

Case Report

Crimean-Congo hemorrhagic fever (CCHF) in Southern Kordofan

Haydar Awad Abdelrazig Abdelhakam (1), Mohamed Ahmed Taha (2)

(1) Children's Hospital, Omdurman Military Hospital, Sudan.

(2) Infectious Diseases Unit, Omdurman Military Hospital, Sudan.

ABSTRACT

Crimean-Congo hemorrhagic fever (CCHF) is a disease that poses a great threat to public health owing to its high mortality rate (30-70%), mode of transmission and geographic distribution. Here, we report on a nine years-old Sudanese boy from Southern Kordofan State who presented with Jaundice, high-grade fever, severe headache, abdominal pain and a history of hematemesis. The diagnosis of CCHF was confirmed based on clinical and serological findings.

Key words:

Crimean-Congo hemorrhagic fever; Tick-borne virus; Southern Kordofan; Sudan.

INTRODUCTION

Congo-Crimean hemorrhagic fever (CCHF) is a viral disease that causes sporadic outbreaks in

a wide geographic area in Central Asia, Central Africa and the Middle East. Severe hemorrhagic disease, causing a large outbreak was reported in 1994 from the Crimean peninsula in the former Soviet Union [1,2]. Several years later, a virus causing a hemorrhagic fever disease was identified in Congo, East Africa. Subsequently, it was found that both diseases are caused by the same virus and was named as CCHF virus (CCHFV) [3-4].

Crimean - Congo hemorrhagic fever virus is the second most widespread Arbovirus of medical importance after Dengue fever virus. Nowadays CCHFV is known to be widely distributed throughout large areas of Sub-Saharan Africa, European Union, Russia, the Balkans, Arab Peninsula, the Far East, the Middle East and Europe [5-9]. CCHFV is endemic in large parts of the world and has one of the most extensive geographic ranges of the tick-borne viruses causing disease.

Correspondence to:

Dr. Haydar Awad Abdelrazig Abdelhakam,
Consultant Pediatrician,
Children's Hospital, Omdurman Military Hospital,
Sudan.

Email: habelhakam1@hotmail.com

Phone (mobile) : +249 123431031

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CASE REPORT

A 9-year-old male from a village near Kadogli in South Kordofan was referred to the Emergency Military Hospital in Omdurman from Kadogli Civil Hospital in January 2013. The patient presented with Jaundice, high-grade fever, severe headache, abdominal pain and a history of hematemesis, epistaxis and hematuria. Hemorrhagic fever was suspected and the patient was transferred to the Children's Military Hospital, where he was strictly isolated with access only to senior medical and nursing staff.

A blood sample was obtained from the patient and his father (the co-patient), sent to the Central National Health Laboratory (Stack Laboratory). The blood sample was investigated by polymerase chain reaction (PCR) and the enzyme-linked immunosorbent assay (ELISA) for IgG and IgM antibody for both yellow fever and CCHF. The laboratory findings showed no reactivity for PCR to both viral infections as the patient passed the viremia stage of the illness but the results clearly showed reactivity to CCHF IgM, which indicated current CCHF viral infection. The patient was managed by supportive therapy and he received blood and fresh frozen plasma (FFP) transfusions, analgesics, antibiotics, hematonics and eventually discharged in good condition after complete recovery.

DISCUSSION

Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic viral disease that is characterised by high morbidity and mortality (30-70%) in humans when it reaches the hemorrhagic phase. It is widely distributed around the globe and has been reported in Eastern Europe, South East Asia, the Middle East, East and West Africa. It belongs to the arthropod-borne (ARBO) viral group, specifically, the tick-borne subgroup. It is a very difficult infection to control in the lack of appropriate containment facilities required for isolation and personal protection, in the absence of a proper vaccine and specific antiviral treatment. Humans are the only known hosts that develop the disease after infection with CCHF virus. The

infection can result in CCHF, which is a severe hemorrhagic fever that is characterised by fever, prostration, severe hemorrhages and potentially death. The disease progression can be subdivided into four different stages: incubation period, pre-hemorrhagic, hemorrhagic and the convalescent phases [10]. It should be noted that the duration and symptoms of these different phases vary significantly between individuals [11]. The pathogenesis of CCHF is only poorly characterised for several reasons; infections occur sporadically and in areas where facilities are limited for performing complete autopsies, virus handling requires bio-safety level 4 containment laboratories and there is a lack of available animal models of disease. In fatal cases, platelet counts can be extremely low, even from an early stage of the illness. Furthermore, an increase in aspartate and alanine amino transferases (AST and ALT) levels in the serum and prolongation of prothrombin and partial thromboplastin times (PT and PTT) have also been observed [12].

