DENTAL AND MEDICAL JOURNAL - REVIEW

e-ISSN 2667-7288 **Vol** 4, **Issue** 1, (2022) *Review Article / Derleme Makale*

BRUCELLOSIS FROM HEMATOLOGY PERSPECTIVE

HEMATOLOJİ PERSPEKTİFİNDEN BRUSELLOZ

Can ÖZLÜ[1]

[1]Ass. Prof MD, Department of Hematology Kütahya Health Sciences University Faculty of Medicine, Kütahya, Turkey

ORCID ID: 0000-0002-9573-1177

Corresponding Author:

Can ÖZLÜ,

Department of Hematology Kütahya Health Sciences University Faculty of Medicine, Kütahya, Turkey,

E mail: cozlu20@gmail.com, Phone: +90 505 479 18 72

Article Info / Makale Bilgisi

Received / Teslim: December 23, 2021
Accepted / Kabul: January 17, 2022
Online Published / Yayınlanma: February 28, 2022
DOI:

ÖZLÜ C. Brucellosis From Hematology Perspective. Dent & Med J - R. 2022;4(1):72-78.

DENTAL AND MEDICAL JOURNAL - REVIEW

e-ISSN 2667-7288 **Vol** 4, **Issue** 1, (2022) ***Review Article / Derleme Makale***

Abstract

Brucellosis is a zoonotic infectious disease that causes many hematological abnormalities. This review study, it was aimed to evaluate the literature in terms of hematological involvement of brucellosis. As brucellosis may mimic a primary hematological disease but this is reversible after appropriate antimicrobial therapy. For this reason, it should be considered in the differential diagnosis of hematological diseases, especially in endemic areas such as our country where animal husbandry is common.

Keywords: *Brucellosis, hematological involvement, leukopenia, lymphomonocytosis, anemia.*

Özet

Bruselloz, birçok hematolojik anormalliğe neden olan zoonotik bir enfeksiyon hastalığıdır. Bu derleme çalışmasında, brusellozun hematolojik tutulumu açısından literatürün değerlendirilmesi amaçlanmıştır. Bruselloz primer hematolojik bir hastalığı taklit edebilir, ancak bu uygun antimikrobiyal tedaviden sonra geri dönüşümlüdür. Bu nedenle özellikle ülkemiz gibi hayvancılığın yaygın olduğu endemik bölgelerde hematolojik hastalıkların ayırıcı tanısında mutlaka düşünülmelidir.

Anahtar Kelimeler: *Bruselloz, hematolojik tutulum, lökopeni, lenfomonositoz, anemi.*

DENTAL AND MEDICAL JOURNAL - REVIEW

e-ISSN 2667-7288 Vol 4, Issue 1, (2022) Review Article / Derleme Makale

OVERVIEW / GENEL BAKIŞ

Brucellosis is a zoonotic infectious disease caused by Brucella bacteria and causes multi-organ involvement (1). Transmission from infected animals to humans occurs through direct or indirect contact, inhalation of infected droplets, or consumption of unpasteurized milk and dairy products (1,2). It is an important public health problem, especially in countries where animal husbandry is common, such as our country especially in as Southeastern Anatolia, Eastern Anatolia, and Central Anatolia regions (3-5). Its most important feature is that it affects many organs and is included in the differential diagnosis of many diseases as it is an intracellular pathogenic microorganism. This disease causes clinical and laboratory findings depending on the region of involvement (1,6). Brucellosis is included in the differential diagnosis of many diseases due to its systemic symptoms. The most common symptoms in brucellosis cases are fever, joint and muscle pain, arthritis, abdominal pain, headache, weakness, fatigue, loss of appetite, gastrointestinal symptoms, weight loss, and night sweats. In the laboratory examinations of the patients, hepatobiliary enzyme elevations can be detected, except for hematological involvement (1,7).

