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Case Report

Prepubertal Juvenile Myasthenia Gravis; A Case With Early Onset And Bulbar Symptoms

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Summary

Juvenile myasthenia gravis (JMG) is a rare autoimmune disease affecting the neuromuscular junction in children and adolescents. Its clinical presentation is usually associated with ethnicity and pubertal development. We present a 14 month old patient with, bulbar symptoms and a good clinical course. The age of onset in this case is lower than average and the case is in pharmacological remission after medical treatment. Prepubertal JMG is very rare during infancy in Caucasians and ocular symptoms are more common in prepubertal patients. This Caucasian case is uncommon since she has presented with bulbar symptoms and early onset.

Key words: Juvenile myasthenia gravis, neuromuscular junction, autoimmune disease

Prepubertal Juvenil Miyastenia Gravis; Bulber Semptomlar İle Erken Başlangıçlı Bir Olgu

Özet

Juvenil miyastenia gravis (JMG) çocukluk ve adolesan dönemde nöromuskuler bileşkeyi etkileyen nadir bir otoimmün hastalıktır. Klinik görünüm genellikle ırksal özellikler ve pubertal gelişim ile ilişki gösterir. Bu yazıda bulber bulguları olan, iyi bir klinik gidiş gösteren 14 aylık bir hasta sunulmaktadır. Olgumuzun başlangıç yaşı JMG için ortalama yaştan düşüktür ve tıbbi tedavi ile tam klinik remisyon gözlenmiştir. Prepubertal JMG beyaz ırkta bebeklik döneminde çok nadirdir ve prepubertal olgularda daha çok okuler semptomlar görülür. Sunulan beyaz ırktan olan olgu, erken başlangıçlı ve bulber semptomlarla prezente olması ile ender bir olgudur.

Anahtar Kelimeler: Juvenil miyastenia gravis, nöromuskuler bileşke, otoimmün hastalık

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease affecting the postsynaptic acetylcholine receptors at the neuromuscular junction. Juvenile myasthenia gravis (JMG) affects patients aged between 1 and 19 years. JMG has been reported even in the first two years of life.

Although the adult form of MG and JMG are caused by similar pathophysiological mechanisms, the epidemiological and prognostic features of the two diseases as well as therapeutic approaches are different. Racial characteristics and pubertal development affect the clinical presentation and prognosis.[1-5] Prepubertal JMG have some distinct clinical and prognostic features when compared with postpubertal JMG.

In this article, we present a case with very early onset and significant bulbar involvement.

CASE PRESENTATION

A 14 month-old Caucasian girl was referred to our clinic by her paediatrician because of eyelid ptosis, swallowing dysfunction and hypophonation that had

lasted a month. Her complaints had started within two weeks after a fever illness and had fluctuated throughout the day.

She was born by vaginal delivery at full term. Her developmental milestones, family history and general examination were normal. On neurologic examination; bilateral eyelid ptosis and extraocular weakness on both vertical and horizontal gaze were found (Figure 1). She had symmetric facial weakness. Her crying was weak on examination. There was difficulty in swallowing during feeding. Her gait was normal and deep tendon reflexes in both the upper and lower extremities were normoactive. There was no ataxia.

Figure 1: *Eyelid ptosis before treatment*

The complete blood count, erythrocyte sedimentation rate, serum chemistries and thyroid hormone levels were normal. Anti-thyroperoxidase and anti-thyroglobulin antibodies were negative. The neostigmine test showed significant improvement in the patient's eyelid ptosis. Nerve conduction velocities were normal. There was 25% decremental response at 3 Hz repetitive stimulation in the trapezius muscle. The acetylcholine receptor (AChR) antibody titre was 0.6 nmol/L (normal <0.25). Thoracic magnetic resonance imaging was normal.

The clinical features, positive acetylcholine receptor antibody, decremental response on repetitive stimulation and positive neostigmine test confirmed the diagnosis of JMG.

