THYMECTOMY FOR MYASTHENIA AND THYMOMA: PESHAWAR EXPERIENCE OF 63 CASES

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ABSTRACT

Objective: To determine the safety and efficacy of thymectomy is thymomas and myasthenia gravis.

Material and Methods: A prospective observational study was carried out at Cardiothoracic Surgery unit Lady Reading Hospital Peshawar from March 1997 to April 2000. A total of 63 patients with a male and female ratio of 23:40, age range 15-50 years (Mean age 30.5 years) were entered into the study. Thirty nine presented with myasthenia while 24 presented with a mediastinal mass. They all underwent thymectomy via median sternotomy.

Results: There was one mortality due to failure to come off the ventilator in grade IIc. Myasthenia with a malignant thymoma, who was ventilated for 9 days. Out of 39 myasthenias 21 were off medication at 18 months followup, 13 were on reduced medication while 5 continued on the same medication. All thymomas without myasthenia did not need any medication.

Conclusion: Thymectomy in a thoracic surgical unit, with ventilatory backup, is a safe and effective treatment for both myesthenias and non myasthenics with thymomas, and stops the progress of an other wise crippling and fatal disease.

Key words: Thymectomy, Myasthenia, Thymoma.

INTRODUCTION

Although the symptoms of myasthenia gravis were described in 1672 prior to the introduction of anti-cholinesterase drugs, the disease was only recognized because of severe weakness and was fatal with in a short course of time. The association of myasthenia gravis and thymic tumours was first made by Weigert in 1901.[1] Thymectomy for the treatment of thymo-

mas and of myasthenia gravis was first introduced by Blalock and associates in 1939 and 1941.[1]

Myasthenia gravis is an acquired relapsing and remitting autoimmune disorder associated with acetylcholine receptor (AchR) deficiency at the motor end plates, caused by complement fixing antibodies.[2] It has been suggested that auto reactivity in myasthenia gravis is initiated with in the thymus. There is a biphasic mode of distribution with a tendency for population of young women and elderly men to be affected. Women are involved twice as often as men. The mean age of onset of symptoms is 26 years, men tend to be affected at a later age and tend to have higher incidence of thymoma.[3] Weakness and fatigue with activity are the hall marks of myasthenia gravis.[4]

Approximately 10-15% of patients with myasthenia gravis are found to have thymomas where as approximately 30-50% of thymomas are associated with clinical myasthenia gravis.[5]

Thymectomy is increasingly important and standard procedure for resection of thymoma, myasthenia gravis in selected patients or both.[6] The risk involved with thymectomy is small provided the operation is undertaken in a center with good intensive care facilities.[7] The incidence of remission increases with the number of years after thymectomy. Complete remission or substantial improvement may be expected in 80% of patients without thymic tumours, though it may take three to five years before the benefits of surgery are apparent.[8] Moreover the earlier the operation is undertaken in the course of disease the better the results.[9]

The aim of this study was to analyze the role and of midterm results of thymectomy both for thymomas and myasthenia gravis.

MATERIAL AND METHODS

In a 3 year period between March 1997 and April 2000, 39 patients with Myasthenia Gravis and 24 patients with thymoma were studied. Each patient was evaluated and underwent clinical staging based on modified Osserman classification (Table 1). Patients less than 15 years of age and those in stage I (ocular myasthenia) were excluded from the study. Each patient's clinical stage and medication requirement were recorded at the time of surgical referral. Indications for surgery included generalized myasthenia gravis while on a medical regimen, or the presence of thymoma as diagnosed on computed tomography.

Before surgery each patient underwent computed tomographic scan of the chest and pulmonary function studies apart from baseline investigation.

