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CASE REPORT

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Crimean-Congo hemorrhagic fever in the COVID-19 pandemic: A case study

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Abstract

In the COVID-19 pandemic, the overlap of clinical features between other viral infections makes a reliable diagnosis difficult in the initial stage of illness. We describe a confirmed case of CCHF in Tehran Province during this year, who was first misdiagnosed as COVID-19 infection.

KEYWORDS

CCHF, epidemiology, SARS-CoV-2

1 | INTRODUCTION

Viral hemorrhagic fevers are a diverse group of acute tick-borne, zoonotic illnesses. Crimean Congo hemorrhagic fever virus (CCHFV), one of the viral hemorrhagic fever syndromes, is described as an emerging viral infection worldwide with a mortality rate of 30%. This emerging virus has been classified as a *Nairovirus* genus in the *Bunyaviridae* family. It is transmitted to humans by the bite of an infected tick and direct contact with infected blood or tissue from humans and livestock. *Hyalomma* ticks causes to transmit this virus from animals to humans.[1,2] Nonspecific symptoms of the coronavirus disease 2019 (COVID-19) can mimic the clinical manifestations of other infectious viral diseases, including CCHF, which this misdiagnosis can be highly dangerous. Herein, we describe the confirmed case of CCHF in the setting of an ongoing COVID-19 pandemic who was first managed with the diagnosis of COVID-19 infection.

2 | CASE PRESENTATION

A previously healthy 41-year-old Persian male was presented to the emergency department due to a 7-day history of fever, myalgia, malaise, and a 2-day history of

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gastrointestinal (GI) bleeding, including coffee ground vomitus and melena. He was referred to other medical centers two times before admission at our hospital, and he was evaluated for COVID-19 infection owing to fever, myalgia, and malaise with conservative management; at that time, the patient did not have GI bleeding; however, there was no significant improvement. He had a recent history of traveling to Karbala, Iraq, 14 days before admission. On initial examination, he was alert, and his vital signs were as follows: blood pressure, 120/75 mmHg; pulse rate, 100 beats/min; respiratory rate, 17 cycle/min; body temperature, 38.5°c, and SpO2, 93%—room air. Sclera was not icteric. GI bleeding, including coffee ground vomitus and melena, was initiated 2 days before admission. The patient had no respiratory symptoms. Other physical examination was not remarkable except mild tenderness in the right upper quadrant of the abdomen. Findings of abdominopelvic sonography and lung computed tomography were normal. Table 1 shows the laboratory data at admission. Blood cultures were obtained before starting antibiotics, and isolation was recommended. During monitoring, no active GI bleeding was observed, and no drop of hemoglobin level was detected.

According to elevated liver enzymes, viral markers, including IgM anti-HBC-Ab, HBS-Ag, HCV-Ab, IgM anti-CMV-Ab, and IgM anti-HAV-Ab, were checked, and all were negative. Ferritin level was high and reported as >2000 ng/ml. The results of two sets of blood cultures were negative. The serum level of the erythrocyte sedimentation rate and the C-reactive protein were 10 mm/h and 22 mg/dl, respectively. The albumin level was 3.6 gr/dl, and the level of d-dimer was 1.2 micgr/ml (<0.5=negative). According to the recent travel and clinical and laboratory tests, complementary laboratory tests were requested, and a serum sample for CCHF was sent. Based on the national guidelines for CCHF, the patient was a probable case and subjected to the ribavirin therapy. Serological tests, including ELISA IgG and IgM, were reported positive after 5 days. ELISA test was performed by VectoCrimean-CHF-IgM kits (Vector-Best). The polymerase chain reaction (PCR) assay was performed at the National Reference Laboratory of Pasteur Institute of Iran, where the specificity of assays was approved as 100% and was reported positive; hence, the diagnosis of CCHF was confirmed. In addition, the reverse transcriptase-PCR (RT-PCR) of nasopharyngeal samples for *SARS-CoV-2* and *Influenza* A and B was reported negative. Furthermore, 3000 mg of ribavirin was prescribed as the initial dose followed by 1800 mg every 6 h for 4 days, and then 600 mg every 8 h for 6 days, and antibiotic therapy was discontinued. On Day 4, the patient was afebrile, and hemodynamic was stable. He was discharged on Day 7 after hospitalization afebrile and improvement of GI bleeding. Table 1 depicts the laboratory data at discharge. Follow-up for 14 days showed that he was healthy.