Brucella bacteria are viable and reproducible in phagocytic cells of the host and facultative intracellular pathogen. Is not fully understood how Brucella bacteria protect the killing effect of on the phagocytic cells. Primary and secondary degranulation, myeloperoxidase-H2O2 system, and reactive oxygen Cu-Zn superoxide, which removes its intermediates dismutase inhibition are theoretically suspected mechanisms. Brucella survival of phagosome-lysosome fusion and apoptosis in mononuclear phagocytes is thought to be facilitated by inhibition (1,6,8). Reticuloendothelial system (RES) involvement such as bone marrow and spleen are observed in brucellosis. Therefore, abnormalities may be seen in laboratory findings (6-8). Hematological complications due to brucellosis are common. They thought to be occurred Brucella spp. have tropism of the RES such as bone marrow and peripheral organs. Changes in hematological parameters are observed in most of the patients (8). Hematologically, brusellosis often can cause leukopenia, lymphomonocytosis, and mild anemia. Although rare, it has been reported to cause pancytopenia and severe thrombocytopenia by causing hemophagocytosis, hypersplenism, and granulomatous changes in the bone marrow. Even it can cause disseminated intravascular coagulation (DIC), but this complication is rare (6-13).

This review study, it was aimed to evaluate the literature in terms of hematological involvement of brucellosis.

a. Anemia

In the literature, the most common hematological finding in pediatric cases with brucellosis has been reported as anemia with a frequency of 20% to 50%. [6] Changes in iron metabolism secondary to an infection, hypersplenism, bleeding, bone marrow suppression, and autoimmune hemolysis are blamed for the development of anemia. [10] Even cases of microangiopathic hemolytic anemia and severe thrombocytopenia due to severe brucellosis have been reported (11,12). In studies conducted in our country, anemia was detected in 37.8- 48.6% of the cases (2,13).

e-ISSN 2667-7288 Vol 4, Issue 1, (2022) Review Article / Derleme Makale

b. Thrombocytopenia

Although hematological complications such as anemia, thrombocytopenia, and leukopenia are frequently reported in acute brucellosis, severe thrombocytopenia is rare. Hypersplenism, reactive hemophagocytosis, and immunosuppression are possible causes of thrombocytopenia shown as (13-17). Thrombocytopenia seen in brucellosis is usually isolated thrombocytopenia. Clinical and laboratory idiopathic thrombocytopenic purpura imitates. Thrombocytopenia in patients with brucellosis. Although the pathogenesis is clear; platelet damage caused by hypersplenism, hemophagocytosis, endotoxin, and exotoxins increase the clearance of platelets to vascular surfaces various types of adhesion, such as bone marrow suppression. It is thought that the mechanisms may play a role. Although antiplatelet antibodies can cause peripheral immune destruction of platelets, it is quite difficult to detect these antibodies with routine tests (18). Clinical evaluation of patients with brucellosis presenting with thrombocytopenia symptoms and signs, similar to patients without thrombocytopenia. Findings such as petechiae, ecchymosis, and bleeding are mostly related to the depth of the thrombocytopenia. Although there is mild thrombocytopenia bleeding may occur. In rare cases, this condition is associated with platelet function. It was thought that it may be related to vasculitis, which is rare (18-23). There are even cases of immuno thrombocytopenia reported in the literature (16). In a study conducted in our country, thrombocytopenia was detected in 2.7-% of the cases (2).

c. Leukocyte Abnormalities (Leukopenia and leukocytosis)

In brucellosis, leukopenia has been reported with a different frequency of 6-31%, and leukocytosis 3-16% (21-23). Among the leukocyte count abnormalities secondary to brucellosis, the most common leukopenia and relative is lymphocytosis. Both leukocytosis and lymphopenia are less common. Hemophagocytosis, hypersplenism, and granulomatous lesions are thought to be played in etiopathogenesis (18).

d. Pancytopenia

Pancytopenia incidence varies according to the reported series (3-21%). In pathogenesis as with other hematological findings, multiple factors play a role. Hemophagocytosis, hypersplenism, granuloma formation in the bone marrow, bone marrow hypoplasia, and immune destruction are the main mechanisms. Bone marrow is mostly hypercellular. Histiocytic hemophagocytosis is in the foreground. pancytopenia can be seen alone such as hepatitis, arthritis, meningoencephalitis, kidney failure, epididymoorchitis, liver abscess, spleen focal abscess, and capillary leak syndrome. It may also appear with systemic manifestations (8,18,24).

e. Other Hematological Findings

Thrombotic microangiopathies (Thrombotic thrombocytopenic purpura, disseminated intravascular coagulation), Coomb's positive autoimmune hemolytic anemias, cold agglutinin disease can be counted among. It can trigger hemolytic anemia in patients with G6PD deficiency. It can also be seen together with hematological and oncological malignancies. hairy cell leukemia. It can be seen simultaneously with multiple myeloma, Hodgkin's, and non-Hodgkin's lymphomas, acute leukemias, polycythemia vera and myelofibrosis.

e-ISSN 2667-7288 Vol 4, Issue 1, (2022) Review Article / Derleme Makale

In addition, in febrile neutropenia development can be seen due to brucellosis during (chemotherapy and bone marrow transplant) hematological treatments of diseases (usually malignancies) (18).

