

# Crimen-Congo Hemorrhagic Fever Without History Of Tick Bite

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## Abstract

Crimean-Congo hemorrhagic fever is an endemic disease in Kosovo appearing each year as sporadic or epidemic form. Infection of people is usually caused by tick bite. We report a fatal case of Crimean-Congo hemorrhagic fever without history of tick bite. The diagnosis of Crimean-Congo hemorrhagic fever was confirmed by reverse transcription-PCR. Diagnosis of the disease, in pre-hemorrhagic phase is difficult but essential for the prognosis of the disease and prevention of spreading the infection among contact persons. Absence of history of the tick bite does not exclude the Crimean-Congo hemorrhagic fever in patients with febrile syndrome in endemic regions of Kosovo. From these data's we conclude that early diagnosis of the disease is a key factor in the outcome of the disease and efficacy of therapy.

## INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne viral disease presenting with flu-like symptoms, hemorrhage and petechia. The virus (CCHFV) is a member of the Nairovirus genera of Bunyaviridae family and can be transmitted to humans by Hyalomma tick-bite, by exposure to infected blood and fomites of patient with CCHF or contact with animal tissue in viremic phase<sup>1</sup>. Milkers and shepherds are frequent victims. Asymptomatically viremic sheep and cattle have been implicated in transmission to abattoir workers, even outside known endemic areas, and it is also hazardous to crush infected ticks<sup>2</sup>. The CCHF virus has a wide geographic distribution, circulating in Africa, the Middle East, Asia, and Central and South-Eastern Europe<sup>3,4</sup>. The disease was first clinically described in 1944 in Crimea in the former Soviet Union during a large outbreak of over 200 cases<sup>4,5</sup>. The CCHF virus was identified in 1967, from a patient in Uzbekistan, and was found to be similar to a virus isolated in 1956 in Congo, hence the name Crimean-Congo<sup>4,6</sup>. In 2001, were register outbreak of CCHF in Kosova, Albania, Pakistan, Iran, and South Africa<sup>8,9,10</sup>. Since 1995, Kosovo is facing almost every year sporadic or epidemic form of CCHF. In Kosovo the main mode of transmission of the infection is through tick named hyalomma marginatum, and also are registered cases of intrahuman and nosocomial transmission of the virus.

## CASE REPORT

We present a 24 year old male patient with previously good health from Gjakova (Kosovo) who denies to be bitten by a tick. Last two weeks before coming to the family doctor, he was working as a deminer in endemic region for CCHF. The disease begins with general symptoms, fever, chills, headache and was treated for 6 days as an outpatient by the family doctor with analgetics, antipyretics and infusions. On day seven starts cutan hemorrhagic syndrome with subcutaneous hematoma on the hands and feet and the patient is referred to the Clinic of Infectious Diseases in Prishtina as febrile state.

On admission, the patient was orientated but prostrate, without fever, with headache, arthralgia, injected sclera, petechial bleeding in axillar and pectoral region, subcutaneous hematoma at the sites of venepuncture.

The number of red blood cells were  $5.6 \times 10^{12}$  cells/liter (normal range  $4.5 \times 10^{12}$ - $5.9 \times 10^{12}$  cells / liter), hemoglobin level 15.7 g/dl (normal range 13.5-17.5 g / dl ) and number of platelet count was reduced to  $23 \times 10^9$ /liter (normal range  $140 \times 10^9$ /liter -  $400 \times 10^9$ /liter ). Indirect hyperbilirubinemia, hyperuremia, prolonged prothrombin time, high levels of alanine and aspartate transaminase, high levels of lactate dehydrogenase and creatine phosphokinase were also noticed.

The same day of hospitalizations the condition of the patient deteriorates with intensive hemorrhagic syndrome, gingival bleeding, petehial bleeding, subcutan hematoma, hemoperitoneum, low level of consciousness. Abdominal ultrasonography revealed hepatosplenomegaly, hemorrhagic cholecystitis and presence of free fluid in the abdominal cavity, suggestive of hemoperitoneum. Chest radiograph showed haemorrhagic pleuritis.

