

Report of nine cases of Crimean-Congo haemorrhagic fever From Iran

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ABSTRACT

Crimean-Congo haemorrhagic fever (CCHF) is an often fatal viral infection described in about 30 countries around the world. It is transmitted to humans by the bite of an infected tick and by direct contact with blood or tissue from infected humans and livestock. In the following, we report nine cases of CCHF disease. This paper reported nine human CCHF cases, two in Tabas and Bandar Abbas and seven in Yazd. They were 21-, 33-, 28-, 29-, 61, 34, 35, 36 and 52 year-old men. The first, second and third patients were butchers and other patients were farmers. CCHF should be investigated in the patients with fever, bleeding and low platelet counts.

Key words: Bleeding and low platelet counts, Crimean-Congo, haemorrhagic fever

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INTRODUCTION

The viral haemorrhagic (or hemorrhagic) fevers (VHFs) are a diverse group of animal and human illnesses. They may be caused by five distinct families of ribonucleic acid (RNA) viruses: The families *Arenaviridae*, *Filoviridae*, *Bunyaviridae*, *Flaviviridae* and *Rhabdoviridae*.¹

Crimean-Congo hemorrhagic fever virus (CCHFV) or Central Asian haemorrhagic fever virus is an RNA virus of the genus *Nairovirus* (family: *Bunyaviridae*).²

Clinical features usually include a rapid progression characterized by haemorrhage, myalgia and fever, with a mortality rate of up to 30%.³

This disease is a particular 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 become an important public health issue, including its wide and extending 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. Due to its potential to cause community and nosocomial outbreaks, a quick and accurate diagnosis of CCHF is important for case management and protection of medical staff. In fact, 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

This paper report nine human Crimean-Congo fever cases, two in Tabas and Bandar Abbas and seven in Yazd, during 2010 to 2013.

CASE REPORT

During 5 June 2010 to 8 June 2013, nine patients were admitted to Shahid Sadoughi Hospital in Yazd. The cases have been reported in the following:

Case 1

On June 2010, a male, 21 years of age, from Yazd presented with a 4-day of fever of 38.2°C, malaise, body ache, nausea, vomiting, abdominal pain and headache. On examination, he had not any symptom for hepatosplenomegaly or lymphadenopathy. He was butcher. The patient did not report any travel history abroad. He had experienced CCHF 3 years ago. On admission, urine analysis showed protein (+) and blood (+++). Finally, he was treated.

Case 2

On September 2010, a male, 33 years of age, from Yazd presented with a fever about 39.1°C and vomiting. He

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10.4103/0300-1652.153409

was butcher and had a normal antenatal course with a history of excessive nausea and vomiting. On examination, he had not any symptom for hepatosplenomegaly or lymphadenopathy. He had also severe eczema on the skin and a previous experience for CCHF. Finally, he was treated.

Case 3

The third case (November 2010) was admitted with hepatosplenomegaly. He was a male, 28 years of age, from Tabas. His complaints started several days before admission. Physical examination revealed mild tenderness on deep palpation in 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. Finally, he was treated.

Case 4

On March 2011, a male, 29 years of age, from Bandar Abbas 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. Finally, he was treated with ribavirin in combination with folic acid.

Cases 5-9

In March 2013, three butchers and two worker in an ostrich farm were infected with CCHF in central part of Iran. They were admitted to shahid sadoughi hospital. Considering the role ostriches play in transmitting the disease, serum samples from five ostriches of that farm were taken and sent to the laboratory for CCHF ELISA tests. The result of the IgG test was positive for one (20%) of the ostriches. At the same time, serum samples of eight sheep from the same farm were sent for IgG testing, two (25%) of which were positive.

Tables 1 and 3 show the laboratory parameters of the patients on admission.

Serological tests for differential diagnosis such as Epstein-Barr virus (EBV) infection, brucellosis, toxoplasmosis, cytomegalovirus, hepatitis A, B and C were performed. These tests were negative.

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 pack cell.

Differential diagnosis is necessary for other infectious diseases showing similar symptoms as well as it is vital to consider CCHF in the differential diagnosis. Therefore, polymerase chain reaction (PCR) was performed.

Blood samples of the patients taken on days 3 and 6 during hospital stay were sent to the National Laboratory of Research and Diagnosis of Arboviruses and Viral Haemorrhagic Fevers Tehran. PCR result and Immunoglobulin M (IgM) and Immunoglobulin G (IgG) [by enzyme-linked immunosorbent assay (ELISA)] for CCF were reported to be positive in our samples.

Over a period of 4-6 days, the patients showed progressive improvement in clinical and biochemical parameters.

Tables 2 and 4 show the biochemical parameters in the patients after treatment with ribavirin (on discharge). Finally, the patients were discharged well.

