Case Report

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Longitudinal Extensive Transverse Myelitis Secondary to Lyme Disease

Lyme Hastalığına Bağlı Gelişen Longitudinal Extensive Transvers Myelit

Nihal AYDIN, Dilara Füsun İÇAĞASIOĞLU

Bezmialem Vakif University Faculty of Medicine, Department of Child Health and Diseases, Division of Child Neurology, İstanbul, Turkey

ABSTRACT

Transverse myelitis (TM) is a rare disease. It may present as the primary case or it may present as associated with inflammatory diseases following an autoimmune or infectious condition. Lyme disease involves cranial nerve neuropathy, meningitis, and radiculopathy neurologically, while only 4-5% of cases with neuroborreliosis show TM. Here we present a 3-year-old male patient with longitudinal extensive TM (LETM) secondary to Lyme disease.

Keywords: Transvers myelitis, lyme, neuroborreliosis

ÖZ

Transvers myelit (TM) nadir görülen bir hastalıktır. Primer bir olay olarak oluşabildiği gibi; otoimmün, enfeksiyöz veya enfeksiyon sonrası enflamatuvar hastalıklarla da ilişkili olabilir. Lyme hastalığında nörolojik tutulum daha çok kraniyal sinir nöropatileri, menenjit ve radikülopati şeklinde olurken TM nöroborreliosis vakalarının sadece %4-5'inde oluşmaktadır. Bu yazımızda lyme hastalığına bağlı longitudinal extensive TM (LETM) gelişen 3 yaşındaki erkek hastayı sunuyoruz.

Anahtar Sözcükler: Transvers myelit, lyme, nöroborreliosis

Introduction

Transverse myelitis (TM) is an inflammatory disease of the spinal cord that causes sensory and autonomic dysfunction in a few hours or days (1). It may primary or secondary toautoimmune, infectious or postinfectious disorders. Infectious etiologic agents include Herpes simplex type 1 and 2, Varicella zoster, West Nile virus, human immunodeficiency virus (HIV), human T-lymphotropic virus, *Borrelia species*, *Mycoplasma pneumoniae* and *Treponema pallidum*. TM due to *Borrelia species* is very rare (2).

Lyme is a disease caused by Ixodes ticks carrying 3 pathogenic species of Borrelia (*B. burgdorferi*, *B. afzelii* and *B. garinii*). It has a wide range of clinical manifestations. The clinical spectra includes cutaneous, joint, cardiac and neurological symptoms. Neurological manifestations mostly include cranial nerve neuropathy (most common is the 7th cranial nerve), meningitis and radiculopathy (3). However, it may rarely manifest in the form of TM (4,5). Primary infection and neural damage caused by post-infection immunity are responsible for central nervous system involvement (6).

The number of patients with Lyme and TM published in the literature is limited. It is known that a rapid response can be obtained with appropriate antibiotic therapy (2). Early diagnosis is critical in terms of treatment before the disease progresses.

Case Report

A 3-year-old male patient was admitted with weakness in legs and arms. The patient's history revealed that the weakness in both lower extremities started 5 days before, progressed within 3 days and weakness in the upper extremities was added. Physical

Address for Correspondence: Nihal AYDIN, Bezmialem Vakif University Faculty of Medicine, Department of Child Health and Diseases, Division of Child Neurology, İstanbul, Turkey
E-mail: nihalsoylutp@hotmail.com **ORCID ID:** orcid.org/0000-0003-3384-1677

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examination revealed that he was conscious, cooperated and oriented. His pupils were isochoric, bilateral light reflexes were positive and eye movements were free in all directions. The fundus examination was normal. During motor examination, flask tetraparesis was detected. Bilateral deep tendon reflexes were normal and bilateral foot sole reflexes were extensor . There were no signs of meningeal irritation or nuchal rigidity. He could not cooperate to the sensory examination. The autonomic examination revealed constipation and urinary retention. No characteristics were detected in his blood tests. In cerebrospinal fluid (CSF) analysis, CSF pressure was normal, protein level was 20 mg/dL, glucose level was 60 mg/dL and direct microscopic examination revealed 40/mm^3 lymphocytes. CSF oligoclonal band was negative and immunglobulin (Ig)G index was normal. Electromyography findings and tests for connective tissue diseases did not show any characteristics of the disease. There were no radiological or biologic findings suggestive of malignancy in our patient.

His cranial magnetic resonance imaging (MRI) was normal while his spinal MRI revealed a longitudinal extensive TM (LETM) on the cervical spinal cord, distal thoracic cord and conus medullaris (Figure 1). Serum serological tests were negative for HIV, Herpes virus, Cytomegalovirus, Toxoplasmosis, Mycoplasma, Chlamydia, Tuberculosis, Brucella, Varicella zoster virus and syphilis. He was negative for Borrelia burgdorferi IgM and positive for Borrelia burgdorferi IgG. Anti-Borrelia antibodies were detected by Western Blotmethod. Ceftriaxone treatment was completed in 7 days and oral amoxicillin treatment was continued for 21 days. Oral low dose steroid treatment was started after intravenous pulse steroid was given for 3 days. During this time the patient received physical therapy. Low-dose steroid treatment was prescribed for the first month and then the dose was gradually reduced and it was terminated one month later. The patient started walking in the second week of steroid treatment, but his arms were still weak. By the end of the first month of treatment he could use his arms fully.