On day eight of illness, the patient's condition deteriorates further with sopor, fasciculations and massive hemorrhagic syndrome with hematemesis, melena, epistaxis. The patient was anemic, with decreased levels of red blood cells  $3.8 \times 10^{12}$  cells/liter and hemoglobin 11.8 g/dl and decreased platelet count to  $16 \times 10^9$ /liter. The alanine and aspartate transaminase were up to 823 U/liter (normal range 5-40 U/liter) and 2320 U/liter (normal range 5-40 U/liter). Also lactate dehydrogenase and creatine phosphokinase levels were elevated, 4442 U/liter (normal range 114-240 U/liter) and 14 405 (normal range 10 to 120 mcg/L). Prothrombin time was prolonged 46 % (70-120 %).

Hemorrhagic fever with kidney syndrome and severe form of leptospiroses were excluded. Based on epidemiological data, clinical and laboratory performance the treatment consisted on supportive therapy with hydration, antibiotics, ribavirin given parenterally, blood transfusions, plasma and platelets solutions.

Even despite intensive treatment, the patient's condition deteriorates and ends with death on the eighth day of the disease, due to hemorrhagic shock and pulmonary edema. Diagnosis was confirmed by reverse transcription-PCR for CCHF. The case was identified as CCHF on the seventh day of illness, due to the lack of history of the tick bite. Initially the patient was treated as a fly like syndrome.

## **DISCUSSION**

The CCHF is a zoonotic viral infection associated with high rate of morbidity and lethality. The main mode of transmission of the infection is through tick bite and also are registered cases of intrahuman and nosocomial transmission of the virus. Infection can also occur via skin lesions when crushing an infected tick and also associated with the slaughtering of infected animals via small-particle aerosol from infected rodent excreta, and from contaminated needle sticks or infected fomites<sup>10,11,12,13</sup>. CCHF is a severe hemorrhagic fever with shock, disseminated intravascular coagulation, frequent extensive bleeding, and severe thrombocytopenia<sup>8,10</sup>. The virus infects the

reticuloendothelial system and frequently involves hepatocytes extensively, leading to icteric hepatitis<sup>15</sup>.

Clinical features usually include a rapid progression characterised by haemorrhage, myalgia and fever, with a mortality rate of up to 30%<sup>4</sup>. Since 1995, Kosovo is facing every year cases of CCHF (except year 1997) with reported high mortality rate<sup>16</sup>. The first symptoms of our patient were chills, fever, muscle aches, loss of appetite, headache and arthralgia. The most common symptoms reported in the literature have been fever, fatigue, headache, loss of appetite, and myalgia<sup>17</sup>. Typically, 5-6 days after exposure to infected blood or tissues, the flu-like symptoms occur that can last up to a week. However, in 75% of cases, hemorrhagic syndrome appears within 3-5 days after onset of illness with gingival bleeding, epistaxis, hematuria and melena. In our case hemorrhagic syndrom appears in seventh day of illness. From laboratory tests were very significant thrombocytopenia, high liver enzymes and prolonged prothrombin time, indicating severe damage of the liver. This accords with the data of other authors<sup>1,4</sup>. Disseminated intravascular coagulation can present a result of acute kidney weakness and shock, and following acute respiratory distress syndrome<sup>13,17</sup>. Treatment with ribavirin may be useful if given within the early stage of disease<sup>18</sup>. Diagnosis of CCHF is important to prevent the spread of CCHF virus among the health-care workers and relatives of patients<sup>4</sup>.

## **CONCLUSION**

From these data's we conclude that early diagnosis of the CCHF is a key factor in the outcome of the disease and efficacy of therapy. Diagnosis of the disease, in pre-hemorrhagic phase is difficult but essential for the prognosis of the disease and prevention of spreading the infection among contact persons. Absence of history of the tick bite does not exclude the CCHF in patients with febrile syndrome in endemic regions of Kosovo.

