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Brief communication

Clinical and laboratory characteristics of severe fever with thrombocytopenia syndrome in Chinese patients

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ABSTRACT

Severe fever with thrombocytopenia syndrome (SFTS) associated with severe fever with thrombocytopenia syndrome virus (SFTSV) is an emerging infectious disease. 12 patients with severe fever with thrombocytopenia syndrome in our study were presented mainly with fever and severe malaise. The clinical manifestations typically became worse on the 6th or 7th day. The average fever time is 9.11 ± 1.54 days. Most of them had multiorgan dysfunction, and part of them had hemophagocytic lymphohistiocytosis histiocytosis (HLH). The characteristic laboratory findings in the early stage were the drop of white blood cells (WBC), platelets (PLT) and serum Ca++, while increase of aspartate amino transferase (AST), creatine kinase (CK), and lactate dehydrogenase (LDH). CD3+CD4+ were significantly decreased, while CD3-CD56+ were significantly increased, whereas CD3+CD8+ were constantly elevated throughout the disease course. Ten to 14 days after illness onset, symptoms were improved, accompanied by resolution of laboratory abnormalities. These results indicate that severe fever with thrombocytopenia syndrome has an acute onset and self-limited course. It is a systemic infection. The host immune response caused tissues and organs injury. The improvement of symptoms and laboratory tests is consistent with the elimination of the virus and recover of immune response. Further investigation should be done in order to better understand this disease and guide the clinical treatment.

Accumulating clinical cases with fever, thrombocytopenia and multiorgan dysfunction have been reported in Jiangsu Province of China since middle 1990s.[1,2] In 2010, newly emerging patients with the same symptoms in Hubei, Henan provinces and several other provinces were reported,[3,4] and then a new virus named severe fever with thrombocytopenia syndrome bunyavirus (SFTSV) was confirmed[5] by sequencing the whole genome of the virus. Viruses of the Bunyaviridae family are classified into five genera: Orthobunyavirus, Hantavirus, Phlebovirus, Nairovirus, and Tospovirus. The first four genera can infect mammalian hosts. Most bunyaviruses are transmitted by arthropod vectors such as sandflies, mosquitoes, and ticks, whereas the Hantaviruses are maintained in the natural environment as persistent infections of rodents.[6] These viruses can cause hemorrhagic fevers such as Rift Valley fever (RVF), Crimean-Congo hemorrhagic fever (CCHF), hemorrhagic fever with renal syndrome (HFRS), and Sicilian sandfly fever (SFS) in human beings. They may also

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cause encephalitis and acute respiratory diseases.[7] Currently, HFRS and CCHF are endemic in China, and HFRS is an important infectious disease in Jiangsu province.[8]

Twelve SFTS patients who were admitted to our department from May to August 2011 were enrolled in this analysis. The disease was confirmed according to the Clinical Guidelines on Severe Fever with Thrombocytopenia Syndrome (2010 Edition)[9] released by the Ministry of Health of the People's Republic of China. All the data including the clinical data, laboratory findings, imaging results, and outcomes were retrospectively collected by infectious disease physicians. The disease course was divided into four phases: phase1 (days 1–7), phase2 (days 8–10), phase3 (days 11–13), and phase4 (after the 14th day). The changes in serum creatinine, kinases, electrolytes and peripheral blood lymphocyte subsets were monitored and analyzed. All laboratory tests were performed in the First Affiliated Hospital of Nanjing Medical University, except for the real-time PCR to confirm SFTSV RNA from patients in acute stage (within 14 days since onset) that was performed in Jiangsu CDC.

The statistical analysis was performed using SPSS software 17.0 for Windows. Means for continuous variables were compared using independent-group Student's *t* tests when the data were normally distributed after Kolmogorov–Smirnov test; otherwise, the rank sum test was used. A p-value of <0.05 was considered statistically significant.