Discussion

TM is a rare disease with rapid onset motor weakness, sensory changes, and bowel or bladder dysfunction (7). Immunopathogenesis is very diverse. There is evidence of perivascular infiltration of monocytes and lymphocytes in the lesions and axonal degeneration (8). The involvement of both gray and white matters with this pathological heterogeneity suggests that TM is a mixed disorder affecting neurons, axons, oligodendrocytes and myelin rather than a pure demyelinating disorder (8).

Idiopathic TM usually occurs as a post-infectious complication which is thought to be caused by the autoimmune process. Of patients 30-60% have a history of respiratory, gastrointestinal or systemic diseases (9). TM may develop due to direct infections or may be secondary to systemic rheumatic diseases (e.g. ankylosing spondylitis, antiphospholipid antibody syndrome, Behçet's disease, mixed connective tissue disease, rheumatoid arthritis, scleroderma, Sjögren syndrome, and systemic lupus erythematosus), paraneoplastic syndromes, post-vaccination reactions or multifocal central nervous system disorders (multiple sclerosis, neuromyelitis optica, acute disseminated encephalomyelitis, and neurosarcoidosis) (10-13).

Lyme disease due to *Borrelia species* is presented in three stages as early localized (erythema migrans), early disseminated and late disseminated disease. Clinical symptoms usually begin as erythema migrans and then disseminate to other systems. Arthritis, carditis, cranial nerve neuropathies (mostly 7th cranial nerve), meningitis or radiculopathy are the most common clinical spectra. Most discussions about Lyme disease are related to its nervous system involvement because neuroborreliosis usually causes nonspecific symptoms such as fatigue, headache, impaired cognitive function and memory. These symptoms are not specific for central nervous system infections but can also be seen in many other infectious and inflammatory conditions (14-16). Therefore, especially in pediatric patients, the diagnosis is difficult. TM, on the other hand, is only found in about 4-5% of patients with neuroborreliosis (17). Due to the small number of patients with TM secondary to Lyme disease, TM is not usually considered in the differential diagnosis. However, there are rare case reports in the literature. TM in those reported patients is in the form of LETM. LETM is defined as a type of TM involving three or more vertebra in the spinal cord (18). This relationship is considered important even though the underlying mechanism is unclear (4,19).

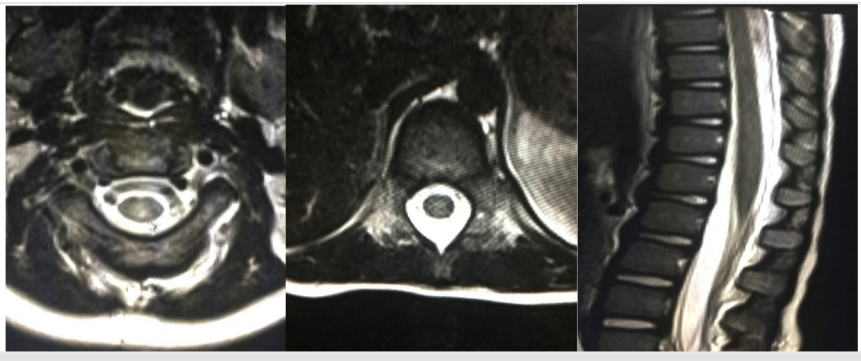

Figure 1. Spinal MRI shows LETM on cervical spinal cord, distal thoracic cord and conus levels
MRI: Magnetic resonance imaging, LETM: Longitudinal extensive transverse myelitis

In our patient, collagen tissue diseases and malignancy were excluded since these tests gave negative results. The clinical data, MRI and CSF findings were not consistent with acute disseminated encephalomyelitis, multiple sclerosis, and neuromyelitis optica spectrum disorder; therefore, these diseases were not considered. Serological tests in serum for infectious etiologies were positive only for Borrelia burgdorferi.

Leukocyte cell count in CSF and Borrelia burgdorferi antibody index in CSF and serum should be evaluated for the diagnosis of neuroborreliosis. However, 30% of patients may have a negative antibody index in CSF. Therefore, a diagnosis of neuroborreliosis can be made with typical clinical symptoms, presence of B. burgdorferi antibodies in serum, positive response in pleocytosis to antibiotic therapy (20,21).

Although our patient did not have a history supportive of Lyme disease, a diagnosis of TM due to neuroborelliosis was made with serum borrelia antibody positivity, confirmatory tests, andclinical response to antibiotherapy and steroid treatment. Control CSF examinations of the patient could not be performed because the family did not give consent.

As a result; due to the absence of features in the tests for autoimmune and demyelinating diseases (CSF oligoclonal band, Ig G index, serum Aquoporin 4 antibody, serum Anti MOG, C3, C4, cANCA, p ANCA etc.), they were not considered in the diagnosis. However, the patient was followed up for these diseases. Even if there is no history of tick bite or erythema migrans; neuroborreliosis should be considered in the differential diagnosis of TM, and if there are strong clinical findings, appropriate treatment should be initiated accordingly.

Ethics

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: N.A., D.F.İ., Design: N.A., D.F.İ., Data Collection or Processing: N.A., D.F.İ., Analysis or Interpretation: N.A., D.F.İ., Literature Search: N.A., D.F.İ., Writing: N.A., D.F.İ.

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