PO Box 2345, Beijing 100023, China
www.wjgnet.com
wjg@wjgnet.com

ELSEVIER

World J Gastroenterol 2005;11(19):2971-2974
World Journal of Gastroenterology ISSN 1007-9327

• *BRIEF REPORTS* •

Clinical features of probable severe acute respiratory syndrome in Beijing

Hai-Ying Lu, Xiao-Yuan Xu, Yu Lei, Yang-Feng Wu, Bo-Wen Chen, Feng Xiao, Gao-Qiang Xie, De-Min Han

Hai-Ying Lu, Xiao-Yuan Xu, Department of Infectious Diseases, Peking University First Hospital, Beijing 100034, China
Yu Lei, Department of Hepatic Disease, Renmin Hospital of Fangxian, Fangxian 442100, Hubei Province, China
De-Min Han, Beijing TongRen Hospital, Beijing 100730, China
Yang-Feng Wu, Gao-Qiang Xie, Chinese Academy of Medical Sciences, Fu Wai Hospital, Beijing 100037, China
Bo-Wen Chen, Feng Xiao, Capital Institute of Pediatrics, Beijing 100020, China
Supported by the National High Technology Research and Development Program of China (863 Program), No. 2003AA208107
Correspondence to: Xiao-Yuan Xu
Correspondence to: De-min Han, Beijing TongRen Hospital, 2 ChongNei Street, DongCheng District, Beijing 100730, China. handemin@trhos.com
Received: 2004-07-09 Accepted: 2004-08-30

Abstract

AIM: To summarize clinical features of probable severe acute respiratory syndrome (SARS) in Beijing.

METHODS: Retrospective cases involving 801 patients admitted to hospitals in Beijing between March and June 2003, with a diagnosis of probable SARS, moderate type. The series of clinical manifestation, laboratory and radiograph data obtained from 801 cases were analyzed.

RESULTS: One to three days after the onset of SARS, the major clinical symptoms were fever (in 88.14% of patients), fatigue, headache, myalgia, arthralgia (25-36%), *etc*. The counts of WBC (in 22.56% of patients) lymphocyte (70.25%) and CD_3, CD_4, CD_8 positive T cells (70%) decreased. From 4-7 d, the unspecific symptoms became weak; however, the rates of low respiratory tract symptoms, such as cough (24.18%), sputum production (14.26%), chest distress (21.04%) and shortness of breath (9.23%) increased, so did the abnormal rates on chest radiograph or CT. The low counts of WBC, lymphocyte and CD_3, CD_4, CD_8 positive T cells touched bottom. From 8 to 16 d, the patients presented progressive cough (29.96%), sputum production (13.09%), chest distress (29.96%) and shortness of breath (35.34%). All patients had infiltrates on chest radiograph or CT, some even with multi-infiltrates. Two weeks later, patients' respiratory symptoms started to alleviate, the infiltrates on the lung began to absorb gradually, the counts of WBC, lymphocyte and CD_3, CD_4, CD_8 positive T cells were restored to normality.

CONCLUSION: The data reported here provide evidence that the course of SARS could be divided into four stages, namely the initial stage, progressive stage, fastigium and convalescent stage.

Key words: SARS; Clinical features; Clinical stage

Lu HY, Xu XY, Lei Y, Wu YF, Chen BW, Xiao F, Xie GQ, Han DM. Clinical features of probable severe acute respiratory syndrome in Beijing. *World J Gastroenterol* 2005; 11(19): 2971-2974
http://www.wjgnet.com/1007-9327/11/2971.asp

INTRODUCTION

A novel coronavirus[1-3] has been identified as an etiologic agent for severe acute respiratory syndrome (SARS), which caused about 8 437 SARS cases in the world between December 2002 and October 2003. The previous reports[4-7] described the clinical features of SARS, but there is little information available in literature about features of this illness in a large SARS population. In this paper, we will describe the characteristics of SARS during the whole course systematically, through investigation of the data derived from 801 cases of probable SARS.

MATERIALS AND METHODS

Patients

This study includes 801 cases of patients admitted to hospitals between March and June 2003 in Beijing. These cases are consistent with the criteria of WHO for a probable SARS, with fever, abnormality of chest radiograph or CT scan and history of exposure to an index patient suspected of SARS or to have had direct contact with an individual who became ill after exposure to a patient with SARS.

