ORIGINAL ARTICLE

Relationship of Myasthenia Gravis with Thymic Pathology

AAMIR MAHMOOD IJAZ.[1]; SYED M. NAQVI[1], RAZA IQBAL[1], *H. DOGAR*[2]

ABSTRACT

Aim: To study the relationship of Myasthenia Gravis with different Thymic Pathologies.
Methods: This descriptive study was performed at the Department of Thoracic Surgery, Mayo Hospital, Lahore between January 2010 and January 2012. A total of 60 consecutive cases of Myasthenia Gravis aged 15 and above were included in this study.
Results: Out of 60 cases included in this study, 41(68.3%) were females. Based on Thymic Pathologies, 52(86.7%) cases were found to have Thymic hyperplasia while 8(13.3%) cases had Thymoma. Of the 60 cases included in this study, 54(90.0%) had features suggestive of Myasthenia gravis whereas 6(10.0%) had no such evidence.
Conclusion: In conclusion it was observed that there is a strong relationship of Myasthenia Gravis with thymic pathology, with Thymic hyperplasia accounting for a greater majority of cases than Thymoma. Moreover, a significant female predominance is observed when both thymic hyperplasia and thymoma are collectively taken into consideration as one of the likely causes of Myasthenia Gravis.
Keywords: Thymic Hyperplasia, Thymoma, Myasthenia Gravis.

INTRODUCTION

Myasthenia Gravis (MG) is an autoimmune disorder which roots neuromuscular disease leading to fluctuating muscle weakness and fatigue in which weakness is caused by circulating antibodies. Mechanically antibodies block acetylcholine receptors at the postsynaptic neuromuscular junction inhibiting the excitatory effects of neurotransmitter acetylcholine on nicotinic receptors throughout the neuromuscular junction[1]. The thymus gland, which lies in the chest area beneath the breastbone, plays an important role in the development of the immune system in early life. Its cells form a part of the body's normal immune system. The gland is somewhat large in infants, grows gradually until puberty, and then gets smaller and is replaced by fat with age. In adults with MG, the thymus gland remains large and is abnormal. It contains certain clusters of immune cells indicative of lymphoid hyperplasia; a condition usually found only in the spleen and lymph nodes during an active immune response[2]. Some individuals with MG develop thymomas (tumors of the thymus gland). Thymomas are generally benign, but they can become malignant[2].

The relationship between the thymus gland and MG is not yet fully understood. MG occurs in all ethnic groups and both genders. It most commonly affects young adult women under 40 and older men over 60, but it can occur at any age. In neonatal myasthenia, the fetus may acquire immune proteins (antibodies) from a mother affected with MG. Generally, cases of neonatal myasthenia gravis are temporary and the child's symptoms usually disappear within 2-3 months after birth[2]. Although MG may affect any voluntary muscle, the degree of muscle weakness involved in MG varies greatly among individuals, ranging from a localized form limited to ocular muscles to a severe or generalized form in which many muscles sometimes including those that control breathing are affected. Symptoms, which vary in type and severity, may include a drooping of one or both eyelids, blurred or double vision due to weakness of the muscles that control eye movements, unstable or waddling gait, a change in facial expression, difficulty in swallowing, shortness of breath, impaired speech, and weakness in the arms, hands, fingers, legs, and neck[2].The prevalence of MG in the United States is estimated at 14 to 20 per 100,000 population, approximately 36,000 to 60,000 cases in the United States. However, MG is under diagnosed and the prevalence is probably higher. Almost 20% of patients with MG whose symptoms begin between the ages of 30 and 60 years have thymoma; the frequency is much lower when symptom onset is after age 60.Most patients with MG demonstrate thymic abnormalities, including thymic lymphoid follicular hyperplasia (LFH) and thymoma[4].The pathogenesis of MG, including the

---

[1]Department of Thoracic Surgery, King Edward Medical University/Mayo Hospital, Lahore, Pakistan
[2]Department of Radiology, King Edward Medical University/Mayo Hospital, Lahore Pakistan
Correspondence to Dr. Aamir Mahmood Ijaz, Associate Professor Email: draamirijaz@gmail.com
Cell:0300-84438000

role of the thymus and the factors that initiate and maintain the autoimmune response, is not fully understood; however, the thymus is thought to play a critical role[5].

MATERIAL AND METHODS

This descriptive study was conducted at the Department of Thoracic Surgery King Edward Medical University/Mayo Hospital, Lahore between January 2010 and January 2012. A total of 60 patients of age 15 and above were registered in this study. Patients were evaluated clinically and history was taken on a pre-defined questionnaire. Patients were checked for presence of ocular symptoms like ptosis and diplopia along with extra-ocular symptoms like proximal muscle weakness, dysphagia, regurgitation, drooling, dysarthria, generalized weakness, easy fatigability, exertion dyspnea, resting dyspnea and respiratory failure. They were then subjected to tests like Repetitive Nerve Stimulation test and Prostigmine test to ascertain the diagnosis of Myasthenia Gravis. Patients were also looked for any signs and symptoms suggestive of an antero-superior mediastinal mass like vague chest pain, SVC syndrome or stridor. Additionally, patients with or without symptoms or confirmatory diagnosis of myasthenia gravis having a radiological evidence of an Anterior Mediastinal mass with a thymic origin were also included in this study. The symptoms of Myasthenia Gravis mentioned above were used as a guideline to grade the severity of the disease and to ensure proper pre-operative preparation of patients for thymectomy. Surgery was only performed in cases whose symptoms had already been controlled either by drugs or through plasmapheresis. Paediatric patients, patients with poor control of myasthenic symptoms, patients with anterior mediastinal masses other than Thymoma, patients with inoperable Thymic masses involving SVC, Aorta, Pulmonary Artery or heart and patients with other medical conditions involving skeletal muscle were excluded from this study. Histopathological results of the samples taken during thymectomy were obtained as either Thymoma or Thymic Hyperplasia. These results were then brought in association with presence or absence of Myasthenia Gravis in respective cases. Finally, both these parameters were analyzed to establish a relationship of Myashenia Gravis with Thymic pathologies.

