

Hepatosplenik *Bartonella henselae* Infection in an Immunocompetent Patient

Bağıışıklık Sistemi Yeterli Bir Hastada Hepatosplenik *Bartonella henselae* Enfeksiyonu

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ABSTRACT

Cat scratch disease often presents with limited regional lymphadenomegaly. In addition, atypical manifestations such as retinitis, tendinitis, osteomyelitis, oculaglandular syndrome, encephalopathy and granulomatous hepatitis have been reported.

The patient was hospitalized with a diagnosis of fever of unknown origin. Apart from fever, no clinical complaints and no pathological examination findings were found. Since the patient identified erythema migrans-like lesions before the application, doxycycline treatment was started with the suspicion of Lyme disease. However, *Borrelia burgdorferi* immunoglobulin (IgM) and IgG resulted as negative. A fever response was received from the patient at the 48th hour to doxycycline treatment, and *Bartonella henselae* IgG (IFA) evaluation was requested because the patient said they had a cat. *Bartonella henselae* IgG was positive in 1/512 titers and the diagnosis of bartonellosis was made. A liver biopsy was performed with positron emission tomography-computed tomography because of malignancy and microabscess suspicion. Histopathological findings have been reported to be compatible with granulomatous inflammation in the liver. Doxycycline treatment was discontinued and rifampicin was completed on the first day as 14 mg 600 mg/day + azithromycin 500 mg and 250 mg. The patient was discharged with healing. No relapse occurred after his first year of follow-up. *Bartonella henselae*, which is often the cause of cat scratch disease, can rarely cause hepatosplenic involvement secondary to bacteremia. As in our case, it should be kept in mind in the etiology of fever of unknown origin.

Keywords: *Bartonella henselae*, cat scratch disease, hepatosplenic involvement

ÖZ

Kedi tırmığı hastalığı, genellikle sınırlı bölgesel lenfadenomegali ile kendini gösterir. Ancak retinit, tendinit, osteomyelit, oküloglandüler sendrom, ensefalopati ve granülomatöz hepatit gibi atipik klinik tablolar da bildirilmiştir.

Hasta nedeni bilinmeyen ateş tanısı ile yatırıldı. Hasta başvurudan önce eritema migrans benzeri lezyonu tanımladıktan sonra borreliyoş şüphesi ile doksisisiklin tedavisi başlatılmıştır. Ancak *Borrelia burgdorferi* immünoglobulin (IgM) ve IgG negatif sonuçlandı. Doksisisiklin tedavisine 48. saatte ateş yanıtı alınan hastadan, evde kedisi olması nedeniyle *Bartonella henselae* IgG (IFA) istendi. *Bartonella henselae* IgG, 1/512 titrede pozitif olarak sonuçlandı ve hastaya bartonelloz tanısı konuldu. Pozitron emisyon tomografi-bilgisayarlı tomografide malignite ve mikroabselerden şüphelenildiği bildirildiği için karaciğer biyopsisi yapıldı. Histopatolojik bulguların karaciğerdeki granülomatöz enflamasyonla uyumlu olduğu bildirilmiştir. Doksisisiklin tedavisi kesildi ve rifampisin ilk gün 14 mg 600 mg/gün + azitromisin 500 mg ve 250 mg olarak tamamlandı. Hasta iyileşerek taburcu edildi. İlk takip yılı bitiminde nüks görülmedi. Sıklıkla kedi tırmığı hastalığı etkeni olan *Bartonella henselae*, çok nadir olarak bakteriyemiye sekonder hepatosplenik tutulumu neden olabilir. Olgumuzda olduğu gibi nedeni bilinmeyen ateş etiolojisinde bartonelloz akılda bulundurulmalıdır.

