Clinical Diagnosis and Management of Ocular Myasthenia Gravis

Abstract

Introduction

Ocular Myasthenia Gravis may be the first initial symptoms encountered in the disease course. Among patients presenting with ocular symptoms, 20–50% remain purely ocular, whereas the remainder progress to generalized disease. Ocular manifestations can masquerade as a variety of ocular motility disorders, including central nervous system disorders and peripheral cranial nerve palsies. Therefore, it is important for clinicians to recognize a correct clinical assessments and prompt management as it may provide patient's prognostic information.

Purpose

To describe a case of ocular myasthenia gravis

Case report

A 36-year-old woman came to Neuro-ophthalmology unit National Eye Center Cicendo Eye Hospital with a chief complaint of droopy eyelid on the left eye which was worsened in the evening and improve after taking rest since 1 month ago. Ophthalmic examination revealed visual acuity on both eyes was 1,0. No ocular motility disturbance and anterior segment and posterior segment were within normal limit on both eyes. The examination showed positive result of Cogan's eyelid twitch, orbicularis weakness, stare test, ice pack test and prostigmin test. There was no signs of generalized type Myasthenia Gravis. She was diagnosed ocular myasthenia gravis and was treated with pyridostigmin tablet 60 mg three times a day orally and showed symptoms improvement at 1 month follow up.

Conclusions

Several diagnostic and treatment options are available for Ocular Myasthenia Gravis. Correct and prompt clinical assesment is important in making diagnosis and treatment of myasthenia gravis.

I. Introduction

Myasthenia gravis (MG) is a an autoimmune disorder in which antibodies are produced against the nicotinic acetylcholine receptors on the postsynaptic membrane. Clinically, it is characterized by ptosis, diplopia, dysphagia, dysarthria, and general muscle weakness and fatigue. Autoimmune myasthenia gravis may affect all races and ages, with an incidence of 4 to 5 per 100.000/year and prevalence ranges estimated of 0.5-12.5 per 100.000/year. Onset of symptoms in the first decade or after the age of 70 years is less common. The ratio of affected females: males is 3:2 or higher in Generalized MG, more males are affected by solely Ocular MG. Onset occurs at an earlier age in women (around twenties and thirties) than in men (around sixties of seventies).[1,2,3]

Until today, the pathophysiology of the immune system malfunctions in people with myasthenia gravis remains unclear. Many factors likely contribute to the risk of developing this complex disorder. Whether there are predisposing factors is not established, but in some cases the presence of infection, emotional stress, smoking, surgeries, trauma, use of antibiotics, or pregnancy have been related to the onset of disease manifestation.[3,4,5]

Despite advanced diagnostic and treatment techniques, MG still represents a challenge. Diagnosing MG in patients with solitary ocular manifestation must be apprehended since not all supportive tests may give satisfying diagnostic result. Awareness of the characteristics of Ocular MG is important in order to avoid delayed or misdiagnosis of MG. This case report aimed to describe clinical characteristics and management of myasthenia gravis.[5,6]

II. Case Report

A 36 year-old woman came to neuro-ophthalmic unit at Cicendo Eye Hospital with a chief complaint of droopy eyelid on left eye for one month. The droopy eyelid was better in the morning and was worsened in the evening, mostly associated with physical exertion. No complaints of headache and double vision. No history of trauma, pain, fever, muscle weakness, difficulty in swallowing and breathing, hoarseness, nor articulation changes. She had denied any consumption of medication and presence of systemic illness such as hypertension, diabetes mellitus and dyslipidemia. She was married and had one child, history of using contraception was denied. No history of the same complaints within patient's family.

All general examinations were within normal limit. Motoric examinations were normal in four extremities. No signs of lateralization in cranial nerve examinations.

Ophthalmic examination showed the visual acuity was 1.0 on both eyes. Intraocular pressure was 17 for both eyes. Hirchberg test showed orthotropia, with neither restriction nor pain on both ocular motility (see nine-gaze position in Figure 2.1).

