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Caso clinico

Case report

A case of Crimean-Congo haemorrhagic fever with normal laboratory findings

Descrizione di un caso di febbre emorragica Congo-Crimea con normalità degli indici di laboratorio

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INTRODUCTION

Crimean-Congo haemorrhagic fever (CCHF) is a tick-borne disease caused by Nairovirus, of the family Bunyaviridae. Crimean- Congo haemorrhagic fever virus (CCHFV) is transmitted to humans through infected tick-bites or direct contact with viremic animals or humans [1, 2]. CCHF is a severe viral infection and it is observed in many parts of Africa, Asia, Eastern Europe, and Middle East [1]. CCHF causes direct multiplication in the endothelial cells or direct activation under the effect of the cytokine, chemokine and other mediators from mononuclear cells and impairment of barrier function [3].

After a short incubation period, it is characterized by fever, myalgia, malaise, nausea and vomiting, headache, diarrhea, and bleeding [3, 4]. Laboratory findings include leucopenia and thrombocytopenia, elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), prolonged prothrombin time (PT), and activated partial thromboplastin time (aPTT) [3, 4]. IgM and IgG antibodies are detectable by enzyme-linked immunosorbent assay (ELISA) and immunofluorescence assays from approximately 7 days after the onset of the disease. Recent infection is confirmed by demonstrating seroconversion, or a fourfold or greater increase in antibody titer in paired serum samples, or IgM antibodies with IgM antibody in a single sample. Reverse transcriptase-polymerase chain reaction (RT-PCR) is the method of choice for rapid laboratory diagnosis of CCHF virus infection because this method is highly specific, sensitive, and rapid and allows early diagnosis [5, 6].

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CASE DESCRIPTION

A 36-year-old woman was admitted to our clinic with the complaints of fever, chills, myalgia and vomiting. She had a history of anemia for six years. She was living in an endemic region for CCHF and had a history of tick bite ten days ago. Her complaints had started five days after the tick bite, and bleeding of the nose and vagen followed.

At initial presentation her general condition was average, and she exhibited full consciousness, orientation and cooperation. Her body temperature was 37.6°C, pulse 88 beats/min. Any abnormality was not noted on systemic examination except vaginal hemorrhage.

The epidemiological and clinical features of the patient were typical for CCHF but the laboratory investigation was normal except anemia. Under laboratory analysis, serum WBC was 7300/mm^3, Hb 11.9 g/dL, Plt count 293000/mm^3, AST was 23 U/L, ALT 14 U/L, LDH 139 U/L, CK 39 U/L, INR 0.8 and APTT 26.2 seconds. Vaginal hemorrhage stopped in the third day of the hospitalization, and hemorrhage of the nose also stopped one day after it.

Based on these clinical and epidemiological findings, a diagnosis of CCHF infection was suspected, and the diagnosis of CCHF was confirmed with blood sample tested in Refik Saydam National Public Health Agency Virology Reference and Research Laboratory by TaqMan-based one-step RT-PCR positivity and IgM antibody positivity.
Laboratory values were closely followed-up and any abnormality was not detected. Her symptoms regressed gradually.
She was discharged from the hospital on sixth day of the hospitalization; all the clinical and laboratory findings were normal except anemia.

DISCUSSION

CCHF has four distinct phases: incubation, prehemorrhagic, hemorrhagic, and convalescence. The incubation period depends on the host, route of exposure, and viral inoculum, and it is estimated that it lasts 1-3 days after a tick bite, 5 days after contact with livestock blood or tissue, and 5-6 days after contact with human blood. The prehemorrhagic period lasts 3-6 days and it is characterized by sudden onset fever (39-41ºC), rigor, severe headache, myalgia, lower backache, abdominal pain, and photophobia [1].
The hemorrhagic period develops from various sites 3-6 days following the onset of illness and lasts 2-3 days. On mucous membranes and skin, hemorrhagic manifestations range from petechiae to large ecchymoses.
Bleeding of the nose, gums, and buccal cavity occurs frequently. In severe cases of CCHF, gastric, uterine, intestinal, genitourinary, cerebral and pulmonary hemorrhages occur with decreasing frequency [7, 8].
While the pathogenesis of CCHF is still not completely understood, the endothelium and mononuclear phagocyte system are the main targets of the virus [9]. Thrombocytopenia, disseminated intravascular coagulation, shock, vascular endothelial injury, and liver dysfunction can lead to bleeding tendencies in CCHF [10]. Since endothelial damage is a main contributor in the pathogenesis of CCHF, it can be seen in many different clinical manifestations and complications. CCHF may be explained with reaction of endothelial cells and diffuse inflammation caused by cytokine storm [11].
Viral hemorrhagic fevers share some pathophysiologic, clinical, and laboratory features. Capillary fragility is a common feature of viral hemorrhagic fevers, suggesting that infection of the endothelium plays a major role [8].
As with Ebola haemorrhagic fever, the general pathogenetic characteristic of the infection is estimated to stem from suppression of type 1 interferon response as a result of necrosis of dendritic cells and macrophages that would initiate antiviral response, and immune response defect developing in the host as a consequence [12].
Together with this damage, the virus spreads to organs with a similar structure containing macrophage and dendritic cells, such as the liver, spleen and lymph nodes [12].
Proinflammatory cytokines, chemokines and other mediators released from infected cells cause vascular permeability, rapidly increasing systemic inflammation, and widespread intravessel coagulation [12].

CONCLUSIONS

This is the first case in the literature of confirmed CCHF case without laboratory abnormality. This case is important because of bleeding despite normal laboratory findings. We suggest that patients from endemic region who have typical epidemiological and clinical findings should be evaluated as a possible case for CCHF even if the laboratory findings are not compatible.

