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Epidemiological characteristics of severe fever with thrombocytopenia syndrome in Zhejiang Province, China

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SUMMARY

Objectives: To summarize the epidemiological characteristics of severe fever with thrombocytopenia syndrome (SFTS) in Zhejiang Province, China.
Methods: A standardized questionnaire was used to collect information on demographic features, exposure history, clinical symptoms, and timelines of medical visits. Descriptive statistics were used to analyze the characteristics of SFTS.
Results: A total of 65 cases of SFTS were identified in Zhejiang Province from 2011 to 2013, of whom 34 were male and 31 were female. The median age was 66 years and 60 cases occurred in persons aged ≥50 years. The majority (91%) of SFTS cases occurred between May and August. With regard to exposure history, patients had pursued outdoor activities (63%), had a history of exposure to a tick (68%) or tick bite (29%), bred domestic animals (31%), or had a history of exposure to a mouse (57%), and some patients had a multi-exposure history. Approximately 98.46% of patients were hospitalized, and symptoms of the illness included fever (98%), fatigue (71%), chills (51%), etc. Two family clusters occurred, although there was no person-to-person transmission.
Conclusions: In Zhejiang Province, SFTS is prevalent between May and August among elderly persons who live in hilly areas, and clinical features are not specific. More emphasis should be given to this disease and further training of medical personnel should be carried out to prevent misdiagnosis.

1. Introduction

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging infectious disease discovered in China and is caused by a novel bunyavirus, SFTS virus (SFTSV). SFTSV is classified in the family *Bunyaviridae*, genus *Phlebovirus*, and is believed to be transmitted by ticks because the virus has been detected in *Haemaphysalis longicornis* ticks.[1] The major clinical symptoms and laboratory abnormalities of SFTS are fever, thrombocytopenia, leukopenia, and elevated serum hepatic enzymes, and death in SFTS patients is usually the result of multiple organ failure.[1] The clinical symptoms, however, are less specific and need to be differentiated from those of various other infectious diseases, in particular from hemorrhagic fever with renal syndrome (HFRS) caused by hantavirus and human anaplasmosis.[2,3]

In 2011–2012, 2047 cases of SFTS and 129 deaths were reported in over 206 counties of eastern and central China.[4] Cases of SFTS were also identified in Zhejiang Province, and a total of 65 cases were reported in recent years according to the information system for disease control and prevention.[5–7] Here, we analyze the epidemiological and clinical characteristics of SFTS in Zhejiang Province to provide scientific information for the control and prevention of SFTS.

2. Methods

2.1. Case definition

In accordance with the document entitled "The diagnosis and treatment programs of severe fever with thrombocytopenia syndrome" issued by the Chinese Ministry of Health,[8] an acutely ill person with acute onset of fever (≥38.0 °C) and other symptoms (e.g., gastrointestinal symptoms, bleeding), epidemiological risk factors (being a farmer or being exposed to ticks 2 weeks before

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illness onset), and laboratory data showing thrombocytopenia and leukocytopenia, was defined as a suspected case of SFTSV. Confirmed cases of SFTSV infection were defined as those who met the criteria for a suspected case of SFTSV and who also met one or more of the following criteria: (1) detection of SFTSV RNA by a molecular method, (2) seroconversion or ≥4-fold increase in antibody titers between two serum samples collected at least 2 weeks apart, and (3) isolation of SFTSV in cell culture.

2.2. Laboratory test assays

Serum samples obtained from the patients with suspected SFTS were sent to the laboratory of the Zhejiang Provincial Center for Disease Control and Prevention (CDC). Laboratory measurements of SFTSV RNA by real-time reverse-transcription PCR (RT-PCR), of SFTSV-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies, and isolation of SFTSV were performed as described previously.[6]

2.3. Data collection

The aims of our study were explained to all patients and their consent was obtained prior to inclusion in this study. A standardized questionnaire was used to collect information on demographic features (age, gender, occupation, and residential address), exposure history, clinical signs and symptoms, date of onset, date of first medical visit, and date of confirmation. Exposure history collected included habitats of their place of residence, outdoor activities within 2 weeks before illness onset, exposure to a tick within a month before illness onset, history of tick bite within 2 weeks before illness onset, skin breakdown within 2 weeks before illness onset, breeding domestic animals, contact with wildlife, and history of exposure to a mouse within a month before illness onset.

