

Crimean–Congo hemorrhagic fever: a report of four cases

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Crimean–Congo hemorrhagic fever (CCHF) is an often fatal viral infection described in about 30 countries worldwide. It is transmitted to humans through the bite of an infected tick and via direct contact with blood or tissue from infected humans and livestock. In this article, we report four cases of CCHF disease in men of age 21, 28, 29, and 33 years. Two patients were butchers and two were farmers. CCHF should be considered in patients with fever, bleeding, and low platelet counts.

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Introduction

The viral hemorrhagic (or haemorrhagic) fevers are a diverse group of animal and human illnesses, which include five distinct families of RNA viruses (*Arenaviridae*, *Filoviridae*, *Bunyaviridae*, *Flaviviridae*, and *Rhabdoviridae*) [1]. Crimean–Congo hemorrhagic fever (CCHF) virus or Central Asian hemorrhagic fever virus is an RNA virus of the genus *Nairovirus* (family: *Bunyaviridae*) [2]. Clinical features usually include a rapid progression of symptoms characterized by hemorrhage, myalgia, and fever, with a mortality rate of up to 30% [3].

CCHF is a threat to farmers and other agricultural workers, veterinarians, laboratory workers, and hospital personnel. CCHF virus can be inactivated by disinfectants, including 1% hypochlorite and 2% glutaraldehyde. It is also destroyed by heating at 56°C (133°F) for 30 min [3–5].

Several factors have made CCHF virus an important public health concern, which include its wide and extended geographical distribution, its potential to cause outbreaks and highly fatal disease in humans, the lack of vaccine, limited treatment options, as well as fears about

its use as a biological agent by terrorists or criminals. Owing to its potential to cause community and nosocomial outbreaks, a quick and accurate diagnosis of CCHF is important for case management and protection of the medical staff. Late diagnosis of patients decreases treatment efficacy and increases the risk of fatal outcome [6]. Virus isolation is very constraining as it must be performed in high biocontainment laboratories of biosecurity level 4 (BSL4) [7].

Cases reports

Between June 2010 and June 2011, four patients were admitted to Shahid Sadoughi Hospital in Yazd. The cases have been reported in the following.

Case 1

A 21-year-old man from Yazd presented with a 4-day history of fever of 38.2°C, malaise, body ache, nausea, vomiting, abdominal pain, and headache. On examination, he did not exhibit any signs of hepatosplenomegaly or lymphadenopathy. He was a butcher and did not report any travel history abroad. He had experienced CCHF 3

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years earlier. On admission, urine analysis showed protein (+) and blood (+++).

Case 2

A 33-year-old man presented with a fever of about 39.1°C and vomiting. He was a butcher and had a history of excessive nausea and vomiting. On examination, he did not exhibit any signs of hepatosplenomegaly or lymphadenopathy. He had also severe skin eczema and had experienced CCHF earlier.

Case 3

The third case was admitted with hepatosplenomegaly. He was a 28-year-old man. His complaints started several days before admission. Physical examination revealed mild tenderness on deep palpation in the epigastrium region. On examination, he had not any symptom for hepatosplenomegaly or lymphadenopathy. On admission, he had a fever of 38°C and abdominal discomfort. This patient was a farmer.

Case 4

A 29-year-old man presented with fever, vomiting, headache, and hematuria. On examination, he had a slight hepatosplenomegaly. He was a farmer. The patient did not report any travel history abroad.

Table 1 shows the laboratory parameters of the patients on admission. Serological tests for differential diagnosis such as Epstein–Barr virus infection, brucellosis, toxoplasmosis, cytomegalovirus, and hepatitis A, B, and C were performed. These tests were negative.

Differential diagnosis is necessary for other infectious diseases showing similar symptoms and it is vital to consider CCHF in the differential diagnosis. Therefore, PCR was performed.

Blood samples of the patients taken on days 3 and 6 during the hospital stay were sent to the National Laboratory of Research and Diagnosis of Arboviruses and Viral Hemorrhagic Fevers Tehran. PCR result and immunoglobulin M and immunoglobulin G (by ELISA) for Crimean–Congo fever were reported to be positive in our samples.

Table 1. Laboratory parameters of the patients on admission.

