International Journal of Infectious Diseases 45 (2016) 109–111

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Possible sexual transmission of Crimean-Congo hemorrhagic fever

Natalia Yurievna Pshenichnaya [a,*], Irina Stanislavovna Sydenko [b], Elena Pavlovna Klinovaya [b], Elena Borisovna Romanova [a], Alexey Sergeevich Zhuravlev [c]

[a] Rostov State Medical University, Rostov-on-Don, Russia
[b] Central District Hospital of Salsk District of the Rostov Region, Russia
[c] First Moscow Medical University "I.M. Sechenov", Moscow, Russia

ARTICLE INFO

Article history:
Received 12 January 2016
Received in revised form 27 February 2016
Accepted 29 February 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:
Crimean-Congo hemorrhagic fever
Family cluster
Sexual contact
Transmission of infection

SUMMARY

Three cases of family transmission of laboratory-confirmed Crimean-Congo hemorrhagic fever (CCHF) among spouses are reported. These spouses had sexual contact at the end of the incubation period or during the early stage of the mild form of CCHF, without any hemorrhagic symptoms in the first infected spouse. This report demonstrates that sexual contact may represent a real risk of CCHF transmission, even if the patient only experiences mild symptoms.

1. Introduction

Crimean-Congo hemorrhagic fever (CCHF) most frequently occurs among inhabitants of rural areas and agricultural workers. The disease occurs following the bite of an infected Hyalomma tick, or by direct contact of unprotected hands with ticks, and more rarely through exposure to the blood and tissues of infected livestock, particularly among slaughterhouse workers.[1]

Medical personnel and family members usually contract CCHF through contact between body fluids of infected patients and unprotected skin or eye mucosa.[2] The performance of aerosol-generating medical procedures in CCHF patients can also lead to the nosocomial distribution of the infection among healthcare workers (HCWs).[3]

The southern regions of Russia (Astrakhan, Rostov, Volgograd, Krasnodar, and Stavropol regions, and Kalmykia, Dagestan, and Ingushetia Republics) are endemic for CCHF. One thousand seven hundred and forty-five CCHF cases with 75 fatalities (case-fatality rate 4.3%) were recorded between 1999 and 2014; 487 cases of CCHF were diagnosed in the Rostov region alone between 2001 and 2015.[4] The most affected territory in this region has been the district of Salsk, where 122 CCHF cases (25% of all cases in the Rostov region) were recorded during the last 10 years. The present researchers recently described probable CCHF virus transmission after aerosol-generating medical procedures, which led to a nosocomial cluster involving eight HCWs in the district of Salsk.[3]

Three cases of family transmission of laboratory-confirmed CCHF among spouses are reported herein. These spouses had sexual contact with the index cases at the end of the incubation period or during the early stage of a mild form of CCHF, without any hemorrhagic symptoms in the first infected spouse.

2. Case reports

The three cases were diagnosed in the district of Salsk in Rostov region within the last 10 years (2005–2015). The authors believe that CCHF virus could have been transmitted sexually in 2.5% of the 122 cases occurring during the last 10 years.

Ribavirin was administered to all of the patients, and all recovered successfully. PCR confirmation of CCHF became available in the region in 2008; prior to this, only ELISA was available.

2.1. Case 1

A 27-year-old man, a slaughterhouse worker, was admitted to hospital on day 7 of disease (May 22, 2005). On days 1 and 2 of illness, he had a fever of up to 38.0–39.0 °C, but during the next

* Corresponding author. Tel.: +7 918 553 53 06; fax: +7 863 234 91 83.
E-mail addresses: pshenichnaya.natalia@gmail.com, natalia-pshenichnaya@yandex.ru (N.Y. Pshenichnaya).

http://dx.doi.org/10.1016/j.ijid.2016.02.1008

5 days before hospitalization (days 3–7 of disease), his body temperature was normal (37.2–37.3 °C) and his condition improved. No hemorrhagic symptoms were detected during the entire course. CCHF was suspected and later confirmed by ELISA 3 days after admission. Anti-CCHF virus IgM was positive at a titer of 1:1600 and IgG at a titer of 1:400.

