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Concise Communication

Aerosol transmission of severe fever with thrombocytopenia syndrome virus during resuscitation

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Abstract

We investigated potential nosocomial aerosol transmission of severe fever with thrombocytopenia syndrome virus (SFTSV) with droplet precautions. During aerosol generating procedures, SFTSV was be transmitted from person to person through aerosols. Thus, airborne precautions should be added to standard precautions to avoid direct contact and droplet transmission.

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Severe fever with thrombocytopenia syndrome (SFTS) caused by SFTS virus (SFTSV), a newly discovered emerging infectious disease with a high case-fatality rate recognized in central China in 2007, has recently been reported in China, Japan, and Korea.[1] Although most SFTS cases occur through tick bites, clusters of SFTS in family members and healthcare personnel (HCP) between people in several routes have been reported.[1–5] The major route of human-to-human transmission is direct blood exposure without proper personal protection equipment (PPE).[1,3] For this reason, contact precautions are recommended when caring for suspected or confirmed SFTS patients.[1,6] A recent outbreak of SFTS in a Korean hospital suggests possible droplet transmission.[2] In China, probable aerosol transmission in a family cluster has also been reported.[4]

Considering the increasing incidence and high overall case fatality ratio (~32.6%) of SFTS in Korea,[7] better understanding the mode of SFTS transmission is essential for infection control. We report a cluster of nosocomial person-to-person transmission of SFTSV probably by aerosol and contact routes.

Methods

Case definition and epidemiologic investigations

In September 2017, a SFTS-confirmed patient died at a tertiary-care hospital in Ansan, Korea. Thereafter, a cluster of 2 confirmed or suspected SFTS cases occurred among people exposed to the index case. With suspicion of nosocomial transmission of SFTSV, epidemiologic investigations were performed in all people exposed to the index patient during hospitalization. Epidemiological interviews included demographic data, clinical symptoms, signs of SFTS, history of tick bites, animal contacts, routes of possible exposure to risk factors, the use of protective devices, and protective behaviors. Paired sera 2 weeks apart were collected for confirmatory tests.

Laboratory tests

Confirmatory tests of SFTSV infection were (1) 1-step, real-time, or conventional reverse-transcription polymerase chain reaction (RT-PCR) for detecting M and S segments of SFTSV RNA, (2) immunofluorescence assay (IFA) for detecting anti-SFTSV immunoglobulin G (IgG), and (3) isolation of SFTSV in Vero E6 cell culture.[8] Genome sequences covering partial M (560-bp) and S (563-bp) segments were generated using de novo assembly with DNAStar version 5.06 software (Madison, WI). MEGA 6 software was used for genomic sequence alignment and phylogenetic analysis using the maximum-likelihood method.[8] All confirmatory tests were performed at the Korea Centers for Disease Control and Prevention (KCDC).

Results

The index patient was a 57-year-old man with onset of illness on September 22, 2017, after collecting mushrooms on a mountain to 10 days previously. He visited a local clinic on September 24 with high fever above 38°C, myalgia, watery diarrhea, and decreased urine output. He was transferred to our hospital and admitted to general ward on September 27. Physical examination revealed eschar on his back suggesting a tick bite. The laboratory tests

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Table 1. Clinical and Laboratory Findings of the HCP Contacted the Index Patient

	Classifying HCP	Sex	Age	Blood and/or Body Fluid Exposure	PPE Use	Fever	IFA Acute Phase	IFA Convalescence	RT-PCR
Case 1	Doctor	M	31	Try of endotracheal intubation, September 30	Fluid shield mask, glove	Yes	< 1:32	1:256	Positive
Case 2	mortuary beautician	M	26	Clean the deceased, October 1	Gown	No	1:128	1:256	Negative
Case 3	Doctor	F	33	Try of endotracheal intubation, September 30	Fluid shield mask, glove	No	<1:32	<1:32	Negative
Case 4	Doctor	M	26	Try of endotracheal intubation, September 30	Fluid shield mask, glove, gown	No	<1:32	<1:32	Negative
Case 5	Nurse	F	24	Assistance of endotracheal intubation, September 30	Fluid shield mask, glove	No	<1:32	<1:32	Negative
Case 6	Nurse	F	26	Assistance of endotracheal intubation, September 30	Fluid shield mask, glove	No	<1:32	<1:32	Negative
Case 7	Nurse	F	26	Assistance of endotracheal intubation, September 30	Fluid shield mask, glove	No	<1:32	<1:32	Negative
Case 8	Nurse	F	29	Assistance of endotracheal intubation, September 30	Fluid shield mask, glove	No	<1:32	<1:32	Negative
Case 9	Nurse	F	26	Suction, September 30	Glove	No	<1:32	<1:32	Negative
Case 10	Nurse	F	26	Suction, October 1	Glove	No	<1:32	<1:32	Negative
Case 11	Nurse	F	23	Suction, October 1	Glove, gown	No	<1:32	<1:32	Negative
Case 12	Nurse	F	24	Suction, October 1	Surgical mask, glove	No	<1:32	<1:32	Negative
Case 13	Nurse	F	24	Suction, October 1	Surgical mask, glove, gown	No	<1:32	<1:32	Negative
Case 14	Doctor	M	47	Assistance of endotracheal intubation, September 30	Fluid shield mask, glove	No	<1:32	<1:32	Negative

