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Ocular Manifestations of Myasthenia Gravis

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1. Introduction

Myasthenia Gravis (MG) is presently an incurable antibody-mediated autoimmune disorder characterized by generalized voluntary skeletal muscle weakness. Literally translated from its Latin and Greek etymological roots, myasthenia gravis means, “grave muscle weakness.” The cause of the weakness is due to a defect at the level of the neuromuscular junction in which autoimmune antibodies block the receptors responsible for initiating muscular contraction. The neurotransmitter that is subject to this competitive inhibition is acetylcholine (ACh). The muscles commonly affected include those of the neck, limbs and chest cavity with regards to breathing. The muscles of the eye, including those responsible for eye movements, as well as those involved with swallowing, chewing, and speaking, are most notably affected. Muscle weaknesses involving the eye produce symptoms of blurred vision, variable diplopia, and ptosis. Colavito et al. noted that nonstriated ocular muscles can also be involved in MG. They cautioned that when patients with myasthenia present with complaints of asthenopia and blur, resulting from accommodative dysfunction and vergence insufficiency, the underlying systemic disease process may be missed. Ptosis is defined as an abnormal eyelid “drooping” beyond the normal 1-2 mm of the upper limbus of the cornea.

Since the process in which the muscular weakness manifests is a result of competitive inhibition, the weakness observed is transient and improves with periods of rest. Likewise, muscular weakness increases during periods of increased or prolonged physical activity.

Even though MG is an antibody-mediated autoimmune disease, a reported 15% of patients with systemic or generalized MG have no detectable antibodies to acetylcholine receptors (i.e., they have “seronegative” MG). Seronegative MG is common in children; 40% of cases present before the age of 10 years.

It is estimated that 85-90% of all reported MG cases, whether seropositive or seronegative, present with ocular symptoms. Additionally, it has been reported that 20-50% of all cases of MG are purely ocular. Ocular myasthenia is considered a distinct diagnosis from generalized MG. Although there is evidence of ocular MG progressing to generalized MG, it has been reported that those with purely ocular symptoms for a period of 1-3 years have a greatly reduced chance of progressing on to generalized MG. Furthermore, a reported estimate of 55% of all cases of ocular MG are seropositive.
Two reasons have been suggested to explain the high proportion of MG cases that present with ophthalmic manifestations. The first is the susceptibility of ocular muscles to the disease process. The second reason is that ocular involvement in MG is relatively easy to recognize compared to that of other muscle groups. The exact reasoning why is unknown, but the following four reasons are hypothesized to contribute in part or in whole: First, even the slightest extraocular muscle (EOM) weakness will sufficiently misalign the visual axis to produce symptoms of diplopia. This is in contrast to an affected muscle in a limb, where an individual would not notice minute reductions in muscle-generated forces most likely.

Moreover, the ocular motor system relies primarily on visual feedback, not so much on proprioceptive mechanisms, thereby making its ability to adapt swiftly to asymmetric or variable weakness more limited compared to an extremity muscle. Second, the high firing frequencies of ocular motor neurons might contribute to neuromuscular transmission fatigue. No other motor neuron in the body exhibits the rate of firing frequency of the ocular motor neurons. It is estimated ocular motor neurons fire at a frequency exceeding up to 600 Hz during saccades. Motor neurons found elsewhere in the body rarely exceed a firing frequency of 100 Hz. Therefore, any disruption in the ability of these ocular neurons to maintain a high firing rate would cause a decrease in effectiveness and appropriate output. Myasthenia gravis produces this kind of disruption. Third, several anatomic and physiologic properties of EOM fibers make them more susceptible to neuromuscular transmission blockade. EOM nerve fibers possess anatomical characteristics that possibly make them more susceptible to neuromuscular transmission block. The fibers of the EOMs have less prominent synaptic folds, and the conclusion is drawn that there are fewer ACh receptors and sodium channels on the postsynaptic membrane. Much has been previously documented in that the mean quantal content (in other words, the average number of vesicles released during a synaptic event) of ocular motor neurons is lower than motor neurons innervating other muscles. Fourth is the preferential immunologic targeting of EOM synapses. This theory remains purely speculative, but it has been observed that the sera from some MG patients bind only to multi-innervated fibers’ synapses, and the use of EOM as a source of ACh receptors for ACh antibody assays leads to higher rates of autoantibody detection, which suggests that EOMs have unique antigenic targets.

