



A Neuroborreliosis Case Presenting with Asymmetric Painful Radiculoneuritis

Asimetrik Ağrılı Radikülonevritle Prezente Bir Nöroborelyoz Olgusu

Helin Cansu Serindağ, Eda Çoban, Yeşim Kayı, Aysun Soysal

Bakirkoy Prof. Dr. Mazhar Osman Mental and Neurological Diseases Hospital, Clinic of Neurology, Istanbul, Turkey

Abstract

Lyme disease (LD) is a tick-borne multisystem disease caused by infection with the spirochete *Borrelia burgdorferi*. LD is associated with numerous neurologic, rheumatologic, and cardiac manifestations. Neurologic manifestations are seen in 12-15% of untreated patients. LD is endemic in North America and Northern Europe. It is easy to diagnose LD in an endemic area if tick bite is recognized and the typical lesion erythema migrans is seen; however, it is a diagnostic challenge if the typical lesion is not seen in a country in which LD is not endemic. These cases may be underdiagnosed in Turkey because of the imitator nature of the disease and the belief that LD does not exist in Turkey. We report a patient who presented with acute asymmetrical paraparesis and was diagnosed and treated as having LD and discuss our case accompanied a literature review.

Keywords: Neuroborreliosis, *Borrelia burgdorferi*, meningoradiculitis

Öz

Lyme hastalığı (LH), kene ısırığı ile bulaşan, etkeni spiroket *Borrelia burgdorferi* olan, deri, kas iskelet sistemi, kardiyovasküler sistem ve sinir sistemini tutan bir hastalıktır. Sinir sistemi tutulumu tedavi edilmemiş olguların %12-15'inde görülür. Kuzey Amerika ve Kuzey Avrupa'da endemik olarak bulunur. Endemik sayıldığı bir bölgede, hatırlanan kene ısırığı varsa, tipik lezyon görülüyorsa tanı koymak kolay olsa da; Türkiye gibi endemik olmayan bölgelerde akla gelmesi zor bir tanıdır. Türkiye'de LH'nin görülmediğine dair genel bir kanı olmasından ve LH'nin taklitçi doğası nedeniyle bu olguların tanısı konamayabilir. Bu yazıda bacaklarında ağrı ve güçsüzlük nedeniyle kliniğimize başvuran ve nöroborelyoz tanısı konan bir olgu sunulup literatür bilgisi eşliğinde olgumuz tartışılacaktır.

Anahtar Kelimeler: Nöroborelyoz, *Borrelia burgdorferi*, meningoradikülit

Introduction

Lyme disease is clinically divided into three stages: early localized, early disseminated, and late disease. Erythema migrans lesions are seen in the early localized stage and in 80% of patients. Typically, a raised, sharply demarcated, salmon-red-colored lesion appears at the site of tick bite after 1-2 weeks and gradually expands. After a few weeks, the agent spreads hematogenously or through peripheral nerves and may present with neurologic, cardiac, and rheumatologic findings. In the late period it may present as arthritis, late neuroborreliosis, and chronic acrodermatitis (1,2,3).

Case Report

A 17-year-old male patient was admitted to our emergency service with symptoms of pain and weakness in the legs and difficulty in walking. First, he was given a painkiller injection for low back pain with a diagnosis of lumbar disc herniation 1.5 months ago. After 1-2 weeks, the back pain decreased, but pain started especially in the proximal muscles of the knees and legs with increasing severity with movement. In the last 2 weeks, he began to report weakness in both legs, which was more obvious on the right, and he had difficulty climbing the stairs. The neurologic examination showed that the muscle strength of the patient was full in the upper extremities and the cranial nerve was intact. A

Address for Correspondence/Yazışma Adresi: Helin Cansu Serindağ MD, Bakirkoy Prof. Dr. Mazhar Osman Mental and Neurological Diseases Hospital, Clinic of Neurology, Istanbul, Turkey

Phone: +90 530 942 40 04 E-mail: cansuserindag@gmail.com ORCID ID: orcid.org/0000-00024359-3008

Received/Geliş Tarihi: 25.01.2018 **Accepted/Kabul Tarihi:** 30.03.2018

©Copyright 2018 by Turkish Neurological Society
Turkish Journal of Neurology published by Galenos Publishing House.

