Thymectomy in Myasthenia Gravis

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ABSTRACT:

BACKGROUND:

Thymectomy is a good option for the treatment of patients with myasthenia gravis (MG).

OBJECTIVE:

To show the effect of thymectomy as treatment for patients with myasthenia gravis.

PATIENT AND METHODS:

A retrospective study of 75 patients admitted to AL-Hariri martyr hospital from January 2010 to December 2014. They were reviewed using special form included patients' (age, sex, hospitalization period, CT-findings, preoperative medication, respiratory care unit (RCU) admissions, plasmapheresis sessions, number of drains in operation, complications post operatively, type of surgery, histopathological findings) with their symptoms being staged according to Osserman classification. All patients managed with trans-sternal thymectomy and extensive tissue removal of the thymus and fatty tissue around it.

RESULTS:

From 75 patients, 33% achieved complete remission, 27% had partial improvement, 32% with no changes and 8% got worse. 45 patients (60%) are between 20ys and 40ys with female predominance and good responses to surgery. 30 patients (40%) are above 40 with less improvement after thymectomy. Patients with severe symptoms (32 patients) appear to improve. This is also true in patients underwent thymectomy and the histopathological findings of thymic follicular hyperplasia (35 patients).

CONCLUSION:

Trans-sternal thymectomy is a safe treating method for patients with myasthenia gravis. Age, sex of the patients and presence or absences of thymoma are significant predictors. Patients with severe symptoms and those with a biopsy of thymic follicular hyperplasia improve remarkably.

KEY WORDS: myasthenia gravis, thymectomy, neuromuscular junction, thymoma.

INTRODUCTION:

Myasthenia gravis is an autoimmune neuromuscular transmission disease that leads to fluctuating muscle weakness and fatigue.[1] Previous studies, disclose that female are more often affected than male. The most common age at onset is the 2nd and 3rd decades in female and the 7th and 8th decades in male. [2] Usually the initial complaint is localized muscle weakness rather than generalized. Ocular motor disturbances are the initial symptom of MG in 2/3 of patients; almost all progress to generalized myasthenia gravis within 2 years. About 70% of patients with MG have hyperplastic changes that indicate an active immune response and 15% have a thymic tumor [3,4] the association of MG with abnormal thymus gland is clear but the real cause of MG not yet fully understood. Thymic tumors mostly benign in patients with MG, well encapsulated, and can be totally resected. Most Textbook describe that clinical diagnosis of MG must be unpretentious. However, this is not constantly true. [5] Most studies recommend Thymectomy for most patients with MG. Studies do not correlate the rate of improvement after thymectomy to the stage of disease before surgery. The maximal improvements usually happen 2 to 5 years after thymectomy. However, significant impairment may continue for long time after. The response is relatively unpredictable and the best response to surgery is in young patients in early stages of their disease. Onset of MG disease in patients above 60ys age rarely show fundamental improvement after thymectomy. Patients without thymomas respond to thymectomy better than those patients with thymoma.[6]

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PATIENTS AND METHODS:

This is a retrospective study of 75 patients with Myasthenia Gravis who were admitted in Ghazi AL- Hariri surgical specialties hospital, underwent trans-sternal total thymectomy during the period of January 2010 to December 2014. All patients were evaluated preoperatively by the clinician and diagnosis was depending on clinical presentation, electromyography and laboratory tests. All patients underwent clinical staging depend on the OSSERMAN classification. The study was a retrospective study using the data available in the hospital records, surgeons' personal data and sometimes by direct contact with patients. Data form sheet was prepared include age, sex, occupation, hospitalization period, signs and symptoms, histopathological findings, preoperative medications, plasmapheresis, respiratory care unit admission period, type of operation and complication during operation. All patients were underwent routine chest x-ray, chest C-T scan.. Laboratory studies included complete blood picture, blood group, random blood sugar, virology screen, pulmonary and renal function test, and formal cardiology evaluation. Plasmapheresis has been done to all the patients in our hospital routinely before surgery. Indications for thymectomy included persistent generalized myasthenia refractory to medical treatment, persistent ocular myasthenia in spite of proper medical treatment regime and the presence of a thymoma as diagnosed by computerized tomography. General anesthesia used and the patients underwent complete or hemi-sternotomy and trans-sternal thymectomy. Our patients were given pyridostigmine 60mg, two tablets, in the nasogastric tube immediately after surgery, while the patient on table. All thymic tissue and anterior Mediastinal fat were removed from the pericardium inferiorly to the cervical thymic tissue superiorly and from the left parietal pleura to the right one. Tissues taken as a biopsy including the thymus gland and the surrounding fatty tissue sent post operatively to the histopathological study. All patients were immediately extubated postoperatively and referred to the RCU, only one patient need assisted ventilation after surgery. All of the malignant thymoma patients were referred to the oncology department and had courses of chemotherapy and radiotherapy.

