Case series

Crimean-Congo hemorrhagic fever following consumption of uncooked liver: case series study

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Abstract

We have described four patients with Crimean- Congo hemorrhagic fever which acquired the illness following consumption of uncooked sheep liver. Three patients admitted to hospital nearly 36 hours after eating the liver with acute fever and with quick treatment they respond to therapy. Unfortunately, one patient who was referred late to hospital and treatment was after 5 days of the beginning of the first sign, died. Here in, we described four patients who consumed uncooked liver together in a party and apparently there were no other routes for transmission. Three of them were members of a family (one sister and two brothers) and the fourth was their friend who invited to their party

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a fatal viral disease and caused by an infection with a tick-borne virus in the family of *Bunyaviridae[1-3]*. In endemic areas, animal holders, slaughter houses, livestock workers and farmers are at risk of CCHF[3-5]. Healthcare workers are also at risk of infection through unprotected contact with infectious blood and other infected body fluids. Travelers with contact to livestock in endemic regions also are at risk[1,2]. Tick bite is one of the most important risk factors for CCHF acquisition[1,5, and6]. Consumption of meat (not raw meat) is not an important risk factor by itself because the virus is usually inactivated by postslaughter acidification[7,8]. There is no published report of CCHF following consumption of raw liver during the last epidemic in Iran and especially from the Southeast of Iran [7-8]. Here, we present four patients who got CCHF following the consumption of uncooked liver of sheep. They were from Zahedan and there was no prior history of travel to rural area or contact to livestock or tick.

Case 1

On 25 June 2008, a previously healthy 16-year-old female from Zahedan (Southeastern Iran) was admitted to our hospital (Boo-Ali Hospital, Zahedan University of Medical Sciences) because of acute fever, myalgia,,abdominal pain, headache, nausea and vomiting from 5 days ago. She had also watery diarrhea. The above manifestations were appeared about 8 hours after she ate an uncooked liver. Her oral temperature was 38.5°C and blood pressure was 85/50 mmHg. Her pulse and respiratory rates were 115 and 28/min, respectively. The cardiac examination was normal. No other abnormal signs were elicited. On admission, a complete blood count revealed a white blood cell count of 2.3 x 10^9/l (neutrophils 22% and lymphocytes 61%), hemoglobin of 7 g/dl, and a platelet count of 16 x 10^9/l. Blood urea nitrogen was 19 mg/dl and serum creatinine was 0.8 mg/dl. Other findings were a blood glucose of 82 mg/dl, sodium of 137mEq/l, potassium of 4.5mEq/lL.The patient's prothrombin time was 23s (normal 11–15) and partial thromboplastin time was 65 s (normal 30–45). Since, the South east of Iran is an endemic for CCHF, the patient was placed on a high dose of ribavirin (1200 mg/day, orally) and a blood transfusion was begun. She also received Platelets and FFP. A peripheral blood smear (PBS) obtained on second day of admission revealed a white blood cell count of 2.4x 10^9/l (neutrophils 47% and lymphocytes 41%), hemoglobin of 12.8 g/dl, and a platelet count of 5x 10^9/l. Repeated peripheral blood smears for *P.Malaria* were negative.Proteiuria and and microscopic hematuria were detected in the urinalysis throughout the patient's hospital stay. Two Blood cultures and urine culture were negative. Bone marrow aspiration was performed on day 2, and it rouled out hematologic malignancy. On 3 days of hospitalization she had hematemesis and melaena. This time, she was confused and went to ICU. Despite the measures, the patient's clinical status worsened rapidly on 4th day. Nasal, lower gastrointestinal, and vaginal bleeding as well as extensive ecchymosis and petechia were observed. The patient's platelet count, white blood cell count, and hemoglobin further dropped to 1.5 x 10^9/l, 1.8 x 10^9/l and 6 g/dl, respectively. At this time, the prothrombin time was >34 s and partial thromboplastin time was >70 s. Despite supportive measures, the patient died due to extensive hemorrhage on day 4 post-onset of symptoms. The serologic samples (IgM & IgG) were negative for CCHF but RT-PCR was positive.

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Case 2

A 22-year -old man with a history of acute onset of fever, myalgia and bone pain who had epistaxis admitted to our hospital. He had a history of consumption of raw liver in a party about 24 hour ago. Twelve hours later, he had upper gastrointestinal (GI) bleeding secondary to severe thrombocytopenia (less than 20,000). So, his friend who had participated in the same party and had eaten uncooked liver, was admitted to the same hospital at the same time and was treated for CCHF, we started ribavirin for him and blood samples were sent to reference laboratory for more evaluation for CCHF. He also received Platelet and FFP due to thrombocytopenia and decreased PT and PTT. Serology test (IgM-ELISA) and RT-PCR were positive for CCHF. Fortunately, by adequate and prompt management, he responsed to the therapy.

