Biosc.Biotech.Res.Comm. Special Issue Vol 14 No 06 (2021) Pp-52-54

BBRC
Bioscience Biotechnology Research Communications

Myasthenia Gravis: And Updated Review

Arya Dahane[1], Ranjit S. Ambad[2] and Swarupa Chakole[3]
[1]MBBS student atDatta Meghe Medical College, Wanadongri, Nagpur, India
[2]Department of Biochemistry Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre, Nagpur, India
[3]Dept. of Community Medicine Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences Sawangi (Meghe), Wardha
Corresponding author email: abad.sawan@gmail.com

ABSTRACT
This article aims to discuss an autoimmune disorder of postsynaptic membrane where auto-antibodies are deposited at neuromuscular junction (NMJ) against ACh receptor (AChR) named MG.Discussing normal neuromuscular transmission .Alongwith (EAMG) Experimental autoimmune myasthenia gravis in which rabbits were immunised with AChR shows an allergic reaction to muscle AChR which usually occurs in MG patients. Furthermore, prognosis of specific antibodies namely AChR-Ab, MuSK-Ab, LRP4-Ab is discuss with clinically recommended tests. And ending with thymoma in MG patients and discussing necessity for thymus imaging of MG patients.

KEY WORDS: MYASTHENIA GRAVIS, AUTO-ANTIBODIES , NEUROMUSCULAR JUNCTION, EXPERIMENTAL AUTOIMMUNE MG, ACHR, MUSK, LRP4, THYMOMA.

INTRODUCTION

Myasthenia gravis is an autoimmune disorder of postsynaptic membrane where auto-antibodies are deposited at neuromuscular junction (NMJ) against ACh receptor (AChR). The clinical signature of MG is fluctuating fatigability which gets worsen with exertion and improves with rest, weakness affecting bulbar, ocular and proximal limb skeletal group of muscles (Rousseff, 2021; Melzer et al., 2016). It was found that animals immunized with acetylcholine receptors purified from electric organs of *Electrophorus electricus* or *Torpedo californica* demonstrate remarkable resemblance with patients of MG (Mantegazza et al., 2016).

Beside such animal experiments the search for other pathogenic antigens were also conducted which leads to detection of antibodies against muscle specific tyrosine kinase (MuSK) and low- density lipoprotein-releated protein 4 (Lrp4). Both of which causes pre and post synaptic deformities. Alongwith this Agrin was also detected as fourth pathogen (Masaharu et al, 2020).

DISCUSSION

Neuromuscular Transmission: The action potential reaching to axonal end, depolarizes it which leads to opening of voltage gated calcium channels. The influx of calcium ions triggers release of acetylcholine (Ach) in synaptic cleft which then attatches to acetylcholine receptors (AChR), which are present on the crest of post-synaptic membrane, depolarizing it and thus further creating end plate potential (EPP). Which then spreads over sarcolemma generating muscle action potential, leading to initiation of reactions muscular contration (For detailed information you can refer{6}). Then ACh is hydrolysed by enzyme named acetylcholinesterase (AChE) into it'sconstitutive which are taken up back by pre-synaptic membrane for resynthesis of Ach (Martyn 2009).

Biosc Biotech Res Comm P-ISSN: 0974-6455 E-ISSN: 2321-4007

Identifiers and Pagination
Year: 2021 Vol: 14 No (6) Special Issue
Pages: 52-54

Article Information
Received: 24th March 2021
Accepted after revision: 29th May 2021

DOI: http://dx.doi.org/10.21786/bbrc/14.6.12

Beside this for regulation of ACh at end plate,there is release of Argin protein which activates enzyme muscle-specific tyrosine kinase(MuSK) In complex with low-density lipoprotein-releated protein 4(Lrp4) This is how normal NMJ works.

Experimental Autoimmune MG: Rabbits immunised with AChR isolated from the Electrophorus electricus electric organ acquired MG-like symptoms, according to the first article on an experimental form of MG released more than 35 years ago. Many animal tests later demonstrated that an allergic reaction to muscle AChR occurs in MG patients, and that anti-AChR antibodies are responsible for the structural and functional changes (Lindstrom, 1980).