## **References**

1. Kaya Kiliç E, Yilmaz U, Cesur S, Koçak Tufan Z, Kurtoğlu Y, Bulut C, et al. Two Crimean-Congo hemorrhagic fever cases without history of tick contact from Ankara region. *Mikrobiyol Bul* 2009; 43(4):677-81.
2. Rodriguez LL, Maupin GO, Ksiazek TG, et al. Molecular investigation of a multisource outbreak of Crimean-Congo hemorrhagic fever in the United Arab Emirates. *Am J Trop Med Hyg* 1997; 57:512.
3. Lindenbach BD, Rice CM, Chanock RM. Flaviviridae: the viruses and their replication. In *Fields virology*. 4th edition. Edited by Knippe DM, Howley PM, et al. Philadelphia, PA: Lippincott, Williams & Wilkins; 2001; 991-1041.
4. Ahmeti S, Raka L. Crimean-Congo Haemorrhagic Fever in Kosovo: a fatal case report. *Virology* 2006; 3:85.
5. Hoogstraal H. The epidemiology of tick born Crimean-

- Congo haemorrhagic fever in Asia, Europe and Africa. *J Med Entomol* 1979; 15:307-417.
6. Cagatay A, Kapmaz M, Karadeniz A, Basaran S, Yenerel M, Yavuz S et al. Haemophagocytosis in a patient with Crimean–Congo haemorrhagic fever *J Med Microbiol* 2007; 56(8):1126-1128.
7. Jauréguiberry S, Tattevin P, Tarantola A, Legay F, Tall A, Nabeth P, et al. Imported Crimean-Congo Hemorrhagic Fever. *J Clin Microbiol* 2005; 43(9):4905-4907.
8. Swanepoel R. Crimean-Congo haemorrhagic fever. In: Palmer SR, Soulsby EJJ, Simpson DIH, eds. *Zoonoses*. Oxford: Oxford University Press; 1998:461-470.
9. Capua I. Crimean-Congo haemorrhagic fever in ostriches: a public health risk for countries of the European Union, *Avian Pathology* 27, 117-120; Guest Editorial 1998.
10. Papa A, Bino S, Llagami A, et al. Crimean-Congo hemorrhagic fever in Albania, 2001. *Eur J Clin Microbiol Infect Dis* 2002;21:603-606.
11. Morikawa, S, Saijo M, Kurane I. Recent progress in molecular biology of Crimean-Congo hemorrhagic fever. *Comp Immunol Microbiol Infect Dis* 2007; 30(5-6):375-389.
12. Heymann DL. An Official Report of the American Public Health Association. In D. L. Heymann (Ed.), *Control of Communicable Diseases Manual*. (18th ed., pp. 35-37). Washington, D.C.American Public Health Association, 2004.
13. Crimean-Congo Haemorrhagic Fever Virus. Health Agency of Canada [www.publichealth.gc.ca](http://www.publichealth.gc.ca).
14. Mardani M, Keshtkar-Jahromi M. Crimean-Congo hemorrhagic fever. *Arch Iran Med* 2007; 10(2):204-214.
15. Burt FJ, Swanepoel R, Shieh WJ, Smith PA, Leman PW, Greer LM. et al. Immunohistochemical and in situ localization of Crimean-Congo hemorrhagic fever virus in human tissues and pathogenic implications. *Arch Pathol Lab Med* 1997;121:839.
16. Humolli I, Dedushaj I, Zupanac TA, Muçaj S. Epidemiological, Serological and Herd Immunity of Crimean-Congo Haemorrhagic Fever in Kosovo. *Med Arh* 2010; 64(2).
17. Yilmaz GR, Buzgan T, Irmak H, Safran A, Uzun R, Cevik MA, et al. The epidemiology of Crimean-Congo hemorrhagic fever in Turkey, 2002–2007 *Int J Infect Dis* 2009; 13(3): 380–386.
18. Ergonul O, Celikbas A, Dokuzoguz B, Eren S, Baykam N, Esener H. The characteristics of Crimean-Congo Hemorrhagic Fever in a recent outbreak in Turkey and the impact of oral ribavirin therapy. *Clin Infect Dis* 2004;39:285–89.

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