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A Five-Member Family With Crimean-Congo Hemorrhagic Fever; A Case Series Study

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Introduction: Crimean-Congo Hemorrhagic fever (CCHF) is a viral hemorrhagic fever which transmitted by tick-bites, or through contact with infected animal tissues or secretions during and immediately post-slaughter. It can be responsible for severe outbreaks in humans.
Case Presentation: We have explained five patients of a family with (CCHF), which acquired the illness at one time. Every five patients were admitted to our hospital and they treated by ribavirin promptly. Unfortunately, one patient was referred late to the hospital and the treatment started 96 hours after the beginning of the first sign who expired
Conclusions: CCHFV can infect human clustering in a family. To our knowledge, this is the first report of this form in Iran.

*Keywords:*Hemorrhagic Fever, Crimean; Cluster Analysis; Family

1. Introduction

Crimean-Congo hemorrhagic fever (CCHF) is caused by infection with a tick-borne virus (Nairovirus) in the family Bunyaviridae (1-3). In endemic areas, farmers, slaughters, animal holders, and livestock workers are at risk of CCHF (4, 5). Nosocomial outbreaks have been reported and occurred due to exposure to infected blood and secretions (1, 2). Tick bite is one of the most important risk factors for CCHF acquisition (1, 5, 6). Consumption of raw meat is another risk factor (7). The virus is stable under wet conditions for 7 hours at 37 °C, 11 days at 20 °C, and 15 days at 4 °C. Under dry conditions, the virus is stable for at least 90 minutes, but less than 24 hours (8). The onset of CCHF is sudden, with initial signs and symptoms including high fever, headache, back pain, joint pain, stomach pain, and vomiting. Symptoms may also include jaundice, and in severe cases, changes in mood and sensory perception. As the illness progresses, petechia, ecchymosis, nose bleeds, and uncontrolled bleeding at injection sites can be seen. In confirmed outbreaks of CCHF, fatality rates in hospitalized patients have ranged from 9% to as high as 70% and recovery is slow (1, 7). Diagnostic tests include indirect haemagglutination inhibition (IHA), Enzyme -linked immunosorbant assay (ELISA), RT-PCR, and immunofluorescence (IF). The ELISA test has a high sensitivity and specificity, and can be easily reproducible. Here, we present five patients of a family who got CCHF at one time. They were from Khash (a city in Sistan & Balouchestan Province) and among the patients four cases were cured and the father unfortunately died.

2. Case Presentation

2.1. Case 1

On January 5th 2014, a previously healthy 48-year-old man from Khash (Southeastern Iran) was admitted to our hospital (Boo-Ali Hospital, Zahedan University of Medical Sciences) because of acute fever, myalgia, nausea and vomiting from 3 days ago. The above manifestations were appeared about 3 day after he butchered a cow. His oral temperature was 38.5°C and blood pressure was 100/600 mmHg. His pulse and respiratory rates were 80 and 19/min, respectively. The cardiac examination was normal. No other abnormal signs were observed. On admission, a complete blood count revealed a white blood cell count of 12.4×10^9/L (neutrophils 22% and lymphocytes 75%), hemoglobin of 12.7 mg/dL, and a platelet count of 11×10^9/L. Blood urea nitrogen (BUN) and creatinine (Cr) were normal. Other findings were a blood glucose of 92 mg/dl, sodium of 137 mEq/L, and potassium of 3.9 meq/lL. The

Implication for health policy/practice/research/medical education:
CCHF virus can infect human clustering in a family. Health education is very important for the prevention of CCHF.

patient's prothrombin time (PT) was 23s (normal 11 – 15), partial thromboplastin time (PTT), 75 s (normal 30 – 45) and INR was 3. Since, the South east of Iran is an endemic area for CCHF, the patient was placed on a high dose of ribavirin (1200 mg/day, orally) and a blood transfusion was begun. He also received platelets and fresh frozen plasma (FFP). A peripheral blood smear (PBS) obtained on second day of admission revealed a white blood cell count of 1.2×10^9/L (neutrophils 75% and lymphocytes 24%), hemoglobin of 12.9 g/dl, and a platelet count of 10×10^9/L. PT and PTT were 18 and 65 s respectively and INR was 1.8. Repeated peripheral blood smears for P. Malaria were negative. Two blood cultures and urine culture were negative. On 3 days of hospitalization he had hematemesis and referred to ICU. Despite the measures, the patient's clinical status worsened rapidly. Despite supportive measures, the patient died due to extensive hemorrhage on day 6 post-onset of symptoms. The serologic samples (IgM & IgG) were negative for CCHF but RT-PCR was positive.

2.2. Case 2

On January 7th 2014, a 17-year -old man who was the son of our patient was admitted to hospital with a history of acute onset of fever, myalgia and bone pain. He helped his father in butchering. Eight days later (two days after his father died), he was symptomatic and had severe thrombocytopenia (9,000). We started ribavirin for him and blood samples were sent to reference laboratory for more evaluation for CCHF. He received platelet due to severe thrombocytopenia. PT, PTT, and INR, were normal. Serology test (IgM-ELISA) and RT-PCR were positive for CCHF. Fortunately, by adequate and prompt management, he responded to the therapy.