Anahtar Kelimeler: *Bartonella henselae*, kedi tırmığı hastalığı, hepatosplenik yayılım



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Introduction

Bartonella is an oxidase and catalase negative, facultative, intracellular gram negative bacteria (1). *Bartonella henselae*, *Bartonella quintana* and *Bartonella bacilliformis* can infect healthy people (2). Cat scratch disease often presents itself with limited regional lymphadenomegaly. Papules or pustules occur 3-10 days after animal contact. Growth and pain in the ipsilateral lymph nodes occurs 1-2 weeks later (3). Fever, weakness, myalgia, arthralgia, headache, and sore throat can be observed. Atypical manifestations such as hepatosplenic involvement, neuroretinitis, endocarditis, tendinitis, osteomyelitis, oculoglandular syndrome and fever of unknown origin have been reported. Hepatosplenic bartonellosis is a clinical condition that makes lesions characterized by granulomatous inflammation in the liver and spleen, after the bacteria pass into the systemic circulation. *Bartonella* infections should be considered in the case of fever of unknown origin. The aim of this case report is to present the case who was being observed due to fever of unknown origin, that was diagnosed with isolated hepatosplenic bartonellosis without the presence of lymphadenopathy.

Case Report

A 48-year-old female patient was admitted to our outpatient clinic due to fever that had been ongoing for a month. She had 39.5 °C degrees of fever every evening for a month; the patient had no additional complaints. There was no chronic disease except hypothyroidism and using levothyroxine. There was no history of traveling abroad, and no smoking and alcohol use. The patient had a history of visiting the countryside but did not describe a tick contact. The only animal that the patient contacted was her cat at home. In her family history, her father had only diabetes mellitus. It was learned that he had received meropenem + vancomycin treatment in a private hospital 15 days before her application to our hospital, and then she used levofloxacin for five days on suspicion of atypical pneumonia. There was no regression in the patient's fever with the current treatments. No pathological examination findings were found. The patient was hospitalized with a diagnosis of fever of unknown origin. In routine examinations, C-reactive protein resulted in 8.4 mg/dL (range <0.5), sedimentation was 85 mm/hour, ferritin was 456 ng/mL. Other biochemical and complete blood count results were within normal limits (white blood cell: 8,900, leukocyte: 5,400, lymphocyte: 2,600, hemoglobin: 11 g/dk, platelet (Plt): 414,000/u). There were no atypical cells in the peripheral smear; malaria parasite was not found in thin and thick smear preparations. Infiltration-cavitation-consolidation or mass image was not detected on lung X-ray. Cytomegalovirus (CMV) immunoglobulin (IgM): 1.68 (0-0.84) and CMV

immunoglobulin (IgG): >250 (0-5.9) were obtained in serological examinations. Hepatitis B, hepatitis C, toxoplasmosis, brucella, Epstein-Barr virus (EBV) and syphilis tests of the patient were negative. Because the CMV IgG avidity test was high (83.3), acute infection possibility was disregarded. antinuclear antibody, rheumatoid factor and Quantiferon tests were negative; C3-C4 was within normal limits. Vegetation was not observed in transthoracic echocardiography for endocarditis exclusion. "Liver and spleen sizes were normal and diffuse hypoechoic smooth limited millimetric (the largest is 9 mm in diameter) multiple lesions" was observed in the abdominal ultrasonography. Thereupon, upper abdominal magnetic resonance (MR) with contrast was planned. *Borrelia burgdorferi* IgM and IgG were sent for the patient who described the lesion in the forearm in Figure 1 before applying to hospital. Doxycycline 2x100 mg was started after getting this information. *Borrelia burgdorferi* IgM and IgG resulted as negative. After the 48th hour of doxycycline treatment, the patient's fever did not recur, and his CRP and sedimentation values decreased after the treatment. Because the patient's fever resolved after doxycycline treatment, we started to research which bacteria that doxycycline killed. Multiple millimetric lesions were detected in the liver by abdominal ultrasonography. Abdominal MR showed hypointense in T1 sequence, hyperintense in T1 and T2, and diffusion



