Virologica Sinica 39 (2024) 513–515

Contents lists available at ScienceDirect

Virologica Sinica

journal homepage: www.keaipublishing.com/en/journals/virologica-sinica
www.virosin.org

Letter

Severe fever with thrombocytopenia syndrome virus infection attributed to cat contact: A case report in Beijing, China

Shuo Zhang [a,b,1], Yu Leng [b,1], Fa-Xue Zhang [c], Bo-Kang Fu [b,d], Bing-Zheng Wu [b], Jia-Hao Chen [b], Ning Cui [e], Ning Zhao [a,*], Wei Liu [a,b,d,*], Hao Li [b,c,*]

[a] College of Life Sciences, Southwest Forestry University, Kunming, 650224, China
[b] State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, Beijing Key Laboratory of Vector Borne and Natural Focus Infectious Diseases, Beijing, 100071, China
[c] School of Public Health, Wuhan University, Wuhan, 430071, China
[d] The First Affiliated Hospital of Anhui Medical University, Hefei, 230022, China
[e] Xinyang 154 Hospital, Xinyang, 464000, China

Dear Editor,

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging tick-borne infectious disease caused by a novel bunyavirus called SFTS virus (SFTSV). It was initially identified in China in 2009 (Yu et al., 2011). Since then, the number of reported SFTS cases has rapidly increased in China, South Korea, and Japan (Li, et al., 2018; Takahashi et al., 2014; Kim et al., 2018). Sporadic SFTS cases have also been identified in several other Asian countries, such as Vietnam, Pakistan, Myanmar, and Thailand (Takahashi et al., 2014; Tran et al., 2019; Li et al., 2021). This disease is recognized as a highly lethal viral hemorrhagic fever with a mortality rate ranging from 12% to 50% (Yu et al., 2011; Li et al., 2018; Takahashi et al., 2014; Kim et al., 2013). SFTS primarily spreads to humans through bites from ticks infected with SFTSV, with the *Haemaphysalis longicornis* tick acting as the predominant vector for SFTSV (Zhuang et al., 2018). *H. longicornis* typically thrives in shrub grasslands and shows a positive association with the coverage of rural settlement. By far, it is the most widely distributed tick species in eastern and northeastern China. Individuals residing in rural or mountainous areas are facing a high risk of infection (Zhao et al., 2021). Local infections of SFTSV among individuals residing in rural–urban fringe or highly urbanized areas dominated by artificial forests, rather than natural habitats, are extremely rare. Human-to-human transmission of SFTSV through exposure to blood or bloody secretions from SFTS patients has been increasingly reported (Wu et al., 2022). Additionally, citizens living in areas endemic for SFTS may be at risk of infection through contact with infected community cats (Kida et al., 2019; Yamanaka et al., 2020; Tsuru et al., 2021).

A 60-year-old male was admitted to Xinyang 154 Hospital of Henan Province on July 13, 2023, presenting with a fever (temperature up to 38.8 °C), fatigue, myalgias, anorexia, and nausea for a duration of five days. He had previously received treatment with ibuprofen and cephalosporin for three days without any improvement of the conditions. The diagnosis of SFTSV infection ($10^{5.4}$ copies/mL) was confirmed through reverse-transcription quantitative real-time polymerase-chain-reaction (RT-qPCR) analysis of the serum sample collected upon admission. Upon admission, the physical examination showed swollen lymph nodes in the groin area, with no rash or eschar observed. Blood test showed leukopenia (white blood cell count, 2.6×10^9/L), thrombocytopenia (platelet count, 80×10^{12}/L), as well as elevated levels of aspartate transaminase (AST, 179 U/L), alanine transaminase (ALT, 155 U/L), lactate dehydrogenase (LDH, 548 U/L), and creatine kinase (CK, 971 U/L). On July 14th, he developed coughing, vomiting, and diarrhea, along with multiple organs dysfunction characterized by decreased platelet count (64×10^{12}/L), increased liver enzymes, including LDH (926 U/L), CK (1188 U/L), and elevated viral load ($10^{5.9}$ copies/mL). After receiving supportive therapy for five days, he tested negative for SFTSV RNA detection using RT-qPCR assay (Supplementary Table S1). His clinical manifestations and laboratory abnormalities were resolved, except for a slight increase in ALT (95 U/L) and LDH (322 U/L).

