

RESEARCH ARTICLE

## A nosocomial outbreak of Crimean-Congo hemorrhagic fever

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### ABSTRACT

**Objectives:** An outbreak of nosocomial Crimean-Congo Hemorrhagic Fever (CCHF) occurred in a university hospital in May 2014. The index case was hospitalized with a preliminary diagnosis of intoxication, liver failure and disseminated intravascular coagulopathy (DIC). The index case, a farmer, died a few hours later with signs of bleeding.

**Outbreak Investigation:** Crimean-Congo Hemorrhagic Fever Polymerase Chain Reaction (PCR) was positive in the index case serum. RT-PCR and/or IgM serology were reported as positive for CCHF virus in all cases.

Six health care workers and two relatives in direct or indirect contact with the index case were infected. The main symptoms were myalgia, fatigue, headache, anorexia, sore throat and eruption. Maculopapular rash was observed in five cases. Three patients had exudative tonsillitis. Emergency workers and internal medicine intensive care, radiology and infectious disease personnel had a history of contact with index and/or secondary cases. Ribavirin was given to all patients. One health care worker died because of CCHF.

**Conclusion:** A healthcare worker died due to nosocomial CCHF. This presentation emphasized importance of universal precautions. *J Microbiol Infect Dis 2015;5(1): 5-9*

**Key words:** Crimean-Congo hemorrhagic fever, nosocomial, outbreak, prevention

### Kırım kongo kanamalı ateşi hastane salgını

#### ÖZET

**Amaç:** 2014 yılı Mayıs ayında hastanemizde nozokomiyal Kırım Kongo Kanamalı Ateşi (KKKA) salgını meydana geldi. İndeks vaka toksikasyon, karaciğer yetmezliği, diseminan intravasküler koagülasyon (DİK) ön tanıları ile yatırıldı. Çiftçilikle uğraşan hasta kanama belirtileri ile birkaç saat sonra öldü.

**Salgın Araştırması:** İndeks vakanın serumundan çalışılan KKKA PCR'ı pozitif sonuçlandı. Tüm olgularda KKKA virüsü için RT-PCR ve / veya IgM serolojisi pozitif olarak rapor edildi.

İndeks vaka ile doğrudan ve dolaylı teması olan altı sağlık çalışanı ve iki akrabasına hastalık bulaştı. Başlıca yakınmalar iştahsızlık, halsizlik, kas ağrısı, baş ağrısı, boğaz ağrısı ve döküntü idi. Makulopapüler döküntü beş vakada mevcut idi. Hastaların üçünde eksüdatif tonsilit vardı. Acil servis, dâhiliye yoğun bakım, radyoloji ünitesi, enfeksiyon hastalıkları ve laboratuvar çalışanlarının indeks vaka ve/veya sekonder vakalarla teması oldu. Hastaların tamamına ribavirin tedavisi verildi.

**Sonuç:** Bir hastane çalışanı KKKA nedeni ile kaybedildi. Bu sunum universal korunma önlemlerinin önemini vurgulamaktadır.

**Anahtar kelimeler:** Kırım kongo kanamalı ateşi, nozokomiyal, salgın, korunma

#### INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal viral infection.<sup>1</sup> The CCHF virus is member of the Nairovirus genus of the Bunyaviridae family.<sup>2</sup> The disease is a major public health prob-

lem in some countries. It is a serious pathogen and causes acute hemorrhage and nosocomial epidemics. The incubation period changes from one to nine days.<sup>3</sup> Hyalomma type ticks infected with the virus can infect humans in endemic regions, especially

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those with hot climates. The virus can be transmitted through contact with body fluids. Clinical symptoms are not specific. The disease starts with loss of appetite, malaise, myalgia, fever, headache, nausea, vomiting and non-bloody diarrhea. Typical disease does not develop in all patients. The mortality rate is between 3% and 30%.<sup>4,5</sup> Nosocomial transmission is well-known, although uncommon.<sup>6-9</sup> CCHF nosocomial transmission have been reported from various countries, including Pakistan, Dubai, North Africa, Iran and Turkey.<sup>4,5,7,10,11</sup> In general terms, during post-exposure prophylaxis, health care workers take ribavirin if they are exposed to the CCHF virus.<sup>3,12</sup> According to our knowledge this is the first nosocomial outbreak report due to CCHF virus in Turkey.

