LFP, Chee RE, Stanton LW, Long PM, Liu ET. Comparative full length genome sequence analysis of 14 SARS coronavirus isolates and common mutations associated with putative origins of infection. Lancet 2003;361:1779-85.
24. Dwosh HA, Hong HHL, Austgarden D, Herman S, Schabas K. Identification and containment of an outbreak of SARS in a community hospital. Can Med Assoe J 2003;168:1415-20.
25. Twu SJ, Chen TJ, Chen CJ, Olsen SJ, Lee LT, Fisk T, Hsu KH, Chang SC, Chen KT, Chiang IH, Wu YC, Wu JS, Dowell SF. Control measures for severe acute respiratory syndrome (SARS) in Taiwan. Emerg Infect Dis 2003;9:718-20.
26. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, Abu-Raddad LJ, Ho LM, Thach TQ, Chau P, Chan KP, Lam TH, Tse LY, Tsang T, Liu SH, Kong JHB, Lau EMC, Ferguson NM, Anderson RM. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Lancet 2003;361:1761-6.