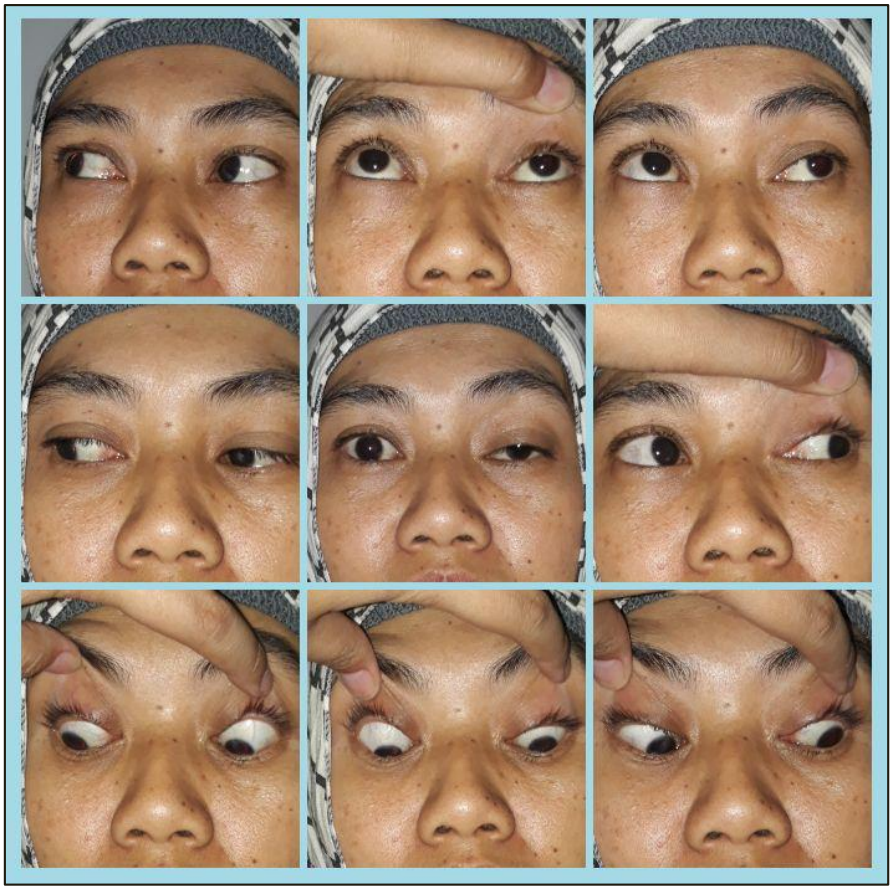
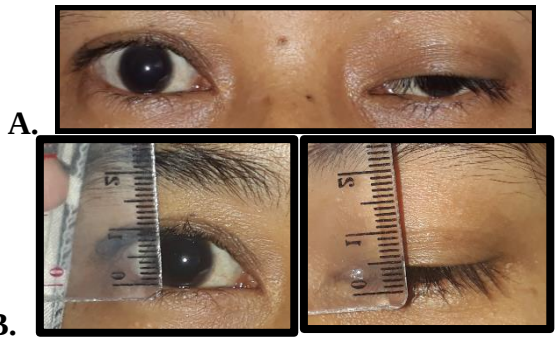


Figure 2.1 Nine-gaze position at first visit
Source : Cicendo Eye Hospital

Left eye showed ptosis (Figure 2.2 A and B) with margin reflex distance (MRD) 1 was 0 mm, MRD 2 was 5 mm, interpalpebral fissure (IPF) width was 5 mm, and levator function was 14 mm. Right eye was normal with MRD 1 was 5 mm, MRD 2 was 5 mm, IPF width was 10 mm, and levator function was 15 mm.



A.

B.

Figure 2.2 A Ptosis on the left eye. B. Margin Reflex Distance and Interpalpebral Fissure Measurement
Source : Neuroophthalmology Unit Cicendo Eye Hospital

Further examination regarding ptosis showed positive result of stare test (Figure 2,3A), cogan eyelid twitch, and orbicularis oculi muscle weakness on the left eye (Figure 2.3B). Ice pack test showed improvement of droppy eyelid (Figure 2.4). Interpalpebral fissure was 5 mm before the ice pack test and 9 mm (MRD 1: 4mm, MRD 2: 5 mm) after the test.