### Outbreak Investigation

In May 2014, an outbreak of CCHF was occurred in Ataturk University Hospital, Erzurum, Turkey. The index case died soon after being placed in intensive care. The disease was transmitted to six health care workers and two relatives. When the epidemic was realized the analysis was started. Blood specimens were collected from the family members and health care workers who came into contact with the index case. After hospitalization, routine laboratory tests were performed, including whole blood count, liver enzymes, creatine kinase, prothrombin time and partial thromboplastin time. For serological (IgM and IgG) and molecular (RT-PCR) testing, blood samples were forwarded to the CCHF reference laboratory. Although endemic cases of CCHF had previously been seen in our region, no epidemic had been reported. All patients presenting with febrile hemorrhagic syndrome in an endemic region in Turkey must be assessed for CCHF until this has been excluded. Use of personal protective equipment is essential. This paper describes an epidemic that infected health care workers and relatives because safety measures were not taken or protective precautions were not sufficient.

### INDEX CASE

A 69-year-old man was admitted to the intensive care unit with initial suspicion of intoxication, liver failure, toxic hepatitis and disseminated intravascular coagulopathy. He lived in a rural area endemic for CCHF and worked in animal husbandry. Abdominal pain, high fever, nausea, vomiting, impaired general condition and confusion were observed. Abdominal pain had commenced after treating animals with a

chemical substance 6 days previously. The following day he had been bitten on the inside of the right leg. High fever and confusion began one day later. On admission to hospital (04 May 2014), the patient was somnolent and not fully oriented or cooperative. Rash was observed in both malar area, and widespread hemorrhagic incrustation in the mouth, tongue and palate. Secretory rales were present in the physical examination. The patient was hospitalized, transferred to the intensive care unit and intubated but he died in hours after hospitalization. Retrospectively, he was thought to have had CCHF. CCHF PCR from his serum was reported as positive.

### SECONDARY CASES

#### Family member 1

A son of the index case was applied and hospitalized one week later (May 12, 2014) with headache, high fever, sore throat and diarrhea seven days after the death of the father. Possible transmission had occurred with blood and/or body fluids during treatment of the index case. The patient was discharged in a healthy condition on the 8<sup>th</sup> day.

#### Family member 2

A nephew of the index case had wiped her uncle's hands and blood without using gloves during admission to the hospital. The nephew was hospitalized (May 12, 2014) seven days after the death of the index case with weakness, high fever and vomiting. She was discharged in a healthy condition on the 10<sup>th</sup> day of hospitalization.

#### Health care worker 1

This 28-year-old male is a research resident physician in the emergency department. We learned that there had been no contact with blood, apart from examination wearing gloves, in the index case. Five days later he developed nonspecific symptoms. The patient was admitted to the infectious disease clinic with high fever, fatigue, sore throat and muscle pain (09 May 2014). A maculopapular rash appeared on the skin on the third day and diarrhea developed on the fourth day. The patient was discharged 12 days after admission.

#### Health care worker 2

This 27-year-old male nurse in the emergency department, he had performed vascular access in the fatal index case using no protection except for

gloves. Four days after contact with the patient, he was hospitalized (09 May 2014) with a severe headache and high fever. Antibiotherapy was started due to the presence of an exudative lesion in the throat. The patient eventually recovered.

#### Health care worker 3

This 33-year-old male was a health worker in the emergency department. He had come into contact with the index case' blood and belongings while wearing gloves. Four days after initial contact, the patient was hospitalized (08 May 2014) with nausea, fever and joint pain. A skin rash was seen on the second day. On the third day, the patient developed diarrhea. His results were positive. Platelet suspension was given by apheresis. On the eighth day, all complaints resolved, and the patient was discharged from hospital on the 12<sup>th</sup> day.