Methods

Clinical manifestation, laboratory and chest radiographic data were documented prospectively. Investigations included a complete blood count, CD3, CD4, CD8 positive T cell, lymphocyte count, and serum biochemical measurements (including electrons, renal function and liver function, creatine kinase, creatine kinase MB and lactate dehydrogenase). After the patients were admitted to hospitals, the above examinations were performed every week during the entire course of this illness.

Statistical analysis

All analyses were performed using Statistica software. Data are expressed as mean±SD and percentage.

RESULTS

Our cohort comprised 801 cases of probable SARS, the mean age of the study population was 37.04±15.64 years (range, 0.72-92.89 years), 412 cases (51.56%) were female, and 154 patients (9.23%) were medical personnel. Sixty-five patients (8.1%) had coexisting conditions, hypertension in 21 cases, hepatitis cirrhosis in 13 cases, diabetes mellitus in 9 cases and cardiovascular disease in 8 cases. The mean day of hospitalization was 29.02±9.07 d, and that of the entire course was 32.79±10.82 d. 64.17% of patients were admitted to hospital 1-3 d after onset of illness, 88.9%, 4-7 d, 93.51%, 8-11 d, 95.51%, 12-14 d, 95.76%, 15-21 d. In later days, the percentages gradually decreased.

Temperature

The range of patient's temperature on admission during 1-14 d after onset of illness was 38.11-38.36 ℃. On d 1, 88.14% of patients had a documented fever, and 98.12% with a reported fever. The percentages of patients with fever declined to 40.31%, 15.13%, 5.07% and 6.02% on the 7th, 14th, 21st and 28th d respectively, the mean time taken for the patient's temperature to drop below 37.2 ℃ after admission was 5.69±4.53 d.

Hypoxemia findings

The oxygen saturation (SaO_2) went down below 93% in 1.39-3.13% of patients, the mean of oxygen saturation was more than 96%. The partial arterial pressure of oxygen (PaO_2) was noted below 12.7±3.4 kPa in 65.74% of patients (mean 12.4±1.6 kPa) from the 1st to the 3rd d, then the percentage subsequently reduced. On the 4th wk, 40% of patients presented low PaO_2, and the mean of PaO_2 was 15.5±2.4 kPa. The medians of low PaO_2 and SaO_2 occurred at the 3rd and 1st d respectively, and recovered to the normal levels in the later 8 and 9.5 d, respectively.

There were seven cases of patients who required noninvasive ventilation and one case with mechanical ventilation at the 1st-3rd d, and 18 cases with noninvasive ventilation at the 4th-7th d, 15 cases at the 8th-11th d, 7 cases at the 12th-14th d, and 3 cases at the 3rd wk.

Clinical features

At the 1st-3rd d, the predominant symptom was high fever, and other common symptoms were fatigue (in 33.85% of patients), headache (21.34%), myalgia (22.17%), sore throat (18.66%), arthralgia (16.01%), chills, rigors, or both (12.6%).

At d 4-7 above prodromal symptoms appeared less worsening, but the low respiratory tract symptoms appeared obvious, such as cough (in 24.28% of patients), sputum production (14.26%), chest distress (21.04%) and shortness of breath (9.23%). These respiratory symptoms deteriorated progressively and touched the peak at the periods from d 8-16 then alleviated gradually in the subsequent days.

The prodromal symptoms that usually persisted for 3-5 d are cough and sputum production, occurring at the 2nd and 3rd d, and disappeared later at d 13 and 7 respectively, chest distress and shortness of breath at d 7th and 5th, and recovered later in d 10 and 17.5 respectively. The positive rates of symptoms in our study cohort during the whole course are listed in Table 1.

Hematologic findings

In the early phage (1-3 d) of the course for SARS, the white blood cell count, lymphocyte cell count and its subtype cell count (CD4, CD3, CD8 positive cell) presented reduction, and touched bottom at the 4th to 7th d, then gradually went up to the normal levels at the 4th wk. The Table 2 shows the abnormal rates and means of hematology in our study cohort during the course.

Radiographic findings

At the 1st to 3rd d after onset of illness, 96.65% of patients had abnormal chest radiographs, most of them showed a unilateral one focal infiltrates, but some patients (11.45%) presented unilateral or bilateral multifocal involvement and had a dramatic worsening in the period from the 8th to 14th d. After that, the majority of patients had radiographic evidence of improvement in lung consolidation. There were, however, 17.35% and 10.24% of patients with abnormal chest radiograph at the 6th and 7th wk after onset of this illness, and 4.37% at the 8th wk. The abnormal change in SARS patients' chest CT scans also showed the same trend, but CT scan is more sensitive than X-ray examination. The abnormal rates of chest radiographs and CT in our study cohort during the course are presented in Table 3.