Clinical evaluation of EAMG symptoms

Clinical score	Symptoms
Grade 0	Normal power and no fatigability
Grade 1	Mildly reduced movement and shaky grip
Grade 2	Clinical symptoms present prior to exercise
Grade 3	Severe healh symptoms at rest, no grip and state of moribundity
Grade 4	Fatal

Abbreviation: EAMG, experimental autoimmune myasthenia gravis.

Antibodies Inmg Prognosis: Detecting proven pathogenic antibodies against certain synaptic molecules in a patient with standard clinical features is almost diagnostic of MG and aids in the classification of disease types and subtypes (Jayam et al, 2012). Assays are readily obtainable for inspection of AChR-Ab , MuSK-Ab , Lrp-4-Ab which are found causative in MG patients (Hoch et al, 2001; Osamu, 2011). While some antibodies found use ful in detection of MG-thymoma. Where patient develop tumors in thymus gland which is usually difficult to recognize.Some patients were detected with absence of AChR-Ab those were classified under “seronegative MG” group.

Antibodies Inmg Prognosis: Detecting proven pathogenic antibodies against certain synaptic molecules in a patient with standard clinical features is almost diagnostic of MG and aids in the classification of disease types and subtypes (Jayam et al, 2012). Assays are readily obtainable for inspection of AChR-Ab, MuSK-Ab, Lrp-4-Ab which are found causative in MG patients (Hoch et al, 2001; Osamu, 2011). While some antibodies found use ful in detection of MG-thymoma. Where patient develop tumors in thymus gland which is usually difficult to recognize.Some patients were detected with absence of AChR-Ab those were classified under “seronegative MG” group.

MuSK autoantibodies, the postsynaptic receptor for agrin, were discovered to be the cause of “seronegative MG” in a large number of patients in 2001. Soon MuSK-MG was detected as notably different from AChR-Ab –MG so discovered new subtype.{13,14} 6-8% MuSK antibodies are found in all types MG cases. Those can be detected by RIPA by using radiolabel antigen 125I MuSK (domain extracellular) (Cao et al., 2020). Elisa kits are available but are not extremely used MuSK-Ab was observed by CBA (Cell Based Assay) in patients who were RIPA negative for both AChR-Ab and MuSK-Ab. Since some of them had unidentified IgM MuSK-Ab, an IgG-specific CBA for MuSK-MG was created .{15}.

Antibodies TO ANTI-LRP4: Argin signaling is mediated to MuSK via lipoprotein receptor releated protein (LRP-4). Their anibodies can be detected by RIPA, ELISA CBA methods. LRP4-Ab is also used in up to 23% of ALS (Amyotrophic lateral sclerosis) patients, a proportion of patients with other neuroimmune conditions, and up to 20% of MuSK-MG patients (as defined by serological and clinical criteria). It’s not directly diagnostic and thus it must be understood solely in the sense of clinical practice (Huda et al., 2017; Zisimopoulou et al., 2013).

Thymus Imaging: Thymoma (i.e. tumors in thymus gland)can be seen in up to 15% of MG patients, with the majority having detectable AChR-Ab. Imaging of thymus is strictly recommended in all confirmed or suspected MG patients and all patients with thymoma, on the other hand, should be tested for MG since up to one-third of them experience the condition.CT, PET, MRI and radioisotopic methods can be used for diagnosis but CT is most favoured (Melzer et al., 2016).

CONCLUSION

MG an autoimmune disorder of NMJ is specified with having antibodies against ACh-R ,with variations thus making it’s different subtypes namely AChR-MG,MuSK-MG ,LRP4-MG. RIPA ,CBA ,FIPA are some of assays usually used to detect presence of particular Ab . Patients with any type of MG have following symptoms-

Drooping eyelid
Blurred vision
Slurred speech
Weakness in the arms and legs
Difficulty chewing or swallowing
Difficulty breathing

Moreover, thymoma is generally seen in MG patients and vice-versa. Thus making thymus-imaging mandatory in MG suspected patients.

REFERENCES

Cao, M., Koneczny, I. and Vincent, A., 2020. Myasthenia gravis with antibodies against muscle specific kinase: an update on clinical features, pathophysiology and treatment. Frontiers in molecular neuroscience, 13, p.159.

