

A Case of Crimean-Congo Hemorrhagic Fever in Oman

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Abstract

In the summer of June 2011, the first case of Crimean-Congo hemorrhagic fever (CCHF) was observed in Oman since the last fifteen years. The first blood sample using reverse transcriptase polymerase chain reaction (PCR) test were sent looking for CCHF, tick-borne encephalitis, dengue, Japanese encephalitis, Chikungunya and West Nile. All resulted as negative. 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.

Keywords: Crimean-Congo hemorrhagic fever; Oman; Arab peninsula; PCR; Cytokines.

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a severe viral human disease with fatality rates up to 30%. It is a tick-borne disease described in more than 30 countries in Europe, Asia and Africa.^{1,2} The causative agent is the Crimean-Congo hemorrhagic fever virus (CCHFV) that is a member of the genus *Nairovirus* of the family *Bunyaviridae*. An additional mode of transmission is direct contact of broken skin or mucous membranes with blood or tissues of infected livestock or CCHF patients.²

Because of the associated high fatality rate,³ CCHF is considered to be a major public health threat. In addition, the absence of an FDA-approved vaccine, and the potential for human-to-human transmission and nosocomial outbreaks, it is also considered to be a significant public health issue. CCHF is noted to be endemic in the neighboring countries in the Arabian Peninsula for instance, in the United Arab Emirates (UAE), Saudi Arabia and Kuwait.⁴⁻⁸ CCHF cases had not been reported in Oman for the last 15 years; however, evidences from the literature indicate that clinical CCHF was first isolated in Oman in 1995 by using either ELISA for antigen or antibody or reverse transcriptase polymerase chain reaction testing, and the disease was found in three unrelated cases, one each in January, May, and June. A subsequent case occurred in August 1996. It also found that all four individuals had exposure to domestic livestock and/or their associated ticks, and no secondary cases were reported.^{9,10}

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As no CCHF case in details had been reported in Oman since the last 15 years, it was suggested that it would be beneficial to present and report in detail the first clinical CCHF case in Oman after a long period of time.

Case Report

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. The patient did not report any travel history abroad. Physical examination revealed mild tenderness on deep palpation in epigastrium and right hypochondriac region.

Laboratory examination on admission showed leukocytes at 16 with 14 neutrophils, a hemoglobin of 16 mg/dL, platelets of 38, an aspartate transaminase (AST) level of 1600 IU/L (reference range <31 IU/L), an alanine transaminase (ALT) level of 850 IU/L (reference range <34 IU/L), a c-glutamyl-transpeptidase level of 1113 IU/L (reference range 9-38 IU/L). Activated partial thromboplastin time (APTT) was prolonged, International Normalized Ratio (INR) was prolonged, and D-dimers were high.

A few hours after admission, blood re-examination revealed that the platelet level was low, and the fibrinogen level was very low. The patient also had hemorrhages, namely, hematuria, melena, gingival bleeding, and the most common manifestation was epistaxis. A chest X-ray showed bilateral lower and mid zone haziness with obliteration of costophrenic angles (picture of plural effusion). An ultrasound of the abdomen revealed some fluid collection. Portal vein cannot be visualized. The advice was to do computed tomography (CT) scan of abdomen. Supportive treatment was initiated. CCHF was not included in the initial differential diagnosis.

On the next day, APTT could not be determined, D-dimers were high. The AST, ALT, and the LDH level were all deranged. The patient developed disseminated intravascular coagulation (DIC), and fresh frozen plasma was given. Serological examination for hepatitis A, B, and C was negative. The PCR for CCHF, tick-borne encephalitis, dengue, Japanese encephalitis, Chikungunya, and West Nile was negative. On the same day, oliguria, mental disturbance, and severe lactic acidosis were established. Bone marrow aspiration, which was performed to exclude hematological malignancy revealed hemoglobinopathy trait, leukoerthroblastic picture with toxic changes, reactive plasmoid lymphocytes and other suspicious cells, high n/c ratio, dark cytoplasm and homogeneous chromatin, and bone marrow irritation and infiltration.