Biochemical findings

A substantial proportion of patients had several abnormal serum chemical values, which could occur early but progressively worsened at the 2nd and 3rd wk. 64.66% of patients had an elevated serum alanine aminotransferases levels (>40 IU/L, ALT), 44.34% of patients with an elevated serum AST levels

Table 1 Positive rates of symptoms in our study cohort (%)

Variable	1–3 d	4–7 d	8–11 d	12 d-	15 d-	22 d-	29 d-
Chill	12.6	9.34	4.32	2.4	1.43	0.31	0.57
Rigor	4.29	2.39	0.61	1.05	0.29	0	0.19
Fatigue	33.85	27.59	22.65	14.16	3.3	8.47	4.32
Headache	21.34	12.03	7.45	3.18	13.88	1.99	1.89
Arthralgia	16.01	9.64	5.31	3.53	2.87	2.31	2.29
Myalgia	22.17	13.23	7.63	5.38	4.3	2.92	1.52
Diarrhea	9.88	12.09	5	3.71	3.14	1.8	2.7
Cough	23.76	24.18	29.18	28.68	20.85	8.02	4.23
Sputum production	8.02	14.26	13.09	11.36	8.56	3.08	2.01
Chest distress	8.43	21.04	31.83	35.23	35.34	26.09	17.15
Breath shortness	8.24	9.23	15.65	20.35	18.01	7.12	5.01
Rales	6.2	4.78	5.08	4.65	3.12	1.25	1.01

Table 2 Abnormal rate (%) and value of hematology in our study cohort

Variable	1 d-	4 d-	8 d-	12 d-	15 d-	22 d-	29 d-
WBC							
Abnormal rate	22.56	38.93	16.45	8.44	6.44	6.81	8.66
Mean	5.15	4.75	7.46	4.75	8.42	8.22	7.33
SD	2.56	2.73	4.21	4.83	3.96	3.76	3.49
Lymphocyte							
Abnormal rate	70.25	78.81	58.9	45.21	39.29	25.8	29.94
Mean	1.11	1.19	1.50	1.70	1.75	1.87	1.74
SD	0.51	0.64	0.81	0.91	0.92	0.94	0.75
CD8							
Abnormal rate	68.42	80.33	75.81	67.35	51.58	48.15	35.42
Mean	307.23	244.14	306.19	318.28	453.06	534.37	511.31
SD	274.19	182.34	251.53	227.91	433.46	428.46	269.11
CD3							
Abnormal rate	68.42	87.1	82.26	71.43	60	54.43	49.94
Mean	690.97	568.03	711.48	787.24	1 068.9	1 184.5	1 148.3
SD	576.36	434.18	515.14	559.83	788.19	713.17	620.1
CD4							
Abnormal rate	69.05	84.38	72.58	60.78	48.42	44.44	36
Mean	367	295.28	377.66	430.92	582.21	656.78	670.32
SD	300.64	248.96	326.16	325.07	464.04	576.2	447.19

Table 3 Abnormal rates of chest radiographs in our study cohort

Variable	1 d-	4 d-	8 d-	12 d-	15 d-	22 d-	29 d-
Abnormal rate X-ray	96.65	94.3	97.04	80.68	74.96	64.98	56.37
Multifocal opacities X-ray	11.45	15.19	25.44	25.18	20.38	15.82	16.56
Abnormal rate CT	95.45	95.92	95.56	91.67	84.21	73.97	82
Multifocal opacities CT	21.88	28.21	42.5	37.5	24.14	20.31	20.19

(>45 IU/L), and 29.72% of patients with an elevated serum bilirubin levels. Serum urea (>7.85 mmol/L) and creatinine (>106.5 mmol/L) were elevated in 20.87% and 11.16% of patients respectively.

