



## CASE REPORT/OLGU SUNUMU

# Neuroborreliosis and autoimmunity, Guillain Barré syndrome: two case reports

Nöroborelyoz ve otoimmünite, Guillain Barre sendromu: iki olgu sunumu

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### Abstract

Lyme disease is a multisystemic disease and involvement of the nervous system is called neuroborreliosis. Clinical manifestations of peripheral neuroborreliosis include asymmetric polyradiculopathy, cranial nerve paralysis, multifocal mononeuropathies and sensorymotor polyneuropathies. Guillain-Barré syndrome also known as acute inflammatory demyelinating polyneuropathy is an immune-mediated neuropathy. Only limited number of cases with Lyme disease presented with Guillain-Barré syndrome symptoms are encountered in the literature reviews, which are mostly seen during paediatric age. Herein we will report two patients with Guillain-Barré syndrome who presented with atypical findings and followed up in our clinic. In these cases diagnosis of Lyme disease was confirmed by Western Blot technique which demonstrated the presence of antibodies formed against *Borrelia burgdorferi*.

**Key words:** Guillain-Barré Syndrome; Lyme disease; neuroborreliosis; autoimmunity

### Öz

Multisistemik bir hastalık olan Lyme Hastalığının sinir sistemi tutulumu nöroborelyoz olarak isimlendirilmektedir. Klinikte periferik nöroborelyoz asimmetrik poliradikülopati, kranyal sinir felçleri, multifokal mononöropatiler, ve sensorimotor polinöropatiler şeklinde görülmektedir. Guillain Barre Sendromu immün ilişkili akut nöropati tablosudur. Literatür tarandığında Guillain Barre sendromu bulguları ile presente olan Lyme olguları sınırlıdır. Burada kas ve eklem ağrıları gibi atipik bulgular ile gelen ve takibinde Guillain Barre sendromu bulguları yerleşen iki olgu bildirilmiştir. Bu olguların her ikisinde de kene ısırığı hikayesi yoktu ve 15 gün kas ve eklem ağrıları nedeniyle ortopedi ve fizik tedavi kliniklerinde takip edilmişlerdi. Aynı zamanda tiroid otoantikorlarının yüksekliği tespit edilen hastaların Lyme hastalığı tanısı *Borrelia burgdorferi*ye yönelik oluşmuş antikorları belirleyen Western Blot tekniği ile doğrulanmıştır.

**Anahtar kelimeler:** Guillain Barre Sendromu, Lyme Hastalığı, nöroborelyoz, tiroidit, otoimmünite

## INTRODUCTION

Lyme disease is a multisystemic disease caused by a spirochete *Borrelia burgdorferi*<sup>1</sup>. The first few weeks after tick bite is called Stage 1 and clinically skin rashes described as erythema migrans are seen. During the following 6 months named as Stage 2, meningoradiculitis (Bannwarth Syndrome), meningitis, peripheral facial paralysis, encephalitis, myelitis, arthritis and myalgia can be seen. After that period Stage 3 is seen which is characterized by

encephalitis or encephalomyelitis, polyneuropathy, monoarthritis or oligoarthritis<sup>2,3</sup>.

Involvement of the nervous system is encountered in 10-15 % of the patients and its clinical picture is called neuroborreliosis<sup>1</sup>. The most frequently seen manifestations of neuroborreliosis are headache and meningismus, involvement of cranial nerve and meningoradiculitis. However, chronic neuroborreliosis, which progresses with cognitive involvement, paresis, extrapyramidal symptoms and psychosis, can manifest itself with stroke-like symptoms and vasculitis<sup>4</sup>. In Lyme disease,

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peripheral nerve lesions can be seen in nerve roots, plexus or peripheral nerves. Even though clinical discrimination is hard to make, electromyography (EMG) and studies on nerve conduction velocities can sometimes be helpful. EMG can be completely normal or it can demonstrate axonal damage or slowing down of nerve conduction velocity<sup>5</sup>. Clinical manifestations of peripheral neuroborreliosis include asymmetric polyradiculopathy, cranial nerve paralysis, multifocal mononeuropathies and sensorymotor polyneuropathies<sup>6</sup>.