Note. HCP, healthcare personnel; IFA, immunofluorescence assay; PPE, personal protective equipment; RT-PCR, reverse transcriptase polymerase chain reaction.

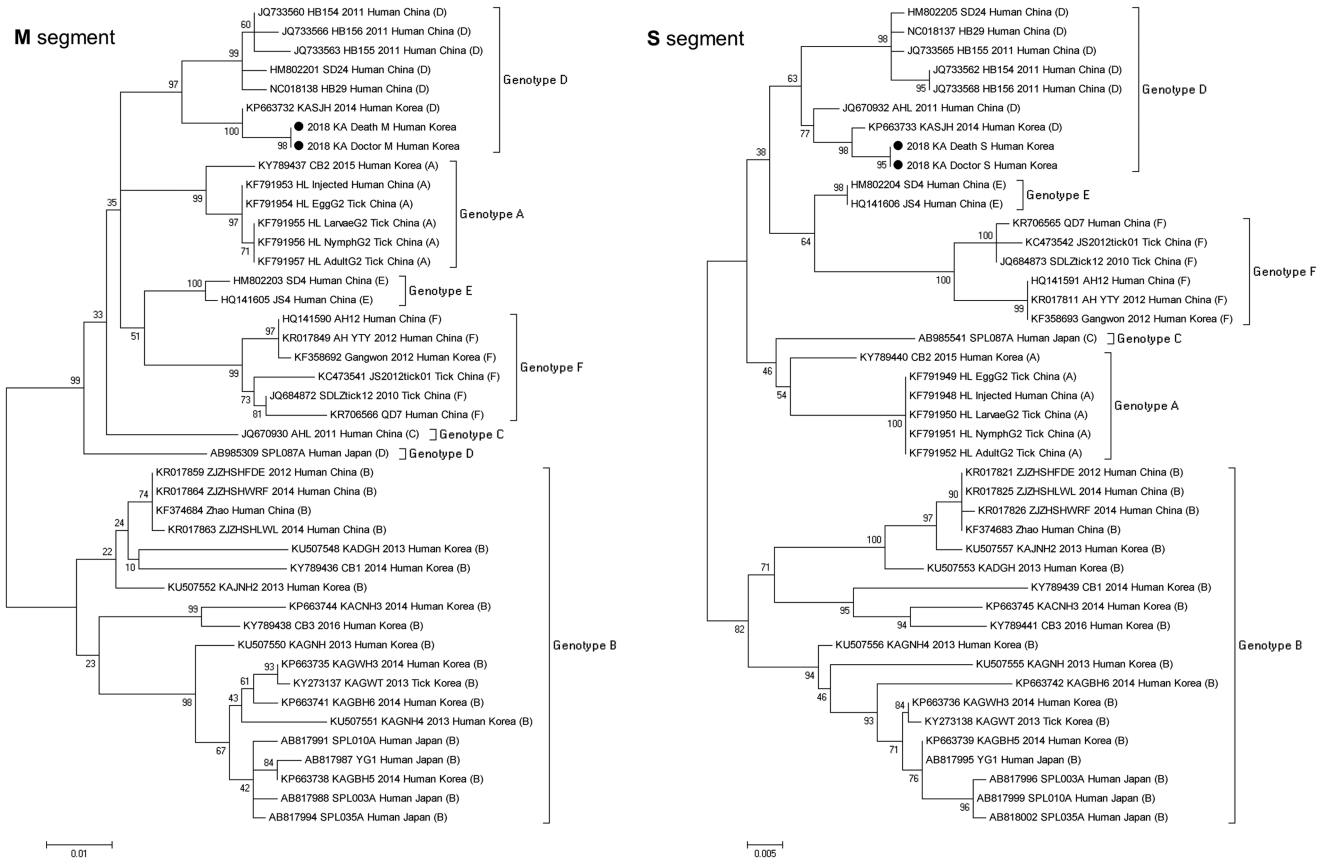

Fig. 1. Phylogenetic analysis based on partial nucleotide sequences of M and S segments of severe fever with thrombocytopenia syndrome virus (SFTSV) strains using the maximum likelihood (ML) method and the Kimura 2-parameter model. Numbers on branches indicate bootstrap percentages based on 1,000 replications, and the scale bar indicates nucleotide substitutions per site. The index patient and case 1 are marked with closed circles.