TABLE 1 Laboratory data on admission and at discharge

Laboratory test	Reference range	At admission	At discharge
WBC(μ/l)	4000–10,000	4700	6250
Hb (gr/dl)	13.5–17.5	15	16.1
PLT(/μl)	150,000–450,000	45,000	240,000
PTT(sec)	30–45	57.3	40
PT(sec)	12–14	14.2	13.3
INR	1–1.19	1.1	1.03
BUN (mg/dl)	8.9–21	11	12
Cr (mg/dl)	0.9–1.3	1	1.16
AST(IU/L)	Up to 37	690	142
ALT(IU/L)	Up to 41	700	298
ALP	80–306	240	219
LDH (IU/L)	Up to 480	1276	588

Abbreviations: ALP, Alkaline phosphatase; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BUN, Blood Urea Nitrogen; Cr, Creatinine; Hb, Hemoglobin; INR, International normalized ratio; LDH, Lactate dehydrogenase; PLT, Platelets; PT, prothrombin time; PTT, partial thromboplastin time; WBC, White blood cells.

3 | DISCUSSION

CCHF is the second most widespread of viral hemorrhagic fever viruses, after dengue virus, and its vector and reservoir are *Hyalomma* species of thick. This infection is endemic in many countries in Asia, Africa, and Southeastern Europe.[3,4] The clinical characteristics of the patients with this thick born viral disease are from mild to fatal outcomes. The clinical course of CCHF infection is divided into four categories: incubation period, pre-hemorrhagic phase, hemorrhagic phase, and convalescent-phase. After a variable incubation phase, clinical features in the pre-hemorrhagic period are characterized by sudden onset of fever, chills, headache, abdominal pain, and myalgia that typically last <1 week. Accordingly, 3–6 days later, in severe cases, hemorrhagic manifestations, such as petechiae and disseminated intravascular coagulation, occur.[5,6] Suppression of the host immune system by the virus and consequently rapid virus proliferation and dysregulation of the vascular system play a role in the disease pathogenesis. It is described that inflammatory mediators and consequent endothelitis and activation of the intrinsic coagulation cascade play a crucial role in leading to disseminated intravascular coagulation and multi organ failure.[7]

Several laboratory data, including platelet count, hemoglobin, prothrombin time, activated partial thromboplastin time, international normalized ratio, aspartate

aminotransferase, alanine aminotransferase, lactate dehydrogenase, and creatine kinase, were reported to be the prognostic factors.[1] Diagnosis of CCHF is suspected based on clinical, epidemiologic, and laboratory criteria. Prompt diagnosis is critical for therapy and prevention of transmission of infection. The diagnosis is confirmed by RT-PCR, or positive anti-CCHFV IgM or a four-fold increase in specific IgG. These serologic tests are useful in the second week of disease.[8,9] Supportive therapy, including blood or platelet transfusion, is the cornerstone of management. Ribavirin is the only antiviral drug that may be beneficial for CCHFV treatment, particularly in the early phase of therapy.[10]

CCHF has been documented as the most frequent tick-borne viral infection in Iran. The first human infection in Iran was diagnosed in 1999, and then, the incidence of CCHF had a significant rise.[4] It has been described that most of the cases of CCHF in Iran are related to people exhibiting close contact to the tissue or blood of affected livestock. This rout of transmission is more common in eastern parts of Iran. CCHF has been documented in most of the provinces of the country, with highly endemic areas, such as Isfahan, Sistan, and Baluchestan, Razavi Khorasan, Khuzestan, and Fars.[11–13] Approximately 40% of CCHF cases have been reported from Sistan and Baluchestan.[4]

We describe the confirmed case of CCHF who presented with acute onset of fever, malaise, and myalgia and was initially managed with the diagnosis of COVID-19 owing to similar SARS-CoV-2 symptoms, but then GI bleeding manifested. After hospitalization in our hospital, careful history and laboratory data, the diagnosis of CCHF was established. The early symptoms of CCHF, such as fever, myalgia, headache, weakness, and diarrhea, are similar to symptoms of COVID-19 infection; therefore, a misdiagnosis of COVID-19 instead of CCHF can be extremely dangerous and problematic. Clinical and epidemiological findings are the most important strategies to diagnose CCHF disease.

4 | CONCLUSION

During a pandemic, other infections with similar signs and symptoms to COVID-19 should be considered in patients with vague clinical symptoms, particularly in countries, where other endemic diseases occur. This case highlights the significance of considering other differential diagnoses in the COVID-19 era.

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CONFLICT OF INTERESTS

The authors declare that they have no competing interest.

AUTHOR CONTRIBUTION

M,M; K.A; S.N; and A.H acquired data and analyzed and interpreted the data. A.H wrote the first draft of the manuscript. M.M; K.A and S.N revised the manuscript. All authors read and approved the final manuscript.

CONSENT

This research was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and written informed consent was obtained from the patient.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this case report type article as no new data were created or analyzed in this study.

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