Original Article / Özgün Araştırma

Clinical and Laboratory Findings of Paediatric Patients with Brucellosis

Çocukluk Çağı Bruselloz Hastalarının Klinik ve Laboratuvar Bulguları

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Abstract

Objective: Brucellosis is the most common bacterial zoonotic disease transmitted via unpasteurised milk and dairy products from infected animals. This study aimed to evaluate paediatric patients treated for brucellosis and followed for 2 years.

Materials and Methods: The records of 73 patients with childhood brucellosis who had undergone treatment and follow-up for 2 years were retrospectively evaluated.

Results: The patient age ranged from 1 to 14 years, with 39 boys (53%) and 34 girls (47%). Fever (94%) was the first common symptom. Other symptoms, in the order of frequency, were myalgia (80%), arthralgia (75%), fatigue (38%) and anorexia (33%). Complications included sacroiliitis (12%), hemophagocytic lymphohistiocytosis (4%), epididymo-orchitis (1.3%), focal abscess (1.3%) and meningitis (1.3%). Splenomegaly, hepatomegaly and lymphadenopathy (24%, 33% and 5%, respectively) were also reported. Moreover, 18% of the patients had hepatosplenomegaly at initial admission. Dermatological involvement revealed maculopapular rash in 4.1% and petechial rash in 9.6% of patients. Body weight loss was observed in 14% of the cases. In addition, 76.3% and 23.7% of the patients had acute and sub-acute forms, respectively.

Conclusion: Brucellosis can display several different clinical presentations. This diversity can lead to diagnostic delay. In settlements where the disease is common, patients with fever and joint pain should be treated early and the disease should be ruled out.

Keywords
Brucellosis, childhood, clinical characteristics, epidemiology

Anahtar Kelimeler
Bruselloz, çocukluk çağı, klinik özellikler, epidemiyoloji

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Öz

Amaç: Bruselloz, enfekte hayvanlardan pastörize edilmemiş süt ve süt ürünleriyle bulaşan en yaygın bakteriyel zoonotik hastalıktır. Bu çalışmada bruselloz tedavisi gören ve 2 yıl boyunca takip edilen pediatrik hastaların değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Çocukluk çağı brusellozlu olan 73 hastanın 2 yıllık süredeki tedavi ve takip kayıtları geriye dönük olarak incelendi.

Bulgular: Yaşları 4-14 arasında değişen 73 hastanın 39'u erkek (%53) ve 34'ü kız (%47) idi. En sık görülen semptomlar ateş (%94), artralji (%75), miyalji (%80), yorgunluk (%38) ve iştahsızlık (%33) idi. Komplikasyon olarak sakroileit (%12) ve hemofagositik lenfohistiyositoz (%4) saptandı ve diğer yaygın komplikasyonlar epididimoorşit (%1,3), fokal apse (%1,3) ve menenjit (%1,3) idi. Splenomegali, hepatomegali ve lenfadenopati sıklıkları sırasıyla %24, %33 ve %5 idi. Çalışmaya alınan olguların %18'inde tanı anında hepatosplenomegali varlığı saptanmıştır. Dermatolojik tutulum üçünde makülopapüler döküntü, yedisinde peteşiyal döküntü

şeklindeydi. Olguların %14'ünde kilo kaybı tespit edildi. Akut form %76,3 hastada mevcutken subakut form %23,7 hastada mevcuttu. **Sonuç:** Bruselloz çok farklı klinik tablolarla ortaya çıkabilir. Hastalığın spektrumundaki bu çeşitlilik tanıda gecikmelere yol açabilir. Hastalığın sık görüldüğü yerleşim yerlerinde ateş ve eklem ağrısı olan hastalarda öncelikli olarak düşünülmeli ve hastalık ekarte edilmelidir.