2.4. Data analysis

Descriptive statistics were used to analyze the epidemiological characteristics and clinical characteristics of SFTS in Zhejiang Province, China. We used the Wilcoxon Rank Sum W test to compare the age distribution of patients with SFTS who survived and those who died. The Chi-square test or Fisher's exact test were used to compare symptoms between survivors and those who died. The difference was considered statistically significant when $p < 0.05$. The statistical analysis was performed using SPSS software (SPSS 17.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Epidemiological characteristics

A total of 65 laboratory confirmed cases of SFTS were identified in Zhejiang Province from 2011 to 2013, of whom 34 were male and 31 were female. All patients lived in wooded, hilly areas and the majority of them were farmers (92%). The median age of confirmed patients was 66 years (range 31–84 years), and 60 cases (92%) occurred in persons aged ≥50 years (Figure 1). Moreover, nine deaths occurred (case fatality rate, 14%) and the age distribution of patients who died was significantly different to that of survivors ($Z = -2.034$, $p = 0.042$ (<0.05)). The majority (91%) of SFTS cases during 2011–2013 in Zhejiang Province occurred yearly between May and August (Figure 2). However, two cases were reported in March and two cases were reported in October in 2013.

All cases occurred in 13 counties that were members of five cities, and the number of counties in which SFTS was identified increased from 2011 to 2013 (Figure 3). The cities with the highest

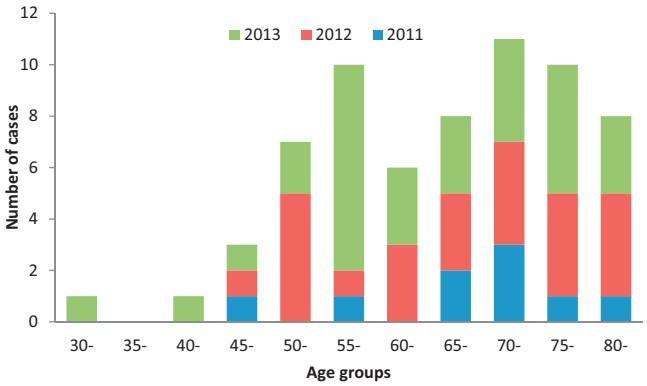

Figure 1. Age distribution of SFTS in Zhejiang Province, China.

numbers of reported cases were Zhoushan (69%) and Ningbo (18%). Of note, 63% (41/65) of cases were identified in Daishan County, which is a part of Zhoushan located in eastern Zhejiang Province. Daishan County is comprised of seven towns, and SFTS was indentified in five of them (Figure 4). Gaoting town and Dongsha town accounted for 68% (28/41) of patients in Daishan County.

All cases lived in hilly areas within a month before illness onset and 63% (41/65) of cases had performed outdoor activities within 2 weeks before illness onset. Of these, 36 cases farmed, 10 cases mowed, and three cases grazed (Table 1). Six cases had a history of farming and mowing, and one case had a history of farming, mowing, and grazing. Among the 65 cases, 27 of 40 with data available had a history of exposure to a tick in the month before illness onset, but only 12 of 41 cases with data available had a history of a tick bite before illness onset. In addition, 14% (9/65) of cases had skin breakdown within 2 weeks before illness onset, 31% (20/65) of cases bred domestic animals, and 57% (30/53) of cases had a history of exposure to a mouse within a month before illness onset. However, no case had a history of contact with wildlife. Of note, nine cases had a multi-exposure history to domestic animals and mice; four cases had a multi-exposure history of tick bite and mouse contact; two cases had a multi-exposure history of tick bite and contact with domestic animals; two cases had a multi-exposure history of tick bite and contact with domestic animals and mice. The estimated median incubation period for 12 confirmed cases with a history of tick bite was 12 days (range 2–47 days).

3.2. Clinical characteristics

Approximately 99% of patients were hospitalized, and symptoms of the illness included fever (98%), fatigue (71%), chills (51%),

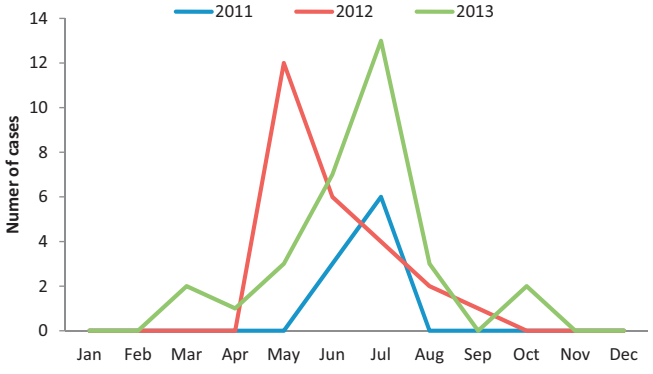

Figure 2. Monthly distribution of SFTS in Zhejiang Province, China.