Figure 1. Erythema migrans-like lesion on the left forearm

sequence in necular lesions in the T1 sequence, heterogeneity in the spleen parenchyma, and intra-parenchymal lesions in the spleen. The radiologist evaluated the current findings as metastasis if the patient had a history of primary malignancy. In addition, it was stated that it should be evaluated for specific granulomatous infections and microabscess. The infections that caused granulomatosis infections in the liver namely, tuberculosis, brucellosis, secondary syphilis, toxoplasmosis, CMV, EBV, hepatitis A, B, C were disregarded after necessary tests. *Bartonella henselae* IgG (IFA) was requested from the patient who had a clinical and laboratory response to doxycycline therapy, which was started with the suspicion of Lyme. The patient was found to be positive at *Bartonella henselae* IgG 1/512 titer*, and thus was diagnosed with bartonellosis. Doxycycline treatment was discontinued and rifampicin was completed to 14 days as 600 mg/day + azithromycin 500 mg

on the first day and 250 mg on maintenance. Positron emission tomography-computed tomography (PET-CT) was taken to the patient because malignancy and infectious processes could not be distinguished in abdominal MR. A liver biopsy was performed in PET-CT as the lesions were reported as suspicious for malignancy and microabscess. Histopathological findings were reported as compatible with granulomatous inflammation in the liver (Figure 2). The patient was discharged with healing. *Indirect immunofluorescence assays (IFA) were performed using the *Bartonella henselae* (IgG) kit (Euroimmun, Lübeck, Germany) in Istanbul Sistem Tip Laboratory.

Conclusion

Bartonella henselae can be presented with atypical clinical pictures besides cat scratch disease and bacillary angiomatosis.