Introduction

Brucellosis continues to be an important public health problem in many developing countries. Brucellosis can be seen at any age. Childhood cases constitute 20% to 25% of brucellosis cases (1). The disease agent is immobile, small, gram negative coccobacillus (2). *Brucella abortus, Brucella melitensis, Brucella suis* and *Brucella canis* are species pathogenic to humans (3). More than 500,000 new cases are reported worldwide each year. In some endemic countries the prevalence is greater than 10/100,000 (4). Animals and their products are sources of brucellosis contamination. Transmission is usually through direct contact of the infected animal's secretions with disintegrated skin or mucosa, use of unpasteurized milk and dairy products, inhalation of infected aerosols and contact with the conjunctiva. Brucellosis may present with a wide variety of signs and symptoms, multisystem involvement such as cardiovascular, skeleton, neural, skin and intestinal system. Brucellosis is a benign disease that often responds well to treatment, however; involvement in the bone, cardiovascular and nervous system can cause significant illness and death (5). Transmission through consumption of unpasteurized milk and dairy products is the most common route of transmission. The frequent clinical symptoms and signs of the disease are high fever, myalgia, arthralgia, sweating, weakness, and splenomegaly. Weight loss, arthritis, vomiting, abdominal pain, headache, cough may be seen (3). A definitive diagnosis is made by isolating *Brucella* spp. from blood, bone marrow or other tissue cultures, body fluids such as cerebrospinal fluid (4-6). However, the commonly used diagnostic method is serum agglutination test, which reveals IgG and IgM type *Brucella* spp. antibodies. A single serum brucella titer of 1:160 or above is considered to support the diagnosis (7,8). Here, we retrospectively evaluated 73 brucellosis cases who applied to the General Pediatric Outpatient Clinic and Pediatric Emergency Outpatient Clinic between August 2018 and December 2019.

Materials and Methods

In this study, 73 brucellosis cases who applied to Van Yüzüncü Yıl University, Faculty of Medicine Hospital Pediatrics General Pediatric Outpatient Clinic and Pediatric Emergency Outpatient Clinic between December 2017 and December 2019 were evaluated retrospectively. Diagnosis of the disease was made by positive brucella agglutination titers (titers 1:160 or higher) or isolation of the causative agent in the presence of clinical findings consistent with brucellosis. The cases were grouped according to the duration of symptoms as acute (0-2 months), subacute (2-12 months) and chronic (>12 months) (6). The available data of the cases in the study were obtained from electronic medical records and files. Patients with recurrent disease were interviewed by phone and confirmed. Recurrence of disease was defined as recurrence of symptoms within 6 months of treatment or a positive blood culture (9). Patients age, gender, city of residence, season at the time of admission and whether there was a family history of similar disease were recorded. The first admission clinical symptoms and examination findings of the patients and the treatments given were evaluated. Necessary imaging methods (direct radiography, magnetic resonance, ultrasonography imaging) were used in cases with suspected complicated brucellosis. Since bone marrow aspiration was performed in cases with suspicion of pancytopenia and hemophagocytic lymphohistiocytosis as hematological involvement, the available data were recorded. The presence of neurobrucellosis was investigated by lumbar puncture performed in patients diagnosed with brucellosis, with headache, seizures, impaired consciousness, and vomiting. The presence of neurobrucellosis was detected by the presence of Wright agglutination titer in the cerebrospinal fluid, the presence of lymphocytic

pleocytosis, protein increase, low glucose level and positive detection in the standard tube agglutination test. Informed consent forms were collected from the parents of the patients.

Ethics

The study was initiated after being approved by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (decision no: 2020/06-04, date: 18.09.2020). All analyzes were carried out in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

The analysis of the data was done with the SPSS 13.0 package program. Descriptive statistics are results for continuous and sortable variables as mean ± standard deviation, median (maximum-minimum); categorical variables were expressed as "%".

Results

The ages of the patients ranged from 1 to 14 years, with 39 boys (53%) and 34 girls (47%). The mean age of the subjects included in the study was 10.2 years (±3.4). The characteristics and clinical findings of the patients are shown in Table 1. Sixty six cases (90.6) had a history of consuming unpasteurized milk and dairy products. In 28 (38%) cases, there was a history of both contact with animals and eating fresh cheese. Consumption of unpasteurized milk or dairy products was significantly common in 21 cases with a family history of brucellosis. The disease was more common in those residing in rural areas. The most frequent symptoms were fever (94%), arthralgia (75%), myalgia (80%), fatigue (38%), and anorexia (33%). When evaluated in terms of complications, it was determined as sacroileitis (12%) and Hemophagocytic lymphohistiocytosis (4%), epididymoorchitis (1.3%), focal abscess (1.3%) and meningitis (1.3%), respectively (Table 1). Neurobrucellosis was detected in only 1 of the cases, but the agent could not be isolated in the cerebrospinal fluid culture. This patient was diagnosed with a positivity of agglutination titer in the cerebrospinal fluid. The frequencies of splenomegaly, hepatomegaly and lymphadenopathy were 24, 33, and 5%, respectively. The presence of hepatosplenomegaly at the time of diagnosis was found in 18% of the cases included in the study. Dermatological involvement was maculopapular rash in three of them, and petechial rash in seven. Body weight loss was detected in 14% of the cases. Of the patients in the study, 76.3% had acute form and 23.7% had subacute form. Table 2 shows the results of the Laboratory examinations. The diagnosis of brucellosis was made using the standard tube agglutination test in all cases included in the study. All of these cases

