Clinical features of probable severe acute respiratory syndrome in Beijing

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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 (22.56% of patients) lymphocyte (70.25%) and CD4, CD8 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 (29.96%) and shortness of breath (35.34%) increased, so did the abnormal rates on chest radiograph or CT. The low counts of WBC, lymphocyte and CD4, CD8 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 CD4, CD8 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.

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Key words: SARS; Clinical features; Clinical stage

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 (19.23%) 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, and 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 (SaO2) 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 (PaO2) 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 PaO2, and the mean of PaO2 was 15.5±2.4 kPa. The medians of low PaO2 and SaO2 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 subsequently reduced. On the 4th wk, 40% of patients presented low PaO2, and the mean of PaO2 was 15.5±2.4 kPa. The medians of low PaO2 and SaO2 occurred at the 3rd and 1st d respectively, and recovered to the normal levels in the later 8 and 9.5 d, respectively.

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 level (>40 IU/L, ALT), 44.34% of patients with an elevated serum AST levels
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(>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 °C], 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 lymphopenia, 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 lymphopenia, and low count of CD3, CD4, CD8 positive T lymphocytes reduced dramatically. It has been proved[8-11] that the mechanism of SARS is the SARS-CoV attacking the T lymphocyte and triggering the immune response, causing a series of pathologic 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.

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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 dangerous phase in the whole course of SARS, and is named as festastage period.

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 immunity also returned to normal. The infiltrates in lung were gradually absorbed and disappeared. But we found its subtype cells turned back to the normal levels and body’s symptoms and in the air-space opacities. About 3 wk later, the temperatures 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 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 symptoms and in the air-space opacities.

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.

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