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Case Report

Fatal Crimean-Congo Hemorrhagic Fever with an Atypical Clinical Course during the COVID-19 Pandemic

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Abstract

Background: Crimean-Congo hemorrhagic fever (CCHF) is a viral zoonotic disease characterized by high fever, bleeding manifestations, and a high mortality rate. Most patients begin to experience bleeding 5 to 7 days after the onset of the illness, usually while hospitalized. This report highlights that even though patients may develop shock and multi-organ failure, there might be no visible signs of bleeding until shortly before death.

Methods: This case report describes a 42-year-old male patient with a confirmed diagnosis of CCHF via RT-PCR, who died despite intensive care treatment. Despite receiving intensive care treatment, he did not respond to the septic shock therapy and unfortunately passed away within a few hours. The diagnosis of the disease was made by the reference laboratory with a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test for CCHF.

Results: In this case, the patient exhibited no visible signs of bleeding, such as hematemesis, melena, or gross hematuria, despite being in shock. While CCHF mortality (5–30%) typically occurs during the 3–5-day hemorrhagic phase, this patient died suddenly due to massive intra-abdominal bleeding, skipping the typical bleeding phase.

Conclusion: Clinicians should consider that individual differences may be seen in the clinical course of CCHF disease. In addition, the Coronavirus Disease-2019 (COVID-19) pandemic was experienced worldwide when the patient applied. Given the overlapping initial symptoms of COVID-19 and CCHF, clinicians should prioritize differential diagnosis, especially during the COVID-19 pandemic. During the COVID-19 pandemic, diagnostic delays may occur in the management of CCHF, particularly due to resource allocation.

Keywords: Crimean-Congo hemorrhagic fever; COVID-19; Bleeding; Mortality

Introduction

CCHF is a lethal viral zoonotic infection with a high fatality rate. It is a single-stranded, lipidencased RNA virus belonging to the Bunyaviridae genus Nairovirus. The virus is primarily transmitted through the bites of infected ticks belonging to the genus *Hyalomma*. It can also spread through contact with the blood or bodily fluids of infected hosts. The initial manifestations of CCHF illness are nonspecific. Common symptoms include weakness, broad muscular pains, headache, fever, chest discomfort, arthralgia, and diarrhea. In severe cases, vascular complications such as conjunctival erythema, facial flushing, edema, hemorrhages, hypotension, shock, and proteinuria may occur, along with bleeding manifestations. Hematemesis, melena, hematochezia, metrorrhagia, petechiae, purpura, epistaxis, bleeding from gingiva and puncture sites, hemoptysis, and hematuria are all forms of bleeding. Also reported seldom are hemothorax and cerebral hemorrhages. Central nervous system manifestations in the advanced stage of a disease have been regarded as an indicator of a poor prognosis (1, 2). Thrombocytopenia is a consistent feature of the infection. Patients exhibit leukopenia and elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and creatinine phosphokinase (CPK) levels.

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Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were extended among the hemostasis assays. Fibrinogen concentration may decline, and fibrin breakdown products may rise (3). In the study by Swaneopoel et al. a leukocyte count of more than 10,000/mm3 was related to an increased risk of death (4). While the typical clinical and laboratory features of CCHF are well-documented, individual cases may present with unusual or atypical findings. Here, we report a case of CCHF with an unexpected clinical course, including the absence of visible bleeding despite severe complications. The patient in this case had no history of tick contact and initially presented with non-specific symptoms. Laboratory tests revealed normal leukocyte and thrombocyte counts, as well as normal AST, ALT, LDH, and CPK levels. However, within three days, the patient developed shock and multi-organ failure. Notably, there were no visible signs of bleeding, despite the progression of the disease.

Case Presentation

A 42-year-old male patient was brought to the emergency room by his relatives due to fever, weakness, lack of appetite, and general malaise. Three days prior, he had visited the hospital with similar symptoms, including muscular and joint discomfort. The hemogram and biochemical tests were ordinary. A COVID-19 PCR test, performed due to the ongoing pandemic, was negative, and a lung CT scan showed no abnormalities. The patient was discharged from the emergency room with a prescription for non-specific therapy for his symptoms. Despite initial discharge with non-specific therapy, the patient's condition deteriorated rapidly, prompting his return to the emergency room three days later. When we evaluated the patient in the emergency room, he was unstable, sleepy, restless, and disoriented. On examination, the skin was cold and clammy. There was no evidence of skin ecchymosis, oral mucosal bleeding, hematuria, hematemesis, hemoptysis, hematochezia, or melena. The temperature was 37.8 degrees Celsius; blood pressure was 80/30 mmHg, pulse was 117 beats per minute, and respiration was 45 beats per minute. Arterial blood gas analysis revealed a pH of 6.68. The white blood cell count was 26,350/mm³. Hemoglobin was 19.1 g/dL, hematocrit was 62.1%, and platelet count was 45.000/mm^3. Laboratory testing indicated significant liver damage (ALT: 2565 IU/L, AST: 2068 IU/L). LDH: 6371 IU/L, CPK: 9393 IU/L, urea: 108 mg/dL, creatinine: 5.12 mg/dL. Similarly, coagulation tests revealed excessively high levels (International normalized ratio (INR): 20.3; prothrombin time (PT): 128 seconds; activated partial thromboplastin time (aPTT): 101 seconds). In addition, 90 mg/L of C-reactive protein (CRP) and 0.94 ng/ml of procalcitonin were measured (Table 1).

