J Chin Med Assoc
2004;67:472-475

Case Report

Clinical Manifestations of Two Cases with Severe Acute Respiratory Syndrome (SARS) in I-Lan County

Yu-Jiun Chan[1,6]
Shew-Dan Chen[3]
Kuei-Hsia Hsueh[4]
Nai-Wei Hsu[3,6]
Chin-Lin Perng[3,6]
Nan-San Chou[2]
Gau-Jun Tang[5,6]

[1] *Section of Infectious Diseases, Department of Medicine,* [2] *Su-Ao Veterans Hospital;*
[3] *Department of Medicine and*
[4] *Intensive Care Unit,* [5] *I-Lan Hospital, Department of Health; and*
[6] *National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.*

Severe acute respiratory syndrome (SARS) is a new respiratory tract infectious disease caused by a novel coronavirus. As of this report, there were 3 probable SARS cases in I-Lan County. Of them, 1 was deceased in another hospital and the remaining 2 were cured and discharged. This report describes the clinical manifestations of the 2 surviving probable cases. The first case had a travel history to Guangdong province, China, and the second case probably contracted the disease from a hospital outbreak. They both developed infiltrations over uni- or bilateral lungs but recovered without intubations. Their treatment modalities included empirical antibiotics, steroids, and anti-viral agents. As SARS becomes an emerging infectious disease in the 21st century, its clinical manifestations and treatment will be discussed.

Key Words
coronavirus;
pneumonia;
severe acute respiratory syndrome

Severe acute respiratory syndrome (SARS) was first defined by the World Health Organization (WHO) to describe a mysterious "atypical pneumonia" which attacked Guangdong province, China, starting November 2002.[1] According to the definition for SARS proposed by the WHO, there are 2 categories, namely suspected and probable SARS. The suspected SARS case is defined if the patient has clinical symptoms of fever higher than 38 °C, cough, breathing difficulty and a positive SARS contact history or a travel history to an endemic area of SARS within 10 days prior to onset of symptoms. In the presence of acute respiratory distress or radiological infiltrations compatible with pneumonia, the suspected case of SARS becomes a probable case. Recently, identification of the SARS coronavirus has become another criteria for a probable case (www.who.int/csr/sars/en/).

The first SARS case reported in Taiwan was a merchant who frequently visited China and became ill in the early March 2003. His wife (the second case) was ill later. I-Lan County is located in eastern Taiwan. Herein, we reported the first case in this county who got infection from China and a second SARS probable case, who might have been infected in a hospital outbreak.

CASE REPORT

Case 1

This 64-year-old woman had been relatively robust except for a history of subtotal thyroidectomy due to hyperthyroidism and subtotal gastrectomy due to peptic ulcer disease. She denied any other disease history such as diabetes mellitus or heart diseases. She joined a 7-day tour to Guangdong, China, and returned to Taiwan in

Received: June 6, 2003.
Accepted: March 10, 2004.

Correspondence to: Gau-Jun Tang, MD, I-Lan Hospital, Department of Health, 152, Xin-Min Road, I-Lan 260, Taiwan.
Tel: +886-3-932-5192; Fax: +886-3-935-1838; E-mail: ilan@ilan-tpg.gov.tw

early March. She began to suffer from cough with mild sore throat 1 week before admission and sudden onset of chills, high fever up to 39 °C accompanied by poor appetite, nausea, and vomiting on March 13, 2003. The initial clinical examination showed negative findings in chest and abdomen. The chest X-ray revealed mild cardiomegaly and some infiltrations at the right cardiophrenic region. The complete blood count revealed a white cell count of 9,710/mm^3 with neutrophils 90.9% and lymphocytes 7.3%, a hemoglobin level of 10.3 g/dL, and a platelet count of 222 × 10^3/mm^3. Routine serum biochemical tests, such as aspartate transaminase (AST) and alanine transaminase (ALT) were within reference limits. She fulfilled the criteria for a probable SARS case according to the SARS definition proposed by the WHO on March 15. A team of specialists from the Centers for Disease Control (CDC) of the USA inspected the patient on March 17 and agreed with the diagnosis of SARS. She was initially treated with ofloxacin 400 mg intravenous injection every 12 hours. The body temperature returned to normal on the fourth day after admission. Bacterial cultures for blood, urine, and sputum failed to yield microorganisms. Serology for *Mycoplasma* and *Chlamydia* IgM antibodies was negative.

