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Erythema migrans in Lyme disease: Diagnostic challenge without tick bite history

Lyme hastalığında eritema migrans: Kene ısırığı öyküsü olmadan tanısal zorluk

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ABSTRACT

Erythema migrans, the hallmark rash of early Lyme borreliosis, is caused by *Borrelia burgdorferi sensu lato* and transmitted through the bite of infected *Ixodes* species ticks. We report a case of a 25-year-old woman with no history of tick bite who presented with pruritic annular erythematous plaques on the lower extremities following recent travel to a Lyme-endemic region. Serological testing revealed elevated *Borrelia burgdorferi* IgM antibodies, and Western blot analysis corroborated the diagnosis of early disseminated Lyme disease. This case highlights the importance of suspecting Lyme borreliosis in patients presenting with characteristic skin lesions and relevant travel history, even in the absence of a recalled tick bite. Given the risk of progression to serious late-stage complications, including arthritis, neuropathy, and carditis, prompt clinical recognition and early initiation of appropriate antimicrobial therapy are essential to minimize morbidity.

Keywords: Erythema migrans, Lyme borreliosis, early disseminated Lyme disease, atypical presentation, travel-associated infection

ÖZ

Lyme borreliyozu, Borrelia burgdorferi kompleksine bağlı gelişen ve genellikle kene ile bulaşan, insanlarda farklı organları etkileyebilen multisistemik bir enfeksiyondur. Hastalığın en karakteristik bulgusu olan eritema migrans, erken dönemde ortaya çıkmakta olup çoğunlukla klinik olarak tanı konur. Lyme borreliyozunun tanısı ve yönetimi açısından bu bilgiler önem taşırken, sunacağımız olgu bu çerçevede ele alınmıştır.

Bu olguda, kene ısırığı öyküsü bulunmayan 25 yaşında kadın bir hastada gelişen, klasik görünümlerden farklı, atipik eritema migrans lezyonları ayrıntılı şekilde sunulmuştur. Hastanın detaylı epidemiyolojik öyküsü, semptomlarının başlangıcı ve seyriyle birlikte serolojik bulguları, Lyme hastalığını düşündürmüştür. Elde edilen bulgular ışığında, olgunun değerlendirmesi ve klinik yaklaşımımız aşağıda ayrıntılı olarak ele alınmıştır.

Bu olgu, kene ısırığı öyküsü olmadan da Lyme hastalığının gelişebileceğini ve eritema migransın klinik tanı açısından önemini vurgulamaktadır.

Anahtar Sözcükler: *Eritema migrans, lyme borreliozisi, erken dissemine lyme hastalığı, atipik prezentasyon, seyahatle ilişkili enfeksiyon*

INTRODUCTION

Lyme borreliosis is a multisystem infection caused by the *Borrelia burgdorferi sensu lato* complex and is typically transmitted by *Ixodes* ticks (1).

The disease is classically divided into three overlapping stages: early localized (characterized by a typical rash), early disseminated (with multisystem involvement occurring weeks to months later), and late (manifested by articular or neurological involvement).

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The most characteristic finding of early Lyme disease is erythema migrans, which usually appears 3–30 days after tick exposure. Diagnosis can be challenging when the tick bite is not noticed or when the lesion presents atypically. Serological testing may be helpful; however, timing is important as IgM antibodies appear before IgG, and false-positive results may ocur (1). Erythema migrans is a clinical diagnosis, and treatment should be initiated without waiting for serological confirmation. In this case, erythema migrans was observed, supporting the diagnosis of early Lyme disease and prompting immediate initiation of appropriate antibiotic therapy.

CASE REPORT

A 25-year-old woman presented to our clinic with a 7-day history of pruritic lesions on her right lower extremity, which had begun to spread to the contralateral side with similar morphology. She did not report systemic symptoms such as fever, chills, arthralgia, or malaise; however, mild fatigue was noted. Notably, there was no recent history of tick or insect bites. The patient had recently traveled abroad and visited a rural, Lyme-endemic area in Lithuania one month before her emergency department visit. Additionally, she had a history of outdoor exposure near a lake in a rural area of Bandırma, Türkiye, seven days before admission. She had no past medical history of comorbid conditions but had a documented allergy to amoxicillin-clavulanate, with a history of maculopapular rash. Her only regular medication was an oral contraceptive pill, with no recent changes in medication.

At her initial emergency department visit, her vital signs were as follows: temperature, 36.0°C; blood pressure, 133/78 mmHg; pulse rate, 89 beats/min; and SpO2, 98%. She was alert, afebrile, and clinically stable. Skin examination revealed multiple annular, erythematous plaques with central clearing on the medial aspect of the left thigh, consistent with atypical erythema migrans (Figure-1a). Additionally, several targetoid macules with punctate centers were noted on both lower extremities. Mild bilateral erythema and warmth were present on the dorsum of the great toes, along with a few scattered scratch marks (Figure-1b). Due to upcoming school examinations, the patient declined immediate dermatology and infectious disease consultation. She was prescribed doxycycline and scheduled for outpatient follow-up.

Figure-1a. Annular erythematous plaque with central clearing and an external small central punctum on the medial aspect of the thigh, compatible with an atypical erythema migrans lesion.

Figure-1b. The features of erythematous, indurated plaques with a central punctum on the dorsum of the feet would hint at a localized inflammatory response, and possibly at the site of entry of the arthropod.