showed leukopenia, thrombocytopenia, and elevated levels of aspartate transaminase, alanine transaminase, and creatine phosphokinase. On September 29, he rapidly deteriorated with hypersomnia and disorientation. He was transferred into the intensive care unit (ICU). On September 30, incidental epistaxis and oral bleeding appeared. The patient was intubated for mechanical ventilation following a seizure attack with hypoxemia. On October 1, he expired from progression of multiorgan failure. Confirmatory RT-PCR test revealed that he was positive for SFTSV, with 1.9×10^6 copies/mL of viral titer at admission. During ICU hospitalization, standard and contact precautions were implemented with suspicion of SFTS.

Epidemiologic investigation revealed that a total of 14 HCP contacted the index patient during his hospitalization (Table 1). Of these, 2 were confirmed or suspected to have SFTS, including a 31-year-old male doctor who tried endotracheal intubation for the index patient (case 1) and a 26-year-old male mortuary beautician (case 2). Case 1 was admitted with fever of 39.3°C and chills on October 10. SFTS was confirmed by detecting SFTSV RNA (6.6×10^4 copies/mL) from his serum and ≥4-fold increase in antibody titers. He had short contact (within 10 minutes) with the index patient during endotracheal intubation, wearing a fluid-shield mask and gloves. During intubation, frequent oro-tracheal suctions were done to ensure visibility due to patient's naso-oral bleeding. Case 2 had contact with the index corpse without gloves or mask. He felt malaise without documented fever 1 week after contact. He had a 2-fold increase in serial IgG titer from 1:128 to 1:256 in sera collected at 25 days and 60 days after contact, respectively, without detection of SFTSV RNA. He denied any recent history of outdoor activity. The remaining 12 HCP were negative for SFTSV by IFA.

PCR sequencing was performed for the index patient and case 1. Sequences of M and S segments from case 1 shared 100% nucleotide identities with the index patient. Phylogenetic analysis for sequences of M and S segments from the isolated virus were classified as genotype D and clustered with sequences of PCR products from case 1 and the index patient (Fig. 1).

Discussion

We have documented a cluster of nosocomial SFTS using epidemiologic and viral genomic evidence. The index patient and case 1 were classified as genotype D, although genotype B strains of SFTS were predominant in Korea during 2013–2017.[9] Genotype D was isolated from only 1 case in 2014. Both M and S segments showed 100% homology in nucleotide sequences, confirming the same origin of SFTS infection between the index patient and case 1. Epidemiological investigation showed that all HCP wore fluid-shield mask and gloves during potential exposure period. However, these PPEs cannot protect conjunctiva or upper respiratory tract against aerosols containing the pathogen. Case 1 might be infected through aerosols generated from suctions of oral bleeding during endotracheal intubation. Previous studies reported that doctors contracted this disease after performing endotracheal intubation[2,3,5] and suggested droplet or possible aerosol transmission.[3,5] We believe that case 2 was infected through direct

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contact with contaminants of blood or bloody secretions produced by index patient's mouth or nose.

In general, transmission of communicable diseases has 3 routes: airborne, contact, and droplet. Unique control procedures and PPE are recommended for each route.[10] However, there is limitation in dichotomization of airborne and droplet transmission. Some viruses such as influenza virus and severe acute respiratory syndrome coronavirus (SARS-CoV) are transmitted through small-particle aerosols in addition to droplet and contact routes. This case supports the hypothesis that a fatally ill patient with high viral loads of SFTS may be highly contagious by releasing viable pathogen through small-particle aerosols. Therefore, additional airborne precautions such as particulate respirator (N95 mask or equivalent), a face shield, and negative pressure ventilation may be needed during aerosol generating procedures for SFTS patients, especially fatally ill patients with high viral loads. Because there is no definitive treatment or vaccine against SFTSV to date, infection control is extremely important in the healthcare setting.

This study has some limitations. Case 2 was not confirmed by detection of SFTSV RNA or 4-fold increase in serial IgG titer because his first sample was taken very late after contact. Although case 1 might have contracted the disease through contact transmission, he also immediately washed a small droplet on his intact skin.

In conclusion, our findings indicate that SFTSV could be transmitted from person-to-person through aerosol, which highlight the importance of adding airborne precaution during aerosol-generating situations.

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