

## CASE REPORT

# THE SEROEPIDEMIOLOGICAL ASPECTS OF CRIMEAN-CONGO HEMORRHAGIC FEVER IN THREE HEALTH WORKERS: A REPORT FROM IRAN

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Crimean-Congo hemorrhagic fever (CCHF) is caused by *Nairovirus*, genus *Bunyavirus* in family of bunyaviridae, and is spread by the tick *Hyalomma* spp or via blood transfusion and contaminated blood of human and animal. CCHF virus infection was rarely reported in Iran before 1999. From January 1st 1999 to October 1st 2002 nearly 144 confirmed sporadic CCHF cases reported from many provinces of Iran. Seroepidemiological details of three cases of nosocomial CCHF that were seen in three different hospitals throughout Iran are described here. Of the three patients in this study, two died. All three patients initially presented with severe Ebola virus-like or influenza-like symptoms, making the disease difficult to diagnose in the early stage. However, petechiae and signs of bleeding distinguish CCHF from influenza, but not from Ebola which is not related to this disease and has not been reported in Iran. Leukopenia and thrombocytopenia were the most important laboratory findings. Rising IgG and IgM titers made the diagnosis certain in two of the cases. Despite the low mortality rate because of very effective treatment with ribavirin among the general population, two of the three CCHF patients died. This poor prognosis for CCHF signals the importance of early diagnosis and admission of suspicious cases to hospital.

**Keywords** • *Bunyaviridae* • Crimean-Congo hemorrhagic fever • *Nairovirus* • Health workers • nosocomial infections

### Introduction

Crimean-Congo hemorrhagic fever (CCHF) is caused by a virus that is widely distributed in wild and domestic mammals, birds and ticks in many regions of Africa, Europe and Asia.<sup>1</sup> CCHF was first observed in the Crimea in 1944 by Russian scientists. The virus was first isolated in Africa from the blood of a febrile patient in Zaire in 1956.<sup>2</sup> In 1967, Simpson et al described 12 cases of a feverish illness with similar signs and symptoms of CCHF, of whom five were diagnosed as infection in the laboratory and the virus was isolated after inoculation of newborn mice with sera samples of

infected patients. They were able to show that these viruses were serologically indistinguishable from the one isolated in 1956, and that this type of Congo virus was also similar to other virus strains from Central Asia, USSR and Bulgaria.<sup>3</sup>

The virus has been classified as a *Nairovirus* genus from the family of *Bunyaviridae*. The virus contains RNA and is inactivated by lipid solvents and detergents.<sup>4,5</sup> In Africa, the virus has been isolated from a variety of animals, including cattle, sheep, goats, and from a number of ticks that parasitize them, including *Hyalomma* spp, *Hyalomma maginatum*, *Hyalomma anatolieum* and *Rhipicephalus* spp.<sup>6</sup> In Iran, *Hyalomma* spp probably plays the main role in transmitting the infection from animals to humans.<sup>7</sup>

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### Clinical presentation

The disease is usually transmitted to man

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following a tick bite, or through contact with the patient's blood or blood-contaminated specimens. Exposure to the blood of infected animals, especially cattle and sheep, has led to severe and often fatal infections. The incubation period for CCHF depends on the mode of transmission. It can extend from 2 to 7 days following a tick bite, or up to 10 to 14 days after blood transfusion or organ transplantation. The onset of the illness is sudden, with fever, chills, severe muscular pains, headache, vomiting, and pain in the epigastric and lumbar regions. A hemorrhagic state develops from the third to the fifth day and manifests with skin petechiae or purpura, and bleeding from the mucous membranes that manifests with epistaxis, hemoptysis, hematemesis, melena and hematuria. At this stage the conjunctiva is infected, face is flushed, tongue is dry, blood pressure decreases and heart sounds become weak. The liver is enlarged and tender, and there is tenderness over the epigastrium and splenic region. In patients who recover, the temperature decreases between the 10th and the 20th days and bleeding stops; however, convalescence can last up to 4 weeks or longer. In fatal cases, death from massive hemorrhage and cardiac arrest occurs 7 to 9 days after onset of the illness.<sup>8-10</sup>

