

## A Case of Crimean-Congo Haemorrhagic Fever (CCHF) Mimicking the COVID-19 Disease

Zahit Taş<sup>1</sup>

ORCID: 0000-0003-1292-5951

Meliha Çağla Sönmezer<sup>1</sup>

ORCID: 0000-0001-6529-5282

Gülçin Telli Dizman<sup>1</sup>

ORCID: 0000-0001-8195-3345

Ahmet Çağkan İnkaya<sup>1</sup>

ORCID: 0000-0001-7943-8715

Ömrüm Uzun<sup>1</sup>

ORCID: 0000-0003-4721-0139

Murat Akova<sup>1</sup>

ORCID: 0000-0002-6904-9473

<sup>1</sup>Hacettepe University, Faculty of Medicine, Infectious Diseases and Clinical Microbiology Department, Ankara, Turkey.

This case presented as an oral abstract at ESCMID Conference on Coronavirus Disease (ECCVID) on 23-25 September 2020.

Corresponding Author: Zahit Taş  
Hacettepe University, Faculty of Medicine, Infectious Diseases and Clinical Microbiology Department, Ankara, Turkey.  
E-mail: zahittas@hotmail.com

### ABSTRACT

A 74-year-old female from a rural district in Central Anatolia, Turkey, was admitted with persisting fever, malaise, cough, and vomiting. There is no abnormal finding on physical examination. There was no petechiae, purpura, ecchymosis, or bleeding in organ systems at any time. Laboratory findings showed increased D-dimer level and acute inflammation biomarkers such as C-reactive protein, ferritin, and thrombocytopenia with prolonged prothrombin time. Since the patient applied with clinic features indicating a viral infection and on a pandemic period, firstly, we focused on coronavirus disease 2019 (COVID-19) disease. However, the probability was reduced with negative chest imaging and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse-transcription polymerase chain reaction (RT-PCR) results. Any patient admitting with symptoms indicative of COVID-19 disease during the pandemic era should also be evaluated for other infections, especially endemic zoonotic infections such as brucellosis, Crimean-Congo hemorrhagic fever (CCHF), Q fever. In this case, serologic tests were all negative (Leptospira Toxoplasma, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Rubella, Brucella, Coxiella, Hepatitis B, Hepatitis C). The patient was found to be IgM and RNA positive for the CCHF virus by ELISA and polymerase chain reaction (PCR) methods, respectively. In endemic areas, CCHF is one of the diseases which should be considered in the differential diagnosis. In addition, it is essential to accurately identify CCHF infection using proper medical tests to prevent misdiagnosis amid this COVID-19 pandemic. Hence, we need to keep an eye on the cases that come from endemic rural areas in the Central Anatolia region of Turkey. Herein, we present a case of CCHF patients initially evaluated to have COVID-19.

Keywords: Crimean Congo Haemorrhagic Fever, zoonotic disease, endemic region, pandemic, COVID-19

Received: 2 August 2021, Accepted: 11 October 2021,  
Published online: 13 June 2022

## INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is an emerging zoonotic disease characterized by flu-like symptoms, fever, hemorrhage, and petechia. The CCHF virus is a member of the Bunyaviridae family and can be transmitted to humans by tick-bite. The disease is widely distributed from the Black Sea to southern Africa. It has been endemic in some parts of Turkey since 2002, with many fatalities, and it is considered a significant public health problem [1,2]. Laboratory findings may include

thrombocytopenia, leukopenia, hyperbilirubinemia with elevated transaminases, prolongation of international normalized ratio, prothrombin time, and activated partial thromboplastin time. In addition, many of the initial nonspecific symptoms of CCHF can mimic other common infections [1,3,4].

Coronavirus disease 2019 (COVID-19) is a respiratory infectious disease in humans caused by a newly discovered virus known as the severe

acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is characterized by fever, cough, dyspnea, myalgia, malaise, and fatigue symptoms like CCHF [1,3,5,6]. Also, laboratory findings are similar to CCHF, such as higher D-dimer, C-reactive protein (CRP), creatine kinase (CK), and lactate dehydrogenase (LDH) levels. Additionally, lymphopenia, thrombocytopenia, and pulmonary opacities on the chest CT [1,3,5,7].

Although CCHF is endemic in some countries, the main admission symptoms are fever, myalgia, malaise, and fatigue, so that it can be misinterpreted mainly due to the ongoing COVID-19 pandemic [9]. In this setting, a complete history and careful physical examinations must be followed by laboratory confirmation. The differential diagnosis should be broad enough when someone comes with a chief complaint of persisting fever, myalgia, and malaise [5,8,9].

Herein, we present some COVID-19 symptoms and their similarities with CCHF. In addition, we also describe similar laboratory findings of both diseases.