Response to surgery and the improvement following the operation was classified into the following categories:

1-Complete remission and improvement of symptoms.

2-Significant disappearance of signs and symptoms.

3-No change can be detected from surgery and the patient condition is the same.

4-Worsening in patient's condition after thymectomy.

RESULTS:

- Seventy five patients with MG were studied, 61(82%) patients were female and 14(18%) were male with male to female ratio was 1/2 in patients more than 40-years of age and 1/5 in age patients less than 40-years and
- The youngest patient in this study was 12 years old female and the oldest was 62 years old male.
- Most of patients were below 40 years in age, and the percentile of male to female ratio is shown in the fig. no. 1 below.

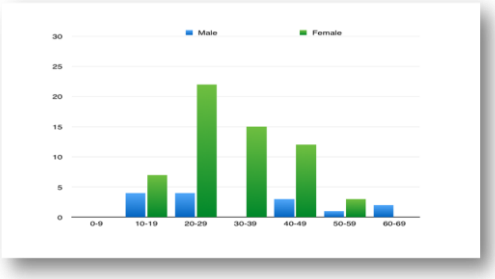

Fig 1: Distribution of patients with MG according to sex and age group.

- Patients with MG who are not responding to medical treatment were 67 (89.3%) patients and those who are diagnosed with an anterior mediastinal mass on chest tomography were 8 (10%) patients with mean interval from presentation to surgery about (6-14months) on medical treatment then underwent thymectomy.

Pre-operative medications were:

1. Pyridostigmine (Mestinon) 60mg (all patients in different doses).
2. Prednisolone (5mg) taken in different doses by 30 patients.

- Plasmapheresis has been done to all of our patients routinely before surgery.
- The pre-operative Osserman stages of our patients were as follows:

1. Class I: (A): 15 (19%)
2. Class II: (A): 16 (21%) (B): 10 patients (13%)
3. Class III: (A): 8 (10%) (B): 14 patients (18%)
4. Class IV: (A): 5 (6%) (B): 7 patients (9%)

- All patients had trans-sternal thymectomy done with removal of all thymic tissue and the surrounding fat.
- Mediastinal drains used in all the patients (100%), pleural drains used only in 30 patients (40%) in case (right or left) pleura were opened.
- No complications recorded during operations; there was no death among the patients with MG after surgery. Most of the patients have no complications in the postoperative period, six patients developed postoperative complications as follow:

- Two cases of wound infection
- Two cases had myasthenic crisis.
- One case with an elevated dome of diaphragm.
- One case had been on ventilator support for 17 days.

- In (Fig. 1) it is obvious that most of the patients included in this study were below 40 years 45(60%) patients, the majority of them had good response to thymectomy, 20(26%) patients of them had complete remission and the other 15 (20%) patients showed partial improvement.
- On the other hand, patients above 40ys were (30 patients, 40%) less responded to thymectomy, 5(6%) patients remissions and 5(6%) patients partial improvement.

Biopsy results were as follows:

- 25(33%) cases had normal thymic tissue.
- 40(53%) cases had thymic hyperplasia.
- 2 (2%) cases had thyomlipoma.
- 8(10%) cases had thymoma.

