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Short Communication

Possible Horizontal Transmission of Crimean-Congo Hemorrhagic Fever Virus from a Mother to Her Child

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SUMMARY: The case of a child with Crimean-Congo hemorrhagic fever (CCHF) presumably infected with CCHF virus from her 27-year-old mother is described. The mother with CCHF was treated with ribavirin and did not present with any symptoms of obvious hemorrhage. The child developed fever on the 5th day after the mother's onset. The partial virus genome was amplified by RT-PCR, and nested PCR from the child and the genome sequence were identical to that from the mother, indicating possible transmission of the virus from mother to child. This case indicates the importance of preventive measures for in-house outbreaks of CCHF.

Crimean-Congo hemorrhagic fever (CCHF) virus (CCHFV), a tick-borne virus distributed across Africa, Eastern Europe, the Middle East, and Asia, causes illness in humans and has a high fatality rate of up to 30% (1). Humans are usually infected with the virus through the bite of a tick (genus, *Hyalomma*) or by close contact with freshly slaughtered meat, or blood from viremic animals such as sheep, cattle, and goats (1). CCHF outbreaks have also occurred as nosocomial infections in several instances (2-5). In a review article by Hoogstraal (6), several cases of human-to-human infection of CCHF in households were described, indicating the importance of this infection route in CCHF outbreaks. However, the impact of human-to-human transmission of CCHFV in a household has not been studied with virological analysis, although in-house outbreaks of CCHF are considered to be relatively frequent, beyond expectations.

A 27-year-old female, who lived in a village in the Western part of the Xinjiang Uygur Autonomous Region, P. R. China, presented with fever, backache, headache, flushed face and general malaise without obvious hemorrhagic symptoms, and was transferred to a local hospital. She was diagnosed as having CCHF based on the epidemiology of CCHF in the area, and was hospitalized and treated with a 0.8 g/dose of ribavirin by drip infusion, twice daily for 7 days. Five days after the onset of the symptoms, her 4-year-old daughter also presented with high fever. She was clinically diagnosed as having CCHF, and was treated with intravenous administration of a 0.4 g/dose of ribavirin through drip infusion, twice a day for 7 days. No other proximate households showed any symptoms such as fever, arthralgia, and bleeding around that time. Both these patients lived in close contact with ticks, though neither recalled being bitten by one. Neither patient developed hemorrhagic manifestations. They recovered without any consequences.

Taking the day on which the fever first appeared as day 1, blood specimens were collected on days 3 and 11 from the mother and on days 3 and 8 from the daughter (Table 1). Serum samples were carefully separated under strict precautions, wearing a mask, protective glasses, double gloves, and a gown. RNA was extracted from serum samples using a High Pure Viral RNA Kit (Roche Diagnostics GmbH, Mannheim, Germany), according to the manufacturer's instructions. The reverse-transcription polymerase chain reaction (RT-PCR) and nested PCR was performed for amplification of a portion of the S-RNA segment according to the previous report (7) with some modifications (8). Serum samples were heat-inactivated at 56°C for 1 h for serological assays.

CCHFV immunoglobulin G (IgG) antibodies were detected by recombinant CCHFV nucleoprotein (CCHFV rNP)-based IgG enzyme-linked immunosorbent assay (ELISA) as described previously (9). CCHFV IgM antibodies were also detected by IgM-capture ELISA format using purified CCHFV rNP as an antigen (8). The cutoff optical density values for both ELISA tests were set at 0.200 (8,9).

The CCHFV genome was successfully amplified from the samples taken from the mother on days 3 and 11 and from the daughter on day 3 (Table 1). The daughter's serum collected on day 8 showed a positive reaction in the IgM-capture ELISA. The serum sample collected from the mother on day 11 also showed a positive reaction in the IgM-capture ELISA. On the other hand, a significant IgG response was demonstrated in the daughter but not in the mother (Table 1). The 262-base viral genome fragments, which were amplified in the sera collected from the mother and the child, respectively, were sequenced using ABI PRISM 310 Genetic Analyzer (Applied Biosystems, Foster City, Calif., USA). The nucleotide sequences of these viral genomes were the same (Accession No. AB102852 and AB102853 in DNA Data Bank of Japan). Furthermore, the sequence was confirmed to be identical to

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Table 1. Results of RT-PCR, IgG ELISA, and IgM-capture ELISA

Virological tests	Serum samples collected from on day	Mother 3	Mother 11	Daughter 3	Daughter 8
RT-PCR		+[1)]	+	+	−[1)]
IgG ELISA (OD_{405})		−(0.071[2)])	−(0.059)	−(0.059)	+(0.310)
IgM-capture ELISA (OD_{405})		−(0.015[3)])	+(0.216)	−(0.021)	+(1.433)

[1)]: + and - indicate positive and negative results, respectively.
[2, 3)]: The OD_{405} values in IgG ELISA and IgM-capture ELISA were measured at the dilution level of 1:400 and 1:100, respectively.

that of CCHFV Chinese strain 66019 (Accession No. AJ101648 in National Center for Biotechnology Information). Although the data are not shown here, the CCHF outbreak in the region of residency in 2002 was caused by multiple strains of CCHFV. The partial viral genomes amplified from three patients, including the mother and her daughter, out of 6 patients from whom CCHFV genomes were amplified, were identical. This result strongly suggests that the pair were infected with the same strain of CCHFV from the same source or that the daughter was infected by her mother.

The incubation period of CCHF is 4-7 days (1). The interval between the onset of the mother and that of the child was 5 days. If both of them were infected with CCHFV simultaneously from the same source on the same occasion, the expected incubation time for the mother and her daughter would be 4-7 and 9-12 days, respectively. The expected incubation time of 9-12 days in the daughter is too long, suggesting that she was not infected with CCHFV at the same time her mother was. Therefore, it is quite likely that she was infected by her mother. However, we must not exclude the possibility that they were infected with CCHFV from the same source but on different occasions.

The mother did not show any symptoms of bleeding; therefore, if the daughter was infected by her mother, the daughter was infected through close contact with visually non-bloody bodily fluids secreted from the mother such as saliva, respiratory secretions, and/or urine. It is also possible that traces of blood were present in the mother's bodily fluids. This case of possible mother-to-child horizontal transmission of CCHFV indicates the importance of preventive measures in a household, even in cases without any hemorrhagic manifestations. In order to prevent in-house outbreaks, it must be emphasized that the education of the residents in endemic areas concerning modes of CCHFV transmission, risk of infection, and preventive measures is essential. In addition, rapid and accurate diagnosis of CCHF is also necessary.

The present study indicates the necessity of preventive measures against transmission of CCHFV to caregivers such as family members and hospital staff. It must be stressed that not only blood but also other bodily fluids should be regarded as possible sources of human-to-human transmission.

These patients were treated with an intravenous administration of ribavirin with favorable outcomes, as reported previously (8). The efficacy of ribavirin should be studied as a treatment of CCHF in the future.

In summary, we reported a pediatric case of CCHF, confirmed by virological studies, in which a child was possibly infected by her mother.

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