### Case presentation

A 74-year-old female from a rural area in Central Anatolia, Turkey, was admitted with malaise, fatigue, persisting fever, cough, and vomiting for three days. She was hospitalized at the Infectious Diseases Service, Hacettepe University in Ankara, Turkey. On admission, she did not report any contact with a COVID-19 patient. There was no petechiae, purpuric lesions, or bleeding. Oxygen saturation was 96% in room air, respiratory rate 16/min, pulse 70/min and body temperature 36°C, and blood pressure 130/80 mm/Hg. There is no abnormal finding on physical examination. Complete blood count revealed Hb:12,5 g/dl, Leukocyte:  $2.2 \times 10^3/\mu\text{l}$ , Lymphocyte:  $0.35 \times 10^3/\mu\text{l}$ , Neutrophil  $1.67 \times 10^3/\mu\text{l}$ , Platelet:  $86 \times 10^3/\mu\text{l}$ . Other blood tests were; total CK: 152 U/L, LDH: 313 U/L, ALT: 23 IU/L, AST: 56 IU/L, Ferritin: 477,5  $\mu\text{g/L}$ , D-dimer: 2,36 mg/L, International normalized ratio (INR): 1,6, CRP: 5,66 mg/dl. Bilirubin levels and other blood tests were normal. Chest X-ray and tomography were evaluated normal, without any pathological finding. SARS-CoV-2 RT-PCR from nasopharyngeal smear was negative in two subsequent occasions.

Lymphopenia resolved spontaneously within seven days, but thrombocytopenia and leukopenia continued. Also, platelet values decreased to its nadir of  $25 \times 10^3/\mu\text{l}$ . The blood smear showed no signs of hemolysis or atypical cells. Abdominal ultrasound imaging was deemed to be normal. All serologic tests against an array of infectious agents were negative (leptospira, toxoplasma, CMV, EBV, rubella, brucella, coxiella, HBV, HCV, HIV, ANA, Antids DNA, etc.). Although patient denied a history of a tick bite, CCHF was considered because the patient hailed from an endemic region and was engaged in animal husbandry. AntiCCHF IgM and RT-RNA were found to be positive.

The patient was followed up with supportive therapy in contact isolation. She did not develop petechiae, purpura, ecchymosis, or bleeding in organ systems at any time. Laboratory parameters normalized during follow-up and she was discharged home with close telemedicine observation.

### DISCUSSION

Crimean-Congo hemorrhagic fever (CCHF) is an acute and fatal zoonotic disease caused by an RNA virus that is a member of the Bunyaviridae family. The fatality rate of the disease is 3%-30%. Hyalomma ticks transmit CCHF through direct contact with the blood and other bodily fluids of patients or infected animals [1,3]. The first Turkish case was reported in 2002. The CCHF disease is one of the most dangerous medically significant tick-borne disease affecting Turkish people and many countries at Africa, Eurasia, Central and Southwest Asia, and the Middle East [1,3]. CCHF is characterized by fever, myalgia, malaise, nausea, vomiting, headache, and hemorrhagic manifestations [1,3]. The laboratory findings of CCHF include anemia, thrombocytopenia, leukopenia, hyperbilirubinemia, elevated transaminases, CK, and LDH; and prolonged INR, higher fibrinogen and D-dimer levels [8,10]. These clinical features and laboratory findings may mimic various other infections [3,8].

COVID-19 infection is characterized by fever, cough, dyspnea, myalgia, malaise, fatigue symptoms, D-dimer elevation, elevated acute inflammation

biomarkers such as c-reactive protein, ferritin, thrombocytopenia, lymphopenia, and prolonged prothrombin time, and pulmonary infiltrate including ground-glass opacities on CT of the chest [5,11].

COVID-19 and CCHF are hard to distinguish because they share similar clinical features [6,8]. Cytokine storms are the underlying reason of increased morbidity and mortality in both diseases. While CCHF results in hemorrhage, COVID-19 can cause thrombosis [6].

To our knowledge no CCHF case mimicking the COVID-19 clinical features and laboratory findings have been reported before. Especially at the beginning of the summer, the incidence of CCHF gradually increases in the rural areas due to the increased contact with infected insects and animals. Our patient presented with myalgia, malaise, fatigue, persisting fever, cough, and vomiting. As Turkey is an CCHF-endemic region, CCHF should be kept in mind in patients especially those that come from the endemic regions ie. Corum, Yozgat, and Kirsehir. Since this patient applied with a clinic resembling a viral infection during the pandemic period, COVID-19 infection was considered firstly. However, COVID-19 was ruled out with chest imaging and negative SARS CoV-2 RT-PCR. Subsequently, we performed an array of infectious disease work-up to diagnose causative disease. CCHF was confirmed with positive RT-PCR and specific IgM and IgG tests [1,3,8,12]. Besides, extensive laboratory work-up ruled out other possible infectious casuses

If this case has not been labeled as COVID-19, the CCHF could be diagnosed earlier and not been overlooked. In a large epidemiologic study including more than 1800 cases of CCHF, nearly one third of cases denied prior history of tick bite or tick contact, 62 %reported close contact with animals, and 10 percent had a history of direct contact with animal body fluids or tissue. Hemorrhagic findings were detected in 23.0% of the patients [11]. In endemic areas, regardless of the history of bleeding and tick bites, especially in viral infection-like diseases accompanied by thrombocytopenia, CCHF should be kept in mind [7,8,11].