The man's wife, aged 29 years and a housewife by occupation, was admitted to the hospital on day 1 of illness (May 25, 2005). On the day of admission, she had a fever of 39.0 °C and the following peripheral blood parameters: hemoglobin (Hb) 14.3 g/ml, white blood cell count (WBC) 4.4×10^9/l, platelets (PLT) 169.0×10^3/l. There was no history of tick bites or contact with animals. She had had several sexual contacts with her husband between day 4 and day 7 of his illness and CCHF was suspected. On days 3 and 4 of disease, small hemorrhages were observed at the locations of intravenous injections. During these days, her platelet count was $95.0–104.0 \times 10^3$/l. CCHF was confirmed by ELISA (June 6, 2005); anti-CCHF IgM was found at a titer of 1:800 and IgG was negative.

2.2. Case 2

A 45-year-old woman, a milkmaid by occupation, was admitted to the hospital on day 2 of illness (April 22, 2010), 5 days after a tick bite. On the day of admission, she was febrile at 38–39 °C, with Hb 11.9 g/ml, WBC 3.4×10^9/l, and PLT 123×10^3/l. Hemorrhages were observed around the intravenous catheter on day 3 of disease. The diagnosis was confirmed by ELISA; the anti-CCHF virus IgM titer was 1:800 and IgG was negative.

The woman's 47-year-old husband, who was jobless, was admitted to the hospital on day 1 of illness (April 25, 2010) with a high fever up to 39–40 °C. He had Hb 10.7 g/ml, WBC 3.2×10^9/l, and PLT 95×10^3/l. On day 3 of illness, he developed gastrointestinal bleeding and massive hemorrhages at the site of the intravenous catheter. His peripheral blood parameters were Hb 7.3 g/ml, WBC 3.1×10^9/l, and PLT 34.0×10^3/l, and several platelet and erythrocyte transfusions were administered to the patient. CCHF was confirmed by ELISA (May 3, 2010); the anti-CCHF virus IgM titer was 1:1600 and IgG was negative.

No risk factors for CCHF were found in the history of the patient, with the exception of living in an endemic area and sexual contact with his wife between 24 and 48 h before the onset of symptoms.

2.3. Case 3

A 55-year-old man, store manager by occupation, was admitted to hospital on day 2 of illness (June 17, 2014), 5 days after a tick bite. On day 1 of illness, his fever was 37.2 °C, and this increased on days 2 and 3 up to 38–39 °C. Blood parameters showed Hb 15.0 g/l, WBC 4.3×10^9/l, and PLT 128×10^3/l on the day of admission. No hemorrhages were detected during the entire course of illness. The disease was confirmed by PCR (June 20, 2014) and ELISA (June 23, 2014); the anti-CCHF virus IgM titer was 1:800 and IgG was negative.

The man's 52-year-old wife, a shop assistant in the same store, was admitted to hospital on day 1 of illness (June 22, 2014). She had a fever up to 39.0 °C on the day of admission, and blood parameters showed Hb 11.8 g/ml, WBC 2.1×10^9/l, and PLT 140×10^3 /l. She had had sexual contact with her husband 2 and 3 days before he became febrile. No hemorrhages were observed during the entire illness. CCHF was confirmed by a positive PCR (June 23, 2014) and ELISA; the anti-CCHF IgM titer was 1:6400 and IgG was negative.

A brief description of these family clusters is provided in Table 1.

3. Discussion

Sexual contact with the infected spouse 1–2 days before the onset of symptoms (at the end of the incubation period) or during a relatively mild course of the disease after an improvement in the patient's condition (4–7 days of illness) was followed by clinical and laboratory-confirmed CCHF a few days later.