#### Health care worker 4

This 20-year-old male was a health care worker in the internal medicine department. During intervention for the index patient, the patient came into contact with blood while wearing gloves. Five days after this contact, he was hospitalized (09 May 2014) with fatigue, nausea, fever, and a sore throat. On the same day the patient was hospitalized, a skin rash and malar rash developed on his face and ampicillin/sulbactam therapy was started for exudative lesions. The next day, he developed diarrhea. The patient was discharged on the 12<sup>th</sup> day.

#### Health care worker 5

This 33-year-old male was employed in biochemistry laboratories. He reported that he was not on duty on the night of the death of the index case. He collected blood from Patient 3. Five days after the death of the index case (12 May 2014), and two days after coming into contact with Patient 3, he applied with symptoms such as fatigue, loss of appetite, body aches, fever and headaches. On the fourth day, he developed a skin maculopapular rash and diarrhea. As with the other patients, he was treated with ribavirin. His PCR results were positive and his liver enzymes rose rapidly. Platelet concentrations decreased rapidly. The patient was given thrombocyte replacement, random platelet suspensions and apheresis. His vital signs were not stable. Double filtration was performed. Acidosis and hypotension developed. The patient died on the ninth day of treatment.

#### Health care worker 6

This 29-year-old male was an emergency service secretary who used the same sink with the index case. He came into hand contact with the index case and with patient relatives. He had high fever, drowsiness, severe headache, malaise, anorexia, diarrhea after one day. The patient was hospitalized (09 May 2014) on the fourth day of symptoms. He had tonsillitis and macular rash on his face. The patient was discharged on the 12<sup>th</sup> day of hospitalization.

Descriptive epidemiology was used in outbreak analysis. PCR results were positive for CCHF in all cases from the reference laboratory. Treatment was initiated with a treatment dose of ribavirin when the PCR results were reported positive. The infection was considered to have been transmitted to the other cases due to the index case having high-level viremia and being intubated, deficiencies in the use of personal protective equipment, inappropriate ventilation in rooms and airborne transmission during aerosol procedures. Cases were evaluated in terms of results of clinical and laboratory tests.

## DISCUSSION

CCHF is more common in people engaged in agriculture and animal breeding and in active workers. In Turkey, 90% of all cases involve farmers.<sup>3</sup> CCHF is a disease that can develop due to exposure among healthcare staff. Health workers represent a second risk group. Surgeons and nurses have both been affected the most common.<sup>2</sup> Levels of education and awareness among such personnel are important. The first nosocomial epidemic was reported in 1976 in Pakistan. Three people were killed and 11 were affected by that epidemic.<sup>13</sup> A study from Iran reported a 3.87% seroprevalence rate among HCWs who had a history of exposure to patients with CCHF.<sup>9</sup> Our index case worked in agriculture and animal husbandry. He had a history of exposure to pesticides and insect bites. In his anamnesis, use of insecticides had caused confusion, and there was difficulty in differential diagnosis.

The fatality rate in CCHF is 30%.<sup>5,7</sup> Nosocomial cases have high mortality rates.<sup>9</sup> The fatality rate can be as high as 66% in secondary and tertiary cases during epidemics.<sup>2,3,9</sup> Eleven secondary cases in healthcare workers resulted in three deaths.<sup>13</sup> A nosocomial epidemic was reported in Sudan in 2008, with eight of the 10 cases involved proving fatal.<sup>8</sup> Cases with a high viral load and those presenting with weak or no antibody response gener-

ally result in death.<sup>2,11,14</sup> Death almost always occurs after 6-10 days due to shock and multiple organs failure.<sup>2</sup> However, our patient who died, a medical worker, exhibited the same course since infection can occur from person to person.

The number of mild cases of CCHF has increased slightly due to higher awareness in society. People report contacts with ticks much earlier, and doctors initiate treatment earlier thanks to early diagnosis.<sup>15</sup> Cases are also confirmed earlier thanks to the provision of training activities. Training is available in terms of clinical symptoms, modes of infection, and protection from the disease. An employee in the laboratory died in addition to the index case in this outbreak. Further training has been provided regarding the clinical symptoms of the disease, the routes of transmission and protection. Laboratories should not be overlooked.