## CONCLUSION

The CCHF cases hailing from rural areas apply to emergency departments overcrowded by COVID-19 pandemic. Despite the pandemic constraints, any patient admitting with symptoms indicative of COVID-19 during the pandemic era should also be evaluated for other infections, particularly endemic zoonotic infections. In endemic areas, CCHF is one of the diseases which should be considered in the differential diagnosis. In addition, it is essential to accurately identify CCHF infection using proper medical tests to prevent misdiagnosis amid this COVID-19 pandemic. Hence, we need to keep an eye on the cases that come from endemic rural areas in the Central Anatolia region of Turkey.

## Author contribution

Study conception and design: ZT, MCS, and MA; data collection: ZT, GTD, ACI, and OU; analysis and interpretation of results: MCS, OU, and MA; draft manuscript preparation: ZT, MCS, and GTD. All authors reviewed the results and approved the final version of the manuscript.

## Funding

The authors declare that the study received no funding.

## Conflict of interest

The authors declare that there is no conflict of interest.

## REFERENCES

- [1] Ergonul O. Crimean-Congo hemorrhagic fever virus: new outbreaks, new discoveries. *Curr Opin Virol.* Apr 2012;2(2):215-20. doi:10.1016/j.coviro.2012.03.001
- [2] Yilmaz GR, Buzgan T, Irmak H, et al. The epidemiology of Crimean-Congo hemorrhagic fever in Turkey, 2002-2007. *Int J Infect Dis.* May 2009;13(3):380-6. doi:10.1016/j.ijid.2008.07.021
- [3] Ertem G, Sönmezer M, Temoçin F, Ataman Hatipoğlu Ç, Tülek N, Oral B. The efficacy of oral ribavirin on clinical and laboratory parameters in Crimean-Congo hemorrhagic fever: an observational study from Turkey. *Turk J Med Sci.* Nov 17 2016;46(5):1407-1414. doi:10.3906/sag-1506-92
- [4] Heydari Aa. Acute Complicated Brucellosis Mimicking Crimean-Congo Hemorrhagic Fever (CCHF) and Vice Versa. Review article. *Journal of Medical Microbiology and Infectious Diseases.* 2019;7(1):1-5. doi:10.29252/JoMMID.7.1.2.1
- [5] Sonmezer MC, Inkaya AC. COVID-19: Virology, pathogenesis, Clinical Features, Treatment. *Turkey Clinics special issue COVID-19.* 2020. p. 1-8. Online ISBN: 978-625-401-397-3.
- [6] Pazarlı AC, Parlak Z, Ekiz T. COVID-19 and Crimean-Congo Hemorrhagic Fever: Similarities and Differences. *Heart Lung.* Nov-Dec 2020;49(6):892-893. doi:10.1016/j.hrtlng.2020.05.013
- [7] Kara SS, Kara D, Fettah A. Various clinical conditions can mimic Crimean-Congo hemorrhagic fever in pediatric patients in endemic regions. *J Infect Public Health.* Sep-Oct 2016;9(5):626-32. doi:10.1016/j.jiph.2016.01.007
- [8] Tasdelen Fisgin N, Doganci L, Tanyel E, et al. Initial high rate of misdiagnosis in Crimean Congo haemorrhagic fever patients in an endemic region of Turkey. *Epidemiol Infect.* Jan 2010;138(1):139-44. doi:10.1017/s0950268809990318
- [9] Butt MH, Ahmad A, Misbah S, Mallhi TH, et al. Crimean-Congo hemorrhagic fever and Eid-UI-Adha: A potential threat during the COVID-19 pandemic. *J Med Virol.* Feb 2021;93(2):618-619. doi:10.1002/jmv.26388
- [10] Zayet S, Kadiane-Oussou NJ, Lepiller Q, et al. Clinical features of COVID-19 and influenza: a comparative study on Nord Franche-Comte cluster. *Microbes Infect.* Oct 2020;22(9):481-488. doi:10.1016/j.micinf.2020.05.016
- [11] Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis.* Mar-Apr 2020;34:101623. doi:10.1016/j.tmaid.2020.101623
- [12] Onguru P, Dagdas S, Bodur H, et al. Coagulopathy parameters in patients with Crimean-Congo hemorrhagic fever and its relation with mortality. *J Clin Lab Anal.* 2010;24(3):163-6. doi:10.1002/jcla.20383