DISCUSSION

SARS is a new contagious and rapidly progressive infectious disease with substantial morbidity and mortality. SARS-CoV antibodies (IgM or IgG) cannot be tested until 10 d later after infection[8-11]; and virus RNA (by RT-PCR) can be found in nasopharyngeal aspirates or blood samples of patients at the early stage of illness, but it is difficult to be used in all hospitals. So, in 2003, reliable, rapid and simple diagnostic test was not available for the diagnosis of SARS. The criteria for SARS relied on the definition by the World Health Organization (WHO), a probable case of SARS is an individual with fever [temperature >38 ℃], low respiratory tract symptoms, and contact with a person believed to have had SARS or a history of travel to a region where there has been documented transmission of the illness, and present abnormality on chest radiograph. All our subjects matched with the above criteria. Though a worldwide SARS outbreak in 2003 was controlled, it is unfortunate that several cases of SARS have been reported in the early spring of 2004. Therefore, SARS is still a potential health crisis putting humans at danger. Then, a clear picture of clinical feature for SARS is very valuable to medical personnel to alert the possibility of SARS. In this study, our aim is to describe the characteristics of SARS in different periods of the course. In the data derived from 801 probable SARS cases, at the initial stage of this illness (1-3 d), the predominated symptom was fever, accompanied with the prodromal symptoms due to the viremia. An important abnormality in routine blood count was to present lymphonemia, especially, the counts of CD3, CD4, CD8 positive T lymphocytes reduced dramatically. It has been proved[12,13] that the mechanism of SARS is the SARS-CoV attacking the T lymphocyte and triggering the immune response, causing a series of pathogenic immune damage in tissue or organs of the infected patients. SARS presents predominantly with infiltrates on chest radiographs[14-17]. In our study, the chest radiographic examination showed the infiltrates occurred early (in more than 90% of patients), which is different from the pneumonia caused by the bacteria and common virus.

In the later 4-7 d, the vast majority of patients persisted with high fever, but the prodromal symptoms appeared to be alleviated, the low respiratory tract symptom and abnormalities on chest radiographs began to deteriorate. The most specific feature in this period was that the lymphonemia, and low count of CD3, CD4, CD8 positive T lymphocytes had worsened. These data indicate that the immune response in body caused by SARS-CoV reaches the highest peak and starts to produce pathologic lesions in tissue and organs. We take the name of this period as progressive stage.

In the period from 8 to 16 d, the patients had progressive low respiratory symptoms, the air-space opacities in chest increased in size, extent and severity in majority of patients, some of them appeared to have diffuse opacification and required noninvasive ventilation, even the mechanical ventilation

owing to the respiratory failure. Some patients developed damage of liver, kidney or other organs. The lung biopsy specimen obtained at autopsy[18,19] had shown diffuse alveolar damage with pulmonary congestion, edema and formation of hyaline membrane. So, this period is the most danger phage in the whole course of SARS, and is named as fastigium stage.

When the first 2 wk passed, the patients presented the normal temperature and hardly had the prodromal symptoms, with the exception of some patients having only fatigue. The counts of lymphocyte and its subtype cells (CD3, CD4, CD8) gradually increased, meaning the pathologic damage by immune response stopped. Patients showed an improvement of respiratory symptoms and in the air-space opacities. About 3 wk later, the symptoms almost disappeared, the counts of lymphocyte and its subtype cells turned back to the normal levels and body's immune function also returned to normal. The infiltrates in lung were gradually absorbed and disappeared. But we found occasionally patients (in 10.29-17.35% patients) still presented abnormal shadows on lung at the 6th and 7th wk after onset of illness. So, the convalescence of SARS in some patients may need a longer time to recover, about 3-4 wk, more ever, some of them could remain with interstitial fibrosis in lung.

In summary, at the early stage of SARS (1-3 d), the most common symptoms were fever and the prodromal symptoms. The low respiratory symptoms also occurred early with moderate hypoxemia, but usually lacking of rales. The majority of patients had the reducing counts of CD3 (+), CD4 (+) and CD8 (+) T cells, about one-third of the patients developed lymphopenia. Most patients presented infiltrates on chest radiograph, but about 20% and 10% of patients had normal results of chest X-ray and CT examination respectively on admission. At the progressive stage (4-7 d), the patients still had high fever, the low respiratory symptoms and inflammation in lung began to progress, almost all patients had abnormality on chest radiograph, the counts of CD3 (+), CD4 (+) and CD8 (+) T cells reached the lowest levels. The fastigium stage (8-16 d), patients may occur with serious chest distress and shortness of breath, some with cough and sputum produce, the air-space opacities on chest deteriorated quickly, some of them showed diffuse infiltrates and developed respiratory function failure, even ARDS. At the convalescent stage (17-28 d), patients' temperature were normal, symptoms almost disappeared, the counts of lymphocyte and its subtype cells increased to the normal values, and the infiltrates in lung were gradually absorbed and disappeared.