### Diagnosis

The diagnosis is based on epidemiologic studies and clinical presentation. The diagnosis may be confirmed in a reference laboratory by detection of a rise in specific IgG or IgM titers using ELISA.<sup>10</sup>

### Treatment

Meticulous patient care is the mainstay of treatment. Intensive monitoring and blood transfusion are mandatory in some cases. Prescription of antiviral medication such as ribavirin may show some benefit in established cases.<sup>7-10</sup>

## Case Reports

CCHF has been reported as a nosocomial infection among medical staff. Three cases are reported here.

### Case 1

A 26-year-old female medical student became ill in August 1999 at Shahrekurd (southcentral Iran) and presented with severe undulant fever,

vomiting and diarrhea. Laboratory investigations revealed thrombocytopenia. After 2 weeks, the patient was transferred to a University Hospital in Tehran because of severe dizziness and a sudden onset of gastrointestinal bleeding. Three days later, she died of disseminated intravascular coagulation (DIC). A serum sample that was sent to South Africa showing a rise in CCHF IgG ( $> 0.2$ ). These results confirmed the presence of CCHF virus.

### Case 2

A 32-year-old male physician presented to a clinic in Isfahan (central Iran) with severe malaise, fever, vomiting, diarrhea, petechiae, epistaxis and oral bleeding. Based on these clinical findings, the patient was diagnosed with CCHF. There was no history of recent travel to suspicious regions or contact with domestic animals. Despite leukopenia, thrombocytopenia and a high titer of IgG ( $> 0.2$ ), the patient recovered quickly. During hospitalization, antibiotics, steroids and intravenous immunoglobulin were administered. At the time of writing, the patient was well and without CCHF-associated sequelae.

### Case 3

A 29-year-old female staff member of the Blood Transfusion Center in Shahrekurd, Iran, presented with high fever, petechiae, epistaxis and oral bleeding. A diagnosis of CCHF virus was made. The patient had no history of recent travel or contact with domestic animals. Laboratory investigations showed no evidence of severe thrombocytopenia and there was no rise in IgG or IgM titers. Despite these results, the patient died as a result of DIC.

## Discussion

CCHF virus is most often transmitted to man following a tick bite (genus *Hyalomma*),<sup>11</sup> however, an increasing number of cases have occurred among medical, laboratory and nursing staff in hospitals. In nosocomial cases, the infections have apparently been acquired by direct contact with patients' blood or blood-contaminated specimens. There have been reports that exposure to the blood of infected animals, especially cattle and sheep, have led to severe and often fatal infections. The disease has recently been reported from several countries including China,<sup>4</sup> Oman,<sup>12</sup> Senegal,<sup>11-14</sup> Pakistan,<sup>15</sup> United Arab Emirates,<sup>16,17</sup> Saudi

Arabia,<sup>5</sup> South Africa,<sup>6</sup> Republic of Guinea,<sup>18</sup> Central African Republic,<sup>19</sup> Niger,<sup>20</sup> Sudan<sup>21</sup> and Iran.<sup>22</sup> The CCHF virus has been reported as a nosocomial infection from Iraq,<sup>23</sup> South Africa,<sup>8,9,24,25</sup> United Arab Emirates,<sup>26</sup> and Pakistan.<sup>27</sup> More than 144 cases of CCHF have been reported from Iran (between January 1st and October 1st 2002); however, few were identified as nosocomial infections.<sup>28</sup> This paper suggests that medical staff who works in hospitals or laboratories may acquire the infection directly from patients or contaminated human products. Other studies support these types of transmission.<sup>8,9,23-27</sup>

It is of utmost importance to diagnose suspicious cases of CCHF in the early stages and initiate treatment as early as possible. Blood samples from suspected CCHF virus cases should be handled carefully, following stringent safety guidelines in the laboratory to prevent the transmission of CCHF among medical and laboratory staff.

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