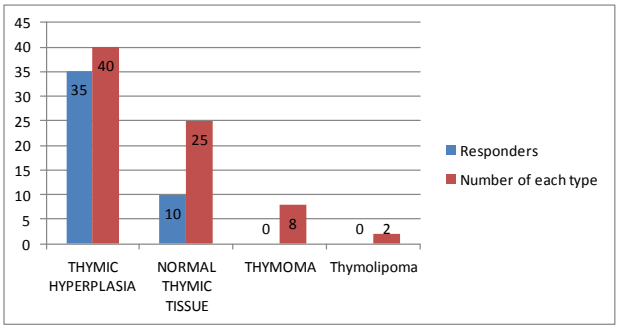

Figure 2: Distributions of patients according to histopathological results versus response.

- Malignant thymomas are found in 8(10%) patients with MG. These tumors are rare in patients younger than age of 20; the number of patients with thymoma is (6 patients) old men, 2 females (above 40ys). 6 patients out of 8 with malignant thymomas had their conditions deteriorate after thymectomy, 1 patient had passed in the next few years and one had no change.
- Patients with hyperplasia had the greatest benefit from thymectomy as 20 patients show complete remission and 15 patients have partial improvement and 5 patients had no change.

- 2 cases of thymolipoma recorded which is a rare type also and shows no obvious change after surgery.
- Normal thymic tissue was found in 25 cases, complete remission seen in 5 patients, improvement in 5, and no change in 15.

Post-surgery results show that:

1. Forty four patients were in Osserman stage IIB, III and IV pre-operative, 18(40%) of these patients were in complete remission and an additional 14 (31%) patients were partially improved post-surgery, 9 had no change and 3 got worse at the follow-up.
2. There were 16(20%) patients in Osserman stage IIA preoperatively, 4 patients show complete remission (25%) and 5 improved (31%) and 7 with no change post-op.
3. On the other hand, of the 15(21%) patients in preoperative Osserman stage I , only 3 (20%) were in complete remission, 1 (6%) partially improved, 8 patients with no change and 3 deteriorated. Fig(3)

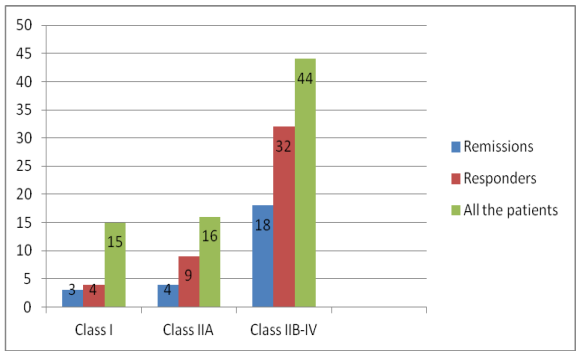

Figure 3: Preoperative Osserman stage versus response (patients in remission or improved) after thymectomy.

- Improvement in our patients started (6 months-2years) after surgery.
- At the follow up Improvement in thymectomy patients occurred as follows: Out of 75 patients, 33% achieved complete remissions (no symptoms, no medication required), 27% achieved partial improvement (freedom of symptoms, specific medication required), 32% have no change, and 8% get worse.

DISCUSSION:

As the majority of our patients were females 61 (82%), 44 of them were young (below 40ys) and the male to female ratio was 1/5 and 17 were above 40ys and the male to female ratio was 1/2, this was similar to what was found by Detterbeck; et al [7] in which 57 patients were below 40 years and 25 were above 40ys, the male to female ratio in general was 1/1.9. In this study the patients' age have been associated with the outcome of surgery as patients below 40ys (45 patients) responded better to thymectomy, as 20 (26%) of them in complete remission and 15 (20%) in partial improvement. While those above 40ys (30 patients) had only 5 remissions and 5 improved. In contrast, patients' age was not found to be significant predictors as in Takanami, Iwao et al[(8)].

Our surgical approach involves a trans-sternal incision and total resection of the thymus gland including the cervical parts. Resection of all anterior mediastinal fat is also advocated. This agreed with the opinion saying that the rationale for trans-sternal thymectomy is based on the thymus arising from several sites, and there may be ectopic nests of thymic tissue scattered throughout the anterior mediastinum and even the retro-thyroid space as in Takanami, Iwao et al[(8)].

