Leonid Skorin Jr, OD, DO

Testing for myasthenia gravis

Myasthenia gravis is an autoimmune disease which affects the neuromuscular junction. It is characterised by fatiguability, abnormal rapid exhaustion and loss of strength in muscles under voluntary control - particularly the ocular and facial muscles[1]. Symptoms increase over the course of the day and after exertion. Ptosis and extraocular muscle motility disturbances with diplopia are frequently the first indicators of myasthenia[2]. In 20-30% of patients, the condition remains confined to the region of the eyes, whereas 90% of patients with generalised myasthenia also have ocular involvement[3].

SIGNS AND SYMPTOMS

An accurate history will help point to the diagnosis of myasthenia gravis. Patients will complain of double vision, blurry vision and eyelid drooping, all of which seem to improve after rest. If the facial muscles are involved, the patient will have difficulty chewing, an abnormal smile or nasal speech. Weakness of the tongue and palatal muscles will cause dysphagia (difficulty in swallowing)[4]. Patients may present with symptoms, which either began abruptly or developed gradually over an extended period of time.

Unilateral or bilateral ptosis, which is often asymmetric, is the most common sign of ocular myasthenia gravis[5]. The ptosis can even shift from one eyelid to the other. Testing the eyelids for fatiguability can be done by asking the patient to open and close their lids several times or gaze upward for an extended time (Simpson test). Increased drooping is a sign of fatigue. The phenomenon of 'enhanced' ptosis can be demonstrated in patients with bilateral ptosis by elevating and maintaining the more ptotic eyelid in a fixed position[6]. The opposite eyelid slowly falls and may close completely. The lid-twitch sign is another way to test for fatiguability[7]. The patient is directed to look down for 10-15 seconds and then to refixate quickly in the primary position. Observation of an upward overshoot of the lid with several twitches, followed by repositioning of the lid to the original ptotic state, identifies the easy fatiguability and rapid recovery of the levator muscle.

Diplopia secondary to extraocular muscle involvement may occur separately or accompany eyelid ptosis and can be variable. Variability in measuring phorias and tropias during the same examination or on different examination days is highly suggestive of myasthenia. Extraocular muscle weakness can also mimic oculomotor nerve palsies, vertical or horizontal gaze palsies or even internuclear opthalmoplegia[8].

Orbicularis oculi muscle strength can be tested by having the patient forcefully close their eyes while the practitioner attempts to open the eyelids manually. In myasthenics, it will be relatively easy to open the eyelids[5]. The 'peek' sign occurs when the palpebral fissure widens after a period of voluntary eyelid closure[9]. This results from orbicularis oculi fatigue.

DIAGNOSTIC EVALUATION

Diagnostic pharmacologic evaluation is done with edrophonium chloride (Tensilon) (**Figure 1**). Tensilon is an anti-cholinesterase agent, which inactivates the enzyme acetylcholinesterase. This permits the accumulation of excessive amounts of acetylcholine causing prolonged neurotransmitter activity on the muscle fibre's specialised motor endplate. Tensilon is an ideal drug because it acts rapidly, usually within 30-60 seconds, and has a short duration of action of only about 10 minutes. Overall, Tensilon is relatively safe to administer to most patients, but it can cause severe adverse effects such as hypotension, bradycardia, cardiac arrest and respiratory distress. Because of these potential side-effects, Tensilon testing should be performed only if appropriate resuscitation equipment is available. The ideal testing protocol involves two examiners, one giving the injection and the other recording the results.

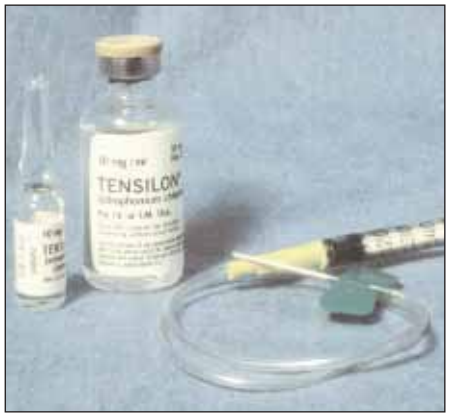

Figure 1
Edrophonium (Tensilon) with butterfly infusion set for intravenous administration

A mixture of 10mg per 1cc of Tensilon is used. A test dose of 0.2ml or 2mg is given intravenously and, after 60 seconds, another 0.4ml or 4mg is again administered. If there is no definitive clinical improvement, the remaining 0.4ml or 4mg is administered until a total of 1ml or 10mg has been given[4].