MODIFIED OSSERMAN STAGING CLASSIFICATION

Stage	Symptoms
Group I	Ocular myasthenia gravis
A	Ocular muscle weakness only, stable for 4 year
B	Ocular muscle weakness with history of previous generalized symptoms
Group II	Generalize myasthenia gravis
A	Mild Generalized
	Ocular muscle weakness spreading to skeletal muscle involvement Respiratory and bulbar muscles not involved
B	Moderate generalized
	Progression to generalized involvement of skeletal & bulbar muscle
	Dysarthria dysphagia
C	Severe generalized
	Skeletal and bulbar muscles weakness respiratory muscles involvement

TABLE – I

SURGICAL CONSIDERATION

Out of 63, 57 patients underwent complete median sternotomy while 3 had right and 3 had left thoracotomy, due to predominant extension of thymus to respective hemithorax. Upon exploration all thymic tissue and anterior mediastinal fat were removed from the mid pericardium inferiorly, to the cervical thymus extension superiorly and to each phrenic nerve laterally. Attempts were made to excise all involved tissue in the presence of an invasive thymoma. Extreme caution was exercised to protect the phrenic nerves. Transcervical approach was not undertaken because of possibility of phrenic nerve injury, bleeding in the depths of mediastinum in the areas of compromised visibility, and because complete clearance of all mediastinal fat is technically difficult through this approach. Following surgery, time to extubation, thymic abnormality and length of hospitalization were recorded.

PREOPERATIVE DATA OF 63 PATIENTS

Variable	No	% of Patients
Sex		
Male	23	(37)
Female	40	(63)
Age Year		
Male		
<40	8	(35)
>40	15	(65)
Female		
<40	30	(75)
>40	10	(25)
Duration of symptoms, mo		
<24	43	(68)
>24	20	(32)
Tensilon Test	39	(100)
Computed tomographic scan		
Normal	39	(62)
Thymoma	24	(38)

TABLE – 2

CLINICAL MANIFESTATION (OSSERMAN'S SCALE) AND DURATION OF SYMPTOMS OF 39 MYASTHENICS

Stage	No(%) of Patients	Duration months
II_C	8 (21)	>24
II_B*	18 (46)	<24
II_A	13 (33)	<24

*Group II_B also includes 8(30%) patients who had thymoma associated with myasthenia gravis.

TABLE– 3

After discharge patients were followed up for varying interval to measure outcome. Patients were categorized as follows: remission: no symptoms and no medication: improved: on less medication and better control of symptoms, and unchanged: if the changes were minimal or equivocal.

RESULTS

A total of 63 patients were included in this study. There were 24 male and 40 female patients ranging in age from 15 to 50 years. Most of the male patients were older than 40 years while female patients tended to be younger. Table 2 summarizes preoperative data. The duration of symptoms ranged from 2 to 24 months. Forty patients (68%) experienced symptoms for less than 2 years while the rest were symptomatic for longer periods. Tensilon test was positive in all 39 patients who presented with myasthenia gravis. Computed tomographic study was performed on all patients before surgery in an attempt to identify and determine the extent of thymoma. In 24 patients CT thorax showed thymoma.

Clinical staging by Osserman class is shown in Table 3. Before undergoing thymectomy for myasthenia there were 8 patients with Stage II_c disease, 18 with Stage II_b and 13 with Stage $II_\pm$. Group II_b also included 8 (30%) patients who had thymoma associated with myasthenia gravis. Table 4

HISTOPATHOLOGY OF THYMIC SPECIMENS

Pathologic findings	Mean age year	No (%) of patients
Normal	44	17 (27
Involved Thymus	45	14 (22)
Lymphoid Hyperplasia	32	20 (32)
Benign thymoma (Stage I, II)	43	10 (16)
Malignant Thymoma	53	2 (3)

TABLE – 4

shows the histological features of 63 excised specimens. The mean age of patients with thymic hyperplasia was lower than that in other group and two patients with malignant thymoma were both older than 50 years.

Table 5 shows overall postoperative clinical status. 21 patients (54%) were in complete remission over a 18 months follow up and 13 (33%) showed improvement, while only 7 (8%) needed medication in the same dosage as preoperatively. Benefit from the operation was thus achieved in 34 (88). Out of 39 patients operated for myasthenia gravis. While 70% of patients with thymoma only were asymptomatic over a 12 months follow up.