A face-to-face interview was conducted, revealing that the patient has been residing in Baixi Village located in Fengtai District of Beijing, China (Fig. 1A) for the past six months, without a history of travel, field activity, or tick bite within the last month. The patient reported having frequent direct contact with four stray cats in the courtyard where he lived and was scratched by one cat two days before the onset of fever. Four days after the onset of illness, he departed from Beijing to seek treatment at Xinyang 154 Hospital in his hometown, Xinyang City, Henan Province, where his medical insurance was active. One week after the patient's illness onset,

* Corresponding authors.
E-mail addresses: lihao_1986@126.com (H. Li), liuwei@bmi.ac.cn (W. Liu), lijiangzhaon@swfu.edu.cn (N. Zhao).
[1] Shuo Zhang, Yu Leng contributed equally to the work.

https://doi.org/10.1016/j.virs.2024.03.006
Received 24 December 2023; Accepted 14 March 2024
Available online 20 March 2024

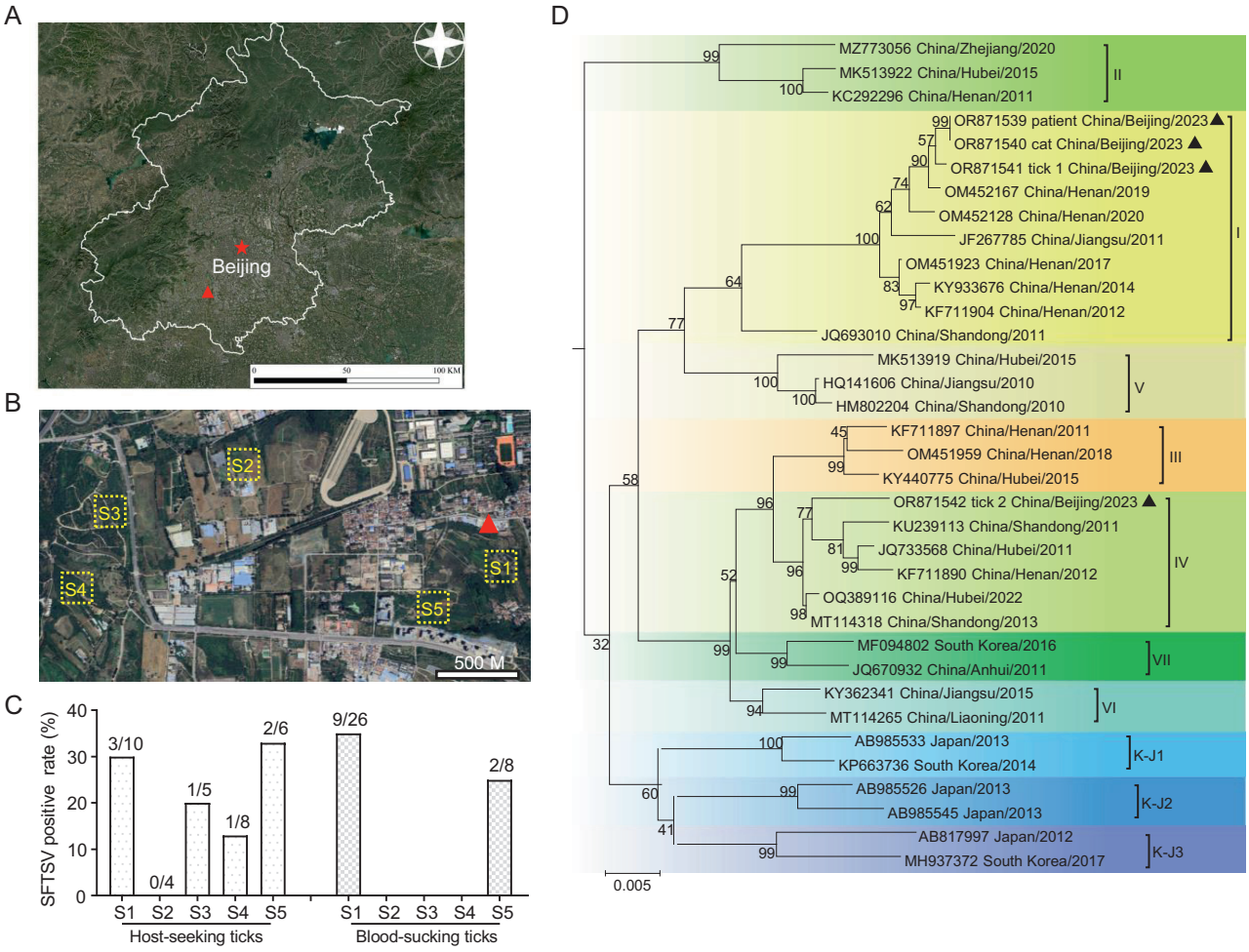

Figure 1. Detection of SFTSV in urbanized areas in Beijing. **A** The location where the patient acquired SFTSV infection, indicated by red triangle. **B** Five sites (S1 to S5) from where tick and cat samples were collected. Cats were living in site 1 (S1). Host-seeking ticks were collected by dragging fabric over vegetation at five sites. Blood-sucking ticks were collected from goats at site 1 (S1) and site 5 (S5). The red triangle indicates the location of the patient. The dotted box indicates the area size of the field survey (200 m*200 m). **C** The positive rate of SFTSV in host-seeking or blood-sucking ticks. Host-seeking ticks were pooled (4–5 ticks per pool) for the detection of SFTSV RNA. The blood-sucking ticks collected from goats were individually tested. **D** Phylogenetic tree was conducted based on nucleotide sequence of nearly complete S segment (1743 bp) of SFTSV with Neighbor-Joining method and 1000 bootstrap replicate using MEGA X software. Corresponding nucleotide sequence of Heartland virus (GenBank accession number JX005842) was used as outgroup. Sequences obtained in this study were indicated as black triangle, with GenBank accession numbers of OR871539 (patient), OR871540 (cat), OR871541 and OR871542 (tick).

whole blood samples were collected from all four cats. SFTSV RNA was detected in one cat that had scratched the patient, with a low viral load ($10^{4.82}$ copies/mL). IgM (titer ≥1:320) and neutralizing antibodies (titer ≥1:200) against SFTSV were detected in two other cats. Additionally, the patient's wife and three neighbors who lived in the same courtyard tested negative for SFTSV RNA, as well as *anti*-SFTSV IgM and IgG antibodies.

To identify local natural foci, a field investigation was conducted to study SFTSV infections in ticks from the areas where the patient resided, 10 days after the patient's illness onset. A total of 168 host-seeking *H. longicornis* adult ticks were collected by dragging fabric over vegetation at five sites, and 34 blood-sucking *H. longicornis* adult ticks were collected from goats at two sites (Fig. 1B and Supplementary Fig. S1). It is worth noting that no ticks were collected from the vegetation in the courtyard or captured from the four cats. SFTSV RNA was detected in 7 out of 33 pooled host-seeking ticks (4–5 ticks per pool) from four sites, with a minimum infection rate of 4.2%, Additionally, SFTSV RNA was found in individually tested blood-sucking ticks from two sites, with an infection rate of 32% (11/34) (Fig. 1C).

