Clinical Findings, Treatment and Prognosis in Patients with Severe Acute Respiratory Syndrome (SARS)

Shan-Chwen Chang*

Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, R.O.C.

Severe acute respiratory syndrome (SARS) is a new infectious disease in humans caused by SARS-associated coronavirus (SARS-CoV). The syndrome was first noted in late 2002 in southern China, but had spread to more than 30 countries in early 2003, when it was particularly evident in China, Hong Kong, Singapore, Vietnam, Taiwan, and Canada. Through international cooperation, the causative agent, SARS-CoV, was quickly identified and confirmed.[1,2] The pandemic was controlled several months later, after major efforts from governments, health societies and the general population in the affected regions. During the pandemic, more than 8,000 cases were reported: many of the patients were health care workers or household contacts of SARS-infected persons, and 774 patients died.

During the early phase of the pandemic, the diagnosis could be made only from clinical findings and patient-contact histories. Even after discovery of the causative agent, many patients could still not be diagnosed by a specific laboratory test, such as reverse-transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV, or viral culture. Therefore, many cases were actually diagnosed according to the World Health Organization (WHO) definition. Reports about clinical manifestations, laboratory and radiologic findings, and prognoses, for SARS patients from different parts of the affected regions showed similar clinical pictures.[3–6]

Patients infected with SARS-CoV usually experience fever 2–7 days (sometimes up to 10 days) after infection has occurred. Many patients also experience chills, rigor and myalgia; some may have cough, diarrhea and shortness of breath a few days later. Patients then visit a hospital, where some have abnormal laboratory findings: for example, elevated levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and creatine kinase (CK); low lymphocyte and platelet counts; and pulmonary infiltration on chest radiographs. Many patients may have aggravated signs and symptoms, abnormal laboratory findings and pulmonary lesions during hospitalization. Around 20% of patients infected with SARS-CoV may progress to respiratory failure or acute respiratory distress syndrome, and the overall mortality rate is about 5–15%. Although several agents have been used for the treatment of SARS, there is still no definitive, effective, treatment regimen.

Liu et al reported clinical characteristics, management, and analysis of prognostic factors in patients with probable SARS who were treated at a specially designated hospital in Taipei City during the SARS epidemic from late April to July 2003.[7] The number of cases included in the analysis was small. However, as only patients with suspected SARS (patients without pneumonia) were transferred to the investigators' hospital during the early epidemic, the clinicians may have been able to observe clinical pictures and disease progression in SARS patients without pneumonia during the early disease course. During later epidemic stages, patients with pneumonia were also transferred to the investigators' hospital. Therefore, the clinicians had an opportunity to observe a whole spectrum of SARS patients with various disease severities. In total, 30% of patients had no pneumonia at presentation, but all except 1 patient progressed to pneumonia during hospitalization. These clinical findings are similar to other reports, except that a higher percentage of patients had diarrhea at presentation; the latter finding differs from reports in other countries, but is similar to another report from Taiwan.[6]

In the report of Liu et al,[7] few patients had major

*Correspondence to: Dr. Shan-Chwen Chang, Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital, 7, Chung-Shan South Road, Taipei 100, Taiwan, R.O.C.
E-mail: sc4030@ha.mc.ntu.edu.tw • Received: November 4, 2004 • Accepted: December 16, 2004

underlying disease, which might explain the low fatality rate that was documented. In many other reports, the proportion of patients with various major underlying diseases was greater, such that the prognosis was worse once patients got SARS.[6] Conversely, Liu et al did not identify major underlying diseases as predictors of respiratory failure or death once patients had developed SARS.[7]

A high level of C-reactive protein (CRP) was predictive of poor prognosis,[7] as also evident in another report from Taiwan.[6] However, this finding was not reported in other regions, because other investigators probably did not measure CRP routinely or statistically analyze CRP data.[3–5] Nonetheless, a high CRP level may represent increased inflammation at certain body sites and, in SARS, it is likely that an elevated CRP level represents tissue damage in the lung, thus increasing the risk of respiratory failure and death.

Similar to other studies, ribavirin and corticosteroids were not effective in treating SARS patients in Liu et al's report.[7] In fact, ribavirin has no efficacy against SARS-CoV *in vitro*.[8] In one study of a small series of SARS patients, ribavirin was also ineffective *in vivo* after serial quantitative RT-PCR assays for the detection of viral load in clinical specimens.[9] Although intravenous immunoglobulin (IVIG) was tried in Taiwan for the treatment of SARS, it did not effectively reduce the probability of respiratory failure or death.[6] However, in another report, IVIG effectively reversed leukopenia and thrombocytopenia associated with SARS.[6]

Nobody knows whether SARS will reappear and cause outbreaks in the future. However, understanding the clinical picture of SARS could help physicians be more alert and consider SARS as a possible diagnosis when patients with similar clinical pictures are encountered. Clearly, early identification of the infection, and initiation of the necessary isolation precautions, may reduce the spread of SARS-CoV and prevent another large outbreak of SARS.

References

1. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, Tong S, et al. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1953–66.
2. Drosten C, Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, Rabenau H, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1967–76.
3. Peiris JS, Chu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLH, Law KI, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *Lancet* 2003;361:1767–72.
4. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;348:1986–94.
5. Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, Walmsley SL, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA* 2003;289:2801–9.
6. Wang JT, Sheng WH, Fang CT, Chen YC, Wang JL, Yu CJ, Chang SC, et al. Clinical manifestations, laboratory findings, and treatment outcomes of SARS patients. *Emerg Infect Dis* 2004;10:818–24.
7. Liu CY, Huang LJ, Lai CH, Chen HP, Chen TL, Fung CP, Liu CY. Clinical characteristics, management and prognostic factors in patients with probable severe acute respiratory syndrome (SARS) in a SARS center in Taiwan. *J Chin Med Assoc* 2005;68:110–7.
8. Cinatl J, Morgenstern B, Bauer G, Chandra P, Rabenau H, Doerr HW. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. *Lancet* 2003;361:2045–6.
9. Wang WK, Chen SY, Liu IJ, Kao CL, Chen HL, Chiang PL, Wang JT, et al. Temporal relationship of viral load, ribavirin, interleukin (IL)-6, IL-8, and clinical progression in patients with severe acute respiratory syndrome. *Clin Infect Dis* 2004;39:1071–5.