CLINICAL OUTCOME AFTER THYMECTOMY

	No (%) of patients	Follow up
A. Myasthenic Group 39		
• Remission	02 (54)	18 months
• Improvement	13 (33)	12 months
• Unchanged	05 (13)	06 months
B. Thymoma Group 24		
• Asymtomatic	17 (70)	12 months
• Symtomatic	07 (30)	18 months

TABLE – 5

DISCUSSION

Myasthenia gravis is a disorder of neuromuscular junction with a population prevalence of 1:75000. Younger women and older men tend to be affected at a male female ratio of 1:2.[2]

It is a recognized auto immune disease; thymus gland seems to play a central role in the pathogenesis although the exact role has yet to be elucidated.[10] Weakness results from reduction in acetylcholine receptors at the neuromuscular junction.[11] Despite significant advances in therapy, myasthenia remains a potentially debilitating and life threatening disease.

Currently four methods of treatment are available for patients with myasthenia; anticholinesterase drugs to enhance neuromuscular transmission; immunosuppression (prednisolone) to decrease immune response; plasmapheresis to remove some of the circulating auto antibodies and thymectomy to remove a major source of antibody production.[12] For this complex auto immune disorder while all or any of the above modes of therapy may be necessary, it is now generally accepted that removal of the thymus gland is distinctly beneficial in the majority of patients with generalized myasthenia gravis.[13]

Age of the patient, duration of symptoms and response to medication are all a consideration in recommending thymectomy. Thymectomy is rarely advocated for ocular myasthenia gravis. Most Neurologists recommend thymectomy for selected patients with generalized myasthenia without thymomas. Nevertheless, with few exceptions; thymectomy is recommended for virtually all patients with thymoma. Most authors[14] agree with the indications for surgery in our study. Several advocate thymectomy at the time of initial diagnosis and demonstrate good results.

Thymectomy for ocular myasthenia gravis only; is not recommended and several studies have shown lower remission rates in their small number of Stage I patients.[15,1]

A variety of surgical approaches to the thymus have been described. Some authors advocate a transcervical approach while most now favor a Transsternal approach both for thymomatous and non thymomatous myasthenia gravis.[16,17,18] It is associated with minimal morbidity and no mortality and results in long term improvement in the symptoms of patients with myasthenia gravis. Fifty seven (90%) of our patients had Transsternal thymectomy while 3 had right thoracotomy and other 3 left thoracotomy due to predominant extension of thymic tumours to respective hemithorax. Histopathology of 10 patients were benign thymoma. (Stage I, II)

Improvement in Stage was noticed in 34 of 39 patients with myasthenia gravis; 21 (54%) experienced remission and 13 (33%) noticed improvement over 18 and 12 months follow up respectively. Our results are consistent with other reported data.[19,20] Out come of myasthenia gravis with thymoma is worse than with out thymoma at one year follow up.[1] Patients with (Stage I, II) thymoma have better survival than advanced thymoma.

Some of the factors which have been known to favorably affect the results of thymectomy are, a shorter duration of disease with milder symptoms, the absence of a thymoma, and the presence of hyperplasia in the thymus removed.[21]

Thymectomy has the most to offer for the young female patients with myasthenia gravis of short duration, because time lapsed from diagnosis to operation is the main determinant is of the outcome.[21] In our study we found that 68% of patients exhibiting symptoms for less than 24 months had better outcome compared with those (20%) with a longer duration of symptoms. The clinical and neurophysiological changes in myasthenia gravis with and without thymoma do not differ. However patients with thymoma have a worse outcome.[3] We had one mortality, a male patient of 50 years with advanced myasthenia and marked involvement of respiratory muscles and malignant thymoma who was reintubated and ventilated for 9 days but finally succumbed to the fatal illness. On the other hand patients with follicular hyperplasia have significantly higher remission rates.[19] Out study supports the use of thymectomy in the treatment of all patients with generalized myasthenia with and without thymoma. The procedure should be accomplished through a Transsternal incision and all mediastinal thymic tissue and fat should be excised.

CONCLUSION

Thymectomy through a full sternotomy for myasthenia gravis, a thymic mass, or both provides excellent exposure and the ability to treat all aspects of the problem with low mortality and morbidity. A team approach has been beneficial in the post operative care of the myasthenic patients undergoing thymectomy with early extubation, individualized care, and close observation being paramount.

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