

Multiple Sclerosis Co-Occuring with Myasthenia Gravis: Case Report

Miyastenia Gravis ve Multipl Sklerozun Beraber Görüldüğü Bir Olgu

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ABSTRACT We report the development of multiple sclerosis in a patient with myasthenia gravis. A 14-year-old girl had the symptoms of central nervous system damage and physical signs of myasthenia gravis. Myasthenia gravis was the predominating disease, but in later stages of the disease multiple sclerosis became the dominating one. To our knowledge, there are variety of claims for cerebral white matter involvement in myasthenia gravis, and subclinical impairment of neuromuscular transmission in some multiple sclerosis patients, but the immunological explanation for these findings is still unremarkable. We want to share this report to provide a further evidence for co-occurrence of these two diseases and discuss the common mechanisms of pathogenesis.

Key Words: Multiple sclerosis; myasthenia gravis

ÖZET Bu yazıda miyastenia gravis olan bir hastada multipl skleroz gelişimi sunulmuştur. 14 yaşında kız çocuğu santral sinir sistemi hasarını gösteren semptomlara ve miyastenia gravisin fiziksel bulgularına sahipti. Miyastenia gravis olgudaki primer hastalıktı. Fakat hastalığın daha ileri dönemlerinde multipl skleroz dominant olan hastalık halini almıştır. Myastenia gravisde serebral beyaz cevher tutulumunun ve multipl sklerozda nöromusküler iletimin subklinik etkilenimine ait çeşitli hipotezler mevcuttur. Fakat bu bulguların immunolojik açıklaması halen belirgin değildir. Bu vaka, bu iki hastalığın birlikte görülebileceği gerçeğini hatırlatmak ve patogenezdeki muhtemel ortak mekanizmaları tartışmak için sunduk.

Anahtar Kelimeler: Multipl skleroz; miyastenia gravis

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Multiple sclerosis (MS) is an inflammatory condition associated with demyelination. The immunological system plays a crucial role in its pathogenesis. Myasthenia gravis (MG) is a common primary disorder of neuromuscular transmission. The usual cause is an acquired immunological abnormality.¹ The first data about unusual accompaniment of MG and MS has come from Aita et al in 1974.² Some other studies and case reports were also documented the rare coexistence of multiple sclerosis and myasthenia gravis.³⁻⁵ In this report, we suggest that patients with myasthenia gravis who have unusual findings as in the patient reported must be investigated for the presence of multiple sclerosis, because of the common mechanisms of the pathogenesis.

CASE REPORT

A 14-year-old girl was first admitted to our clinic with left-sided ptosis, slurring of speech, fatigue, which became more evident in the evening. Edrophonium test was applied and found to be pathological. Anti-acetylcholine receptor antibody was positive at $3,1 \times 10^{-10}$ mol/L (normal $<2 \times 10^{-10}$). Her cranial magnetic resonance imaging and computerized tomography of the mediastinum were normal. EMG showed decremental evoked muscle action potentials (tibialis anterior) with repetitive nerve stimulation and single fiber EMG of orbicularis oculi muscle showed dysfunction of the neuromuscular junction. The patient improved with anticholinesterase medication. Pyridostigmine (60 mg tablets) was administered in a dose of 60 mg every 6 hours. Her second admission to the hospital was eight weeks later, with double vision, weakness in the right leg and difficulty in speaking. The lesions which were seen in the cranial magnetic resonance imaging (MRI) led to the diagnosis of a demyelinating process (Figure 1, 2, 3). The diagnosis was supported by analysis of

