Indian J. Hematol. Blood Transfus 24(1):35–38

CASE REPORT

Crimean congo hemorrhagic fever infection simulating thrombotic thrombocytopenic purpura

Siavash Vaziri · Jafar Navabi · Mandana Afsharian · Babak Sayad · Feizollah Mansouri · Alireza Janbakhsh · Keighobad Ghadiri

Received: 16 February 2008 / Accepted: 10 March 2008

Abstract Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne disease that may also be transmitted through person-to-person transmission by exposure to infected body fluids. Despite its wide geographic distribution in animals, CCHF virus is rarely associated with recognized human diseases. We report the first case of CCHF in Kermanshah province, Iran. Clinical presentation was characterized by fever, myalgia, and hemorrhage. The levels of liver enzymes, creatinine phosphokinase, and lactate dehydrogenase were elevated, and bleeding markers were prolonged.

Keywords Crimean-Congo hemorrhagic fever · Viral infection · Hyalomma spp.

S. Vaziri[1] · J. Navabi[2] · M. Afsharian[1] · B. Sayad[1] · F. Mansouri[1] · A. Janbakhsh[1] · K. Ghadiri[3]
[1]Assistant Professor of Infectious Disease
[2]Assistant Professor of Internal Medicine
[3]Assistant Professor of Pediatrics

Kermanshah University of Medical Sciences, Kermanshah, Iran

S. Vaziri (✉)
e-mail: vaziri15@yahoo.com

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a fatal viral infection described in about 30 countries over the world. It has the most extensive geographic range among the medically significant tick-borne viruses [1]. The occurrence of CCHF closely approximates the known world distribution of Hyalomma spp. ticks. The virus belongs to the genus Nairovirus in the Bunyaviridae family and causes severe diseases in humans, with a reported case fatality rate of 3–30% [1]. No local case was reported from Kermanshah province (west of Iran) yet. However, cases were recently observed in other regions of the country. Humans become infected through the bites of ticks, by contact with a patient with CCHF during the acute phase of infection, or by contact with blood or tissues from viremic livestock [2]. In 1969, the antigenic structures of the viruses from various geographic regions were reported to be indistinguishable [3]. CCHF virus can infect a wide range of domestic and wild animals, including sheep and cattle. Animals are infected with CCHFV by the bite of infected ticks. Seroprevalence is 13–36% in animals [4, 5]. A seroepidemiological study of CCHF in local and imported sheep in Isfahan Province of Iran revealed the endemic spreading of the virus in sheep and the need for special attention to prevent the infection in the community and during occupational exposures [6]. This is the first diagnosed and reported case in Kermanshah province.

Case

On 25 May 2007, a previously healthy twenty six year old male dealing with handling uncooked meat in a restaurant

in a marginal region in Tehran was admitted to Imam Reza Education and Research Hospital in Kermanshah (west of Iran). His complaints started 10 days before admission, with fever, malaise, headache, myalgia, nausea, vomiting, diarrhea, epistaxis, and gastrointestinal bleeding. On admission, he had fever of 39.7 C, epistaxis, conjunctival injection, and abdominal discomfort on palpation. The white blood cell (WBC) count was 1.1 £109/L, hemoglobin was 9.3 g/l, platelet count was 10.3 £109/L, at the second day of hospitalization, his WBC dropped to 0.51 £ 109/L, hemoglobin level to 6.3 g/1, platelet count (PLT) to 7.9 £ 109/L. Large bruises and ecchymoses at the antecubital fossae were detected. The level of AST was 2195 IU, and ALT was 1043 IU. Maximum level of lactate dehydrogenase (LDH) was 4011 IU, creatinine phosphokinase (CPK) 1120 IU, and amylase 458 IU. Prothrombin time (PT) was 23 s, activated partial thromboplastin time (aPTT) was 65 s, INR 1.23 and fibrinogen 2.03 g/l. Since, neutropenic fever was considered as the possible diagnosis, ceftriaxone 2 g bid and amikacin 1 g a day was started on the second day of admission, empirically. Serological tests for differential diagnosis such as EBV infection, brucellosis, toxoplasmosis, cytomegalovirus, hepatitis A, B, and C were performed.

Routine cultures of urine, feces, and blood were done. On the third day of hospitalization, a diagnosis of thrombotic thrombocytopenic purpura was considered, and intravenous Methylprednisolone (500 mg), FFP 4 units, and intravenous immunoglobulin (IVIG), was given. Plasmapheresis 500cc every six hour was initiated for the patient for two consecutive days. On the fourth day of hospital stay, there was a petechial and ecchymotic rash all over the body but more prominent on the extremities. He also had puffiness of the face and edema of the feet. There was no icterus. Examination of the respiratory system revealed crepitations in the right infra-mammary region. Central nervous system examination showed that the patient was unconscious. He responded to painful stimulus with purposeful movements of all four limbs. Planters were bilaterally extensor. The rest of the examination was normal and revealed no focal deficit. The peripheral smear revealed schistocytes, hypochromia and anisocytes. The platelets were markedly reduced with presence of giant forms. BUN was 86 mg% and serum creatinine 10 mg%. Urine output was low and examination showed urine albumin of 2+ and 60-70 RBCs per high power field. SGOT and SGPT were 830 and 180 international units respectively. In this stage of illness the patient received another 3 units of FFP, one unit packed cell and 5 units of platlets.