Parameters (normal limits)	Case 1	Case 2	Case 3	Case 4
Hb concentration (11.8–15.2) (g/dl)	19.1	14.1	14.8	8.5
Leucocytes (4100–11 300) (/mm ³)	4800	1300	3900	3100
Thrombocytes (150 000–450 000) (cells/mm ³)	32 000	23 000	30 000	30 000
AST (8–46) (U/l)	2778	2119	2177	2169
ALT (7–47) (U/l)	1018	1051	1031	1065
PT (11–15) (s)	12	12	13.3	26.4
aPTT (30–46) (s)	49	37	35	81
BUN (5–25) (mg/dl)	49	48	52	38
Creatinine (0.3–1.5) (mg/dl)	8	9.2	10	17

ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Hb, hemoglobin; PT, prothrombin time.

The patients were treated with ribavirin [30 mg/kg loading dose, 15 mg/kg (6 hourly) for 4 days, 7.5 mg/kg (8 hourly) for 6 days]. The fourth case was cured with ribavirin in combination with folic acid (1.5 mg/day) and one unit of packed cells. For a period of 4–6 days, the patients showed progressive improvement in clinical and biochemical parameters.

Table 2 shows the biochemical parameters in the patients after treatment with ribavirin. All patients were discharged well.

Discussion

CCHF virus was identified in 1967, from a patient in Uzbekistan, and found to be similar to a virus isolated in 1956 in Congo, hence the name Crimean–Congo [8]. The history of CCHF in Iran shows that the disease has been detected in Iran since 1970.

Outbreaks of CCHF among shepherds, agricultural and abattoir workers, livestock handlers, skin processors, veterinary personnel, butchers, and other support personnel employed in jobs requiring some contact with animals and animal byproducts [9,10].

This study reports four human CCHF cases from Iran. Finally, the patients showed progressive improvement in clinical and biochemical parameters following ribavirin and were discharged.

Clinical diagnosis of CCHF can safely be made if baseline investigations reveal leucopenia, thrombocytopenia, and raised alanine aminotransferase in the absence of some other obvious causes of bleeding [11].

Ribavirin has been used in CCHF, and its efficacy was estimated at 89% in patients with confirmed Crimean–Congo fever, and 70% in patients with suspected CCHF in a large clinical study of 139 treated patients [12]. Between 1999 and 2004, a total of 255 patients with CCHF were recorded in Southeast Iran. Ninety-three percent of patients were treated with oral ribavirin [13].

Table 2. Laboratory parameters of the patients on discharge.

Parameters (normal limits)	Case 1	Case 2	Case 3	Case 4
Hb concentration (11.8–15.2) (g/dl)	9.6	14.8	13.1	8.1
Leucocytes (4100–11 300) (/mm ³)	12 900	5200	5700	5100
Thrombocytes (150 000–450 000) (cells/mm ³)	348 000	173 000	155 000	319 000
AST (8–46) (U/l)	49	45	71	101
ALT (7–47) (U/l)	45	53	46	43
PT (11–15) (s)	11	11	12.1	14
aPTT (30–46) (s)	42	34	35	47
BUN (5–25) (mg/dl)	13	15	19	16
Creatinine (0.3–1.5) (mg/dl)	1.2	1.9	1.4	0.7

ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Hb, hemoglobin; PT, prothrombin time.

Another study reported a nosocomial spread of the disease in a hospital in, northeastern Iran, with a very short incubation period for one of the secondary cases. The patient was a medical student who had a negligible contact with a CCHF patient during his admission to the hospital. The time interval between contact and the onset of symptoms was only 20 h. Unfortunately, he died within 1 week of exposure [14].

Another study reported a fatal case of CCHF observed in a patient from Kosova. Late diagnosis decreased the efficacy of treatment and the patient died due to severe complications of infection [5].

In 2011, the first case of CCHF was observed in Oman. A 37-year-old man presented to the Sultan Qaboos University Hospital with a 5-day history of fever of 38.5°C, malaise, body ache, nausea, vomiting, and abdominal pain. Repeated serology for CCHF became strongly positive after 5 days from the initial negative test, and accordingly the patient was started on ribavirin and he responded; his condition improved dramatically [15].

Conclusion

This study was interesting because our cases were related to different parts of Iran and included age groups between 20 and 30 years. Despite a number of the mentioned studies in which some patients had died, in the present study all patients improved with treatment. This report of four cases suggests that CCHF should be considered during the differential diagnosis of acute onset of fever, headache, myalgia, and thrombocytopenia, especially if the patient has a history of contact with animals, particularly in areas where this infection is endemic. The quick and accurate diagnosis of CCHF is essential for successful treatment and prevention of spread of the disease.

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Conflicts of interest

The authors have no conflict of interest.

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