The nearly complete genome of the S segment of SFTSV was obtained from the patient, the cat, and two tick pools. The nucleotide sequences of the S segment obtained from both the patient and the cat showed 100% identity (Fig. 1D). Phylogenetic analysis based on a fragment consisting of 1743 bp of S segment revealed two distinct clades of SFTSV. One clade included sequences obtained from both the patient, the cat, and ticks, which suggests a natural focus of SFTSV within surveyed areas in Fengtai District in Beijing.

The detection of SFTSV RNA in cats was initially reported in serum samples from feral cats in South Korea in 2017 (Hwang et al., 2017), and subsequently in pet cats in Japan in 2019 (Kida et al., 2019). Cats were also found to be susceptible to SFTSV through experimental intravenous injection, exhibiting symptoms such as fever, anorexia, leukopenia, thrombocytopenia, and even multiple organs dysfunction post-infection (Park et al., 2019). These findings suggest that cats may play a role in the maintenance and transmission of SFTSV within the natural environment. Recently, several epidemiological studies have disclosed that close contact with infected cats, exposure to blood of infected cats, or

bites from infected cats can transmit SFTSV to humans (Kida et al., 2019; Yamanaka et al., 2020; Tsuru et al., 2021). However, these reports are limited to South Korea and Japan. Here we present the first case of SFTSV infection via cat scratch in China, supported by the following evidence: complete nucleotide sequence analysis showed 100% identity between the patient's and the cat's samples; there were no tick bites or close contact with other SFTS patients; and the onset of SFTS disease developed two days after being scratched by a cat. Importantly, besides a direct bite or scratch from SFTSV-infected cats, transmission of SFTSV from cats to humans may also occur through droplet infection, as SFTSV has been detected in eye swabs, saliva, and urine samples from cats (Park et al., 2019).

Stray cats typically inhabit rural–urban fringe or highly urbanized areas, where they can take advantage of various resources created by human activities. In urban China, cats are the most popular pets, with approximately 65.4 million cats being kept as pets in households in 2022. Consequently, greater attention should be devoted to the potential risk of SFTSV infection through close contact with stray or pet cats among urban residents. Febrile patients who own cats or have had contacts with them should be considered for differential diagnosis of SFTS. Likewise, veterinarians should be aware of potential infection of SFTSV in sick cats in SFTS-endemic regions. Given that stray cats are more susceptible to tick bites, it is imperative to assess the prevalence of SFTSV infection in stray cats residing in urban areas.