2.3. Case 3

On January 7th, a 50–year-old man with history of fever, headache from 48 hours ago referred to Boo-Ali hospital. He also helped his brother (case 1) in butchering. Therefore, he was also admitted to infectious ward. On admission day, he showed severe thrombocytopenia (52000) but, PT, PTT, and INR were normal. He was treated with ribavirin and received platelet. Fortunately, this patient also responded to treatment. RT-PCR for CCHFV was positive but IgM –IgG ELISA was negative.

2.4. Case 4

On January 7th, a 52-year –old women who was the sister of case 3 was referred to our hospital because of acute fever, myalgia, headache and back pain. She had also a history of cutting the meat and skinning the cow, and admitted to infectious ward and received oral ribavirin. She showed severe thrombocytopenia (10,000). PT, PTT and INR were 14, 70 and 1.2, respectively. RT-PCR was positive for CCHFV but IgG & IgG-ELISA were negative. Two days later, she felt well. Her treatment was completed in hospital and discharged in good condition.

2.5. Case 5

On January 7th, a 17-year –old man who was the son of case 3 was admitted to hospital because of acute fever, myalgia, joint pain, and headache. He helped his family in butchering. He was admitted to infectious ward and received oral ribavirin. He also had severe thrombocytopenia (26,000). PT, PTT and INR were 14, 50 and 1.2, respectively. PCR and IgM-ELISA were positive for CCHFV, but IgG-ELISA was negative. Several days later, he felt well. His treatment was completed in hospital and discharged in good condition.

3. Discussion

Crimean-Congo hemorrhagic fever is an important health problem. It is endemic in many countries around the world; in Asia, Africa, Middle East, and East European countries (1, 2). During the last 15 years, a large number of human CCHF virus infection have been reported from many parts of Iran specially from the Southeastern parts (1, 7, 8). About 67 to 75% of cases in Iran have been reported from Sistan and Baluchestan Province in the Southeastern Iran (5-8). Fortunately, with the borders control and further education during the last two years, the number of disease is decreasing. CCHF has a sudden onset, with high fever, chills, myalgia, malaise, photophobia, and head and back-aches. Fever can last between 5 to 14 days and may be biphasic. Other symptoms include abdominal pain, nausea and vomiting, diarrhea, bradycardia, and conjunctiva congestion. Thrombocytopenia, leucopenia, anemia and elevated aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) have been reported in CCHF patients (5-10). These later two findings along with thrombocytopenia, elevated creatine phosphokinase (CPK), confusion, hepatorenal syndrome and pulmonary failure are associated with a poor prognosis. as we observed in case number 1 (5-7). In this case, PT, PTT, and INR were very high and the incubation period was shorter than other cases (less than 4 days). On the other hand, the interval between onset of symptoms and treatment was long (4 days) and he had hemorrhagic event. The hemorrhagic phase of the disease usually begins on day 4, with the most common manifestations being petechia, epistaxis, gums hemorrhages, hematuria, vaginal, and gastric mucosa bleeding. Death occurs when CCHF causes hemorrhagic shock, or neurological complications, pulmonary hemorrhages, or incurrent infection. Our patient (case 1) had hematemesis and despite the supportive measures and good care, the patient's clinical status worsened rapidly and he died due to extensive hemorrhage on day 6 post-onset of symptoms. Treatment is primarily symptomatic and supportive, as there is no established specific treatment. Ribavirin is effective in vitro and has been used during outbreaks. For patients with mild illness and without hemorrhagic complications, treatment with analgesics

and antipyretics, fluid and electrolyte balance is effective. In severe cases, platelets, FFP, albumin, or coagulation factors are administered. Administration of convalescent plasma with a high neutralizing antibody titer is regarded as a useful treatment (11, 12). A Turkish research team led by Refik Saydam has developed treatment-serum derived from blood of several CCHF-patients, which have been proven to be 90% effective in CCHF-patients (11-13). Vaccines based on the inactivated virus have been investigated since the 1970s, and more recently, possible DNA vaccines have been studies; although, the safety and efficacy of these vaccines have not been demonstrated for humans (11, 12). In 2011, a Turkish research team led by Erciyes University has developed the first non-toxic preventive vaccine, which passed clinical trials; although, the vaccine is pending approval by the FDA (14). Control of tick populations with insecticides, and application of insect repellent to limit tick bites in endemic areas is very important (13, 15). Post-exposure prophylaxis with oral ribavirin for those considered to have been in contact with highly viraemic patients (200 mg twice daily, for 5 days (8). In our cases, the first presented patient had an acute onset of disease, a short incubation period with a late onset of treatment. Thrombocytopenia, anemia, leucopenia, elevation of aspartate aminotransferase with an increasing in PT, PTT, and INR were observed. All of these factors were with poor prognosis and despite the suitable management, he died. Other four cases that had a longer incubation period, an earlier onset of treatment with low INR (less than 1.5) survived. This is the first report of a family with CCHF at one time and with same risk factors. Although, in 2011 we reported the first cases of CCHF among 3 friends following consumption of uncooked liver. All three cases in this report were cured and discharged in good condition (7).

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Authors' Contribution

Rakhshani M, Abedi-poor F, Noori-Jangi Z, Khoorgami P, Hajalizadeh A, Kooshki M, Jahantigh A, Safdari A, Abbasi A, wrote the manuscript.

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