Case 3

A 18-year old man with history of fever, headache from 36 hours ago referred to Boo-Ali hospital. He is also a history of eating of uncooked liver with his brother (case2). Therefore, he was also admitted to infectious ward. 18 hours later, he showed severe thrombocytopenia [27000] and uper GI bleeding. He was treated with ribavirin and received platelet On 2th admission he washe was hit with rapidly deteriorating confusion. Brain –CT scan was performed to diagnose probable intracranial hemorrhage due to severe thrombocytopenia(less than 20,000). But, the imaging test was normal.He went to ICU and ribavirin therapy continued. Fortunately, this patient was also respond to treatment. RT-PCR and IgM –ELISA was positive for CCHF.

Case 4

A 19-year –old man who was a friend of two brothers who were discussed before, was referred to our hospital because of acute fever, myalgia, headache. So, he hed a history of eating of raw liver with his friends, he was admitted to our hospital and received oral ribavirin.He showed mild thrombocytopenia (no less than 135,000). PCR and IgM-ELISA were positive for CCHF.Two days later, he felt well. His treatment was completed in hospital and was discharged in good condition.

Discussion

CCHF is a global health problem([1,9]. It is now endemic in many countries around the world; in Asia, in Africa, Middle east and East European countries [1,2]. During the last decade, an increasing number of human CCHF virus infection have been reported from many parts of Iran specially from Southeastern Iran [1,7-8]. About 67% of cases in Iran have been reported from Sistan and Baluchestan, a Southeastern province of Iran [5-8]. Sudden onset of fever, malaise, nausea and vomiting, diarrhea, headache, abdominal pain, myalgia, petech ia and ecchymosis are the most common manifestations of CCHF [1,3–5]. Thrombocytopenia, leucopenia, anemia and elevated aspartate aminotransferase (AST) and lactate dehydrogenase(LDH) have been reported in CCHF patients [5-9]. These latter two findings along with thrombocytopenia, levated creatine phosphokinase, confusion, epatorenal syndrome and ARDS are associated with a poorer prognosis [5-7]. Important risk factors include slaughter, agricultural workers, and veterinarians, having a contact with livestock, and living in a rural area [1,8]. Tick bite history, and living in a rural area were the most common risk factor for occurring CCHF in adults and children in all studies which have been reported from Iran[2-4, 7-12]. Consumption of well-cooked meat is not a risk factor and the virus is inactivated by postslaughter acidification. There is no published report to present uncooked liver or meat has caused the CCHF during last epidemy in Iran and also other countries].

In our cases, the first presented patient had an acute onset of disease. Thrombocytopenia, anemia, leucopenia, elevation of aspartate aminotransferase and lactate dehydrogenase were found. With increasing prothrombin or partial thromboplastin time, three of our patients subsequently went to an extensive hemorrhage and the patients were managed on supportive care (Transfusion of FFP and Platelet). Despite the suitable management, one of them died because of extensive hemorrhage. The patient was referred to the hospital very late and therefore, the treatment was not effective. Molecular genetic analysis of the serum samples was positive for CCHF virus. However, serological tests were negative for anti-CCHF virus IgM and IgG antibodies. Other three cases had referred to hospital, soon. They received oral ribavirin about 36 hours after the beginning of the first sign. Although, two patients had severe thrombocytopenia, they treated quickly by ribavirin and they responsed to therapy. The first patient had a negative serology test.The negative serology is mainly attributed to either the fulminant nature of the infection or blood testing ahead of seroconversion [13,14]. The hallmarks of CCHF are acute onset of fever, headache, myalgia, thrombocytopenia, and hemorrhagic diathesis.[15-16]. Although, CCHF is generally similar to other hemorrhagic fevers, the extensive liver damage and elevated liver enzymes are the prominent findings, as well as disseminated intravascular coagulation (DIC) and generalized endothelial damages [1,6]. One of the major public health hazards of the hemorrhagic fevers including CCHF is person-to-person transmission [1]. Nosocomial and community outbreaks of CCHF have been reported. [1]. In the June 1999, a medical student from Shahrekurd, western Iran) died of extensive gastrointestinal bleeding and disseminated intravascular coagulation due to CCHF [17].Nabeth *et al*., eported a case with CCHF who infected 15 hospitalized individuals and four family members. One physician, one nursing student, a nurse, and two healthcare workers were infected during this outbreak [6]. Crimean-congo hemorrhagic fever can transmit to human by several routes. Tick bite is one of the most important risk factors for CCHF acquisition. In endemic areas, animal holders, slaughter houses, livestock workers and farmers are at risk of CCHF. Healthcare workers are also at risk of infection through unprotected contact with infectious blood and other infected body fluids. Tick bite history, and living in a rural area were the most common risk factors for occurring CCHF in adults and children in all studies which have reported from Iran[7,9 and 12].With review of the literature during the last decade , we couldn,t find a case like our patients.

Conclusion

We advise all clinicians should mind CCHF in the differential diagnosis of acute onset of fever, headache, myalgia and thrombocytopenia, especially, if he or she has a history of contact with animal and consumption of raw liver or meat, particularly in areas where this infection is endemic. Early diagnosis and treatment of CCHF are potentially associated with a lower mortality and better outcome and decreased chance of secondary spread of the infection.

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Conflict of interest statement. None declared.

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