Guillain-Barré syndrome (GBS) also known as acute inflammatory demyelinating polyneuropathy is an immune-mediated neuropathy, which is characterized by acute loss of strength together with sensory symptoms and albuminocytological dissociation in cerebrospinal fluid (CSF)<sup>7</sup>. Only limited number of cases with Lyme disease presented with GBS symptoms are encountered in the literature reviews, which are mostly seen during paediatric age<sup>8</sup>.

Herein we will report two patients with GBS who presented with atypical findings and followed up in our clinic. In these cases diagnosis of Lyme disease was confirmed by Western Blot technique which demonstrated the presence of antibodies formed against *Borrelia burgdorferi*

### CASE 1

A 16-year-old boy scout without any previously known disease presented to our clinic with complaints of gradually worsening loss of strength for the last 15 days, which stemmed from both legs and ascended up to arms. For the last 2 days, his respiratory muscles were also getting weaker. It was learnt that he had been followed up in the polyclinics of orthopedics and FTR for 2 weeks. Upon development of gait disorders, he consulted to the polyclinics of neurology. Neurological examinations revealed loss of strength bilaterally affecting upper (+4/5) and lower (-4/5) extremities. Because of dyspneic complaints he was talking with frequent stops in-between Neurological examination was otherwise unremarkable. On EMG examination, peripheral nerve motor responses with delayed latencies and low amplitudes were obtained; partial conduction blocks and temporally dispersed responses were detected. Her sensory responses were markedly of lower amplitude. Nerve conduction velocities were decreased. Tibial and median F-

responses could not be elicited. The patient's condition was consistent with acute-subacute inflammatory polyneuropathy. Lumbar puncture was performed to obtain CSF samples. CSF was acellular and its opening pressure was within normal limits. Results of laboratory analysis of CSF samples were as follows: CSF albumin, 479 mg/dL (n: 10-30) and protein, 108 mg/dL; (n: 15-40); concentrations; CFS LDH<30 mg/dL, BOS glucose, 58 mg/dl. Results of routine blood analysis were as follows: ESR 83 mm, WBC: 10.9/ mm<sup>3</sup>, LDH: 579 UL (125-220). sT3:3.34 pg/ml (2.56-5.01), sT4:1.62 ng/dl (0.98-1.63), TSH: 4.02 uIU/ml (0.51-4.3), anti TPO: 396.8 IU/ml (0-26), antiTG autoantibody: 202.2 IU/ml (0-64). Thyroid antibody levels were elevated. Other routine laboratory test results were within normal limits. The patient received standard dose of (2 gr/kg) IVIg therapy. Despite lack of any past evidence of tick bite, tests related to the detection of Lyme disease were requested. Blood and CSF Lyme ELISA Ig-M negativity and Ig-G positivity were detected. Western Blot confirmatory test revealed Lyme IgG positivity. Under the surveillance of the department of infection diseases, she received ceftriaxone therapy for one month. She was completely cured with consequently applied FTR therapy.

### CASE 2

A 49-year-old female farmer was living in the countryside and raising cattle. The patient had not any known disease, excluding a fly bite on her left arm 20 days previously. She was followed up in the polyclinics of orthopedics and FTR for her complaints of widespread musculoskeletal pains, numbness felt on hands. We have learnt that her complaints had been aggravated for the last one week so he had been hospitalized in the FTR service. The patient was referred to our clinic when her ESR and CRP levels increased and generalized loss of strength developed.

On neurological examination of the patient who could not sit erect without support, muscle strength of her upper extremities was normal. Muscle weakness were detected in the lower right (2/5) and left (3/5) extremities. DTR could not be elicited. On EMG, peripheral nerve motor responses with delayed latencies and low amplitudes were recorded, while amplitudes of sensory responses were detected at the lower limit of normal. Conduction velocities were decreased. Tibial and median nerve F-

responses could not be elicited. Early stage EMG findings were consistent with inflammatory neuropathy. Her CSF findings were as follows: protein >200 (15-40 mg/dL); elevated CSF albumin 1635 (10-30 mg/dL); CSF glucose 70 mg/dl; CSF LDH<30; acellularity, clear and CSF pressure was normal. WBC 7.2 x10<sup>3</sup>/mm<sup>3</sup>; ESR 101 mm, CRP 36 mg/L, LDH 314 U/L (125-220), anti-TPO 146.8 IU/ml (0-34), antithyroglobulin 249.9 IU/ml (0-115), higher levels of thyroid autoantibodies. sT<sub>3</sub>: 9.87 pg/ml (2.6-4.8), sT<sub>4</sub> 1.41 ng/dL (0.93-1.7) and TSH 1.25 uIU/ml (0.27-4.2). The patient received a standard dose (2 gr/kg) of IVIg therapy. Following IVIg treatment, her complaints were relieved partially. Evaluation with ELISA assays revealed Lyme Ig M negativity and IgG positivity. Western blot confirmatory test detected IgG positivity. Ig-M negativity was also revealed. Under the surveillance of the department of infection diseases, she received doxycycline therapy for one month. She was completely cured with consequently applied FTR therapy.