DISCUSSION

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.⁸

The history of the CCHF in Iran shows that the disease has been detected in Iran since 1970. From 1970 to 1978, some scientists worked on serology and epidemiology of this disease in humans and livestock in Iran.⁹

Table 1: Laboratory parameters of the patients on admission

Parameters (normal limits)	Case 1	Case 2	Case 3	Case 4
Hb concentration g/dl (11.8-15.2)	19.1	14.1	14.8	8.5
Leucocytes/mm ³ (4100-11300)	4800	1300	3900	3100
Thrombocytes cells/mm ³ (150000-450000)	32000	23000	30000	30000
AST U/L (8-46)	2778	2119	2177	2169
ALT U/L (7-47)	1018	1051	1031	1065
PT s (11-15)	12	12	13.3	26.4
aPTT s (30-46)	49	37	35	81
BUN mg/dl (5-25)	49	48	52	38
Creatinine mg/dl (0.3-1.5)	8	9.2	10	17

Hb – Haemoglobin; BUN – Blood urea nitrogen; AST – Aspartat aminotransferase; ALT – Alanine aminotransferase; PT – Prothrombin time; aPTT – Activated partial thromboplastin time

Table 2: Laboratory parameters of the patients on discharge

Parameters (normal limits)	Case 1	Case 2	Case 3	Case 4
Hb concentration g/dl (11.8-15.2)	9.6	14.8	13.1	8.1
Leucocytes/mm ³ (4100-11300)	12900	5200	5700	5100
Thrombocytes Cells/mm ³ (150000-450000)	348000	173000	155000	319000
AST U/L (8-46)	49	45	71	101
ALT U/L (7-47)	45	53	46	43
PT s (11-15)	11	11	12.1	14
aPTT s (30-46)	42	34	35	47
BUN mg/dl (5-25)	13	15	19	16
Creatinine mg/dl (0.3-1.5)	1.2	1.9	1.4	0.7

Hb – Haemoglobin; BUN – Blood urea nitrogen; AST – Aspartat aminotransferase; ALT – Alanine aminotransferase; PT – Prothrombin time; aPTT – Activated partial thromboplastin time

Table 3: Laboratory parameters of the patients on admission

Parameters (normal limits)	Case 5	Case 6	Case 7	Case 8	Case 9
Hb concentration g/dl (11.8-15.2)	18.2	14	14.2	14.1	7.7
Leucocytes/mm ³ (4100-11300)	5800	1200	3800	3800	3200
Thrombocytes Cells/mm ³ (150000-450000)	34000	27000	31000	30000	30000
AST U/L (8-46)	2678	2219	2177	2176	2166
ALT U/L (7-47)	1017	1041	1041	1040	1060
PT s (11-15)	12	12	13.1	13	26
aPTT s (30-46)	48	37	35	36	81
BUN mg/dl (5-25)	48	47	52	45	38
Creatinine mg/dl (0.3-1.5)	6	9.2	9	16	16

Table 4: Laboratory parameters of the patients on discharge

Parameters (normal limits)	Case 5	Case 6	Case 7	Case 8	Case 9
Hb concentration g/dl (11.8-15.2)	9.2	14	13	8	7
Leucocytes/mm ³ (4100-11300)	11900	4200	5700	5600	5110
Thrombocytes Cells/mm ³ (150000-450000)	338000	221000	165000	165000	321000
AST U/L (8-46)	49	46	73	74	102
ALT U/L (7-47)	46	51	47	47	43
PT s (11-15)	11	11	12	12	14
aPTT s (30-46)	43	34	35	35	47
BUN mg/dl (5-25)	13	15	18	18	16
Creatinine mg/dl (0.3-1.5)	1.3	1.9	1.4	0.8	0.7

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.¹⁰

This study reports nine human CCHF cases from Iran. Finally, the patients showed progressive improvement in clinical and biochemical parameters and were discharged. It was an interesting study because our cases were related to different parts of Iran and were included age-groups between 20-60 years.

A study reported the first case of CCHF in Kermanshah province. Clinical presentation was characterized by fever, myalgia and haemorrhage. This patient was treated with ribavirin.¹¹

Clinical diagnosis of CCHF can safely be made if baseline investigations reveal leukopenia, thrombocytopenia and raised Alanine aminotransferase (ALT) 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 CCF and 70% in patients with suspected CCHF in a large clinical study of 139 treated patients.¹²

During June 1999 to February 2004, a total of 255 patients with CCHF were recorded in Southeast of Iran. Ninety-three percent were treated with oral ribavirin.¹³

Another study reported a nosocomial spread of the disease in a hospital in Mashhad, 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 the contact and the onset of symptoms was merely 20 hours. Unfortunately, he died within 1 week of exposure.¹⁴

In 2011, the first case of the 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, bodyache, nausea, vomiting and abdominal pain. The repeated serology for CCHF came strongly positive after five days from the initial negative test, and accordingly patient started on ribavirin and he responded to it. His condition improved dramatically.¹⁵

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

Another study reported three human CCHF cases in Egypt. This study has not spoken about the treatment result in due time.²

CONCLUSION

This study was interesting because our cases were related to different parts of Iran and were included age-groups between 20-60 years. Despite a number of the mentioned studies that some patients had died, in the present study all patients improved with treatment. This report of nine cases suggest that CCHF should be considered during the differential diagnosis of acute onset of fever, headache, myalgia and thrombocytopenia, especially if 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 stopping the spread of the disease.

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How to cite this article: Ayatollahi J, Shahcheraghi SH, Mirjalili M. Report of nine cases of Crimean-Congo haemorrhagic fever From Iran. *Niger Med J* 2015;56:156-9.

Source of Support: Nil, **Conflict of Interest:** None declared.

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