Airborne transmission between husband and wife cannot be excluded, but if that was the case, many more secondary cases to the 122 observed during the period in which these cases were observed would have been expected. However, it is striking that sexual intercourse with a patient incubating CCHF within 3 days before the onset of symptoms was followed by CCHF in the sexual partner.

One case of possible sexual CCHF transmission was reported recently from Turkey. The index case had sexual intercourse with his wife during the convalescent period of CCHF, 3 or 4 days after discharge from the hospital. Seven days after intercourse the woman became ill with CCHF. The authors of that article discussed

Table 1
Description of CCHF family clusters among couples connected by sexual contact

Pair of spouses	Primary case	Day of disease of the primary case when the couple had sexual contact	Difference between dates of onset of symptoms in spouses	Secondary case
1st couple	Husband, 27 years old	Between 4 and 6 days of disease	9	Wife, 29 years old
Tick bite	No			No
Occupation	Slaughterhouse worker			Housewife
Hemorrhages	No			Yes, moderate
Day of disease when hemorrhages occurred	-			3–4
Severity of disease	Mild			Moderate
2nd couple	Wife, 45 years old	1–2 days before the onset of symptoms	4	Husband, 47 years old
Tick bite	Yes			No
Occupation	Milkmaid			Jobless
Hemorrhages	Yes			Yes
Day of disease when hemorrhages occurred	3			3
Severity of disease	Moderate			Severe
3rd couple	Husband, 55 years old	1 day before the onset of symptoms	6	Wife, 52 years old
Tick bite	Yes			No
Occupation	Store manager			Shop assistant
Hemorrhages	No			No
Severity of disease	Moderate			Moderate

the sexual means of CCHF transmission as only 'probable'. They were unable to demonstrate the virus in seminal fluid and also considered that the sexual partner could have become infected with CCHF virus through direct contact with a viremic animal or through a tick bite.[5]

All persons in the cases presented here lived in rural areas and probably had a history of engagement in animal husbandry, both of which are independent risk factors for CCHF.[6] Therefore the sexual mode of CCHF transmission can only be discussed as 'possible'.

Marburg and Ebola viruses have similar routes of transmission to CCHF virus, i.e. infection through body fluids.[7] Furthermore, it is now well documented that Ebola virus, another hemorrhagic virus, can be transmitted in semen.[8,9] The spermatogenic transmission of Marburg virus has also been confirmed in an animal model.[10] The urine of CCHF patients with prolonged viremia can also be infected.[11] Perhaps cervical–vaginal fluid can also contain viruses that cause hemorrhagic fevers, but no confirmation of this hypothesis could be found; this would, however, explain the second pair of cases, where the woman developed CCHF before her husband.

Thus, these three husband–wife pairs of cases of CCHF were all characterized by sexual intercourse within 72 h before CCHF symptoms developed in the index case. It is therefore believed that sexual transmission of CCHF virus, as with Ebola virus, is a distinct possibility, through infected semen or cervical–vaginal secretions from the end of the incubation period. However, close skin-to-skin, mucosa-to-mucosa, and skin-to-mucosa contacts cannot be excluded as possible transmission routes of the virus.

These cases raise the possibility that there is a risk of transmission through sexual contact from the end of the incubation period to the period of convalescence, even if the course of disease in relatively mild and without hemorrhagic symptoms. The transmission of the virus from person to person through sexual contact may lead to a more severe course of the disease. Patients should be questioned regarding sexual contacts within 72 h before symptom development when obtaining the history of CCHF patients.

Conflict of interest: The authors declare that they have no competing financial interests. The content is solely the responsibility of the authors.

Author contributions: N.Y. Pshenichnaya performed the short literature review and drafted the manuscript, I.P. Sydenko and E.P. Klinovaya performed the data collection, E.B. Romanova and A.S. Zhuravlev performed the data analysis and design of the study.

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