Recently, SFTSV was detected in parasitic *H. longicornis* ticks collected from hedgehogs in Shunyi District in Beijing, but not in ticks collected from vegetation (Zhang et al., 2023). Our epidemiological investigation revealed the presence of SFTSV not only in parasitic *H. longicornis* ticks from goats but also in host-seeking ticks collected from vegetation surrounding the patient's residence—an area featured by urbanized ecosystem with artificial forests (Supplementary Fig. S1). This finding strongly supports the natural circulation of SFTSV among ticks and animal hosts within urban areas of Beijing. Our limited-scale field survey identified two viral clades, indicating the existence of multiple genotypes of SFTSV in Beijing. Extensive investigation and active surveillance are necessary to comprehensively determine the distribution and prevalence patterns of SFTSV in ticks and animal hosts across high-risk areas within Beijing metropolitan region. Furthermore, conducting a cross-sectional population-based seroepidemiological study would provide insights into understanding the extent of human exposure and infection rates caused by SFTSV.

Footnotes

This study was funded by the National Nature Science Foundation of China (81,825,019 and 82,330,103). The study was performed with approval from the Ethical Committee of Beijing Institute of Microbiology and Epidemiology (AF/SC-08/02.128). Written informed consent was obtained from the patient. Written informed consent for publication of the clinical details was obtained from the patient. No potential conflict of interest was reported by the authors.

All data generated or analyzed during this study are included in this present study. Supplementary data to this article can be found online at https://doi.org/10.1016/j.virs.2024.03.006

References

Hwang, J., Kang, J.G., Oh, S.S., Chae, J.B., Cho, Y.K., Cho, Y.S., Lee, H., Chae, J.S., 2017. Molecular detection of severe fever with thrombocytopenia syndrome virus (SFTSV) in feral cats from Seoul, Korea. Ticks Tick Borne Dis. 8, 9–12.

Kida, K., Matsuoka, Y., Shimoda, T., Matsuoka, H., Yamada, H., Saito, T., Imataki, O., Kadowaki, N., Noguchi, K., Maeda, K., Mochizuki, Y., Kishimoto, T., 2019. A case of cat-to-human transmission of severe fever with thrombocytopenia syndrome virus. Jpn. J. Infect. Dis. 72, 356–358.

Kim, K.H., Yi, J., Kim, G., Choi, S.J., Jun, K.I., Kim, N.H., Choe, P.G., Kim, N.J., Lee, J.K., Oh, M.D., 2013. Severe fever with thrombocytopenia syndrome, South Korea, 2012. Emerg. Infect. Dis. 19, 1892–1894.

Kim, Y.R., Yun, Y., Bae, S.G., Park, D., Kim, S., Lee, J.M., Cho, N.H., Kim, Y.S., Lee, K.H., 2018. Severe fever with thrombocytopenia syndrome, South Korea, 2010. Emerg. Infect. Dis. 24, 2103–2105.

Li, H., Lu, Q.B., Xing, B., Zhang, S.F., Liu, K., Du, J., Li, X.K., Cui, N., Yang, Z.D., Wang, L.Y., Hu, J.G., Cao, W.C., Liu, W., 2018. Epidemiological and clinical features of laboratory-diagnosed severe fever with thrombocytopenia syndrome in China, 2011–17: a prospective observational study. Lancet Infect. Dis. 18, 1127–1137.

Li, J.C., Wang, Y.N., Zhao, J., Li, H., Liu, W., 2021. A review on the epidemiology of severe fever with thrombocytopenia syndrome. Zhonghua Liuxingbingxue Zazhi 42, 2226–2233.

Park, E.S., Shimojima, M., Nagata, N., Ami, Y., Yoshikawa, T., Iwata-Yoshikawa, N., Fukushi, S., Watanabe, S., Kurosu, T., Kataoka, M., Okutani, A., Kimura, M., Imaoka, K., Hanaki, K., Suzuki, T., Hasegawa, H., Saijo, M., Maeda, K., Morikawa, S., 2019. Severe fever with thrombocytopenia syndrome phlebovirus causes lethal viral hemorrhagic fever in cats. Sci. Rep. 9, 11990.