In ocular myasthenia without systemic manifestations, up to 95% of patients will have a positive Tensilon test[10] **(Figures 2 and 3)**. A negative test does not exclude myasthenia and, occasionally, there is paradoxical worsening or false positives[4].

Another test which can be tried in the practice, particularly if ptosis is the

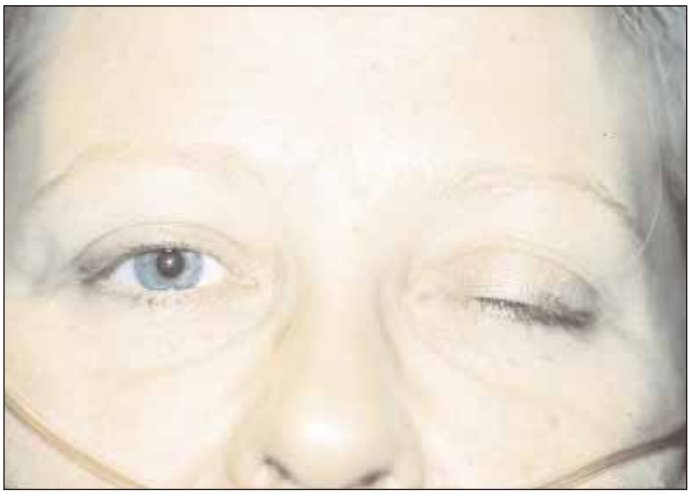

Figure 2
Left eyelid ptosis pre-Tensilon

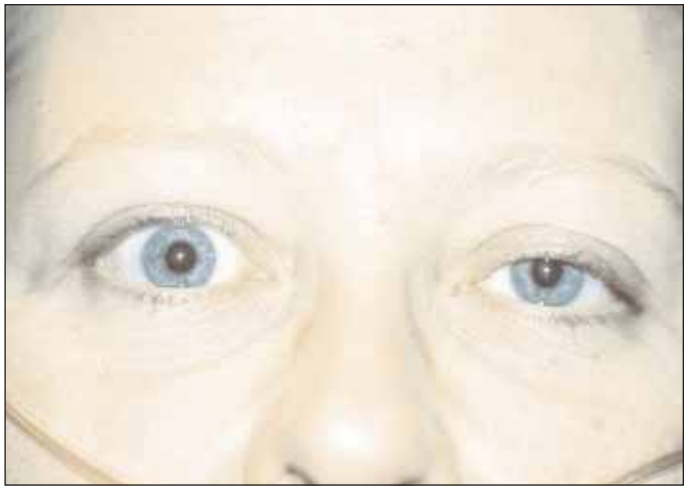

Figure 3
Left eyelid ptosis improved after Tensilon injection

main presenting clinical sign, is the ice-pack test[11]. The ice-pack is applied to the affected eyelid for about two minutes and the eyelid is observed to see if the drooping improves. Improvement may occur in myasthenics since neuromuscular transmission improves at lower temperatures. The ice-pack test can be combined with the sleep test, which is done by asking the patient to rest with their eyes closed for 30 minutes in the practice and then observed immediately upon awakening for symptom improvement[12].

REFERRAL

The patient should be referred to the neurologist for electromyographic testing and to the laboratory for serologic evaluation. About 90% of individuals with generalised myasthenia, and almost 70% of patients with only ocular symptoms, will have circulating antibodies to acetylcholine receptors on serologic evaluation[13,14].

Serologic tests for thyroid disease should be ordered since there appears to be an association between dysthyroidism and myasthenia gravis in up to 9% of males and 18% of females[5].