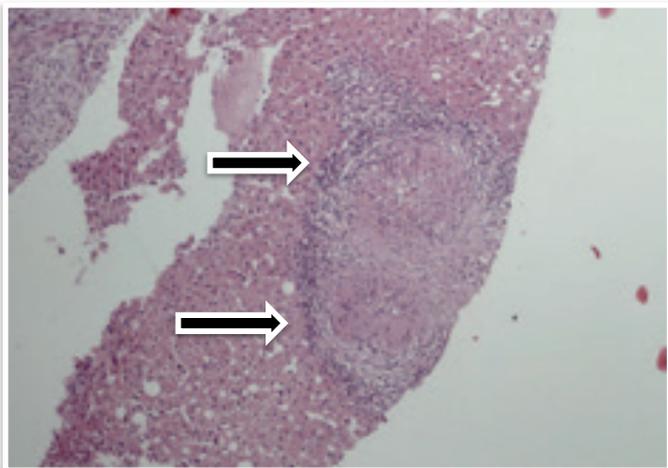


Figure 2a

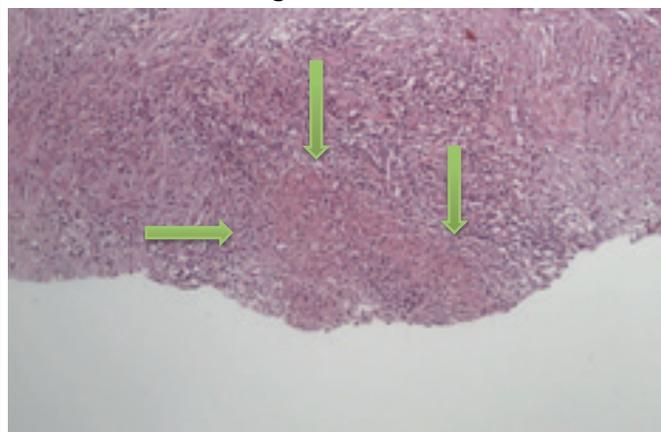


Figure 2b

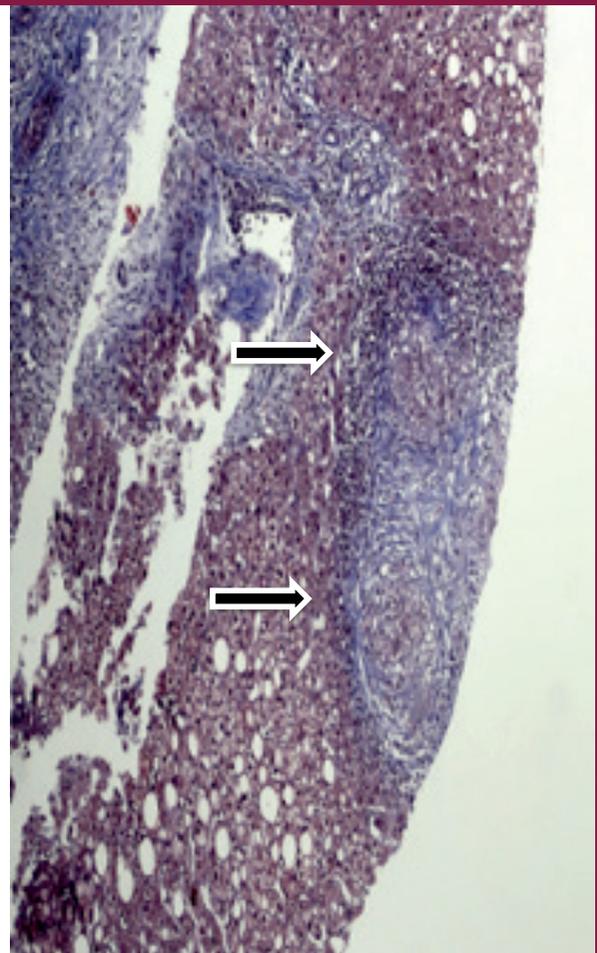


Figure 2c

Figure 2. (a) Two non-necrotizing granulomas in the enlarged portal area, (b) Irregular granuloma structure consisting of epithelioid histiocytes in the portal area with minimal necrosis in the center. H&E X100, (c) Two portal non-necrotizing granulomas surrounded by fibrosis. Masson Trichrome X100

Delays may occur in the diagnosis of atypical course of bartonellosis. The most important diagnostic step in rare infections is the suspicion of the disease. For that, it is very crucial that animal contact is questioned during anamnesis. As in our case, hepatosplenic involvement without lymphadenopathy can progress as an atypical course of bartonellosis (4). In our case, *Bartonella henselae* IgG was positive at 1/512 titers. Culture tests are not used in routine practice because it is difficult to perform. Molecular methods (PCR) and serological tests (IFA) are performed routinely. While titers of *Bartonella henselae* IgG 1/64 and above indicate possible infection, titers above 1/256 strongly suggest acute and recent infection (5,6). Low titer *Bartonella henselae* IgG positivity was found in healthy asymptomatic individuals with cat contact, and serology alone causes deficiencies in diagnosis (7). In fact, false PCR and serology negativities are also observed in blood tests due to temporary and low bacteremia (8). It may be beneficial to go to tissue diagnosis in patients with clinical suspicion whose PCR and serology tests are negative.

There is no consensus in the treatment of cat scratch disease. In the treatment of classical cat scratch diseases, azithromycin is used (6). In the case of bacteremia and endocarditis, gentamicin + doxycycline is used, and in the presence of neuroretinitis and neurological involvement, erythromycin + doxycycline (with or without rifampin combination) is generally used (6). Some clinicians apply long-term (four months) combination therapies to minimize the possibility of sequestration in immunological niches such as thymus, bone marrow, and lymph node (9). In fact, the majority of uncomplicated cases regress without antibiotics (10). In complicated cases, trimethoprim-sulfamethoxazole, ciprofloxacin or azithromycin are recommended. Gentamycin can be reserved for serious patients. We prescribed two-week rifampicin + three-day azithromycin treatment to our patient. No relapse occurred after his first year of follow-up. PET-CT was not taken again because the patient had no suspicion of malignancy and granulomatosis infection was detected in liver biopsy.

Ethics

Informed Consent: The patient signed a written consent form for this case report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Ö., D.Ö.E., S.T.K., O.Ç., C.A., Concept: S.Ö., C.A., Design: S.Ö., D.Ö.E., S.T.K., O.Ç., C.A., Data Collection or Processing: S.Ö., D.Ö.E., S.T.K., O.Ç., A.S., C.A., Analysis or Interpretation: S.Ö., D.Ö.E., S.T.K., O.Ç., A.S., C.A., Literature Search: S.Ö., D.Ö.E., S.T.K., O.Ç., C.A., Writing: S.Ö., D.Ö.E., S.T.K., O.Ç., C.A.

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