First, the patient's body was examined for ticks, but none were discovered. In the patient's relatives' anamnesis, it was found that a tick had not bitten the patient within the previous 15 days. The patient did not reside in a rural area but had handled sheep meat eight days before Eid al-Adha. It was learned that he did not eat meat without cooking it and that he slaughtered and skinned the animal with his bare hands. After consulting with an intensive care expert, the patient was monitored in the tertiary critical care unit with the pre-diagnoses of CCHF, septic shock, and drunkenness. Following cardiac and respiratory arrest, the patient was intubated, mechanically ventilated, and resuscitated. The patient received two replacement units of fresh frozen plasma. Since there was no obvious source of bleeding and the patient's platelet count was 46.000/mm3, immediate platelet replenishment seemed unnecessary. In addition to CCHF, serum samples were collected for differential diagnosis of leptospirosis and hantavirus infection at the appropriate laboratory (leukocytosis, kidney and liver dysfunction, and thrombocytopenia). Intravenous administration of 1 gram of ceftriax-

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one was determined empirically. One hour later, a hemogram revealed that the patient's hemoglobin level had plummeted to 7.2 g/dL. Due to the abrupt distension in the belly, it was believed that the bleeding was occurring in the abdomen. However, imaging to detect intra-abdominal hemorrhage was impossible due to the patient's unstable hemodynamics. Replacement of red blood cells began. The patient's blood pressure did not rise after receiving inotropic therapy and intravenous fluid support. Consequently, the patient could not undergo hemodialysis. One hour after intubation, cardiac arrest developed again in the patient. This time, there was no response to the resuscitation applied, and the patient died approximately three hours after admission to the emergency department. CCHF-PCR test results were positive, while hantavirus IgG and IgM test results were negative. Table 1 shows laboratory findings of blood count, biochemistry, and coagulation parameters of the patient's first admission to the hospital on July 25 and the day of death, July 28. The case was detected in Amasya Province during the summer season. Amasya/Turkey is a region where CCHF disease was endemic.

Table 1. Laboratory data of the patient's first application and the day of death due to Crimean-Congo Hemorrhagic Fever (CCHF), Amasya Province, Turkey, 2019

Test Results	First Application Day (July 25)	Day of Death (July 28)
White Blood Cell (/mm^3)	6990	26.350
Thrombocytes (/mm$^{3)}$	195 000	45.000
Hemoglobin (g/dL)	13.7	19.1
Hematocrit %	43	62.1
AST (IU/L)	27	2068
ALT (IU/L)	32	2565
LDH (IU/L)	243	6371
CPK (IU/L)	91	9393
Creatinin (mg/dL)	1.02	5.12
PT (sn)	13.9	128
aPTT (sn)	30.2	101
INR	1.04	20.3
CRP (mg/L)	5.98	90

AST: aspartat aminotransferase; ALT: alanin aminotransferase; LDH: lactate dehydrogenase; CPK: creatinine phosphokinase; PT: protrombine time; aPTT: activated partial thromboplastin time; INR: international normalized ratio; CRP: C-reactive protein

Discussion

The main mode of transmission of the CCHF virus is a tick bite, and no tick was found on our patient's body. According to the anamnesis taken from the patient's relatives, there is no history of tick bites in the last 15 days. However, it was discovered that he had handled the blood and meat of a sheep slaughtered eight days prior during Eid al-Adha. When the anamnesis was deepened, it was learned that the slaughter of the animal and the processing of the meat were done by our patient alone. In addition, it was understood that our patient and other members of the family did not consume uncooked meat. In this case, the likely route of transmission was direct contact with infected animal blood during slaughter. Leblebicioğlu et al. (5) reported an increase in CCHF cases during Eid al-Adha. CCHF typically includes

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a bleeding phase lasting 3–5 days (6–8). This period was not observed in the case we presented and it appears as an unusual feature of the case. In CCHF, there is a pre-bleeding period that covers the period 1–7 days after the onset of symptoms. During this period, leukopenia, thrombocytopenia, and elevated transaminase levels due to hepatocellular cytolysis are frequently observed (9). A study of thirty fatal cases reported hemorrhagic symptoms in 86.6% of patients (10). Another unusual feature of this case was the absence of leukopenia, thrombocytopenia, or elevated transaminases at initial presentation, despite the onset of symptoms. Somnolence and leukocytosis are associated with mortality in CCHF (11, 12). In the case we present, both tables are available. The atypical presentation of CCHF in this case underscores the importance of maintaining a high index of suspicion, particularly in endemic regions and during overlapping public health crises such as the COVID-19 pandemic. Although its impact has decreased, the COVID-19 pandemic we are in continues. High fever, headache, muscle and joint pain, nausea, vomiting, sweating, diarrhea, and abdominal pain are the main symptoms of COVID-19 (13). Crimean-Congo hemorrhagic fever disease also progresses with similar symptoms and these two diseases can be confused with each other (14). The case we presented was admitted during the COVID-19 pandemic period and was evaluated by the clinician only for this disease at the first application, and the COVID-19 PCR test result was negative. The region we live in is an endemic area for CCHF disease. The clinician should consider the differential diagnosis of these two diseases during the summer months when ticks are active.

Conclusion

In conclusion; clinicians should take into consideration that individual patient differences may occur in the clinical course of CCHF disease. In addition, high fever, weakness, malaise, muscle, and joint pain are common symptoms at presentation for CCHF and COVID-19 infections, and it should be kept in mind that these diseases may be confused in areas endemic for CCHF during the pandemic period, especially in the summer months.

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Ethical considerations

To carry out the study, approval was obtained from the relatives of the case subject to the article.

Conflict of interest statement

The author declares that there is no conflict of interest.

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