## DISCUSSION

History of tick bite was not elicited in both cases. Our Case 1 was a boy scout and he had encamped in the mountain. The other case was living in the countryside and raising cattle. Within the last two weeks before emergence of neurological symptoms, both of our patients had been monitored in the polyclinics of orthopedics and also physical therapy and rehabilitation with the diagnoses of arthralgia and radiculopathy based on their complaints of musculoarticular pain, which eventually delayed our diagnostic process a little bit. Higher ESR and CRP levels were detected in both of our cases. Increased levels of both ESR and CRP in Lyme disease have been cited in the literature<sup>9,10</sup>. Vaishnavi et al. detected higher baseline CRP levels in patients with GBS and demonstrated that autoimmune conditions as GBS may stimulate a high-level inflammatory response which leads to increased production of CRP<sup>11</sup>. Still as is known, in older patients presenting with clinical picture of polymyalgia rheumatica occasionally increased levels of ESR and CRP are detected in Lyme disease<sup>12</sup>. In patients with increased baseline levels of ESR, CRP and widespread musculoskeletal pain, if clinical manifestations of GBS are delayed, then differential diagnosis presents difficulties with potential delay in diagnosis. In our patients because of

abovementioned reasons diagnosis of GBS was also delayed.

Although, peripheral neuroborreliosis manifests itself with symptoms of GBS, at the same time mild and reversible chronic axonal sensorimotor polyradiculopathy can be observed<sup>13,14</sup>. Some cases with neuroborreliosis associated with GBS have been also reported in the literature<sup>15,16</sup>.

Data obtained by EMG and CSF analysis are valuable in the differential diagnosis of GBS. EMG demonstrates demyelination of motor nerves and axonal type involvement. Classical EMG findings include partial motor conduction block, abnormal temporal dispersion of motor responses, prolonged distal motor and F- wave latencies and decrease in the maximum motor conduction velocity. CSF findings are also important in the diagnosis of GBS. Protein concentration in CSF increases. Number of mononuclear cells is within normal limits or decreased (< 50 cells/ml). During the first week of the disease, CSF findings may be within normal limits<sup>17</sup>. However, in neuroborreliosis, lymphocytic pleocytosis and increased albumin ratios are typically present in CSF. Rarely CSF may not contain cells<sup>18</sup>. In our patients, EMG findings were consistent with GBS with acellular CSF and higher protein content of CSF. Excluding Lyme disease, which was confirmed by Western Blot confirmatory test, any previous history of vaccination or infection was not elicited.

In both of our patients, increased thyroid autoantibody levels were detected, while thyroid function test results were within normal limits, GBS is known as an acute inflammatory process developed as a result of autoimmune reaction related to infectious or non-infectious causes<sup>19,20</sup>. Rarely GBS can be seen together with autoimmune thyroiditis<sup>21-23</sup>. Besides some publications in the literature have demonstrated concomitancy between Lyme disease and autoimmune thyroiditis<sup>24,25</sup>. The role of autoimmune process and autoantibodies has been indicated in the pathophysiology of Lyme disease<sup>26</sup>. Indeed, many studies in the medical literature have investigated the association between Lyme disease and autoimmunity<sup>27</sup>. Literature has been reviewed and any case report which indicated presence of high levels of thyroid autoantibodies in patients followed up for neuroborreliosis has not been encountered .

In both of our cases who presented with clinical manifestations of GBS, higher levels of thyroid antibodies were detected. Besides any other etiological factor other than Lyme disease was not found in these patients. When literature was reviewed, any case with combined manifestations of GBS, Lyme disease and thyroiditis was not encountered. It is important to evaluate the patients with acute inflammatory polyneuropathy demonstrating atypical symptoms as diffuse muscle and joint pains with respect to Lyme disease, which is a treatable etiological factor, considered in the differential diagnosis.

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