Competing interests
The authors declare that they have no competing interests.
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Keywords: Crimean-Congo haemorrhagic fever, haemorrhage, normal laboratory findings.

SUMMARY

Crimean-Congo haemorrhagic fever (CCHF) is a tick-borne disease caused by Nairovirus, of the family Bunyaviridae. This is the first case report of a confirmed CCHF case without laboratory abnormality. A 36-year-old woman was admitted to our clinic with the complaints of fever, chills, myalgia and vomiting. She was living in a CCHF-endemic region and had received a tick bite ten days previously. Her complaints had started five days after the tick bite, and bleeding of the nose and vagen followed. Under laboratory analysis, serum white blood cell (WBC) was 7300/mm3, haemoglobin (Hb)11.9 gr/dL, platelet (Plt) count 293000/mm^3, aspartate transaminase (AST) was 23 U/L, alanine transaminase (ALT) 14 U/L, lactate dehydrogenase (LDH) 139 U/L, creatinine phosphokinase (CPK) 39 U/L, INR 0.8 and APTT 26.2 seconds. Based on these clinical and epidemiological findings, a diagnosis of CCHF infection was suspected, and the diagnosis of CCHF was confirmed with a blood sample tested by TaqMan-based one-step RT-PCR positivity and IgM antibody positivity. We suggest that patients from an endemic region who have typical epidemiological and clinical findings should be evaluated as a possible case for CCHF even if the laboratory findings are not compatible.

RIASSUNTO

*La febbre emorragica Congo-Crimea (*CCHF, Crimean-Congo Haemorrhagic Fever*) è provocata da un virus del genere Nairovirus, della famiglia dei Bunyavirus, che si trasmette per lo più attraverso la puntura di zecche infette. Quello che descriviamo è il primo caso clinico di un episodio confermato di CCHF caratterizzato da assenza di alterazione degli indici di laboratorio.*
Una donna di 36 anni è giunta alla nostra osservazione riferendo febbre, brividi, mialgia e vomito. Residente in un'area endemica per la CCHF, la donna era stata punta da una zecca dieci giorni prima. La febbre e i sintomi erano iniziati cinque giorni dopo la puntura, seguiti da emorragia nasale e vaginale. I parametri di laboratorio erano i seguenti: globuli bianchi, 7300/mm^3; emoglobina, 11,9 g/dL, piastrine 293000/mm^3; AST 23 U/L; ALT 14 U/L; LDH 139 U/L; CPK 39 U/L; INR 0,8; aPTT 26,2 secondi. Sulla base di questi riscontri clinici ed epidemiologici, è sorto il sospetto clinico di CCHF; la diagnosi di CCHF è stata confermata dalla positività di un campione di sangue alla TaqMan-based one-step RT-PCR *e dalla positività delle IgM. Sulla base di questa esperienza, suggeriamo che i pazienti provenienti da un'area endemica per la CCHF che presentino riscontri clinici ed epidemiologici caratteristici debbano essere valutati quali possibili casi di CCHF anche se i riscontri laboratoristici non sono compatibili con la diagnosi.*

REFERENCES

[1] Ergonul O. Treatment of Crimean-Congo hemorrhagic fever. *Antiviral Res.* 78, 1, 125-131, 2008.
[2] Morikawa S., Saijo M, KuraneI. Recent progress in molecular biology of Crimean-Congo hemorrhagic fever. *Comp. Immunol. Microbiol. Infect. Dis.* 30, 375-389, 2007.
[3] Ergonul O. Crimean-Congo haemorrhagic fever. *Lancet Infect Dis.* 6, 4, 203-214, 2006.
[4] Whitehouse C.A. Crimean-Congo hemorrhagic fever. *Antiviral Res.* 64, 3, 145-160, 2004.
[5] Cevik M.A., Erbay A., Bodur H., et al. Clinical and laboratory features of Crimean-Congo hemorrhagic fever: predictors of fatality. *Int. J. Infect. Dis.* 12, 374-379, 2008.
[6] Leblebicioglu H. Crimean-Congo haemorrhagic fever in Eurasia. *Int. J. Antimicrob. Agents* 36, 1, 43-46, 2010.
[7] Tesh R.B. Crimean-Congo hemorrhagic fever. In *Textbook of Pediatric Infectious Diseases* (Feigin R.D., Cherry J.D., Demmier G.J. et al., Eds.) 2004, 2414-2415. Elsevier Inc., Pa.
[8] Sonmez M., Aydin K., Durmus, A., et al. Plasma activity of thrombin activatable fibrinolysis inhibitor in Crimean-Congo hemorrhagic fever. *J. Infect.* 55, 184-187, 2007.
[9] Yilmaz G., Mentese A., Kaya S., Uzun A., Karahan S.C., Koksal I. The diagnostic and prognostic significance of soluble urokinase plasminogen activator receptor in Crimean-Congo hemorrhagic fever. *J. Clin. Virol.* 50, 209-211, 2011.
[10] Schnittler H.J., Feldman H. Viral hemorrhagic fever - a vascular disease? *Thromb. Haemost.* 89, 967-972, 2003.
[11] Guner R., Hasanoglu I., Yapar D., Tasyaran M.A. A case of Crimean Congo hemorrhagic fever complicated with acalculous cholecystitis and intraabdominal abscess. *J. Clin. Virol.* 50, 162-163, 2011.
[12] Ergonul O., Whitehouse C.A. Comperative pathogenesis of Crimean-Congo hemorrhagic fever and Ebola hemorrhagic fever. In *Crimean Congo Hemorrhagic Fever: a global perspective* (Ergonul O. and Whitehouse C.A., Eds.) Springer, Dordrecht, NL. 2007, 221-231.