This current study clearly demonstrates that extended radical thymectomy is a safe procedure since there were no serious complications witnessed. All the patients, except one, were extubated immediately post-operatively. This agreed with Al-Shaikh et al; [(9)] study when they found that although patients with MG have greater preoperative morbidity and a higher frequency of re-intubation thymectomy was found to be a safe procedure overall. Still there's controversy regarding the surgical approach and patient selection to surgery[10]. Most patients in our study had symptoms for an average interval of (6-14 months) before surgery and then an early improvement happened after surgery in a relatively short period of time (6 – 24) months,

when the patients experienced remission and relief of symptoms, this agrees with Busch, christoph et al[11]on the other hand disagrees with Kreel, Isadore, et al.[12] Thymic hyperplasia composes more than a half of the biopsy results (40 patients (53%) , responded better to thymectomy as 20 patients were in complete remission and 15 had partial improvement, while normal thymic tissue (25 patients, 33%) shows 5 in complete remission and 5 in partial improvement. while 8 patients with thymoma (10%) had poor prognosis with no improvement witnessed among them as 6 patients got worse , one had no change and one died in the next few years. This is agreed with Detterbeck; et al. Who had good response for surgery with follicular hyperplasia reached 68% of remission and improvement[7;] thymoma had only 8% improvement. Aghajanzadeh M;et al showed that the patients with follicular hyperplasia had remission and palliation in 84%, those with thymoma had remission and palliation in 10% in all thymoma . [13, 14]

In our study 44 Patients with more severe symptoms of Myasthenia Gravis, as in stage IIB, III and IV patients, clearly benefit from thymectomy, this was obvious when 18 patients had complete remission and 14 in partial improvement. Patients with ocular myasthenia (Osserman stage I), 15 patients (21%) revealed significantly lower response rates than those patients with more severe disease (Osserman stages IIB, III and IV), as 3 (4%) had complete remission and only one patient (1%) had partial cure. This agreed with Hatton et al.[15] Who derive that thymectomy in ocular type of MG is not beneficial, The response rate of 26% in this small group of patients does not differ significantly from the spontaneous improvement that may happen in the natural history of the disease defined by Grob and associates[16]. Surgery may be recommended by neurologist for patients with severe generalized myasthenia gravis refractory to medical treatment[(17)]. It is obvious that in our surgery we did not exclude patients with mild symptoms as in stage I who had only ocular manifestations, the response in this group was poor as 3 of them got remission and 1 improved only. Debate still about thymectomy in ocular type of MG which may show natural remission and it is not life threatening[(18)]. Ocular MG may advance to generalized type for that reason thymectomy may be used in ocular type also [(8)], while others found that only ocular type of MG should be medically treated because of majority of those patients do not improve with thymectomy as described by Hatton et al.[(15)] Plasmapheresis sessions arranged to all our patients pre-operatively. Still there's a difference in the number of these sessions. It has showed an impact on the patient recovery post-operatively as immediate extubation, no assisted ventilation required post-operatively and shorter hospitalization period. This agreed with other Studies which had emphasize that plasmapheresis may have useful effect on patient as an adjunct therapy in patients with impaired respiratory mechanism as demonstrated by d'Empaire G, Hoaglin DC et al [(19)] where they found that their results shows that pre-thymectomy plasmapheresis in patients with severe forms of myasthenia gravis associated with less mechanical ventilation and less time in the intensive care unit postoperatively. The multivariate analysis shows that the severity of MG, age, and presence of thymoma are significant factors that affect the clinical course of MG regardless of treatment and are independent prognostic indicators. . Proper evaluation of treatment modalities is not possible without taking into considerations the influence of these factors

Conclusion and Recommendations

This review demonstrates that

- Trans-sternal thymectomy is effective and safe in symptomatic patients with MG.
- Age, sex of the patients and presence of thymoma are significant predictors.
- Patients with severe symptoms showed a greater degree of postoperative improvement and the younger the patients, the better the results.
- Plasmapheresis should be done to all the patients as it has an impact on the outcome of the operation.
- There should be good communication with the department of neuromedicine to achieve the best results from thymectomy and there should be no delay in operation in patients refractory to treatment or those with thymoma.

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