CCHF is nonspecific because several infection and non-infection pictures may occur at the same time. In the early stages of the disease, high fever, anorexia, acedia, headache, and myalgia can develop suddenly. Gastrointestinal symptoms are prominent for three to seven days in the pre-hemorrhagic period. Hemorrhagic bleeding can be seen in different sites.<sup>2</sup>

The activities with a nosocomial transmission include needle-stick injury, bleeding, emergent operations for unsuspected cases, and unprotected handling of infected materials. Contaminated equipment, insufficient hand hygiene, unsuitable masks and gloves, inappropriate apron use and removal and inappropriate use of N95 respirators are responsible for aerosolization in indirect contact.<sup>9,10,11</sup> Deficient injection sterilization, random use of injections during treatment, and reuse of syringes are also significant factors in terms of contamination and aerosolization.<sup>1,14</sup> Spaces in infection control practices are the common elements in the emergence of nosocomial outbreaks.<sup>9</sup> Nine nosocomial cases were reported between 2004 and 2011 in a study from Ankara, Turkey, that evaluated needle injuries and contacts among health personnel. One died, two were asymptomatic and four involved injection traumatization.<sup>11</sup>

A study of six cases from the same family in Iran reported that transition from person to person can be eliminated by avoiding close contact. Six people were injured due to pinprick and insufficient barrier measures.<sup>5</sup>

It is unclear whether the virus can be transmitted from person to person by air.<sup>2,7,9</sup> Lassa fever can

be transmitted by air from person to person.<sup>3,9</sup> Some patients were infected by CCHF despite following proper prevention procedures. This may be interpreted as evidence of transmission of CCHF by airborne transmission. Training, protective equipment and compliance with safety rules are essential in endemic regions.<sup>1</sup> Nosocomial transmission can be blocked if universal procedures are followed.<sup>5</sup> Epidemics have been reported among medical workers when airborne precautions were not followed. Although standard precautions regarding protection, contact and droplets are sufficient, airborne precautions should still be taken during procedures resulting in aerosol formation.<sup>2,8</sup> Suspected patients should be quarantined in private rooms with negative pressure.<sup>2</sup> The CDC suggests that a face guard, face mask and eye guard be worn when dealing with patients with respiratory symptoms. The use of N95 or FFP2 masks is imperative during procedures resulting in aerosol formation.<sup>3,7</sup> It should not be forgotten that the airborne path is one potential route of transmission.

Ribavirin might be an effective and helpful agent in prophylaxis following exposure to the CCHF virus.<sup>3,7,11,12,14</sup> Use of ribavirin in treatment is controversial. It is unclear how protective ribavirin is, although it is currently used in prophylaxis and treatment. We used oral ribavirin in a 2 g loading dose, followed by 4 g/day for four days and then 500 mg four times/day for 6 days.

All patients in endemic regions should be evaluated for hemorrhagic syndrome until inflammatory diseases are excluded.<sup>7,8</sup> Suitable isolation procedures should be applied, but these patients should not be placed in the same rooms with non-infected patients.<sup>7</sup> Early diagnosis can avoid transmission among medical workers. Ribavirin might help healing of clinical symptoms and enhances prognosis.<sup>7,11</sup> Early identification of such cases and adherence with universal precautions to prevent transmission of CCHF in hospitals is the most useful strategy. Medical workers should take all protective measures (including barrier nursing, isolation, and use of face shields or surgical masks, eye protection, and gloves) when handling infected patients, their blood, and other bodily fluids, or even when simply working in proximity to CCHF patients.<sup>3,11,16</sup>

This study has a number of limitations. The mode of transmission was not fully established in all cases. Virus types could not be confirmed with molecular characterization, and titer assay using ELISA could not be performed.

In conclusion, direct contact can occur with blood and body fluids, and nosocomial transmission can be airborne. Nosocomial infection is more serious and fatal. Laboratory workers are also at risk. In addition to standard precautions, barrier precautions and airborne preventive methods should be applied during procedures resulting in aerosol formation in order to prevent a nosocomial epidemic. Staff training, rapid diagnosis, and an early response can be life-saving.

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