Treatment for systemic or generalized MG includes a wide variety of options, but remains primarily systemic medication. First line therapy typically consists of an acetylcholinesterase inhibitor like pyridostigmine bromide (Mestinon). Although it must be noted that pyridostigmine bromide has rather variable results in pure OMG with an approximate effectiveness ratio of 1 to 2. Another option is immunosuppressant therapy such as prednisolone, cyclosporine, azathioprine, methotrexate and mycophenolate mofetil (Cellcept). Yet again, it must be noted with regards to pure OMG, it is suggested there is not sufficient evidence to warrant the routine use of immunosuppressant therapy (i.e. corticosteroids). More drastic measures attempted in the past include systemic oral medications, plasmapheresis (a.k.a. plasma exchange) and IVIG injections. Plasmapheresis is the removal of antibodies from the blood. An IVIG injection is a sterile solution of plasma proteins containing IgG antibodies from pooled human plasma. Although the mechanism of action is unknown, it is thought to down-regulate the production of antibodies. The preparation contains no less than 90% immunoglobulin consisting of all the IgG substances and trace amount of IgA and IgM. However, this treatment is usually reserved for patients...
demonstrating dysphagia with an associated high risk of aspiration and those who are unable to ambulate without assistance. Although slower-acting than plama exchange, the response is similar and offers advantages when therapeutic plasmaphesis is not available or when vascular access is problematic. Significant improvement is seen in patients whose therapy consist of an initial dose of 400 mg/kg/d for 5 days and followed by maintenance with 400 mg/kg once monthly. Furthermore, it has been noted that with regards to a similarly treated disease, Guillain-Epstein Barr Syndrome, IVIG treatment in many ways is considered to be the more effective successor to plasmapheresis.

Thymectomy, the surgical removal of the thymus gland, is also an effective and accepted treatment for generalized MG; however, while effective, it is controversial as a treatment measure in pure OMG. Recent theories suggest thymectomies could be performed on early presentations of OMG to prevent and/or slow the disease progression and immunosuppressive therapy only if proven necessary. Thymectomies are often performed on young individuals in the early stages of MG regardless of the presence of a tumor. As related to generalized MG and post-surgical improvement, it has been shown both the grade of follicular hyperplasia and density of T-cell subsets in the middle part of the thymus (space between the superior and inferior horns) had a significant correlation with the level of improvement of MG after thymectomy.

Additionally, if there is found to be thyroid involvement, a throidectomy is a viable treatment option.

Treatment for ocular MG specifically may include all the aforementioned options because a report 50-60% of individuals who present with purely ocular MG will eventually progress and develop generalize MG. Nevertheless, ocular MG treatments consist of both surgical and non-surgical treatments. Surgical options for myogenic ptosis are ptosis repair surgery, blepharoplasty, and frontalis suspension for which a Tutoplast sling can be utilized, external levator advancement, and tarsomyectomy. A non-surgical option is Botulinum Toxin Type A (Botox) injection to temporarily treat myogenic ptosis.

The first line of treatment should be a refrac tion in order to achieve the patient’s best corrected visual acuity (BCVA). Assessment of accommodation and vergence testing should also be considered. As for diplopia, standard treatments such as occlusion and prisms are commonly employed. However, with prisms, the practitioner must keep in mind the variability of the disease’s manifestations, thereby making it possible for the angle of deviation to fluctuate.

2. References

Rowland R, Sparr S. Head-drop and shortness of breath as a presentation of myasthenia gravis. J Am Geriatr Soc 2007;55(4):S116
Palace J, Vincnet A, Beeson D. Myasthenia gravis: diagnostic and management dilemmas. Current Opinion in Neurology 2001;14:583-589
Homel P, Kupersmith M. Development of Generalized Myasthenia Gravis in Patinet With Ocular Myasthenia Gravis. Arch Neurol 2003; 60(10):1491-1492
Hilton-Jones D, Palace J. The management of myasthenia gravis. Practical Neurology 2005;5:18-27
A Look into Myasthenia Gravis

http://www.ninds.nih.gov/disorders/myasthenia_gravis/myasthenia_gravis.htm

Golnik K. How to Diagnose and Treat Myasthenia Gravis. Review of Ophthalmology. 2002;9(10):219.

Ubogu E, Kaminski H. The Preferential Involvement of Extraocular Muscle by Myasthenia Gravis. Neuro-ophthalmology. 2001;25(4):219-228

Colavito J, Cooper J, Ciuffreda K. Non-ptotic ocular myasthenia gravis: a common presentation of an uncommon disease. Optometry. 76(7): 363-375.