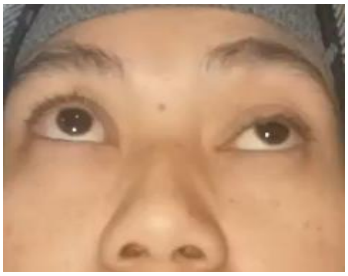
A.  B. 

Figure 2.3 A. The 2-minutes stare test showed worsening of droopy left eyelid. B. Positive orbicularis oculi weakness on the left eye (positive "peek sign")
Source : Neuroophtalmology Unit Cicendo Eye Hospital

Figure 2.4 Positive Ice pack test (improvement of left eye ptosis after 2-minutes application of ice pack)
Source : Neuroophthalmology Unit Cicendo Eye Hospital

Slit-lamp biomicroscopy examination of anterior segment on both eyes were within normal limit. There was no relative afferent pupillary defect. Funduscopy examination on both eyes within normal limit. Amsler grid examination, contrast sensitivity and color vision test were within normal limit.

Patient was diagnosed with left eye ocular myasthenia gravis. She was consulted to Neurology Department in Hasan Sadikin Hospital for prostigmin test and had

positive result. The patient was treated with oral pyridostigmine 3x60mg and artificial tears 4x1 drop on both eyes.

In one month follow up visit, patient showed improvement in ptosis. The interpalpebral fissure of both eyes were the same value which was 10 mm (MRD 1:5 mm, MRD 2:5 mm). No restriction in ocular motility of both eyes (Figure 2.5). Prognosis for this patient quo ad functionam is dubia ad bonam and quo ad vitam dubia.

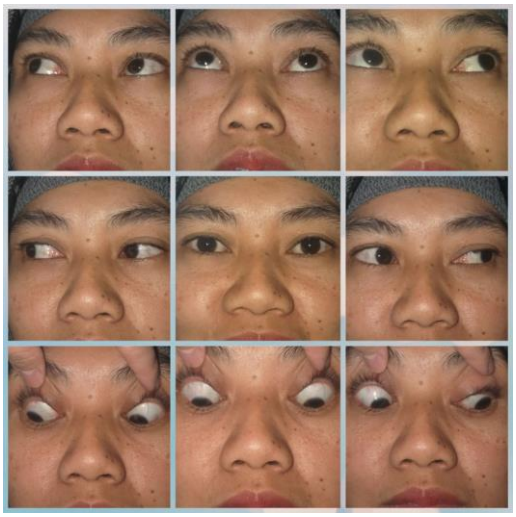


Figure 2.5 Nine-gaze position one month after oral Pyridostigmine was given, improvement in left eye ptosis was seen in primary position
Source : Neuroophthalmology Unit Cicendo Eye Hospital

III. Discussion

Myasthenia gravis is a potentially serious, but treatable autoimmune disease. Clinicians must aware that approximately 50% to 60% initial presentation of myasthenia gravis cases are limited to ocular symptomps which can mimic isolated cranial nerve palsies, gaze palsies, internuclear ophthalmoplegia, and chronic progressive external ophthalmoplegia (CPEO).[6,7]

In this patient all examination regarding ptosis in MG had positive results. The Cogan's lid twitch (CLT) is assessed by having the patient sustain downgaze and saccade back to neutral gaze. Studies had revealed varied results regarding the specificity and sensitivity of CLT in diagnosing the ocular MG. Previous studies assessing CLT revealed trends toward low sensitivity (50%–75%) and high specificity (91.7%–100%). However, Stavern et al prospective study showed the

presence of a lid twitch does not exclude the possibility of either a structural lesion or non-myasthenic disease such as CPEO or levator dehiscence. Thus the positive result of CLT must be accompanied by other MG tests as well.[7-9]

The orbicularis oculi function should be tested as bilateral orbicularis weakness may be encountered in Ocular MG and should not be expected in other causes of ophthalmoplegia. The patient is asked to forcefully close the eyelids. An ease to manually overcome the eyelid closure or presence of 'peek sign' (scleral exposure by fatigue induced opening of the eyelids) are both suggestive of orbicularis oculi weakness. Compared to CLT, the orbicularis oculi muscle weakness test is noninferior with regard to sensitivity and specificity. [9,10]