Table 1. Clinical characteristics and complications of patients with brucellosis

Variable	n (%)
Age at diagnosis, mean	10.2±3.4
Gender	
Male	43 (58)
Female	30 (32)
Consumption of raw or unpasteurized milk and milk products	66 (90.6)
Family history in terms of brucellosis	21 (28)
Symptoms	
Myalgia	59 (80)
Arthralgia	54 (75)
Anorexia	24 (33)
Fever	69 (94)
Fatigue	27 (38)
Abdominal pain	5 (6)
Headache	10 (14)
Signs	
Splenomegaly at diagnosis	17 (24)
Hepatomegaly at diagnosis	24 (33)
Arthritis	21 (29)
Weight loss	10 (14)
Petechiae	7 (10)
Hepatosplenomegaly at diagnosis	13 (18)
Lymphadenopathy	4 (5)
Clinical diagnosis	
Acute	76.3
Subacute	23.7
Chronic	0
Complications	
Meningitis	1 (1.3)
Epididymo-orchitis	1 (1.3)
Focal abscess	1 (1.3)
Sacroileite	9 (12)
Haemophagocytic lympho histiocytosis	3 (4)

had titres of 1:160 or more. *Brucella melitensis* was isolated in only 17 of the cases whose blood culture was studied. While bone marrow aspiration was performed in 7 patients with pancytopenia, bone marrow culture was studied. Culture positivity was detected in 4 out of 7 cases whose bone marrow culture was studied. It was observed that C-reactive protein (CRP) value increased in 41 cases (56%). Although the sedimentation rate was 20-40 mm/h in 41 cases, values above 40 mm/h were found in 5 cases. Anemia was detected in 31 (42%) patients and thrombocytopenia in 11 patients (15%). Leukopenia was found in 17% of the patients, and leukocytosis in 19%. High liver enzymes were found in 49% of 36 cases (Table 2). Oral rifampicin (15-20 mg/kg/day), oral doxycycline (4 mg/kg/day) in patients over 8 years of age; oral rifampicin (15-20 mg/kg/day) and oral trimethoprim-sulfamethoxazole (10-12 mg/kg/day) were given to cases under 8 years of age. The case we detected neurobrucellosis combined treatment with gentamicin (5 mg/kg/day), rifampicin (20 mg/kg/day) and ceftriaxone (100 mg/kg/day) was given. Antibiotic treatment was given for 6 weeks, 4 months in sacroileitis cases and 6 months in meningoencephalitis cases. Except for minor gastrointestinal system complaints (nausea, abdominal pain) related to the treatments, no serious side-effects were observed. Recurrence of the disease developed in 4 patients who were given doxycycline and rifampin as treatment. No recurrence was detected after 6 weeks of the same treatment regimen given to these recurrent cases.

Table 2. Laboratory findings of patients with brucellosis

Variable	n (%)
Anemia (Hgb <12 g/dL)	31 (42)
Leukopenia (4x10^3/mL)	13 (17)
Thrombocytopenia (<150x10^3/mL)	11 (15)
Pancytopenia	7 (9)
Leukocytosis (>10.5x10^3/mL)	14 (19)
Thrombocytosis (>450x10^3/mL)	6 (8)
Elevated aminotransferases (>40 U/L)	36 (49)
ESR (20-40 mm/h)	41 (56)
ESR (>40 mm/h)	5 (6)
Elevated CRP (>5 mg/dL)	41 (56)
Culture positive	21 (28)