Takahashi, T., Maeda, K., Suzuki, T., Ishido, A., Shigeoka, T., Tominaga, T., Kamei, T., Honda, M., Ninomiya, D., Sakai, T., Senba, T., Kaneyuki, S., Sakaguchi, S., Satoh, A., Hosokawa, T., Kawabe, Y., Kurihara, S., Izumikawa, K., Kohno, S., Azuma, T., Suemori, K., Yasukawa, M., Mizutani, T., Omatsu, T., Katayama, Y., Miyahara, M., Ijuin, M., Doi, K., Okuda, M., Umeki, K., Saito, T., Fukushima, K., Nakajima, K., Yoshikawa, T., Tani, H., Fukushi, S., Fukuma, A., Ogata, M., Shimojima, M., Nakajima, N., Nagata, N., Katano, H., Fukumoto, H., Sato, Y., Hasegawa, H., Yamagishi, T., Oishi, K., Kurane, I., Morikawa, S., Saijo, M., 2014. The first identification and retrospective study of Severe Fever with Thrombocytopenia Syndrome in Japan. J. Infect. Dis. 209, 816–827.

Tran, X.C., Yun, Y., Van An, L., Kim, S.H., Thao, N.T.P., Man, P.K.C., Yoo, J.R., Heo, S.T., Cho, N.H., Lee, K.H., 2019. Endemic severe fever with thrombocytopenia syndrome, Vietnam. Emerg. Infect. Dis. 25, 1029–1031.

Tsuru, M., Suzuki, T., Murakami, T., Matsui, K., Maeda, Y., Yoshikawa, T., Kurosu, T., Shimojima, M., Shimada, T., Hasegawa, H., Maeda, K., Morikawa, S., Saijo, M., 2021. Pathological characteristics of a patient with severe fever with thrombocytopenia syndrome (SFTS) infected with SFTS virus through a sick cat's bite. Viruses 13, 204.

Wu, Y.X., Yang, X., Leng, Y., Li, J.C., Yuan, L., Wang, Z., Fan, X.J., Yuan, C., Liu, W., Li, H., 2022. Human-to-human transmission of severe fever with thrombocytopenia syndrome virus through potential ocular exposure to infectious blood. Int. J. Infect. Dis. 123, 80–83.

Yamanaka, A., Kirino, Y., Fujimoto, S., Ueda, N., Himeji, D., Miura, M., Sudaryatma, P.E., Sato, Y., Tanaka, H., Mekata, H., Okabayashi, T., 2020. Direct transmission of severe fever with thrombocytopenia syndrome virus from domestic cat to veterinary personnel. Emerg. Infect. Dis. 26, 2994–2998.

Yu, X.J., Liang, M.F., Zhang, S.Y., Liu, Y., Li, J.D., Sun, Y.L., Zhang, L.H., Zhang, Q.F., Popov, V., Li, C., Qu, J., Li, Q., Zhang, Y.P., Hai, R., Wu, W., Wang, Q., Zhan, F.X., Wang, X.J., Kan, B., Wang, S.W., Wan, K.L., Jing, H.Q., Lu, J.X., Yin, W.W., Zhou, H., Guan, X.H., Liu, J.F., Bi, Z.Q., Liu, G.H., Ren, J., Wang, H., Zhao, Z., Song, J.D., He, J.R., Wan, T., Zhang, J.S., Fu, X.P., Sun, L.N., Dong, X.P., Feng, Z.J., Yang, W.Z., Hong, T., Zhang, Y., Walker, D., Wang, Y., Li, D.X., 2011. Fever with thrombocytopenia associated with a novel bunyavirus in China. N. Engl. J. Med. 364, 1523–1532.

Zhang, X., Zhao, C., Si, X., Hu, Q., Zheng, A., 2023. Natural circulation of tick-borne severe fever with thrombocytopenia syndrome virus in the city ecosystem, China. Virol. Sin. 38, 832–835.

Zhao, G.P., Wang, Y.X., Fan, Z.W., Ji, Y., Liu, M.J., Zhang, W.H., Li, X.L., Zhou, S.X., Li, H., Liang, S., Liu, W., Yang, Y., Fang, L.Q., 2021. Mapping ticks and tick-borne pathogens in China. Nat. Commun. 12, 1075.

Zhuang, L., Sun, Y., Cui, X.M., Tang, F., Hu, J.G., Wang, L.Y., Cui, N., Yang, Z.D., Huang, D.D., Zhang, X.A., Liu, W., Cao, W.C., 2018. Transmission of severe fever with thrombocytopenia syndrome virus by *Haemaphysalis longicornis* ticks, China. Emerg. Infect. Dis. 24, 868–871.