These 12 patients (8 men and 4 women) were aged between 43 and 79 years (mean: 64.0 years). Ten patients were farmers living in hilly regions, one was a forest ranger, and the remaining one was a driver who went fishing in an open-water environment four days before disease onset. Five patients believed that they had ever been bitten by ticks. One had diabetes mellitus and one had undergone prostate resection. All these patients were admitted to the hospital at the 3rd to 7th day from onset of illness (median: at the 6th day). The disease onset was acute in all patients. Whole body sore, extreme fatigue, and fever (temperatures of 38 °C or higher) were also noted. The clinical manifestations typically became worse on the 6th or 7th day when the temperature reached 40 °C. When patients were transferred to our hospital 6–7 days after disease onset, they complained of extreme fatigue (100.0%), dizziness (83.3%) and chest distress (50.0%). Most of them felt abdominal pain (91.7%), diarrhea (91.7%), muscular soreness (75.0%), nausea and vomiting (66.7%). Erosion in the oral cavity (41.7%), mental sluggishness (25%), petechiae and ecchymosis in the skin (33.3%), abdominal tenderness, and superficial lymph nodes (25%) at the same side of the tick-bitted site were also found. Ecchymosis in the skin, and melena and bleeding in the cavity (41.7%) were also observed in patients with severe symptoms. They also presented with wet rales, wheezing sound, hypoxemia, and some nervous system symptoms such as dysphoria, hyperalgia, disturbance of consciousness, hyperspasmia, and status epilepticus. Three patients ultimately died of viral meningoencephalitis, hypoxemia, disseminated intravascular coagulation (DIC), and multiple organ failure. Three of the nine surviving patients persisted with viremia constantly. Viral RNA of one patient was undetectable at day 9 and two at day 10. The body temperature returned normal when virus RNA detection turned out negative, with a temperature recovery time of 9.11 ± 1.54 days.

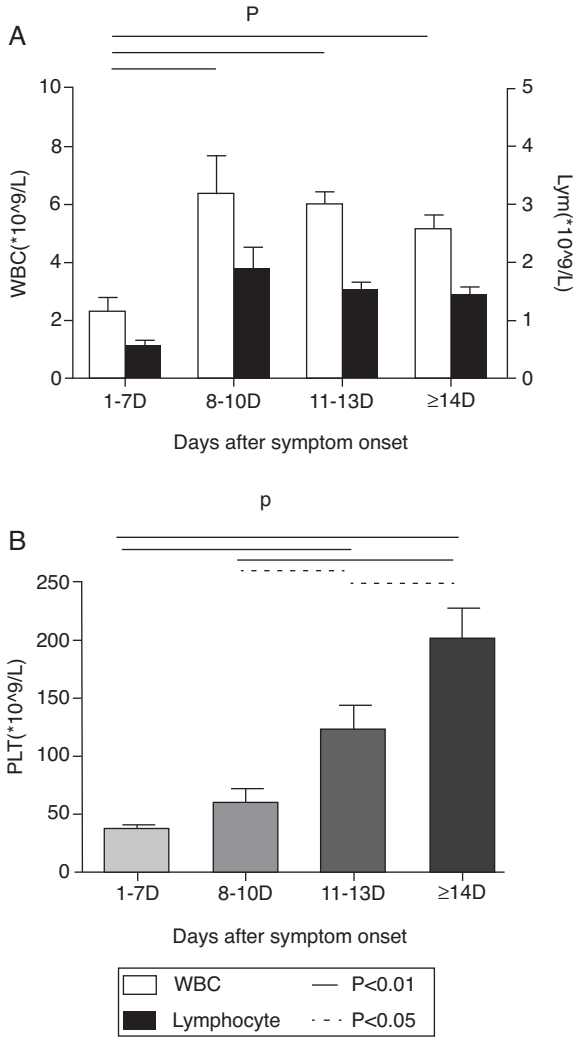

Fig. 1 – Change of WBC, Lymphocytes, and PLT. Changes of WBC and Lymphocyte are shown in A. Changes of PLT are shown in B.

At the first week after disease onset, white blood cell (WBC), lymphocyte and platelet (PLT) counts dropped to the valley levels. Then, at day 8–10, WBC and lymphocyte started to increase, while PLT rose up slowly until day 11–13. The WBC and lymphocyte counts at phase1 were significantly lower than at phases 2, 3, and 4 ($p < 0.01$), while the PLT count at phase 1 was significantly lower than at phases 3 and 4 ($p < 0.01$) and the PLT count at phase 2 was significantly lower than at phase 4 ($p < 0.01$). There was no difference of WBC and lymphocyte counts, but a statistical difference of PLT count was found between phase 2 and phase 3, as well as between phase 3 and phase 4 in pair-wise comparison ($p < 0.05$) (Fig. 1). Urine protein and, microscopically, red blood cells were detected in all 12 patients at the early stage. The average time of urine normalization was 14.11 ± 2.20 days. The LDH, CK, and AST levels remarkably increased at the early stage, and CK and AST remained so for 10 days while LDH returned to normal after 13 days (Fig. 2), in contrast to the ALT level that elevated slightly. BUN and Cr remained normal. Serum Ca^{++} was reduced until day 13. Compared to those in the mid- to late-stage (day 8–13),