The ice test result may be positive in patients with negative edrophonium or anti-AChR-ab testing. A recent review of six studies in which the ice pack test was performed in 76 patients with MG and in 77 controls showed it to have a sensitivity of 89% and a specificity of 100% in these patients, suggesting that it may be useful as an adjunctive diagnostic test in patients with lid ptosis, particularly if the edrophonium test is contraindicated or not available.[10-12]

Edrophonium test is not routinely performed in eye clinics due to possible serious adverse effects which may occur from drug administration. An alternative to the edrophonium test which is more commonly used is the neostigmin methylsulfate test. Neostigmine have the capacity to combine with acetylcholinesterase and prevent the esterase from inactivating acetylcholine. In addition, neostigmine has a direct stimulating action on skeletal muscle. The patient showed positive result of Neostigmine test in which improvement of signs were seen within 30 minutes after drug administration. The sensitivity of Neostigmin test ranges from 70% to 94%. The positive result of prostigmine test combined with positive results in all ptosis examination regarding ocular Myasthenia Gravis are evident in establishing the diagnosis in this patient.[8,11,12]

The initial goal in the treatment of Ocular MG is to control the symptoms. Once this is achieved, therapy is aimed to reduce relapses and minimize drug-induced side effects. According to the International Consensus Guidance for Management of Myasthenia Gravis 2016, Pyridostigmine should be part of the initial treatment

in most patients with MG. Pyridostigmine dose should be adjusted as needed based on symptoms. It is typically started at a dose of 30 mg three to four times a day, and can be increased up to 150 mg four times a day if tolerated and needed. The ability to discontinue pyridostigmine can be an indicator that the patient has met treatment goals and may guide the tapering of the therapies. Corticosteroids or Immunosupressants (IS) therapy should be used in all patients with MG who have not met treatment goals after an adequate trial of pyridostigmine.[13,14]

Nonsteroidal IS agent should be used alone when corticosteroids are contraindicated. A nonsteroidal IS agent should be used initially in conjunction with corticosteroids when the risk of steroid side effects is significant regarding previous medical comorbidities. Nonsteroidal IS agents that can be used in MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. However there is widespread variation in practice in choices of IS agent since there is only limited literature comparing them.[13,14]

In addition when there is not enough evident on clinical assessments, more advanced diagnostic techniques such as serologic tests and electrophysiologic test (Repetitive nerve stimulation or single fiber Electromyography) may be recommended. The diagnosis of Ocular MG can be confirmed by seropositivity to the AChR antibodies or other proteins including antimuscle specific tyrosine kinase (MuSK) and LDL-related receptor protein 4 (LRP4). Elevated levels of AChR antibodies along with the clinical findings is highly specific for Ocular MG, however, only 50% of the patients with Ocular MG have detectable antibodies, which is significantly lower than in patients with generalized MG in which the rate of seropositivity exceeds 85–90%.[14,15]

Patients should also be screened for thymoma, since around 75 % of affected MG individuals have an abnormally large and overactive thymus. However the relationship between the thymus and the specific immune system malfunction that occurs in myasthenia gravis is not well understood.[15,16]

The prognosis in this patient quo ad functionam dubia ad bonam and vitam dubia. Isolated ocular MG may progress to generalization in a high percentage (50%–85%) of adults within 2 years of onset. Due to the risk of developing

respiratory distress and other life-threatening manifestations, it is necessary to manage the patient's care with assistance of neurologist. The subsequent 1–3 years from first intitial symptoms provide important prognostic information. If myasthenia gravis remains ocular for 1 year, the likelihood of progression is 16%, whereas if disease remains localized for 3 years, the likelihood of progression to generalized myasthenia gravis is only 6%. [15-17]

IV.Conclusion

Ocular Myasthenia Gravis can be a challenging diagnosis to make with certainty. Strong clinical suspicion as seen in positive results of stare test, orbicularis oculi weakness test, cogan eyelid twitch, and ice pack test accompanied by positive pharmacological test help confirming the diagnosis. Correct clinical assessment with prompt management are needed, as early disease recognition may offer better clinical improvement as well as better prognosis.

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