Case 2

This 57-year-old woman was relatively robust, and she denied any other history such as diabetes mellitus or heart diseases. Her husband was admitted to a district hospital in Taipei because of vomiting and diarrhea from April 16 to 22, 2003. She took care of her husband during the admission period. That local hospital was later closed because of a nosocomial outbreak of SARS. On April 27, after playing tennis, she felt sudden onset of chills and fever. Myalgia and headache ensued. She was sent to a medical center and then transferred because of rapid progression of chest X-ray findings and the lack of available negative pressure ward there. The initial chest and lungs examination showed mild bilateral rhonchi without wheezing or rales. The chest X-ray revealed an infiltration over the right lung field on the day of admission (Fig. 1), with rapid progression to involve bilateral lung fields on day 7 (Fig. 2). On admission, the complete blood count showed a white cell count of 3,920/mm^3 with neutrophils 88.5% and lymphocytes 6.8%, a hemoglobin level of 13.1 g/dL, and a platelet count of 129 × 10^3/mm^3. Routine serum biochemical tests revealed aspartate transaminase 31 U/L, alanine transaminase 43

Fig. 1. Chest X-ray film of case 2 revealed infiltrations over the right lung field on the day of admission.

Fig. 2. Chest X-ray film of case 2 showed progression of the pulmonary infiltrations on the seventh day after admission.

Fig. 3. Chest X-ray film of case 2 showed resolution of the pulmonary infiltrations on the fourteenth day after admission.

U/L, creatine phosphokinase (CK) 89 U/L, and lactose dehydrogenase (LDH) 199 U/L. She fulfilled the revised criteria for definition of a probable SARS case. Anti-viral agent, ribavirin (Robatrol 400 to 1200 mg bid), and empirical antibiotics (ofloxacin 400 mg q12h and ceftriaxone 2 gm q12h) were administered. However, her clinical symptoms, including chills, persistent fever, and dry cough, exacerbated. Therefore, intravenous immune globulin (IVIG) 1 gm/kg/day was given for 2 days from the fourth to the sixth day after admission, and hydrocortisone sodium succinate 200 mg (Solu-cortef) was given on the fifth day after admission which was followed by prednisolone 40 mg q12h thereafter with tapering. Watery diarrhea was also noted on the fifth day after admission. The body temperature returned to normal on the ninth day after admission. Pneumonic patch resolved on follow-up chest X-ray films 14 days after admission (Fig. 3). Bacterial cultures for blood, urine, and sputum were negative. Serology for *Mycoplasma* and *Chlamydia* IgM antibodies was negative, too. Serology for *Legionella* showed reactive on 1: 100 dilutions but non-reactive on 1: 320 dilutions. Reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS virus from serum and nasal swab on the twelfth day were all negative.

DISCUSSION

SARS is a new disease entity caused by a novel coronavirus. This coronavirus as the SARS etiologic agent has fulfilled the Koch's postulates. Through international cooperation,[6] enormous progress has been achieved, including the identification of the etiologic agent of SARS,[2,3,5] completion of the whole genomic sequences of the virus,[7] and some structural analysis of the main viral proteinase.[8]