RA test was negative. Direct and indirect coombs' test, Anticardiolipin, Anti phospholipids, ANA and dsDNA were negative. C3 level was 50 mg% (normal value 70–110 mg%). VDRL was non-reactive. Serum fibrinogen levels were 656 mg% (normal values 200–400 mg%). Fibrin degradation products were positive in 1 in 5 dilution. Ultrasound revealed the size of kidneys to be 11.6 and 11.9 cm. Parenchymal thickness was increased with decreased echogenicity. The pelvicalyceal system was normal. Other investigations were not contributory. After deterioration of general condition of the patient, he was treated with mannitol, dexamethasone, and supportive measures and transferred to an Intensive care unit. In ICU consultation with an infectious diseases specialist was made and afer discontinuation of all of the above mentioned treatments empiric therapy with Ribavirin [2 gm loading dose, 4 gm/day in 4 divided doses (6 hourly) for 4 days, 2 gm/day in 4 divided doses for 6 days] was started. He rapidly regained complete consciousness in the ICU within 72 hours. No fresh petechiae developed after 2 days of Ribavirin therapy. All skin lesions disappeared by 4 days. Over a period of 5days, the patient showed progressive improvement in clinical and biochemical parameters. At the time of discharge, her clinical examination was totally normal. BUN and serum creatinine were 15 mg% and 1.4 mg% respectively. Urine examination and hemogram were normal. The patient was discharged well (on 8 June 2007), after 15 days of admission. The stored blood samples of the patient taken on days 3 and 8 during hospital stay were sent to the National Laboratory of Research and Diagnosis of Arboviruses and Viral Hemorrhagic Fevers Tehran. IgM and IgG for CCHF by ELISA method was reported to be positive in the patient's sample. None of the members of the ICU and internal medicine and infectious diseases wards had any illness after 20 days of follow up.

Discussion

CCHF was first clinically described in 1944 in Crimea of the former Soviet Union during a large outbreak of over 200 cases. 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 [7, 8]. CCHF virus, from the Nairovirus genus, Bunyaviridae family, is now known to have a wide geographic range, circulating in Africa, the Middle East, Asia, and central and eastern Europe. It may be transmitted by the bite of infected ticks, contact with infected animals, or through person-to-person transmission by percutaneous or permucosal exposure to blood or other infected body fluids [9, 10, 11, 8, 12]. CCHF virus infects the reticuloendothelial system and frequently involves the hepatocytes, leading to icteric hepatitis [13]. CCHF is a severe hemorrhagic fever with shock, DIC, and

frequent extensive bleeding [14, 15, 16]. Case fatality ratios from 20% to 35% have been reported, but the effects of supportive treatment on reducingthe morbidity and the mortality from CCHF can be dramatic [17]. Ribavirin has been used in CCHF, and its efficacy was estimated at 89% in patients with confirmed CCHF and 70% in patients with suspected CCHF in a large clinical study of 139 treated patients [18].

To our knowledge, thrombotic thrombocytopenic purpura like clinical picture is not a common presentation for CCHF so that two important lessons deserve to be outlined from this report. First, recent data showed that CCHF virus can use different means to infect humans. In this observation, the only risk factor (which was ignored in the initial evaluation of the patient) was the patient's occupation. However, the patient didn't recall any occupational exposure to blood during the previous weeks. Apart from his occupation (handling uncooked meat in a restaurant), the patient didn't recall any other classical exposure to CCHF virus such as tick bite or contact with livestock animals or people with hemorrhagic signs. The mode of infection could not be clearly identified, but he was working in close proximity to carcasses of sheeps and cattle.

Second, this observation illustrates that even in the absence of any alert about an ongoing occurrence of viral hemorrhagic fever (VHF), every febrile hemorrhagic syndrome coming from an endemic area where VHF has been reported must be considered as a VHF until proven otherwise. This requires respiratory and contact isolation procedures in a single room with a secure process for obtaining any blood samples. In the observation reported herein, as the physicians in charge of the patient estimated that the probability of CCHF and other forms of viral hemorrhagic fever was low, isolation procedures recommended for any suspicion of VHF were not implemented initially. Consequently, more than 15 patient contacts had to be followed up to ensure that there were no secondary cases. All contacts monitored for 14 days from the day of last contact with the patient but there was no another cases in the patient family and health care workers. Fortunately, CCHF virus is only rarely associated with outbreaks of recognized human diseases, despite its wide geographic distribution, its important circulation in numerous vertebrate species in areas of disease endemicity, and its multiple modes of transmission to humans. Administration of ribavirin in this patient before documentation of clinical diagnosis had significant positive effect on survival. Recovery from CCHF is complete and no relapse has been reported up to now. Therefore, there is no need for follow-up of cases [1].