Diagnosis of brucellosis based on the isolation of the microorganism from clinical specimens, serological methods (Rose Bengal, Wright and Coombs test, Standard agglutination test, etc.), and nucleic acid amplification tests. Definitive diagnosis is made by isolation of bacteria in cultures from sterile sites such as blood, bone marrow, or tissues. The absence of growth in culture does not exclude the diagnosis of the disease. Culture samples that can be used for Brucella isolation are blood and bone marrow, rarely, spleen and liver biopsies, abscess, cerebrospinal fluid, joint, peritoneal, and pericardial fluids, and urine (25).

Treatment is for 42 days to 3-6 months with combination therapy including doxycycline, rifampicin is recommended by the World Health Organization. The duration of treatment and the agents have given vary according to the patient and clinical involvement (1).

There are studies in the literature regarding the hematological involvement of brucellosis (8,18,24,26-30). However, brucellosis studies examining the effect of treatment on hematological findings are limited (26). In studies, it was found that there was no consensus on the cut-off value, especially in terms of anemia (6). In a study in which pediatric brucella patients included from our country reported that because of appropriate antimicrobial treatment of brucellosis may cure hematological findings (26).

SUMMARY / SONUÇ

In conclusion, brucellosis may mimic a primary hematological disease, but this is reversible after appropriate antimicrobial therapy. For this reason, it should be considered in the differential diagnosis of hematological diseases, especially in endemic areas such as our country where animal husbandry is common.

Acknowledgements / Teşekkür

Declaration of conflicting interests: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

References / Referanslar

1. Alp E, Doğanay M. Bruselloz. In Topçu Wilke A, Söyletir G, Doğanay M. (eds) Enfeksiyon Hastalıkları ve Mikrobiyolojisi. Nobel Tıp Kitabevi 2017 İstanbul 4.baskı.863-867.
2. Tatlı Kış T, Kış M, Köse Ş. 111 Bruselloz olgusunun etyoloji, klinik seyir ve komplikasyonlarının değerlendirilmesi; bir retrospektif çalışma. Mersin Üniversitesi Sağlık Bilimleri Dergisi 2020; 13(3): 339-47.
3. Alkan Çeviker S, Elmaslar Mert H, Gedik M. Akut Kolesistit ile Başvuran Atipik Bruselloz Olgusu. Sakarya Tıp Dergisi 2019; 9(4): 702-5.