physical examination revealed that he had 2/5 strength in the right and -4/5 in the left hip flexors, -3/5 in the right and 4/5 in the left hip adductors, 4/5 in the bilateral hip abductors and extensors, and muscular strength was full in the distal muscles of the lower extremities. Right patellar reflex and bilateral Achilles reflexes were absent, and plantar reflexes were bilaterally flexor. The patient, who had hypoesthesia in the right L2-L5 dermatome, could not walk without support. An electromyographic (EMG) examination was requested from the emergency department with a preliminary diagnosis of Guillain-Barré syndrome (GBS), which revealed a lesion more prominent on the right and in L2-L3 roots with asymmetric involvement leading to partial axonal loss in the bilateral L2-S1 roots. The patient was admitted to our clinic for further examination. Contrast-enhanced lumbar magnetic resonance imaging (MRI) revealed pathologic contrast enhancement in the leptomeninges, conus medullaris, and cauda equina (Figure 1A, 1B, 1C) and there were 450 lymphocytes/mm³ in the lumbar puncture (LP) examination of the patient. The investigations of viral and bacterial infections of the patient were normal with high cerebrospinal fluid (CSF) protein (149 mg/dL), normal glucose level (45 mg/dL), positive oligoclonal band (type 2) and high immunoglobulin G (IgG) index (1.62). Contrast-enhanced cranial, cervical, and thoracic MRI examinations were normal. Serum *Borrelia* IgG antibody was positive and IgM antibody was borderline positive. A confirmation test revealed positive IgG antibody and negative IgM antibody results. CSF *Borrelia burgdorferi* DNA polymerase chain reaction (PCR) was negative. The negative result did not exclude the disease because of the low sensitivity of the CSF PCR test. An infectious disease specialist initiated 2x1 g of intravenous (IV) ceftriaxone with a preliminary diagnosis of neuroborreliosis in the patient. When asked again, the patient stated that he had harvested nuts in Ordu 20 days before the symptoms began, that he remained in the open air and did not remember a tick bite, but that at that time he had a homogenous, erythematous, swollen lesion in the sacrum that healed with ointment treatment. Two weeks later, a follow-up LP examination revealed 50/mm³ cells and 91 mg/dL protein. Despite a rapid response in CSF findings, there was no improvement in the clinical status of the patient. His treatment was extended to one month and physical therapy and rehabilitation was started. The patient was pain-free and his paresthesia partly improved, and

he was treated with oral doxycycline 100 mg 2x1 for one month. In the outpatient clinic, the patient's muscular strength was such that he was able to walk without support during the third month of illness.

Discussion

Neuroborreliosis affects both the peripheral and central nervous system, and can present with many different clinical pictures. Cranial neuropathy, lymphocytic meningitis, and radiculoneuritis occur in the early period of neuroborreliosis. Peripheral facial paralysis and meningitis are more common in the United States of America (USA) and subacute painful meningoradiculitis, also known as Bannwarth syndrome, is the most common form in Europe. Lyme meningitis occurs as acute and subacute. It may present with symptoms such as fever, fatigue, and headache (3). The painful asymmetric paraparesis in our patient was consistent with subacute painful meningoradiculitis seen in the early dissemination period of neuroborreliosis due to the presence of lymphocytic cell increase in the LP, polyradiculopathy in the EMG and contrast enhancement in leptomeninges, and conus medullaris and cauda equina fibers in the lumbar MRI examination.

Late neuroborreliosis is much rarer than early disease and presents with clinical pictures regarding central nervous system involvement such as progressive encephalitis, myelitis and encephalomyelitis or peripheral nervous system involvement such as mononeuritis or polyneuritis (3). As in our case, patients can be misdiagnosed and treated as disc herniation because peripheral nervous system involvement can also cause paresthesia and radicular pain in both the early and late neuroborreliosis period.

Although there is no consensus on the mechanism of spread of the agent to the nervous system, it has been suggested that the *Borrelia* strain in North America (*Borrelia burgdorferi* sensu stricto) predominantly spreads hematogenously and the *Borrelia* strain in Europe (*B. garinii*) spreads mostly through peripheral nerves. Aseptic meningitis and multiple erythema migrans in the body are more common in North America, suggesting that the strains in this region are more likely to spread hematogenously. The fact that meningoradiculitis, also called Bannwarth syndrome, is more common in Europe, and that the radicular involvement is seen on the same extremity with the erythema migrans, suggests



Figure 1. A, B) Pathologic contrast enhancement in leptomeninges, conus medullaris and cauda equina in sagittal sections on contrast-enhanced T1-weighted lumbar magnetic resonance imaging, C) Axial view of the section marked in B

that European strains spread through peripheral nerves from the site of tick bite (4). The presence of a lesion in the sacral region in our present case, followed by the involvement of lumbar roots, supports this view.