In conclusion any patient residing in endemic area, presenting with history of fever of less than two weeks duration, with bleeding in the skin and orifices with other manifestation of viral disease in autumn to summer should arouse suspicion of CCHF and it entitles the patient for isolation/ treatment in a specialized center. Clinical diagnosis of CCHF can safely be made if baseline investigations reveal leukopenia, thrombocytopenia and raised ALT in the absence of some other obvious causes of bleeding.

References

1. Ergonul O (2006) Crimean-Congo haemorrhagic fever. Lancet Infect Dis 6(4):203–214
2. Whitehouse CA (2004) Crimean-Congo hemorrhagic fever. Antiviral Res 64(3):145–160
3. Casals J (1969) Antigenic similarity between the virus causing Crimean hemorrhagic fever and Congo virus. Proc Soc Exp Biol Med 131(1):233–236
4. Gonzalez JP, LeGuenno B, Guillaud M, Wilson ML (1990) A fatal case of Crimean-Congo hemorrhagic fever in Mauritania: virological and serological evidence suggesting epidemic transmission. Trans R Soc Trop Med Hyg 84: 573–576
5. Morrill JC, Soliman AK, Imam IZ, Botros BA, Moussa MI, Watts DM (1990) Serological evidence of Crimean-Congo hemorrhagic fever viral infection among camels imported into Egypt. J Trop Med Hyg 93:201–204
6. Darvishi M, Ataee B, Chinikar S, Jalali N, Mardani M, Mirkhani M (2005) Seroepidemiology of Crimean-Congo hemorrhagic fever in local and imported sheep in Isfahan Province of Iran. Clin Microbiol Infect 11(suppl 2):649
7. Casals J (1969) Antigenic similarity between the virus causing Crimean hemorrhagic fever and Congo virus. Proc Soc Exp Biol Med 131:233–236
8. Whitehouse CA (2004) Crimean-Congo hemorrhagic fever. Antivir Res 64:145–160
9. Chapman LEML, Wilson DB, Hall et al. (1991) Risk factors for Crimean-Congo hemorrhagic fever in rural northern Senegal. J Infect Dis 164:686–692
10. Nabeth PD, Cheikh B, Lo O, Faye I, Vall and Niang M (2004) Crimean-Congo hemorrhagic fever, Mauritania. Emerg Infect Dis 10:2143–2149
11. Smego RA, Sarwari AR and Siddiqui AR (2004) Crimean-Congo hemorrhagic fever: prevention and control limitations in a resource-poor country. Clin Infect Dis 38:1731–1735
12. Wilson ML, LeGuenno B, Guillaud M, Desoutter D, Gonzalez JP and Camicas JL (1990) Distribution of Crimean-Congo hemorrhagic fever viral antibody in Senegal: environmental and vectorial correlates. Am J Trop Med Hyg 43:557–566
13. Burt FJ, Swanepoel R, Shieh WJ et al. (1997) Immunohistochemical and in situ localization of Crimean-Congo hemorrhagic fever (CCHF) virus in human tissues and implications for CCHF pathogenesis. Arch Pathol Lab Med 121:839–846
14. Burney MI, Ghafoor A, Saleen M, Webb PA and Casals J (1980) Nosocomial outbreak of viral hemorrhagic fever caused by Crimean hemorrhagic fever-Congo virus in Pakistan, January 1976. Am J Trop Med Hyg 29:941–947

15. Papa A, Bino S, Llagami A et al. (2002) Crimean-Congo hemorrhagic fever in Albania, 2001. Eur J Clin Microbiol Infect Dis 21:603–606
16. van Eeden PJ, Joubert JR, van de Wal BW, King JB, de Kock A and Groenewald JH (1985) A nosocomial outbreak of Crimean-Congo haemorrhagic fever at Tygerberg Hospital. Part I. Clinical features. S Afr Med J 68:711–717
17. van Eeden PJ, van Eeden SF, Joubert JR, King JB, van de Wal BW and Michell WL (1985) A nosocomial outbreak of Crimean-Congo haemorrhagic fever at Tygerberg Hospital. Part II. Management of patients. S Afr Med J 68:718–721
18. Mardani M, Jahromi MK, Naieni KH and Zeinali M (2003) The efficacy of oral ribavirin in the treatment of Crimean-Congo hemorrhagic fever in Iran. Clin Infect Dis 36:1613–1618