e-ISSN 2667-7288 Vol 4, Issue 1, (2022) Review Article / Derleme Makale

4. Alkan Çeviker S, Dindar Demiray E. A Case of Acute Brucellosis that Presenting With Cutaneous Manifestations. Journal of Biotechnology and Strategic Health Research 2020; 4(2): 184-7.
5. Alkan-Çeviker S, Günal Ö, Elmaslar-Mert HT, Köksal E. Brucella septic arthritis and abscess in hand joint. Klimik Derg. 2020; 33(2): 185-7.
6. Justman N, Fruchtman Y, Greenberg D, Ben-Shimol S. Hematologic manifestations of brucellosis in children. Pediatr Infect Dis J 2018; 37:586-91.
7. Okur M, Erbey F, Kaya A, Doğan M, Acar MN, Uzun H. Retrospective clinical and laboratory evaluation of children with brucellosis. Pediatr Int 2012; 54:215-8.
8. El-Koumi MA, Afify M, Al-Zahrani SH. A prospective study of brucellosis in children: relative frequency of pancytopenia. Iran J Pediatr 2014; 24:155-60.
9. Bourantas LK, Pappas G, Kapsali E, Gougopoulou D, Papamichail D, Bourantas KL. Brucellosis-induced autoimmune hemolytic anemia treated with rituximab. Ann Pharmacother 2010;44(10):1677-80.
10. Al-Eissa Y, Al-Nasser M. Haematological manifestations of childhood brucellosis. Infection 1993; 21:23-6.
11. Yaramis A, Kervancioglu M, Yildirim I, Soker M, Derman O, Tas MA. Severe microangiopathic hemolytic anemia and thrombocytopenia in a child with Brucella infection. Ann Hematol 2001;80(9):546-8.
12. Di Mario A, Sica S, Zini G, Salutari P, Leone G. Microangiopathic hemolytic anemia and severe thrombocytopenia in Brucella infection. Ann Hematol 1995;70(1):59-60.
13. Demirdağ K, Özden M, Kalkan A, Çelik İ, Kılıç SS. Bruselloz: 146 Olgunun Retrospektif Değerlendirilmesi. Flora 2002;7(2):120-5.
14. Kiki I, Gundogdu M, Albayrak B, Bilgiç Y. Thrombotic thrombocytopenic purpura associated with Brucella infection. Am J Med Sci 2008;335(3):230-2.
15. Kerget F, Kerget B, Çelik N, İba Yılmaz S. Bruselloz Hastalığının Değerlendirilmesinde Spesifik Testler ve Enflamatuvar Biyobelirteçler. Mikrobiyol Bul 2021;55(2):113-24.
16. Farah RA, Hage P, Al Rifai A, Afif C. Immune thrombocytopenic purpura associated with brucellosis. Case report and review of the literature. J Med Liban 2010;58(4):241-3.
17. Sevinc A, Buyukberber N, Camci C, Buyukberber S, Karsligil T. Thrombocytopenia in brucellosis: case report and literature review. J Natl Med Assoc 2005;97(2):290-3.
18. Sarı İ. Hematolojide Sık Görülmeyen İnfeksiyonlar: Bruselloz. 35. Ulusal Hematoloji Kongresi. 7-10 Ekim 2009, Antalya.
19. Marom R, Miron D, Gabriel H, Horowitz Y. Thrombocytopenic purpura as sole manifestation of brucellosis in children. Harefuah 2000;139(7-8):278–326.
20. Di Mario A, Sica S, Zini G, Salutari P, Leone G. Microangiopathic hemolytic anaemia and severe thrombocytopenia in Brucella infection. Annals of Hematology. 1995; 70:59–60.
21. Ibak G, Hamdi S, Onur K, Unal O, Guloglu G, Akcamet FZ. Brucellosis: Evaluation of 201 cases in an endemic area of Mediterranean Basin. Acta Medica Mediterranea 2014; 30: 121.

e-ISSN 2667-7288 Vol 4, Issue 1, (2022) Review Article / Derleme Makale

22. Yüce A, Alp-Çavuş S, Yapar N, Çakır N. Bruselloz: 55 Olgunun Değerlendirilmesi. Klimik Derg 2006; 19: 13-7.
23. Kazak E, Akalın H, Yılmaz E, Heper Y, Mıstık R, Sınırtaş M. Brucellosis: a retrospective evaluation of 164 cases. Singapore Med J 2016; 57(11): 624-9.
24. Yildirmak Y, Palanduz A, Telhan L, Arapoglu M, Kayaalp N. Bone marrow hypoplasia during Brucella infection. J Pediatr Hematol Oncol 2003;25(1):63-4.
25. Yagupsky P, Morata P, Colmenero JD. Laboratory Diagnosis of Human Brucellosis. Clin Microbiol Rev 2019;33(1): e00073-19.
26. Tural Kara T, Kan A. Hematological findings in children with brucellosis. J Pediatr Inf 2020;14(3): e111-e116.
27. Cesur Salih, Albayrak Fahrettin, Ozdemir Davut, Kurt Halil, Sözen Tuncay Hasip, Tekeli Emin. Akut brusellozise bağli trombositopeni olgulari. Mikrobiyol Bul 2003 Jan;37(1):71–73.
28. Pappas G, Kitsanou M, Christou L, Tsianos E. Immune thrombocytopenia attributed to brucellosis and other mechanisms of Brucella-induced thrombocytopenia. Am J Hematol 2004;75(3):139–41.
29. Benjamin B. Acute thrombocytopenic purpura in childhood brucellosis. Ann Trop Paediatr 1995;15(3):189–92.
30. Iturbe Hernández T, Olave Rubio MT, Arruga A, Sola Sopeña JC, Gutiérrez Martín M. Hemorragia cerebral fatal en un cuadro de trombocitopenia severa asociada a infección por Brucella. Rev Clin Esp 2000 ;200(12):699.