The patient's condition deteriorated rapidly, and he was transferred to the intensive care unit, where he was intubated and given inotropes, fresh frozen plasma, erythrocytes, and corticosteroids. The repeated serology for CCHF came strongly positive after five days from the initial negative test. Accordingly, the patient was started on ribavirin and he responded to it very well. His condition improved dramatically.

Discussion

Although the Arabian Peninsula has been known to be a CCHF-endemic region for a long period of time, no CCHF case was reported in Oman for the last 15 years. After 1995, a cluster of CCHF cases was reported in the neighboring countries for example, in Iran. Additionally, at the same period of time, many CCHF cases were observed in Saudi Arabia and UAE.⁴⁻⁸ We cannot exclude the possibility that unreported CCHF cases may have occurred in previous years in Oman.

The patient had no underlying disease; the presentation of severe illness seems to have been associated with a massive inflammatory response. Evidences from previous studies indicates that increase in the level of inflammatory markers namely IL-6 and TNF- α are associated with disease severity and mortality.^{11,12} In our patient, inflammatory markers such as ANA, lupus anticoagulant, anticardiolipin antibodies and anti-B2-glycoprotein-1 were sent off, and all of them were reported as negative. Regarding the bleeding in this case, the hemorrhages occurred on the same day of admission or the 5th day of the disease, and the most common manifestation was epistaxis.¹³

The first altered parameters in this case were thrombocytopenia, prolonged APTT and International Normalized Ratio (INR). Swanepoel R et al,¹⁴ discussed in their study that leukocytes $>10 \times 10^9/L$, platelets $<20 \times 10^9/L$, AST >200 U/L or ALT >150 U/L, APTT >60 s, and fibrinogen <110 mg/dL are the criteria predicting a fatal outcome, during the first five days of the disease. Another study by Ergonul O et al,¹⁵ found that the criteria for the severity of CCHFV includes AST >700 IU/L and ALT >900 IU/L, and in their study, leukocyte counts was not considered to be a criteria for the severity of the disease. One of the things to note is that our patient fulfilled all four modified criteria. It is shown in the literature that there is a correlation between high viral load and fatal outcome;^{16,17} however, in the present case, the viral load was not done, therefore, it is not possible to observe for the association between viral load and fatal outcome in our study.

The patient did not report any recent travel history abroad. He is a science teacher, and he teaches in one of the secondary schools in the interior region of Oman, but, he was involved in slaughtering goats in one of the farms in the interior region of the country. It has been shown that livestock trade or movements of livestock or wild animals infested with infected ticks might be a culprit in dissemination of infected ticks, and hence spread of CCHFV.² The determination of the exact origin and the conditions that influenced the emergence of CCHF in Oman was observed with great help

for public health experts and veterinary expertise. They conducted environmental sampling as part of their case investigation.

It is difficult to predict whether additional CCHF cases in Oman will occur in the future; however, taking into account that this disease is quite common in neighboring countries considered to be endemic areas, and already one case has been diagnosed after 15 years from the first case discovered in the country in 1996, it can be suggested that the risk of more cases occurring in the future is high. Including CCHF in the differential diagnosis of patients who present with fever accompanied by thrombocytopenia especially in regions of neighboring endemic countries and in individuals returning from an endemic region is warranted. In addition, this case has serious and important public health implications for Oman. More specifically, laboratory capability to safely detect this virus should be evaluated.

Conclusion

To sum up, early diagnosis is important in terms of treatment of patients and prevention of nosocomial infections. Differential diagnosis is also necessary for other infectious diseases showing similar symptoms as well as it is vital to consider CCHF in the differential diagnosis. Apart from intensive supportive therapy, antiviral drug, ribavirin, is a specific treatment of choice for severe case of CCHF.

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