Hgb: Hemoglobin, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

Discussion

Brucellosis is still an important public health problem in our country. It is noticed that this problem is more common in Van than in other cities. The most important reason for its prevalence in regions such as the east and southeast is the prevalence of raw milk and dairy products, nutrition and livestock (10). In our current study, 90.6% of the cases had a history of feeding with raw milk and dairy products, while a history of animal husbandry was found in 53% of the cases. There was a family history in 28% of our cases. In one study, 80.4% of the cases had consumption of raw milk and dairy products, and 33% had a family history (11). In other studies reported in the literature, consumption of unpasteurized milk and dairy products was reported between 62.4% and 94.6% (9,12,13). In the study conducted by Tanir et al. (14), 15.6% of patients with brucellosis had a family history. It was determined from the anamnesis that some patients had past and current cases of brucellosis among their family members. There were no clinical signs of symptomatic infection in all cases. In this study, it was reported that brucellosis is common among other family members and needs attention (15). Therefore, screening family members is essential when a patient with brucellosis is diagnosed. Although standard tube agglutination test is mostly positive in acute cases, seropositivity may occur after a few weeks in some cases. Seropositivity sap 1/160 was found in all of our patients. *Brucella* spp. was isolated from the blood culture of 17 cases and from both the blood and bone marrow cultures of 4 cases. The agent could be isolated in only 4 of 7 patients whose bone marrow culture was studied. The definitive diagnosis is based on isolation of the agent from different samples such as bone marrow and blood (16). Different rates have been reported for blood culture positivity. Culture positivity rates in the range of brucellosis in Turkey is between 12-70%. These rates may be affected by reasons such as not storing the culture samples for a long time and the patient's previous use of antibiotics (17). Blood culture positivity was found to be 28% in our series. This rate can be considered low. We think that this may be due to the previous antibiotic use of our cases. In a study, 83.5% of the cases were evaluated as acute, 8.9% as subacute and 7.6% as chronic brucellosis (18). In another study, the acute

form, chronic form and subacute form were found to be 75.3%, 23.7%, and 1%, respectively (11). In our study, 76.3% of the patients had acute form and 23.7% had subacute form.

Brucellosis can present with a different of symptoms and signs that are not specific and can be confused with many diseases (8). In the literature, fever and joint complaints are the most common clinical findings and were reported as 41-85% and 73-91%, respectively (6,19-21). In one study, osteoarticular involvement was the most common (59.6%), lymphadenopathy (42.1%), hepatomegaly (33.3%), splenomegaly (33.3%) and peripheral nerve involvement (3.5%) (22). 75% of our patients had arthralgia, 94% had fever and 29% had arthritis. The liver is the largest organ of the reticuloendothelial system that is why it can almost always be involved and liver function tests may increase. Tanir et al. (14) reported that, when the examination findings were evaluated, hepatomegaly was observed in 15.6% of the patients, splenomegaly in 11.1% and hepatosplenomegaly in 6.7%, while lymphadenopathy was not detected in any patient. In our study, 33% of the cases had hepatomegaly, 24% had splenomegaly and 18% had hepatosplenomegaly, while lymphadenopathy was detected in 5%.

Laboratory findings in brucellosis are variable, and the elevation of erythrocyte sedimentation rate (ESR) and CRP was found in 40.8-81.1% and 50-87.2%, respectively (17,23-25) of the patients. The data determined in this study are also compatible with the literature, and the elevation of ESR and CRP was found to be 62% and 56%, respectively. Serum transaminase elevation in brucellosis has been reported at a rate of 25-60% (26), and it was found to be 49% similarly in our study. There are few studies in the literature on hematological complications associated with brucellosis in children compared to adults (27). Mild anemia and low white blood cell count are more common than pancytopenia and thrombocytopenia in hematological complications due to brucellosis (28). In a study, the rate of anemia in childhood brucellosis was reported between 20.4% and 53% (11,29). Thrombocytopenia is reported in 1% to 26% in a children series with brucellosis (27-30). Leukopenia has been reported (13.9%) in a children with brucellosis (27). In our study, similar to the previously reported studies, anemia was detected in 42% of our patients, thrombocytopenia in 15% and leukopenia in 17%. When we examined the literature, we found that the hematological involvement in brucellosis patients ranged from 3% to 21% with pancytopenia (27,28). We detected pancytopenia in 7 of our cases. Three patients with pancytopenia had hemophagocytic lymphohistiocytosis syndrome. In these patients, in addition to fever, hepatosplenomegaly, hepatitis, hypofibrinogenemia, and hyponatemia, ferritin values were above 500 mg/dL. There was evidence of hemophagocytosis in the evaluation of bone marrow aspiration of these patients with hemophagocytic lymphohisitiocytosis. With brucellosis treatment, the picture of these three patients resulted in complete recovery. Hematological, osteoarthricular, respiratory and cutaneous complications are more prominent in children. Neurobrucellosis, which is a rare complication, can be suspected due to its clinical features. Neurobrucellosis presents with avariety of clinical manifestations, and the symptoms are sometimes atypical. In our patient with neurobrucellosis, a continuous sleepiness was present in addition to weakness and fever. During the day, he slept an average of 17 hours before the treatment started. After the treatment of neurobrucellosis was started, his clinical findings improved rapidly.