Cameron R, Loehrer P, Thomas C. Thymic Neoplasms; Neoplasms of the Mediastinum. Principles & Practice of Oncology 7th Edition. Chapter 28. Lippincott Williams & Wilkins. 2005.

Donati F, Bevan D. Neuromuscular Blocking Agents. Clinical Anesthesia 5th Edition. Chapter 16. Lippincott Williams & Wilkins. 2006.

Toyka K. Ptosis in myasthenia gravis: Extended fatigue and recovery bedside test. Neurology 2006;67(8):1524

Reddy A, Backhouse O. "Ice-on-eyes", a simple test for myasthenia gravis presenting with ocular symptoms. Practical Neurology 2007;7(2):109-111

Benatar M, Kaminski H. Evidence report: The medical treatment of ocular myasthenia (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2007;68(24):2144-2149

Rudnicky S. Lamber-Eaton Myasthenic Syndrome with Pure Ocular Weakness. Neurology 2007;68(21):1863-1864

Lapido T. Eyelid Crutches for Ptosis: A Forgotten Solution. Plastic and Reconstructive Surgery. October 2000. 106(5): 1213-1214.

Scherer K, Bedlack R, Simel D. Does This Patient Have Myasthenia Gravis?. JAMA 2005;293(15):1906-1914

Morris O, O'day J. Fatiguable Ptosis and Pseudoretraction Caused by Myasthenia Gravis. Clinical and Experimental Ophthalmology. 2004; 32:303-304

Shaw J. When Muscles Falter: Update on Myasthenia Gravis. Clinical Update: Neuro-ophthalmology; http://www.aao.org/publications/eyenet/200607/neuro.cfm. 2006

Golnik K, Pena R, Lee A, Eggenberger R. An Ice Test for the Diagnosis of Myasthenia Gravis. Ophthalmology. 1999; 106(7): 1282-1286

Kennard C. Examine eye movements. Practical Neurology 2007;7:326-330 Tomelleri G, Vattemi G, Filosto M, Tonin P. Eyelid ptosis from sympathetic nerve dysfunction mistaken as myopathy: a simple test to identify this condition. J Neurol Neurosurg Psychiatry 2007;78(6):632-634

Chan J, Orrison W. Ocular Myasthenia: A Rare Presentation with MuSK Antibody and Bilateral Extraocular Muscle Atrophy. Br. J. Ophthalmol. 2007;91:842-843

Kubis C, Danesh-Meyer H, Savino P, Sergott R. The Ice Test versus the Rest Test in Myasthenia Gravis. Ophthalmology. 2000;107(11): 1995-1998

Gilbert M, De Sousa E, Savino P, Peter J. Ocular Myasthenia Gravis Treatment: The Case Against Prednisone Therapy and Thymectomy. Archives of Neurology. December 2007. 64(12): 1790-1792.

Chavis P, Stickler D, Walker A. Immunosuppressive or Surgical Treatment for Ocular Myasthenia Gravis. Archives of Neurology. December 2007. 64(12): 1792-1794.
Kupersmith M, Latkany R, Homel P. Development of Generalized Disease at 2 Years in Patients With Ocular Myasthenia Gravis. Archives of Neurology. February 2003. 60(2): 243-248.

Kaminski H, Daroff R. Treatment of Ocular Myasthenia: Steroids Only When Compelled. Archives of Neurology. May 2000. 57(5): 752-753

Bennett D, Mills K, Riordan-Eva P, Barnes P, Rose M. Anti-MuSK antibodies in a case of ocular myasthenia gravis. Journal of Neurology, Neurosurgery, & Psychiatry. April 2006. 77(4): 564-565.

Caress J, Hunt C, Batish S. Anti-MuSK Myasthenia Gravis Presenting With Purely Ocular Findings. Archives of Neurology. June 2005. 62(6): 1002-1003.

Elrod RD, Weinberg DA. Ocular myasthenia gravis. Ophthalmol Clin North Am 2004 Sep;17(3):275-309.