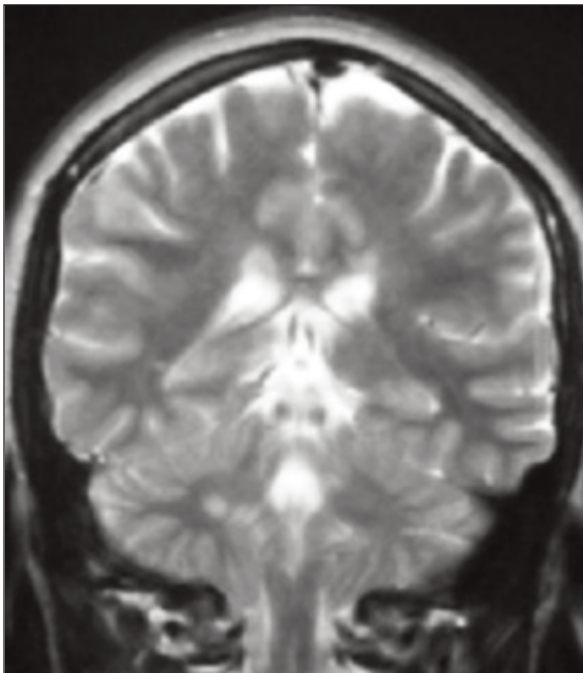


FIGURE 1: Coronal T2-weighted MR image shows two hyperintense foci in the right middle cerebellar peduncle in addition to the lesion locating in the right periventricular white matter.

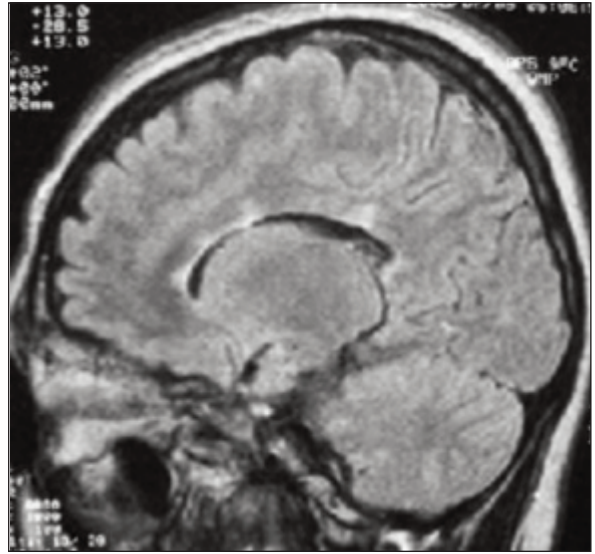


FIGURE 2: Sagittal FLAIR image to the left of the midline shows multiple periventricular plaques affecting the corpus callosum.

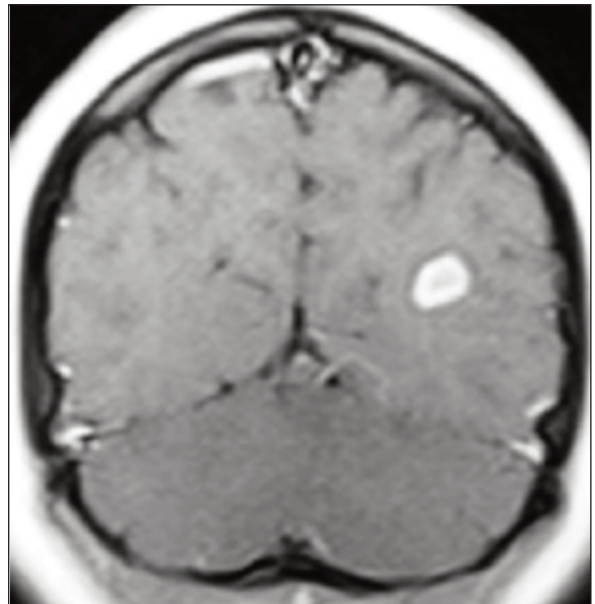


FIGURE 3: Coronal contrast-enhanced T1-weighted image shows an enhancing plaque in the left occipital white matter.

cerebrospinal fluid (CSF) and evoked response testing. Elevated Ig G level in CSF was found. Auditory brain stem evoked responses were normal, visual evoked potentials showed delayed latency and decreased amplitude in right eye and somatosensory evoked potentials were bilaterally delayed.

