

# Severe Fever with Thrombocytopenia Syndrome Virus: The First Case Report in Thailand

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### Abstract

We report a case of a 70-year-old Thai woman with severe fever and thrombocytopenia syndrome, who had lost all seven of her cats from sickness over a week. Diagnosis was established by the detection of viral RNA in serum via real-time polymerase chain reaction. Her symptoms improved after taking doxycycline orally and supportive treatment.

**Keywords:** severe fever with thrombocytopenia syndrome virus, *Phlebovirus*, encephalopathy

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging tick-borne disease in China, South Korea and Japan. This is caused by the SFTS virus (SFTSV), which belongs to the genus *Phlebovirus*, family *Bunyaviridae*.<sup>1,2</sup> We are reporting the first adult case of SFTS discovered, with classical features of SFTS.

### Case report

A 70-year-old woman who was referred from another hospital presented with high-grade fever and diarrhea for 3 days. Upon admission, her body temperature was 39.1°C and her vital signs were stable. The remainder of her detailed physical examination was unremarkable. Laboratory tests showed that her white blood cell count had dropped to 3,700 cells/mm<sup>3</sup> (89% neutrophils and 9% lymphocytes), the platelet count was 177,000/mm<sup>3</sup> and dengue Immunoglobulin M (IgM) was negative. A diagnosis of acute gastroenteritis was made. Ceftriaxone was prescribed intravenously.

After two days of admission, the patient developed an alteration of consciousness. A brain magnetic resonance imaging (MRI) and lumbar puncture were performed. The MRI result was normal. Cerebrospinal fluid (CSF) analysis showed that her red blood cell (RBC) was 20 per microliter, there was no pleocytosis, mildly elevated protein level (67 mg/dl) and normal glucose level. Bacterial culture of CSF yielded had no growth. CSF polymerase chain reaction (PCR) for viral panel was negative. Later, she was referred to Phyathai 3 Hospital.

From the first presentation, she was febrile with temperature of 39°C. The level of consciousness had decreased (Glasgow Coma Score of 9) and she had apparent neck stiffness on physical examination. Motor power was at least grade 3 with a spastic tone of all extremities. An electroencephalogram (EEG) was done. The background activity was moderately slow, indicating the patient had encephalopathy. There was no epileptiform discharge. The laboratory results were remarkable for leukopenia (white blood cell count was 2,100 cells/mm<sup>3</sup> with 45% neutrophils and 50% lymphocytes), and thrombocytopenia (platelet count was 88,000/mm<sup>3</sup>). High D-dimer (2.96 ug/ml), coagulopathy and peripheral blood smear showed decreased number of platelets, few schistocytes, few polychromasia compatible with

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disseminated intravascular coagulation (DIC). Liver function test results were elevated, aspartate aminotransferase, 814 IU/L and alanine aminotransferase, 142 IU/L. Serum creatine phosphokinase and lactate dehydrogenase were elevated at 1,336 U/L and 2,407 U/L. Dengue PCR was negative. Furthermore, serum autoimmune and paraneoplastic encephalopathy panel was also negative. Meningoencephalitis was suspected. Therefore, acyclovir, ceftriaxone, levetiracetam intravenously and doxycycline orally were prescribed.

On the second day of hospitalization, she developed upper gastrointestinal bleeding and gross hematuria. After fluid resuscitation therapy and blood component replacement, she underwent esophagogastroduodenoscopy (EGD) to stop her bleeding. EGD revealed multiple gastric ulcers (GU) with blood oozing at the gastric fundus. Bleeding from GU was endoscopically treated by adrenaline injection, hemoclips, and bipolar probe coagulation.

Further questioning revealed that 1-month prior, her seven cats got sick and died within a week. We obtained saliva, serum, hairline, urine and CSF samples for rabies testing, with the results being negative. Severe fever with thrombocytopenia syndrome virus (SFTSV) RNA was detected in serum samples by real-time PCR, so a diagnosis of SFTS was made. According to the PCR results, acyclovir and ceftriaxone were no longer prescribed, but doxycycline was continued for 10 days. Indirect Immunofluorescence Antibody (IFA) IgM and IgG for *Rickettsia typhi*, *Orientia tsutsugamushi* and Leptospirosis on the fifteenth day of the illness were also negative. The patient gradually improved and was afebrile. Her level of consciousness nearly increased to normal status. She had gradual improvement in orientation, memory, and decreased spastic tone on physical examination.

The standard contact and droplet precautions had been started since we suspected her of being infected by viral encephalitis. There were 56 healthcare workers who had either direct or indirect contact with the patient. Once PCR test revealed that the patient was infected by SFTSV, we followed up signs and symptoms of all contact cases for 14 days, starting from their recent contacts with the patient. Fortunately, none of them had any SFTS-like symptoms.

The Surveillance and Rapid Response Team (SRRT) from the Urban Institute for Disease Control and Prevention, Department of Disease Control, visited the hospital and the patient's house. All patients' family members presented no signs and symptoms. Serum SFTSV PCR tests gave negative results. The samples of ticks from dogs (*Rhipicephalus sanguineus*) and ticks of rats in the neighborhood also showed no infection. However, there was no tick sample from cats.

### Discussion

SFTS is an emerging infectious disease caused by SFTSV, a member of genus *Phlebovirus*, in the family *Bunyaviridae*.<sup>1,2</sup>

This disease was first reported in rural areas of China during 2010. From the initial report, SFTS cases have been described in South Korea, Japan, and Vietnam.<sup>1-5</sup> From our review, there was no report of SFTS indicated in Thailand.

SFTS is mainly transmitted by infected ticks, primarily found in *Haemaphysalis longicornis*, derived from sheep, cattle and dogs.<sup>2,6,7</sup> However, the report of human-to-human transmission by direct contact with blood and body secretions and via needle-stick injury have been found.<sup>8,9</sup>

The clinical manifestations of SFTS begins with a nonspecific prodrome, including fever, anorexia, fatigue, nausea, abdominal pain, vomiting, diarrhea, myalgia, headache, malaise, arthralgia, and dizziness. Meningoencephalitis and multiorgan dysfunction may develop, including acute kidney injury, liver enzyme elevation and disseminated intravascular coagulation.<sup>1-4,10</sup>

Leukopenia and thrombocytopenia are most commonly found in laboratory testing. Other laboratory abnormal results may include elevated serum levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, creatine kinase and ferritin levels.<sup>1-3</sup>

Reverse-transcriptase polymerase chain reaction (RT-PCR) is a method to detect viral RNA in serum, generally 1-6 days after onset. SFTSV virus-specific antibodies are detectable during the second and third weeks of illness.<sup>1</sup>

There is no specific treatment for SFTS. However, there have been a few studies reporting co-infections with SFTSV and Rickettsial infections. Doxycycline could be administered in suspected cases of co-infection.<sup>11,12</sup> Scrub typhus and Murine typhus are endemic in Thailand. Our patient was empirically treated with doxycycline and tested for antibodies against *Rickettsia typhi* and *Orientia tsutsugamushi*.

### Conclusion

The disease begins with fever and nonspecific prodrome symptoms, followed by encephalitis and multi-organ failure. RT-PCR is used for detection of SFTSV in serum. SFTS should be considered in a patient with a history of tick or animal exposure.

### Acknowledgements

We are grateful for the support from the Surveillance and Rapid Response Team (SRRT) from Department of Disease Control who provided us with the case definition information and sample investigations.

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