The following day, during dermatology outpatient clinic evaluation, a 0.5-cm-diameter, firm, and slightly tender nodule was observed on the left upper eyelid, consistent with an inflammatory process. Ipsilateral preauricular and cervical lymphadenopathy were also noted. The remainder of the physical examination, including neurological, cardiovascular, respiratory, and abdominal assessments, was unremarkable. Serological testing revealed elevated *Borrelia burgdorferi* IgM levels (40.50 RU/mL; reference <16 RU/mL), with nonreactive IgG.

Two weeks later, the patient presented to another medical center. Laboratory findings were unremarkable except for a mildly elevated C-reactive protein level (6.1 mg/L). Erythrocyte sedimentation rate (6 mm/h) was within normal limits. Serology for *Borrelia burgdorferi* was positive, with a marked IgM level (38.17 RU/mL; reference <16 RU/mL) and mildly elevated IgG. A Western blot assay was positive for *Borrelia*-specific antibodies, consistent with ongoing *Borrelia* infection and supporting a diagnosis of Lyme disease.

The patient was ultimately diagnosed with early disseminated Lyme disease, presenting with multiple erythema migrans lesions. Treatment was initiated accordingly: doxycycline 100 mg orally twice daily for 10 days. Topical fusidic acid and betamethasone valerate were prescribed for localized inflammation, along with a vitamin B complex supplement. The patient was instructed on the importance of adherence to treatment, sun protection during doxycycline therapy, and early

recognition of any neurological or cardiac symptoms requiring urgent medical attention. Ten days of antimicrobial therapy were planned, with follow-up scheduled for dermatology and infectious diseases within 10 days of initial treatment. During follow-up, no changes were made to the initial treatment. Verbal and written consent were obtained from the patient for publication of this case report.

DISCUSSION

The actual prevalence of Lyme disease is unknown in Turkey, but a few seroepidemiological studies revealed the seropositivity rates between 2-44% (2-4). This case illustrates the difficulties in diagnosing early disseminated Lyme borreliosis, particularly when there is no clear history of tick exposure, which is the most reliable epidemiological risk factor for the disease. Although patients are usually aware of the tick bite early in the clinical course of Lyme disease, erythema migrans can present with an atypical appearance suggestive of early disseminated Lyme disease, particularly in low-endemic areas where it may be missed or misdiagnosed (3). In this case, annular dermatophytic lesions with regional lymphadenopathy were reported recently after returning from an endemic region and traveling in Lithuania. However, she denied a history of tick bites or systemic symptoms. It is worth mentioning that most patients with Lyme disease have no recollection of a tick bite, primarily because *Ixodes* nymphs are small and their bites are painless (1, 4).

Diseases in the differential diagnosis were various cutaneous and infectious conditions. Sensitivity for arthropod bites was initially tested, but no apparent clustering was observed, and the criteria for diagnosing arthropod bites were not sufficient, making this diagnosis less likely (7, 8). In addition, other viral exanthems, such as those caused by Epstein-Barr virus and Parvovirus B19, were considered less likely given the absence of a viral prodrome and the presence of generalized symptoms (7, 9). Chronic spontaneous urticaria and cutaneous vasculitis were ruled out due to the annular morphology of the lesions, absence of weals, and normal systemic laboratory findings (8). The diagnosis of fixed drug eruption was excluded, given the lack of a history of a new drug other than long-term oral contraceptive use (9).

Immunological examination conducted by the dermatology department revealed the presence of *Borrelia*-specific IgM antibodies, but not IgG, indicating a recent infection and consistent with the observed kinetics of antibody formation for seroconversion. IgM testing is known for its higher cross-reactivity, particularly in non-endemic areas; however, in this scenario, the clinical picture and history of heavy epidemiologic exposure rendered the diagnosis appropriate (10). Nevertheless, serological tests should be interpreted cautiously in conjunction with clinical symptoms to prevent overdiagnosis and inappropriate antibiotic use.

If left untreated, Lyme disease can infect various parts of the body and lead to serious complications. Late manifestations such as Lyme arthritis, cranial nerve palsies, meningitis, and rarely, Lyme carditis with atrioventricular conduction abnormalities have also been described (11). The patient in this case did not experience one of these complications, but early detection and treatment were crucial to forestall additional formation.

In the absence of systemic symptoms, the patient was prescribed doxycycline 100 mg twice daily for a 10-day course as the antibiotic of choice for early Lyme disease (6). Doxycycline is more lipophilic, has higher oral bioavailability, higher active tissue concentrations, and crosses the central nervous system, in comparison to tetracycline. Amoxicillin or cefuroxime axetil are reasonable alternatives in some patient groups (children younger than 8 years and pregnant patients). Intravenous ceftriaxone is generally indicated for patients with central nervous system or cardiac disease.

The favorable prognosis in this case could be partly attributed to early and adequate antimicrobial treatment. This highlights the importance of having a high index of suspicion for Lyme disease in patients with dermatologic manifestations who have recently visited an area endemic for the disease, even when they deny recollection of a tick bite (3, 5). Considering the potential for serious late complications, physicians should have a high index of suspicion, especially given the expanding era of international travel and geographic expansion of tick vectors [4]. Erythema migrans remains primarily a clinical diagnosis. Serological testing may yield negative results in the early stages due to delayed antibody production. Therefore, treatment decisions should be based on clinical findings rather than laboratory confirmation.

CONCLUSION

Lyme borreliosis, though uncommon in emergency settings, should be considered in patients with compatible clinical and epidemiological features—even in the absence of a known tick bite. In this case, annular skin lesions, regional lymphadenopathy, recent travel to an endemic area, and positive IgM serology supported the diagnosis of suggestive early disseminated Lyme disease. Early recognition and prompt initiation of appropriate antimicrobial therapy are crucial for preventing long-term complications.

Conflict of Interest: The authors declare no conflicts of interest

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