Vasculitis and connective tissue disease that could mimic demyelination were excluded by performing immunological tests including ANA, ANCA, antiphospholipid antibodies. They were all negative. She was treated with 1 g/day iv methylprednisolone for 7 days. On the third day of treatment, there was a dramatic improvement in her clinical condition. Four months later, clinical relaps with diplopia, and vertigo accompanied with nausea and vomiting necessitated re-admittance, treated with the same five-day intravenous course of methylprednisolone, and showed complete clinical remission in one week. Ten months later, she was admitted with urinary incontinence, weakness in left leg. At every admission, she had new lesions on cranial MRI. Because of these further relapses of multiple sclerosis, glatiramer acetate therapy was begun. During this period there wasn't any exacerbation of MG symptoms in between or during MS relapses. According to these findings she was diagnosed as having an unusual accompaniment of MS and MG.

DISCUSSION

The coexistence of MG and MS is an unusual occurrence. The development of both diseases in the same patient does not seem to be accidental and probably the homogeneity of the diseases lies in impairment of immunological homeostasis characteristic of both autoimmune diseases.⁶ One of these two autoimmune disorders can be the preceding disease but may appear simultaneously.⁵

Myasthenia gravis may appear concomitantly with systemic autoimmune diseases like Grave's disease, Hashimoto thyroiditis, rheumatoid arthritis and systemic lupus erythematosus. Also some neuromuscular disorders (periodic paralysis, myositis, Guillain Barre Syndrome, polyneuropathy) may coexist with MG.⁷

A wide range of "demyelinating diseases" have been seen in patients with MG, and the classic picture of "MS" may be associated with MG less often than other demyelinating patterns such as recurrent myelitis or even ADEM.⁸ The relatives of patients with MS very often have other autoimmune diseases and it has been suggested that there

may be susceptibility genes that are common in this group.⁹

Somer et al reported that in Finland two people in a population of 1,5 million had the combination of MS and MG, both clinically mild, confirmed by elevated serum nAChR antibodies and positive MRI scans. These authors suggested that similar immunogenetic features (DR2, DR3 alleles) can predispose these disorders. But, some unknown genetic and different triggering factors can cause these different clinical diseases.⁵

Besides the coexistence of MG and MS, Kister et al reported an association between MG (after thymectomy) and neuromyelitis optica (NMO) in 4 patients. They suggested that dysregulation of B-cell autoimmunity in myasthenia, possibly exacerbated by loss of control over autoreactive cells as a result of thymectomy, may predispose patients to the development of NMO.¹⁰

Shakarishvili et al presented four patients with thymomogenic myasthenia gravis and demyelinating disorder occurring together.¹¹ They suggested that the key autoantigens of MS and MG are coexpressed in the thymus. The presentation and costimulation by infected antigen-presenting cells may occur in thymic medulla and may cause activation of autoreactive T cells specific to myelin basic protein and acetylcholine receptor. They emphasized that the most important event in development of MS and MG is the activation of specific autoreactive T cells. Another hypothesis for this unusual association can be; the primary activation of myelin reactive T cells can take place in periphery and can cause T cell mediated inflammation against myelin basic protein (MBP) epitope in brain and thymus.¹¹

There's not an information about the cross reactivity between acetylcholine receptor (AChR) and MBP. But the same probable factors (like; viral proteins, superantigens) may trigger these two autoimmune diseases simultaneously or consecutively.¹²

Isbister et al described 8 patients with associated multiple sclerosis and myasthenia gravis. According to their hypothesis; these two autoimmune

neurological disorders share common mechanisms of pathogenesis and lend support to the hypothesis that MS may also have an antibody-mediated component.¹³

The presence of oligoclonal IgG bands in the CSF like our patient indicate that the pathoimmunology of MS may be heterogeneous and that there can exist a sub-group of MS patients with a more antibody mediated form of the disease.¹⁴

MG and MS coexistence is a rare association and the pathogenic mechanisms are unknown. Because of these two reasons, there's not an exact

therapy. Immunosuppressive or immunomodulatory medication can be chosen due to the symptoms of the patients. Our patient had both glatiramer acetate therapy and pyridostigmine therapy.

Although the development of multiple sclerosis in our patient can be coincidental, because of the possibility of a common immunological substrate for both conditions, it is difficult to explain simultaneously coexisting clinical picture with coincidence. To our knowledge; although the pathogenic mechanisms are still unknown, the co-occurrence of MG and MS is a rare but not a random association.

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