

# A case: Rose Bengal test positive Crimean Congo hemorrhagic fever patient

## *Bir olgu: Rose Bengal testi pozitif Kırım Kongo kanamalı ateşi hastası*

**Hatice Bozkurt Yavuz**<sup>ID</sup>

**Atıf/Cite as:** Bozkurt Yavuz H. A case: Rose Bengal test positive Crimean Congo hemorrhagic fever patient. Northwestern Med J. 2023;3(3):197-200.

### ABSTRACT

Brucella is one of the most common bacterial zoonosis. Crimean-Congo Hemorrhagic Fever (CCHF) is a potentially life-threatening infection. They have similar epidemiologic and clinical presentations. A 40-year-old male patient, engaged in animal husbandry, presented to the emergency unit with complaints of weakness, headache, and fever. Because of his low platelet count, he was referred to the internal medicine clinic. The patient did not have a history of contact with a tick or a CCHF patient. The Brucella Rose Bengal Test (RBT) was performed and the result was positive. After he was referred to the infectious diseases clinic, the CCHF RT-PCR test was found to be positive and the Brucella Wright agglutination test was negative. The patient, who was diagnosed with CCHF, was discharged in good condition. A positive RBT result does not always make a definitive diagnosis of Brucella infection. In areas where CCHF and Brucella are endemic, CCHF should be considered even if there is no history of ticks.

**Keywords:** Brucellosis, Crimean-Congo hemorrhagic fever, Rose Bengal, thrombocytopenia

### Öz

Brusella en yaygın bakteriyel zoonozlardan biridir. Kırım-Kongo kanamalı ateşi (KKKA) potansiyel olarak yaşamı tehdit eden bir enfeksiyondur. İki hastalık benzer epidemiyolojik ve klinik prezentasyona sahiptirler. Hayvancılıkla uğraşan 40 yaşında erkek hasta halsizlik, baş ağrısı ve ateş şikayetleri ile acil servise başvurdu. Trombosit sayısının düşük olması nedeniyle dahiliye kliniğine yönlendirildi. Hastanın kene veya KKKA hastası ile temas öyküsü yoktu. Brucella Rose bengal testi (RBT) yapıldı ve sonuç pozitif. Enfeksiyon hastalıkları kliniğine sevk edildikten sonra KKKA RT-PCR testi pozitif, Brucella Wright aglütinasyon testi negatif bulundu. KKKA tanısı konulan hasta sağlık durumu iyi olarak taburcu edildi. Pozitif RBT sonucu her zaman Brucella enfeksiyonunun kesin tanısını koymaz. KKKA ve Brusella'nın endemik görüldüğü bölgelerde kene öyküsü olmasa bile KKKA açısından dikkatli olunmalıdır.

**Anahtar kelimeler:** Bruselloz, Kırım-Kongo kanamalı ateşi, Rose Bengal, trombositopeni

**Received:** 15.12.2022

**Accepted:** 09.05.2023

**Publication date:** 01.10.2023

**Corresponding Author:**

**H. Bozkurt Yavuz**

**ORCID:** 0000-0003-0468-2486

Uşak Training and Research

Hospital, Department of Clinical

Biochemistry Laboratory,

Uşak, Türkiye

✉ haticebozkurtyavuz@gmail.com

## INTRODUCTION

*Brucella*, one of the most common bacterial zoonosis, is seen in more than five hundred thousand new cases each year. *Brucella melitensis*, *Brucella abortus*, and *Brucella suis* are the three species generally associated with human disease (1). The main route of transmission of the disease is the consumption of unpasteurized milk and dairy products, the consumption of undercooked meat or skin penetration of those can also be counted as the other routes of transmission (2).

Brucellosis has a lower fatality rate of 2%, however, it can cause severe disability (3). On the other hand, Crimean-Congo hemorrhagic fever (CCHF) is a life-threatening infection, with reported mortality rates of 13%–30%, caused by the CCHF virus which belongs to the genus *Nairovirus* in the *Bunyaviridae* family. It may exhibit a severe profile with fatal bleeding or may exhibit a mild clinical course (4). The affected population and the clinical presentation of CCHF and brucellosis are similar, so brucellosis should be considered in the differential diagnosis of CCHF in endemic areas.