Conclusion

As a result, brucellosis should definitely be considered in the differential diagnosis of patients who present with nonspecific complaints such as fever, arthralgia, weakness, and hepatosplenomegaly in endemic areas and who have cytopenia and high acute phase reactants in their examinations. Contamination should be prevented with measures such as frequent veterinary studies, identifying and treating sick animals, and increasing animal controls.

Ethics

Ethics Committee Approval: The study was initiated after being approved by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (decision no: 2020/06-04, date: 18.09.2020). All analyzes were carried out in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Informed consent forms were collected from the parents of the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.K., O.T., B.S., Design: S.K., M.B., Supervision: E.Ç.B., S.K., Fundings: E.Ç.B., S.K., Materials: S.K., K.K., Data Collection or Processing: M.B., O.T., Analysis or Interpretation: S.K., B.S., K.K., Literature Search: S.K., Critical Review: O.T., K.K., Writing: M.B., S.K.

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References

1. Akbayram S, Dogan M, Peker E, Akgun C, Oner AF, Caksen H. Thrombotic thrombocytopenic purpura in a case of brucellosis. Clin Appl Thromb Hemost 2011; 17: 245-7.
2. Ekinci O, Ebinc S, Dogan A, Demir C. Frequency of Brucellosis and Hepatitis B Virus Seropositivity in Patients with Chronic Lymphocytic Leukemia. Dicle Tıp Dergisi / Dicle Med J 2020; 47: 609-14.
3. Schutze GE, Jacobs RE. Brucella. In: Kliegman RM, Behrman RE, Jenson HB, et al. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: Saunders 2007; Pp: 1214-6.1214-6.
4. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Infect Dis 2006; 6: 91-9.
5. Aktaş F, Şenol E, Yetkin A, Gürdoğan K, Ulutan F. Brusellozda klinik ve laboratuvar bulgularının hastalık stresi ile ilişkisi. Türk Mikrobiyol Cem Derg 1994; 24: 164-9.
6. Young EJ. Brucella Species. Eds.: Mandell GL, Douglas RG, Bennett JE: Principles and Practice of Infectious Diseases. 6th edition. Philadelphia. Churchill Livingstone, 2005, p. 2670-3.
7. Case definitions for infectious conditions under public health surveillance. Centers for Disease Control and Prevention. MMWR Recomm Rep 1997; 46: 1-55.
8. Alişkan H. Kültür ve serolojik yöntemlerin insan brusellozu tanisindaki değeri [The value of culture and serological methods in the diagnosis of human brucellosis]. Mikrobiyol Bul 2008; 42: 185-95.
9. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, et al. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. Int J Infect Dis 2010; 14: 469-78.
10. Bulut İK, Bulut MO, Büyükkayhan D, İçağasıoğlu D, Kara S, Tanzer F, et al. Çocukluk Çağında Bruselloz: Takip Edilen Olguların İncelenmesi. C. Ü. Tıp Fakültesi Dergisi 2005; 27: 133-6.
11. Yoldas T, Tezer H, Ozkaya-Parlakay A, Sayli TR. Clinical and laboratory findings of 97 pediatric brucellosis patients in central Turkey. J Microbiol Immunol Infect 2015; 48: 446-9.
12. Kursun E, Turunc T, Demiroglu Y, Arslan H. Evaluation of four hundred and forty seven brucellosis cases. Intern Med 2013; 52: 745-50.