REFERENCES

1 **Peiris JS,** Lai ST, Poon LL, Guan Y, Yam LY, Lim W, Nicholls J, Yee WK, Yan WW, Cheung MT, Cheng VC, Chan KH, Tsang DN, Yung RW, Ng TK, Yuen KY. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet* 2003; **361**: 1319-1325

2 **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**: 1953-1966

3 **Drosten C,** Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, Rabenau H,Panning M, Kolesnikova L, Fouchier RA, 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 AD, Schmitz H, Doerr HW. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 2003; **348**: 1967-1976

4 **Lee N,** Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, Yung MY, Leung CB, To KF, Lui SF, Szeto CC, Chung S, Sung JJ. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003; **348**: 1986-1994

5 **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**: 1977-1985

6 Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, Walmsley SL, Mazzulli T, Avendano M, Derkach P, Ephtimios IE, Kitai I, Mederski BD, Shadowitz SB, Gold WL, Hawryluck LA, Rea E, Chenkin JS, Cescon DW, Poutanen SM, Detsky AS. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA* 2003; **289**: 2801-2809

7 **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

8 **Lu HY,** Huo N, Wang GF, Li HC, Nie LG, Que CL, Li J, Li YH, Gao XM, Zhang ZD, Zhuang H, Xu XY. The factors affecting on the produce of IgG antibody in SARS patients . *Shijie Huaren Xiaohua Zazhi* 2004; **12**: 723-725

9 **National Research Project for SARS, Beijing Group**. Serum antibodies detection for serological diagnosis of severe acute respiratory syndrome. *Zhonghua Jiehe he Huxi Zazhi* 2003; **26**: 339-342

10 **World Health Organization**. SARS: availability and use of laboratory testing, 2003/04/24

11 **World Health Organization**. Update 71 Status of diagnostic tests, training course in China, 2003/06/02

12 **Li TS,** Qiu ZF, Han Y, Zhang HW, Wang Z, Liu ZY, Fan HW, Lv W, Yu Y, Wang HL, Zhang HY, Xie J, Zhou BT, Ma XJ, Ni AP, Wang AX, Deng GH. The alterations of T cell subsets of severe acute respiratory syndrome during acute stage. *Zhonghua Jianyan Yixue Zazhi* 2003, **26**: 297-299

13 **Yin CB,** Zhang FC, Tang XP, Chen WL, Chen YQ, Wang J, Jia WD. Measurement of subsets of blood T lymphocyte in 93 patients with severe acute respiratory syndrome and its clinical significance. *Zhonghua Jiehe He Huxi Zazhi* 2003; **26**: 343-346

14 **Zeng QS,** Chen L, Cai X, Chen RC, Xie NW, Zhong NS. Chest Xray and CT in the diagnosis of SARS. *Zhonghua Fangshexue Zazhi* 2003; **37**: 601-603

15 **Du XK,** Yu WJ, Wang SL, Zhu QJ, Hong N. Preliminary analysis of clinical images of SARS. *Zhonghua Fangshexue Zazhi* 2003; **37**: 780-783

16 **Wang W,** Ma DQ, Zhao DW, Chao CH, Guo YB, Wu H, Yuan CW, Duan Y, Lang ZW. CT appearances and dynamic changes in severe acute respiratory syndrome. *Zhonghua Fangshexue Zazhi* 2003; **37**: 686-689

17 **Zhao DW,** Ma DQ, Wang W, Wu H, Yuan CW, Jia CY, He W, Chen JH. Early Xray and CT manifestations of SARS. *Zhonghua Fangshexue Zazhi* 2003; **37**: 597-599

18 **Lai RQ,** Feng XD, Wang ZC, Lai HW, Tian Y, Zhang W, Yang CH. Clinicopathological and ultramicrostructural changes of tissus in a patient with severe acute respiratory syndrome. *Zhonghua Binglixue Zazhi* 2003; **32**: 205-208

19 **Chen J,** Xie YQ, Zhang HT, Wan JW, Wang DT, Hu CH, Wang QC, Xue XH, Si WX, Luo RF, Qiu HM. Lung pathology of severe acute respiratory syndrome. *Acta Acad Med Sin* 2003; **25**: 336-360

Science Editor Guo SY **Language Editor** Elsevier HK