## CASE REPORT

A 40-year-old male patient, engaged in animal husbandry, applied to the emergency unit of our hospital in April 2020 with complaints of weakness, headache, and fever at night. His fever was 37.8°C in the hospital. There was no history of COVID-19 contact. Laboratory results of the patient are shown in Table 1, as 1st day. Since our region is endemic area for CCHF and because the season is favorable for tick cases, the history

of tick was enquired. It was learned that there was no history of ticks or a family member with a recent CCHF disease. The patient was referred to the internal medicine clinic. Two days later, the patient applied to the internal medicine outpatient clinic, thrombocytopenia deepened and the ALT and AST values, which were normal at the emergency admission, increased. The results of the 3rd day are shown in Table 1.

In the internal medicine clinic, while taking the patient's history, it was learned that he had been treated for *Brucella* six years ago. The patient had nausea, vomiting, and diarrhea for two days. It was suspected that the patient, who did not have a history of contact with a tick or a CCHF patient, might have had a *Brucella* infection. Therefore, *Brucella* Rose Bengal agglutination test was performed in the clinical biochemistry laboratory and the result was positive. The patient was referred to the infectious diseases clinic in a tertiary care hospital.

The CCHF RT-PCR (Reverse-Transcription-Polymerase Chain Reaction) test was found to be positive upon his admission to the tertiary infectious diseases clinic. The result of the *Brucella* Wright agglutination test (with Coombs antiserum) was negative with <1/20. The patient was diagnosed with CCHF. After hospitalization, the patient's blood counts were closely monitored (Table 1, days 3-9). Due to the decrease in platelet count, 5 units of platelet suspension and 2 units of fresh frozen plasma were given to the patient. The patient was discharged on the 7th day of his admission. The written informed consent was obtained from the patient for the publication of this case report.

**Table 1. Laboratory results of the patient.**

	1.day	3.day	4.day	5.day	6.day	7.day	8.day	9.day	10.day
PLT (10 <sup>9</sup> /L)	125	43	34	32	32	20	72	91	209
WBC (10 <sup>9</sup> /L)	3,2	1,3	1,5	1,9	2,6	3,2	4,1	5,0	5,7
aPTT (s)	29	28	28	32	28	23	21	-	-
ALT (U/L)	44	125	145	224	271	228	208	125	102
AST (U/L)	32	51	60	118	164	160	202	156	154
CK (U/L)	-	-	450	488	263	188	102	179	50
LDH (U/L)	288	221	625	596	579	548	458	483	549

PLT: Platelets; WBC: White Blood Cells; aPTT: Activated partial thromboplastin time; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; CK: Creatine Kinase; LDH: Lactate Dehydrogenase

## DISCUSSION

Symptoms that are non-specific and easily confused with many diseases are common in brucellosis. Since it can present with hematological findings, it is possible to be confused with any disease that can cause hematological involvement (5). Hematological findings can be seen as a result of bone marrow suppression in brucellosis. Similar laboratory findings such as leukopenia, thrombocytopenia, and anemia can be seen in CCHF. ALT, AST, LDH, and CK elevation can also be seen in both diseases (6,7).

In our case, *Brucella* infection was primarily considered due to the absence of tick history, but CCHF could not be excluded due to the rapid deepening of thrombocytopenia. The main route of transmission of CCHF is tick bite, but humans are also infected by crushing infected ticks, and contact with a CCHF patient, or body secretions of viraemic animals (4). Therefore, it should be kept in mind that CCHF can be transmitted without a history of ticks. CCHF should be considered in deteriorating blood counts, especially in people engaged in animal husbandry.

The Rose Bengal test detects smooth lipopolysaccharide-specific immunoglobulin A (IgA), immunoglobulin M (IgM), and immunoglobulin G (IgG) (8). The Rose Bengal test has high sensitivity and relatively low specificity. However, it may give false positive results in people who have had *Brucella* previously. A study showed that the positive predictive value is 0.89 and the specificity is 76.9% in people who had *Brucella* infection before (9). It is also known that *Vibrio cholerae*, *Francisella tularensis*, and *Yersinia enterocolitica* 0:9 show cross-reactivity in this test (8). Vaccination, antibody residues, and laboratory errors can be considered for cross-reactivity (10). Moreover, a recent study found that the Rose Bengal test may cause false positive results in patients with Coronavirus disease (COVID-19) (11).