The primary pathophysiological event appear to be a leakage of erythrocytes and plasma through the vascular tissues. Endothelial damage can contribute to coagulopathy by deregulated stimulation of platelet aggregation, which, in turn, activates the intrinsic coagulation cascade, ultimately leading to clotting factors deficiency, causing hemorrhage. In case of CCHF, vascular leakage may be caused either by destruction of endothelial cells or by disruption of tight junctions that constitute the endothelial barrier between cells. Moreover, it is unclear whether these events are a consequence of the infection or a virus-induced host factors that cause the endothelial dysfunction [13]. It has been suggested that the hemorrhages and coagulation disturbances may be caused directly, possibly by high levels of pro-inflammatory cytokines. Key players in disease progression are the cytokines IL-10, IL-1, IL-6 and tumour necrosis factor-alpha (TNF-alpha) [14].

Recently, two studies by Ergonul et al [15] demonstrated significantly higher levels of IL-6 and TNF-alpha in CCHF patients with fatal outcome and with the non-fatal cases. Another interesting

observation is the elevated levels of neoprotein in patients with Dengue fever or Ebola hemorrhagic fever [16,17]. Neoprotein is a useful tool to assess the severity of cell-mediated immune response [18]. A recent study noted a correlation between elevated levels of neoprotein in CCHF patients and disease severity [19]. All of these studies suggest that capillary fragility, a common feature of CCHF, is caused by multiple host-induced mechanisms in response to CCHF infection. Endothelial damage would cause the characteristic rash and contribute to hemostatic features. Interestingly, some authors have noticed similarities between various viral hemorrhagic fevers and septic shock caused by severe bacterial infection.

Diagnosis of hemorrhagic fever is primarily based on clinical presentation (major clinical signs and symptoms) such as high grade fever, abdominal pain, epistaxis, hematemesis, hematuria and generalised lymphadenopathy.

Hemorrhagic fevers are generally considered as dangerous pathogens and classified as bio-safety level 4 pathogens, thus processed in specialised laboratories and high containment conditions. General laboratory findings may aid in the diagnosis of CCHF, these include the presence of leucopenia, thrombocytopenia, high level of liver enzymes and renal function parameters. The direct laboratory diagnosis of CCHFV is achieved by virus isolation in mouse cell cultures prepared in specialised laboratory in USA or UK. However, serological tests such as antibody capture, ELISA and immunofluorescence tests can be employed for the detection of specific IgM antibody. These tests can be carried out under less containment conditions in Low-Income Countries. In Sudan, they are made available in the Central National Laboratory coupled with conventional and real-time PCR (RT-PCR) for the detection of viral genome. RT-PCR is considered the gold-standard and the most useful test if it is carried out on blood in the viremia stage which occurs early in the course of infection. Both tests are considered diagnostic and could confirm CCHFV infection.

The possible differential diagnosis includes other hemorrhagic fevers, malaria and Q fever. The

local availability of RT-PCR for the detection of the viral genome via partial S segment sequences of the virus and subsequent phylogenetic analysis are used to confirm the CCHFV infection and to determine the virus genetic lineages and the antibody-captured ELISA used for the detection of specific IgM may lead to the proper confirmation of hemorrhagic fever diagnosis.

In the present study CCHF was confirmed in a 9-year-old boy from a rural area near Kadogli (the capital of Southern Kordofan State). Since 2008, several sporadic cases and nosocomial outbreaks associated with a high fatality rate have been reported in villages and Rural Hospital in Kordofan region. Two outbreaks were reported by Aradaib et al [20,21]. The first nosocomial outbreak of CCHF occurred in Alfulah Rural Hospital in West Kordofan. Two virus strains designated as Alfulah 3 & 4 were identified as etiological agents of this outbreak. The other outbreak was reported in Donkup village in Abyei District, in Southern Kordofan. Detailed analysis of serum samples taken from co-patients in this study was not carried out due to limited resources. However, the presence of virus-specific IgM antibodies was documented later in the course of illness and in persons who survived the infection.

Treatment of CCHF is mainly symptomatic and supportive. The anti-viral drug Ribavirin has never been tested in randomized clinical trials to confirm the efficacy of CCHF treatment, however, observation studies in humans, as well as in vitro studies in mice support the use of this drug [20]. Ribavirin has not been tried in our patient. Supportive and symptomatic therapy proved to be sufficient in that advanced level of infection. In Alfulah outbreak, treatment with oral Ribavirin at a dose of 500 mg/day for 5 days and replacement with fluid and electrolyte therapy, transfusion of whole blood and plasma and the administration of platelet concentrate resulted in rapid improvement in the health condition of the nosocomially infected patients in El-Obeid Hospital (North Kordofan) in a week time post therapy. The CCHFV proved to be susceptible to oral Ribavirin but there is no controlled study evaluating oral versus intravenous

Ribavirin in treating infected patients. An inactivated vaccine produced from mouse brains has been used in Russia and Bulgaria [10]. However, its efficacy and safety has never been seriously tested.

CONCLUSION

This report highlights the need to include CCHF in the differential diagnosis, where fever with

hemorrhagic tendencies is observed in health institutions, especially, in rural areas known to be endemic for the disease. The frequent occurrence of sporadic cases, multiple CCHF outbreaks and the risk these cases pose to medical staff in resource-poor health facilities necessitates the need for improved surveillance programs including molecular typing for emerging viral strains and prevention measures for this important viral disease in Sudan.

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