The patient was started on pyridostigmine 15 mg three times daily and given IVIG (total dose 2 gr/kg for 3 days) for her bulbar symptoms. After IVIG therapy, her bulbar symptoms improved but ptosis and extraocular weakness continued. Oral prednisolone (1 mg/kg/day) was added to the treatment regimen. Her ocular symptoms improved in two months. .(Figure 2) One year after the initial diagnosis, the patient is still in pharmacological remission.

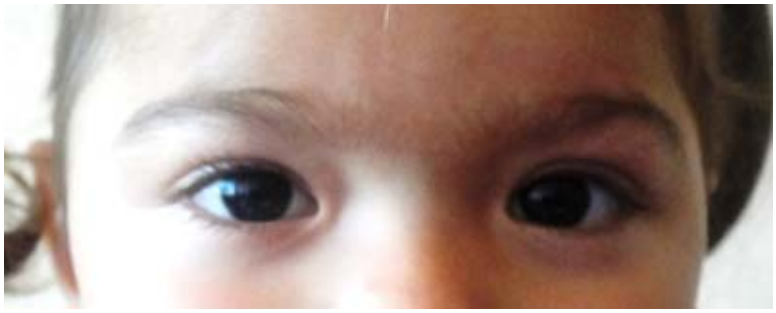

Figure 2: *Improvement of the ptosis after treatment*

DISCUSSION

The pathogenesis and symptoms of JMG are similar to those of adult-form MG, but its epidemiologic and prognostic features, clinical presentation, and treatment approaches are different. Ethnicity and pubertal stage have an effect on the clinical presentation. These effects are likely to be associated with host response and immune maturation as well as, environmental factors.[1-3]

Prepubertal JMG is more common among Asians than Caucasians. Among Asian patients, the disease occurs mostly in children between 2 and 4 years with no sex differences. In these cases, the disease is usually purely ocular and the prognosis is good.[5] Among Caucasians, prepubertal JMG is less common and is very rare in infancy. The disease is more frequently observed in postpubertal patients.[2,10] Prepubertal onset is less than 10% of cases. While prepubertal patients mostly present with ocular symptoms, generalised symptoms are more common in postpubertal patients. There is no gender difference in disease occurrence at prepubertal age, whereas female predominance is present in postpubertal patients.[1,4,5] This female predominance is due to the effects of sex hormones and genetic influences on immune function.[8] Prepubertal patients have a better prognosis with a higher rate of spontaneous remission.

The proportion of prepubertal patients who are seropositive for AChR antibodies is low, whereas in postpubertal patients, the proportion is the same as in adult-form MG. The patients who are seropositive for muscle-specific kinase (MuSK)antibodies has been described in JMG, but its frequency is unknown.[1] Seroconversion has been reported in some patients with JMG who developed MuSK antibodies after thymectomy.[7]

The treatment of JMG should be planned based on clinical presentation, severity and the patient's age. Acetylcholinesterase inhibitors can be used as the first choice in mild cases. Plasmapheresis and IVIG are effective in more severe cases and during myasthenic crises, but the effects of these treatments are temporary. Steroids can be used in severe cases but they should be used with caution due to their long-term side effects. Immunosuppressive agents such as azathioprine, cyclophosphamide, and cyclosporine have been used effectively in JMG. The use of mycophenolate mofetil, rituxumab and tacrolimus has been reported. These immunosupressants should be used for severe cases since serious side effects and risk of delayed malignancy development limit their use.[1-3]

There are few studies on thymectomy in prepubertal JMG due to the low prevalence and high rate of spontaneous remission. Chiang and colleagues reported high remission rates within 1 year after thymectomy in patients with generalised JMG.[1] Thoracoscopic thymectomy has been used in a small sample population.[6] Recent studies revealed that thymectomy causes immunological alterations in very young children, such as premature immune aging.[10] Notably, thymomas are less common in children and adolescents than in adults. Thymic hyperplasia is the most common pathologic finding in JMG.[1,3]

The case of the patient presented here is uncommon because of the early onset with bulbar symptoms. She is currently in pharmacological remission after intravenous immunoglobulin (IVIG) and steroid treatment.

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