All patients suspected of having myasthenia gravis also need a computed tomography (CT) scan of the chest and anterior mediastinum. Up to 20% of patients with myasthenia will have a tumour of the thymus called a thymoma, of which half will be malignant[1].

For treatment, refer these patients to a physician comfortable with the complications of the disease and therapy, usually a neurologist or neuro-ophthalmologist. Treatment options include anti-cholinesterases, steroids and other immunosuppressants, plasmapheresis, intravenous immunoglobulin and thymectomy. Local treatment measures include lid crutches and tape, occlusion. For long-standing, fixed deficits, prisms and ptosis or strabismus surgery can help[15].

ABOUT THE AUTHOR

Leonid Skorin is in private practice in Dixon, Illinois, and is an Assistant Professor of Ophthalmology at the University of Illinois Eye and Ear Infirmary and the Chicago College of Osteopathic Medicine. He has lectured internationally and contributed to over 60 medical and optometric publications. He is co-editor and co-author of 'Ocular Therapeutics Handbook: A Clinical Manual'.

In future issues of *Optometry Today*, Dr Skorin will look at toxoplasmosis, optic disc pits and intracranial hypertension.

REFERENCES

1. Newman, N.M. (1992) 'Neuro-Ophthalmology - A Practical Text'. Nowalk, C.T., Appleton & Lange, pp. 210-212.
2. Fechner, P.U., Teichmann, K.D. (1998) 'Ocular Therapeutics - Pharmacology and Clinical Application'. Thorofare, N.J., SLACK, Inc., pp. 568-569.
3. Sommer, N., Melms, A., Weller, M., Dichgans, J. (1993) "Ocular myasthenia gravis". Documenta Ophthalmalogica 84: 309-333.
4. Skorin, L. (1998) "Neuro-ophthalmic disease". In Onofrey, B.E., Skorin, L., Holdeman, N.R., 'Ocular Therapeutics Handbook - A Clinical Manual'. Philadelphia, Lippincott-Raven, pp. 536-539.
5. Skorin, L. (1991) "Myasthenia gravis". In Onofrey, B.E. 'Clinical Optometric Pharmacology and Therapeutics'. Philadelphia, J.B. Lippincott Co., Chapter 20, pp. 1-17.
6. Gorelick, P.B., Rosenberg, M., Pagano, R.J. (1981) "Enhanced ptosis in myasthenia gravis". Arch. Neurol. 31: 531.
7. Cogan, D.G. (1965) "Myasthenia gravis: a review of the disease and a description of lid twitch as a characteristic sign". Arch. Ophthalmol. 74: 217-221.
8. Alexander, L.J., Skorin, L., Bartlett, J.D. (1995) "Neuro-ophthalmic disorders". In Bartlett, J.D., Jaanus, S.D. 'Clinical Ocular Pharmacology'. Boston, Butterworth-Heinemann, 3rd ed, Chapter 23, pp. 531-535.
9. Osher, R.H., Griggs, R.C. (1979) "Orbicularis fatigue: The 'peek' sign of myasthenia gravis". Arch. Ophthalmol. 97: 678.
10. Evoli, A., Tonali, P., Bartoccioni, E. et al (1988) "Ocular myasthenia: diagnostic and therapeutic problems". Acta. Neurol. Scand. 77: 31-35.
11. Sethi, K.D., Rivner, M.H., Swift, T.R. (1987) "Ice pack test for myasthenia gravis". Neurology 37: 1383-1385.
12. Freidman, D.I. (1998) "Myasthenia gravis". Audio-Digest Ophthalmol 36: Side A.
13. Vincent, A., Newsom-Davis, J. (1982) "Acetylcholine receptor antibody characteristics in myasthenia gravis I. Patients with generalized myasthenia or disease restricted to ocular muscles". Clin. Exp. Immunol. 49: 257-265.
14. Vincent, A., Newsom-Davis, J. (1985) "Acetylcholine receptor antibody as a diagnostic test for myasthenia gravis: results of 153 validated cases and 2,967 diagnostic assays". J. Neurosurg. Psychiatry 48: 1246-1252.
15. Moster, M.L. (1998) "Diplopia diagnosis made easier". Rev. Ophthalmol. 5: 22-36.