RESULTS

The results are summarized in Tables 1. A total of 60 patients presenting with either symptoms suggestive of Myasthenia gravis or an anterior mediastinal mass were then subjected to various tests like Repetitive Nerve Stimulation test, Prostigmine test, Chest Radiographs and Contrast-enhanced Thoracic CT scans. Patients with a confirmed diagnosis of Myasthenia Gravis with or without radiological evidence of a Thymoma, as well as patients with a radiological evidence of an operable thymic mass with or without Myasthenia Gravis were then subjected to Thymectomy via Median Sternontomy. Histological diagnoses were obtained for all cases and an association of Myasthenia gravis with the two major thymic pathologies was observed. Out of 60 cases included in this study, a female to male ratio was found to be 2.15:1 with 41(68.3%) female cases and 19(21.7%) male cases. 8(13.3%) out of 60 cases were less than 20 years of age, 27(45%) out of 60 cases had ages between 20 and 29 years, 17(28.3%) out of 60 cases had ages between 30 and 39 years, while 8(13.3%) out of 60 cases were above 40 years of age. In terms of Thymic pathology ascertained on histopathological results, 8(13.3%) out 60 cases were diagnosed as having Thymoma, while 52(86.7%) out of 60 cases were found to have Thymic Hyperplasia. Finally, 6(10%) of 60 cases did not have Myasthenia Gravis while 54(90.0%) out of 60 cases were confirmed to be having Myasthenia Gravis.

Table 1: Myasthenia gravis and thymic pathology

	=n	**%age**
Gender		
Female	41	68.3
Male	19	31.7
Age		
<20 years	08	13.3
20-29 years	27	45.0
30-39 years	17	28.3
>40 years	08	13.3
Thymic Pathology		
Thymoma	08	13.3
Thymic Hyperplasia	52	86.7
Myasthenia Gravis		
Positive	54	90.0
Negative	06	10.0

DISCUSSION

In present study relationship of Myasthenia Gravis with thymic pathology was clearly seen in 90% of the patients with thymic pathology who were suffering from Myasthenia Gravis. The thymus is a key organ in the production and education of functional T lymphocytes; it may be implicated in the initiation and progress of Myasthenia Gravis. Moreover, an older study has reported approximately 75% of patients of Myasthenia Gravis displaying thymic abnormalities[6]. Furthermore thymectomy has been often reported to

result in improvement in most patients with Maysthenia Gravis[7-8].

Although both genders are affected from Myasthenia gravis however women have a higher prevalence than men, which is generally described as an approximate 2:1 female to male ratio[9]. However a bit higher female to male ratio of 2.15:1 was observed owing to a higher percentage of Thymic hyperplasia included in the present study which is not in an agreement with the study which showed female to male ratio of 1:1.04 and prevalence of 1.41:1[10]. Predominant age range of subjects in present study was 20-39 years which is in agreement with another study which showed age range for disease onset to be 20-40 years[11].

CONCLUSION

In conclusion it was observed that there is a strong relationship of Myasthenia Gravis with thymic pathology, with Thymic hyperplasia accounting for a greater majority of cases than Thymoma. Moreover, a significant female predominance is observed when both thymic hyperplasia and thymoma are collectively taken into consideration as one of the likely causes of Myasthenia Gravis.

REFERENCES

1. Conti Fine BM, Milani M, Kaminski HJ (2006)."Myasthenia gravis: past, present, and future".*J. Clin. Invest.* 2006;116(11): 2843–54.
2. Myasthenia Gravis fact sheet. Last updated in December 2012. Available from: http://www.ninds.nih.gov/disorders/myasthenia_gravis/detail_myasthenia_gravis.htm#222053153
3. Myasthenia Gravis. Foundation of America. Inc. Reviewed in 2010. Available from:http://www.myasthenia.org/HealthProfessionals/ClinicalOverviewofMG.aspx#sthash.GYzjI1Pn.dpuf
4. Wekerle H, Muller-Hermelink HK. The thymus in myasthenia gravis. Curr Top Pathol 1986; 75:179–206.
5. Marx A, Wilisch A, Schultz A, Gattenjohner S, Nenninger R. Pathogenisis of Myasthenia Gravis. Virchows Arch. 1997; 430: 355-64.
6. Castleman B. The pathology of the thymus gland in myasthenia gravis. Ann N Y Acad Sci. 1966; 135:496-505.
7. Gronseth GS, Barohn RJ. Practice parameter: thymectomy for autoimmune myasthenia gravis (an evidence-based review): report of the QualityStandards Subcommittee of the American Academy of Neurology. Neurology. 2000;55:7-15.
8. Rowland LP. Therapy in myasthenia gravis: introduction. Ann N Y Acad Sci. 1987;505:566-567.
9. Andrews P I, Massey J M, Howard J F, Sanders D B. Race, sex, and puberty influence onset, severity, and outcome in juvenile myasthenia gravis.Neurology. 1994; 44(7):1208-14.
10. K Poulas, E Tsibri, A Kokla, D Papanastasiou, T Tsouloufis, M Marinou, P Tsantili,
11. T Papapetropoulos, S J Tzartos. Epidemiology of seropositive myasthenia gravis in
12. Greece. J NeurolNeurosurg Psychiatry. 2001;71:352–356.
13. Myasthenia Gravis. Available from: www.neuroland.com/nn/NeuroMuscular/Myasthenia%20gravis.htm