People who come into contact with livestock in endemic areas, such as shepherds, veterinarians, farmers, and butchers, are at high risk for CCHF. In addition, laboratory workers are at risk of disease transmission (12). Both diseases are common in those living in rural areas and involve animal husbandry.

In conclusion, in areas where CCHF and *Brucella* are endemic, CCHF should be considered in cases of rapid progression of thrombocytopenia, even if there is no history of ticks. Thrombocytopenic patients should be evaluated for CCHF, especially in the epidemic season. A positive Rose Bengal test does not always make a definitive diagnosis of *Brucella*.

**Conflict of Interest:** The authors have declared that they have no conflict of interest.

**Funding:** The authors have declared that they have not received any financial support.

## REFERENCES

1. Mantur BG, Amarnath SK. Brucellosis in India - a review. *J Biosci.* 2008; 33(4): 539-47. <https://doi.org/10.1007/s12038-008-0072-1>
2. Hayoun MA, Muco E, Shorman M. Brucellosis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK441831/>
3. Christopher S, Umapathy BL, Ravikumar KL. Brucellosis: review on the recent trends in pathogenicity and laboratory diagnosis. *J Lab Physicians.* 2010; 2(2): 55-60. <https://doi.org/10.4103/0974-2727.72149>
4. Ergönül O. Crimean-Congo haemorrhagic fever. *Lancet Infect Dis.* 2006; 6(4): 203-14. [https://doi.org/10.1016/S1473-3099\(06\)70435-2](https://doi.org/10.1016/S1473-3099(06)70435-2)
5. Young EJ. *Brucella* species. In: Mandell GL, Bennett JE, Dolin R, editors. *Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases.* 6th ed. Philadelphia: Churchill Livingstone; 2005: 2669-74.
6. Hatipoglu CA, Bulut C, Yetkin MA, et al. Evaluation of clinical and laboratory predictors of fatality in patients with Crimean-Congo haemorrhagic fever in a tertiary care hospital in Turkey. *Scand J Infect Dis.* 2010; 42(6-7): 516-21. <https://doi.org/10.3109/00365540903582418>

7. Ciftçi C, Oztürk F, Oztekin A, et al. Comparison of the serological tests used for the laboratory diagnosis of brucellosis. *Mikrobiyol Bul.* 2005; 39(3): 291-9.
8. Díaz R, Casanova A, Ariza J, Moriyón I. The Rose Bengal Test in human brucellosis: a neglected test for the diagnosis of a neglected disease. *PLoS Negl Trop Dis.* 2011; 5(4): e950. <https://doi.org/10.1371/journal.pntd.0000950>
9. Ruiz-Mesa JD, Sánchez-Gonzalez J, Reguera JM, Martín L, Lopez-Palmero S, Colmenero JD. Rose Bengal test: diagnostic yield and use for the rapid diagnosis of human brucellosis in emergency departments in endemic areas. *Clin Microbiol Infect.* 2005; 11(3): 221-5. <https://doi.org/10.1111/j.1469-0691.2004.01063.x>
10. Chothe SK, Saxena HM. Innovative modifications to Rose Bengal plate test enhance its specificity, sensitivity and predictive value in the diagnosis of brucellosis. *J Microbiol Methods.* 2014; 97: 25-8. <https://doi.org/10.1016/j.mimet.2013.12.005>
11. Gemcioglu E, Erden A, Karabuga B, et al. False positivity of Rose Bengal test in patients with COVID-19: case series, uncontrolled longitudinal study. *Sao Paulo Med J.* 2020; 138(6): 561-2. <https://doi.org/10.1590/1516-3180.2020.0484.03092020>
12. Solís García del Pozo J, Solera J. Systematic review and meta-analysis of randomized clinical trials in the treatment of human brucellosis. *PLoS One.* 2012; 7(2): e32090. <https://doi.org/10.1371/journal.pone.0032090>