The diagnosis of LD is based on either direct isolation of the agent or identification of the resulting immune response (3). The direct isolation is difficult and *Borrelia burgdorferi* antibodies are usually investigated in serum for diagnosis. It is even more difficult to show an antibody response in CSF and it is reported to be positive in 50% of cases in the USA and 85-95% in Europe. In our case, serum *Borrelia* IgG antibody was positive and IgM antibody was borderline positive in the first test, and IgG was positive and IgM was negative in the confirmation test. Our patient was diagnosed with erythema migrans about 2 weeks before the symptoms that started with back pain 1.5 months ago. Our patient presented approximately 2-2.5 months after the inoculation because erythema migrans occurred 1-2 weeks after inoculation. *Borrelia* IgM antibodies for diagnosis are positive after 2-3 weeks of inoculation, reaching a maximum level at 6 weeks and starting to decrease later. IgG antibodies reach the maximum level in 4-6 weeks and can remain high for years. If the antibodies are positive, confirmation with Western Blot is required. In our case, the IgM antibody being positive in the first test and negative in the confirmation test, and the IgG antibody remaining positive also in the confirmation test are related to the duration of the disease. The ratio of CSF antibody level to serum antibody level is the anti-*Borrelia* antibody index (AI), which indicates intrathecal antibody production. In a study of 123 patients with neurologic findings and positive CSF anti-*Borrelia* antibody in 2007, the sensitivity and specificity of the anti-*Borrelia* AI were 75% and 97%, respectively (5). CSF *Borrelia* DNA PCR was performed in our patient because the antibody level in CSF could not be studied in our hospital, but the sensitivity of PCR is much lower than that of the AI. In one study, BOS *Borrelia* DNA PCR was found to be positive in 40% of early neuroborreliosis cases and in 25% of late neuroborreliosis cases (6). PCR negativity did not reduce clinical suspicion and agent-specific treatment was started because the clinical, CSF, and radiologic findings were compatible with neuroborreliosis.

It has been reported that treatment with oral doxycycline 100 mg twice daily for 2 or 3 weeks is effective in uncomplicated cases of neuroborreliosis, such as peripheral facial paralysis (3). In more complicated cases, it is recommended to use IV ceftriaxone

2 g/day, cefotaxime 2 g 3 times a day, and IV penicillin G 20 million units/day. Jassam and Thaler (7) reported that they used oral doxycycline for 6 weeks due to ceftriaxone allergy in a case similar to ours and that the patient recovered at 7 weeks. Due to a lack of sufficient clinical improvement after treatment with IV ceftriaxone 2 g/day for a month in our patient, we continued treatment with oral doxycycline and the patient fully recovered in approximately 3 months.

Although a diagnosis of disc herniation and GBS are reasonable in patients with acute painful limb weakness in our country, questioning the presence of skin lesions and lying in an open field in these patients may help to diagnose and treat neuroborreliosis, thus preventing the development of more serious long-term findings.

Ethics

Informed Consent: Consent form was filled out by the patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

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

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- Halperin JJ. Nervous system Lyme disease. *Infect Dis Clin North Am* 2015;29.
- Koedel U, Fingerle V, Pfister HW. Lyme neuroborreliosis-epidemiology, diagnosis and management. *Nat Rev Neurol* 2015;11.
- Marques AR. Lyme Neuroborreliosis. *Continuum (Minneapolis Minn)* 2015;21.
- Rupperecht TA, Koedel U, Fingerle V, Pfister HW. The pathogenesis of Lyme neuroborreliosis: from infection to inflammation. *Mol Med* 2008;14.
- Blanc F, Jaulhac B. Relevance of the antibody index to diagnose Lyme neuroborreliosis among seropositive patients. *Neurology* 2007;69:953-958.
- Nocton JJ, Bloom BJ. Detection of *Borrelia burgdorferi* DNA by polymerase chain reaction in cerebrospinal fluid in Lyme neuroborreliosis. *J Infect Dis* 1996;174:623-627.
- Jassam YN, Thaler DE. Lyme meningo-radiculitis responsive to oral doxycycline therapy in the USA. *Oxf Med Case Reports* 2014;2014.