Hoch, W., McConville, J., Helms, S., Newsom-Davis, J., Melms, A. and Vincent, A., 2001. Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. *Nature medicine*, 7(3), pp.365-368.

Huda, S., Waters, P., Woodhall, M., Leite, M.I., Jacobson, L., De Rosa, A., Maestri, M., Ricciardi, R., Heckmann, J.M., Maniaol, A. and Evoli, A., 2017. IgG-specific cell-based assay detects potentially pathogenic MuSK-Abs in seronegative MG. Neurology-*Neuroimmunology* Neuroinflammation, 4(4).

Jayam Trouth, A., Dabi, A., Solieman, N., Kurukumbi, M. and Kalyanam, J., 2012. Myasthenia gravis: a review. Autoimmune diseases, 2012.

Latchoumi, T.P., Ezhilarasi, T.P. and Balamurugan, K., 2019. Bio-inspired weighed quantum particle swarm optimization and smooth support vector machine ensembles for identification of abnormalities in medical data. SN Applied Sciences, 1(10), pp.1-10.

Lazaridis, K. and Tzartos, S.J., 2020. Autoantibody specificities in myasthenia gravis; implications for improved diagnostics and therapeutics. Frontiers in immunology, 11, p.212.

Lindstrom J 1980. Experimental autoimmune myasthenia gravis. J Neurol Neurosurg Psychiatry;43(7):568-576. doi:10.1136/jnnp.43.7.568

Mantegazza, R., Cordiglieri, C., Consonni, A. and Baggi, F., 2016. Animal models of myasthenia gravis: utility and limitations. International journal of general medicine, 9, p.53.

Martyn, J.A.J., Fagerlund, M.J. and Eriksson, L.I., 2009. Basic principles of neuromuscular transmission. *Anaesthesia*, 64, pp.1-9.

Melzer, N., Ruck, T., Fuhr, P., Gold, R., Hohlfeld, R., Marx, A., Melms, A., Tackenberg, B., Schalke, B., Schneider-Gold, C. and Zimprich, F., 2016. Clinical features, pathogenesis, and treatment of myasthenia gravis: a supplement to the Guidelines of the German Neurological Society. Journal of neurology, 263(8), pp.1473-1494.

Melzer, N., Ruck, T., Fuhr, P., Gold, R., Hohlfeld, R., Marx, A., Melms, A., Tackenberg, B., Schalke, B., Schneider-Gold, C. and Zimprich, F., 2016. Clinical features, pathogenesis, and treatment of myasthenia gravis: a supplement to the Guidelines of the German Neurological Society. Journal of neurology, 263(8), pp.1473-1494.

Osamu Higuchi,, Hamuro, J., Motomura, M. and Yamanashi, Y., 2011. Autoantibodies to low-density lipoprotein receptor–related protein 4 in myasthenia gravis. *Annals* of neurology, 69(2), pp.418-422.

Rodolico C, Meireles, J. and Massano, J., 2012. Cognitive impairment and dementia in Parkinson's disease: clinical features, diagnosis, and management. Frontiers in neurology, 3, p.88.

Rousseff, R.T., 2021. Diagnosis of Myasthenia Gravis. Journal of clinical medicine, 10(8), p.1736.

Takamori, M., 2020. Myasthenia gravis: from the viewpoint of pathogenicity focusing on acetylcholine receptor clustering, trans-synaptic homeostasis and synaptic stability. Frontiers in molecular neuroscience, 13.

Trakas, N. and Tzartos, S.J., 2018. Immunostick ELISA for rapid and easy diagnosis of myasthenia gravis. Journal of immunological methods, 460, pp.107-112.

Zisimopoulou, P., Evangelakou, P., Tzartos, J., Lazaridis, K., Zouvelou, V., Mantegazza, R., Antozzi, C., Andreetta, F., Evoli, A., Deymeer, F. and Saruhan-Direskeneli, G., 2014. A comprehensive analysis of the epidemiology and clinical characteristics of anti-LRP4 in myasthenia gravis. Journal of autoimmunity, 52, pp.139-145.