13. Tasova Y, Saltoglu N, Yılmaz G, Inal S, Aksu HS. Bruselloz: 238 eriskin olgunun klinik, laboratuvar ve tedavi ozelliklerinin degerlendirilmesi. Turkish J Infect 1998; 12: 307-12.
14. Tanir G, Tufekci SB, Tuygun N. Presentation, complications, and treatment outcome of brucellosis in Turkish children. Pediatr Int 2009; 51: 114-9.
15. Tsolia M, Drakonaki S, Messaritaki A, Farmakakis T, Kostaki M, Tsapra H, et al. Clinical features, complications and treatment outcome of childhood brucellosis in central Greece. J Infect 2002; 44: 257-62.
16. Gotuzzo E, Carrillo C, Guerra J, Llosa L. An evaluation of diagnostic methods for brucellosis--the value of bone marrow culture. J Infect Dis 1986; 153: 122-5.
17. Gür A, Geyik MF, Dikici B, Nas K, Cevik R, Sarac J, et al. Complications of brucellosis in different age groups: a study of 283 cases in southeastern Anatolia of Turkey. Yonsei Med J 2003; 44: 33-44.
18. Demirdağ K, Özden M, Kalkan A, Çelik İ, Kılıç SS. Bruselloz: 146 Olgunun Retrospektif Değerlendirilmesi. Flora 2002; 7: 120-5.
19. Sasan MS, Nateghi M, Bonyadi B, Aelami MH. Clinical features and long term prognosis of childhood brucellosis in northeast iran. Iran J Pediatr 2012; 22: 319-25.
20. Shen MW. Diagnostic and therapeutic challenges of childhood brucellosis in a nonendemic country. Pediatrics 2008; 121: 1178-83.
21. Feiz J, Sabbaghian H, Miralai M. Brucellosis due to B. melitensis in children. Clinical and epidemiologic observations on 95 patients studied in central Iran. Clin Pediatr (Phila) 1978; 17: 904-7.
22. Helvaci M, Atilla D, Barisik V. Çocukluk çağı brusellozlu 57 olgunun geriye dönük değerlendirilmesi. Tepecik Eğit Hast Derg 2011; 21: 135-8.
23. Gürsoy B, Tekin-Koruk S, Sırmatel F, Karaağaç L. Bruselloz: 140 olgunun değerlendirilmesi. Klimik Derg. 2008; 21: 101-4.
24. Aygen B, Sümerkan B, Kardaş Y, Doğanay M, İnan M. Bruselloz: 183 olgunun değerlendirilmesi. Klimik Derg 1995; 8: 13-6.
25. Koşar A, Aygündüz M, Yaylı G. İkiyüzseksen bruselloz olgusunda farklı iki tedavinin karşılaştırılması. İnfeks Derg 2001; 15: 433-7.
26. Yüce A, Alp Çavuş S, Yapar N, Çakır N. Bruselloz: 55 olgunun değerlendirilmesi. Klimik Derg 2006; 19: 13-7.
27. Karaman K, Akbayram S, Bayhan G, Dogan M, Parlak M, Akbayram HT et al. Hematologic Findings in Children With Brucellosis: Experiences of 622 Patients in Eastern Turkey. J Pediatr Hematol Oncol 2016; 38: 463-6.
28. Citak EC, Citak FE, Tanyeri B, Arman D. Hematologic manifestations of brucellosis in children: 5 years experience of an Anatolian center. J Pediatr Hematol Oncol 2010; 32: 137-40.
29. Fanni F, Shahbaznejad L, Pourakbari B, Mahmoudi S, Mamishi S. Clinical manifestations, laboratory findings, and therapeutic regimen in hospitalized children with brucellosis in an Iranian Referral Children Medical Centre. J Health Popul Nutr 2013; 31: 218-22.
30. al-Eissa YA, Assuhaimi SA, al-Fawaz IM, Higgy KE, al-Nasser MN, al-Mobaireek KF. Pancytopenia in children with brucellosis: clinical manifestations and bone marrow findings. Acta Haematol 1993; 89: 132-6.