Sommer N, Sigg B, Melms A, Weller M, Schepelmann K, Herzau V, Dichgans J. Ocular myasthenia gravis: response to long term immunosuppressive treatment. J Neurol Neurosurg Psychiatry 1997;62(2):156-162

Howard J. Intravenous Immunoglobulin for the Treatment of Acquired Myasthenia Gravis. Neurology. December 1998. 51(6) Supplement 5: S50-S56.

http://www.umdnycpic.com/cgi-bin/bookmgr/bookmgr.exe/BOOKS/D971-2A/FRONT

Hilkevich O, Drory V, Chapman J, Korczyn A. The Use of Intravenous Immunoglobulin as Maintenance Therapy in Myasthenia Gravis. Clinical Neuropharmacology. May/June 2001. 24(3): 173-176.

Mechef Schmitz P. A Randomized Trial Comparing Intravenous Immune Globulin and Plasma Exchange in Guillain-Barre Syndrome. Dutch Guillain-Barre Study Group. The New England Journal of Medicine. 1992(17); 326:1123-1129.

Roberts P, Venuta F, Rendina E, De Giacomo T, Coloni G, Follette D, Richman D, Benfield J. Thymectomy in the treatment of ocular myasthenia gravis. The Journal of Thoracic and Cardiovascular Surgery. September 2001. 122(3): 562-568.

Lauriola L, Ranelletti F, Maggiano N, Guerriero M, Punzi C, Marsili F, Bartocci E, Evoli A. Thymus changes in anti-MuSK-positive and -negative myasthenia gravis. Neurology. 8 February 2005. 64(3): 536-538.

Agius M. Treatment of Ocular Myasthenia With Corticosteroids: Yes. Archives of Neurology. May 2000. 57(4): 750-751.

Mori T, Nomori H, Ikeda K, Kobayashi H, Iwatani K, Kobayashi T. The distribution of parenchyma, follicles, and lymphocyte subsets in thymus of patients with myasthenia gravis, with special reference to remission after thymectomy. The Journal of Thoracic and Cardiovascular Surgery. February 2007. 133(2): 364-368.

Periman L, Sires B. Floppy Eyelid Syndrome: A Modified Surgical Technique. Ophthalmic Plastic and Reconstructive Surgery 2002;18(5):370-372Sakol P, Mannor G, Massaro B. Congenital and acquired blepharoptosis. Current Opinion in Ophthalmology 1999;10:335-339Lauriola L, Ranelletti F, Maggiano N, Guerriero M, Punzi C, Marsili F, Bartocci E, Evoli A. Thymus changes in anti-MuSK-positive and -negative myasthenia gravis. Neurology. 8 February 2005. 64(3): 536-538.

Shields M, Putterman A. Blepharoptosis correction. Current Opinion in Otolaryngology & Head and Neck Surgery 2003;11(4):261-266

Sakol P, Mannor G, Massaro B. Congenital and acquired blepharoptosis. Current Opinion in Ophthalmology 1999;10:335-339

www.intechopen.com
Eliasoph I. RE: “Surgical Correction of Blepharoptosis in Patients with Myasthenia Gravis”. Opthal Plast Reconstr Surg 2002;18(4): 312-313
McCord C, Seify H, Codner M. Transblepharoplasty Ptosis Repair: Three-Step Technique. Plastic and Reconstructive Surgery 2007;120(4):1037-1044
Seider N, Beiran I, Kaltreider S. One medial triangular Tutoplast sling as a frontalis suspension for adult myogenic blepharoptosis. Acta Ophthalmologica Scandinavica 2006;84:121-123
Wong, V, Beckingsale P, Olley C, Sullivan T. Management of Myogenic Ptosis. Ophthalmology. 2002;109(5): 1023-1031
Bernardini F, Concillis C, Devoto M. Frontalis Suspension Sling using a Silicone Rod in Patients affected by Myogenic Blepharoptosis. Orbit. 2002; 21(3): 195-198
Gausas R, Goldstein S. Ptosis in the Elderly Patient. Int Ophthamol Clin 2002;42(2):61-74
Bradley E, Bartley G, Chapman K, Waller R. Surgical Correction of Blepharoptosis in Patients With Myasthenia Gravis. Ophthalmic Plastic and Reconstructive Surgery. March 2001. 17(2): 103-110.
Morris O, O’Day J. Strabismus Surgery in the Management of Diplopia caused by Myasthenia Gravis. Br. J. Ophthalmol. 2004; 88: 832-850
Takagi S, Hosokawa K, Yano K, Kunihiro N, Tateki K. Crutches Glasses For Blepharoptosis. Plastic and Reconstructive Surgery. June 2002. 109(7): 2605
Frueh BR. The mechanistic classification of ptosis. *Ophthalmol* 1980; 87(10):1019-21.
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