The most common clinical symptoms of SARS include fever, chills, myalgia, and cough. Features of the clinical manifestations reported from large series of analysis were fever (99-100%), chills and/or rigor (73.2%), nonproductive cough (69%), myalgia (49-60.9%), and dyspnea (42%). Other laboratory findings were lymphopenia (69.9-89%), thrombocytopenia (44.8%), elevated LDH (71.0-80%), AST (78%), and CK levels (32.1-56%). The radiographic appearances and patterns of progression of SARS include 4 types. The more distinctive findings include predominant peripheral location, common progression pattern from unilateral focal air-space opacity to unilateral multifocal or bilateral involvement, and lack of cavitation, lymphodenopathy, and pleural effusion. Wong *et al*.[11] reported the clinical characteristics of 8 fatal cases of SARS in a medical center in Taipei. They suggested close monitoring and active treatment for patients who had advanced age, co-morbid conditions, highly elevated LDH, and multiple infiltrations over chest radiographs.[11,12] Both of our 2 probable SARS cases fulfilled the WHO criteria, with positive SARS contact history or travel history chronologically, fever and cough, and abnormal chest radiographic findings. However, the first case presented a less severe clinical course and the second one a more typical clinical manifestation. Both patients recovered without receiving intubations.

There are new diagnostic tests including RT-PCR and real-time RT-PCR as well as serological methods to detect coronavirus infection. However, the sensitivity is not high enough to exclude patients with negative RT-PCR or real-time RT-PCR results. The serologic meth-

ods require 2 to 3 weeks for seroconversion. Negative results of RT-PCR for coronavirus in our patients may be caused by low viral load. Detection of seroconversion by serial follow-up may confirm a previous infection.

There are neither effective anti-viral treatment nor potent vaccine available at present. Chiang *et al.* proposed a combination protocol including levofloxacin, ribavirin, intravenous immunoglobulin injection (IVIG), and methylprednisolone for patients with different severity.[13] However, all the treatment regimens proposed by different groups need further studies to confirm their efficacy.[4,12] Furthermore, the pulmonary damage associated with SARS may not be caused by the virus but represent a secondary effect of cytokines or other factors. Effective quarantine and strict infectious control policy seem to be the most important approaches to prevent SARS from spreading at the present time.

REFERENCES

1. Acute respiratory syndrome. China, Hong Kong Special Administrative Region of China, and Viet Nam. *Wkly Epidemiol Rec* 2003;78:73-4.
2. Drosten C, Gunther S, Preiser W, van der WS, Brodt HR, Becker S, *et al.* Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1967-76.
3. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, *et al.* A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1953-66.
4. Peiris JS, Lai ST, Poon LL, Guan Y, Yam LY, Lim W, *et al.* Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet* 2003;361:1319-25.
5. Fouchier RA, Kuiken T, Schutten M, van Amerongen G, van Doornum GJ, van den Hoogen BG, *et al.* Aetiology: Koch's postulates fulfilled for SARS virus. *Nature* 2003;423:240.
6. Stohr K. A multicentre collaboration to investigate the cause of severe acute respiratory syndrome. *Lancet* 2003;361:1730-3.
7. Marra MA, Jones SJ, Astell CR, Holt RA, Brooks-Wilson A, Butterfield YS, *et al.* The genome sequence of the SARS-associated coronavirus. *Science* 2003;300:1399-404.
8. Anand K, Ziebuhr J, Wadhwani P, Mesters JR, Hilgenfeld R. Coronavirus main proteinase (3CLpro) structure: basis for design of anti-SARS drugs. *Science* 2003;300:1763-7.
9. Wong KT, Antonio GE, Hui DS, Lee N, Yuen EH, Wu A, *et al.* Severe acute respiratory syndrome: radiographic appearances and pattern of progression in 138 patients. *Radiology* 2003; 228:401-6.
10. Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, *et al.* Clinical features and short-term outcomes of 144 Patients with SARS in the greater Toronto area. *JAMA* 2003;289:2801-9.
11. Wong WW, Chen TL, Yang SP, Wang FD, Cheng NC, Kuo BI, *et al.* Clinical characteristics of fatal patients with severe acute respiratory syndrome in a medical center in Taipei. *J Chin Med Assoc* 2003;66:323-7.
12. Wu JC. Severe acute respiratory syndrome (SARS), a zoonotic infection with rapid spread: are we ready for the coming ones? *J Chin Med Assoc* 2003;66:315-7.
13. Chiang CH, Chen HM, Shih JF, Su WJ, Perng PR. Management of hospital-acquired severe acute respiratory syndrome with different disease spectrum. *J Chin Med Assoc* 2003; 66:328-38.