THYMECTOMY FOR MYASTHENIA GRAVIS : EXPERIENCE AT RATCHABURI HOSPITAL

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ABSTRACT :

Choojai S, Klinjongkol C. Thymectomy for Myasthenia Gravis : Experience at Ratchaburi Hospital. (Region 7 Medical Journal 1996 ; 4 : 437-444).

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Fifteen thymectomies were performed in patients with myasthenia gravis during 1974 - 1994 at Ratchaburi hospital. There were 13 females (86.7%) and 2 males (13.3%). Twelve out of 13 females were 18 - 37 years of age. The two males were 42 and 45 years old at the time of operation. Two patients were in mildly generalised class (2a), while 10 were in moderately generalised (class 2b) and 3 patients were severely affected by the disease (class 3). Outcomes, obtained as the result of the operation, were early remission in 8 (53.5%), late remission in 2 (13.3%), improved status in 1 (6.7%) and not improved in 3 (20.0%). There was 1 opeartive death, and 1 of the non-improved died 2 years after the operation from repeated crises due to therapeutic uncompliance. Results of the operation were more favourable in patients with milder clinical class, shorter duration of symptoms and absence of thymoma.

บทคัดย่อ :

สุเทพ ชูใจ, ชนินทร์ กลิ่นจงกล. การผ่าตัดต่อมไธมัสรักษาโรคไมแอสธีเนียเกรวิส ประสบการณ์ในโรงพยาบาลราชบุรี. (วารสารแพทย์เขต 7 2539 ; 4 : 437-444).

กลุ่มงานศัลยกรรม, รพ. ราชบุรี.

ในช่วงปี พ.ศ. 2517 ถึง 2537 มีผู้ป่วย myasthenia gravis ได้รับการรักษาโดยผ่าตัดเอาต่อมไธมัสออกที่โรงพยาบาลราชบุรี จำนวน 15 ราย เป็นหญิง 13 ราย (86.7%) และชาย 2 ราย (13.3%) ผู้ป่วยหญิง 12 ใน 13 ราย มีอายุอยู่ในช่วง 18 - 37 ปี ส่วนผู้ป่วยชาย 2 ราย นั้นอายุ 42 และ 45 ปี ผู้ป่วยทั้ง 15 ราย มีอาการกล้ามเนื้ออ่อนแรงทั่วตัว และมีความรุนแรงของโรคในระดับอ่อน (class 2a) จำนวน 2 ราย, ระดับปานกลาง (class 2b) จำนวน 10 ราย และมีอาการมาก (class 3) จำนวน 3 ราย ผลการรักษาทำให้ผู้ป่วยหยุดยาภายในกำหนด 3 เดือนหลังผ่าตัดได้ จำนวน 8 ราย (53.3%) ต้องใช้ยานานกว่า 4 เดือนขึ้นไปจึงหยุดยาได้ จำนวน 2 ราย (13.3%) ทำให้อาการดีขึ้นแต่หยุดยาไม่ได้ 1 ราย (6.7%) การผ่าตัดไม่ได้ผล 3 ราย (20%) มีผู้ป่วยเสียชีวิตหลังผ่าตัด 1 ราย (6.7%) ผู้ป่วยในกลุ่มที่การผ่าตัดไม่ได้ผล 1 ราย เสียชีวิตในปลายปีที่ 2 หลังผ่าตัดเพราะหยุดยาเอง ปัจจัยที่เอื้อให้การผ่าตัดได้ผลดีคือ ระดับความรุนแรงของอาการต่ำ ประวัติการดำเนินโรคสั้น และไม่มีเนื้องอก thymoma

Myasthenia gravis is a relatively rare neuromuscular disorder, seen more frequently in females.[1,2,3] It is generally characterised as an autoimmune disease ; specific antibody to postsynaptic acetylcholine receptor (AchR) is positive in 90% of patients. The end result is clinical muscular weakness with a decrease in the number of AchR.[4,5] There is no specific change in striated muscle, grossly or microscopically, other than atrophy dues to hypoactivity. In exceptional cases, there may be spotty lymphocytic infiltration (lymphorrhage) within the muscle bundles ; this can be found in the liver, thyroid and suprarenal glands as well.[6] All muscle groups may be affected, but ocular, upper extremity and other cranial nerves are more severely affected, with extension to other groups as the disease progresses. Consequently, diplopia and ptosis may be early findings, while dysphagia and general weakness of facial muscles and extremities usually are signs of late disorder. Although the disease, mostly runs a chronic course, could well be controlled by anticholinesterase drug, pyridostigmine bromide (Mestinon®), corticosteroids and other immunosuppressive agent (usually azathioprine [Imuran®]) ; thymectomy has continued to gain acceptance as definitive treatment for patients with moderate or severe disability.[7] Thymic pathology, clinical severity, duration and onset of disorder and preoperative intervention are factors influencing the outcome.[8,9,10]

Ratchaburi Hospital has been capable of providing operative treatment for myasthenia gravis since 1970. This report, a review of cases, is aimed at presenting outcomes of 15 thymectomies for the disease during a period of time. However, correlating the factors and results of the operation deems limited due to lack of uniformed details and number of patients.

Patients and Method

Medical records of 15 patients who were admitted to Ratchaburi Hospital of myasthenia gravis and had thymectomies done as an option of curing the disease during 1974 to 1994 were reviewed. The operations were performed by either of us. The pre and postoperative management methods were incidentally more or less similar. That is, muscular fatigue was brought to control by anticholine esterase, with or without prednisolone. The thymectomies were carried out via median sternotomies. Glandular removals were to be completed with the adjoining fatty tissue, even at the expense of pleural and pericardial resection. The anaesthetic was light halothane, without preanaesthetic ever given. The patients must be fully alert before transferring to the intensive care unit unextubated. The endotracheal tubes could be removed only after respiratory assessment was satisfied by the operating surgeon. The patients were kept in the intensive care unit until no respiratory support of any kind was assurred.

Patients who were able to be removed early from the intensive care unit, were observed for reoccurrence of muscular weakness. Anticholine esterase (Mestinon®) orally, or acetylcholine agonist, prostigmine hydrochloride intramuscularly in titrating dosages would be given if indicated. For those who were not performing well postoperatively and kept in the intensive care unit, the drug was given while

closely assessing the respiratory effort. Respiratory support was indicated in the patients who did not respond to medication. All 15 patients, except one medical referred case, were observed postoperatively in the general surgical ward or general intensive care unit. The exceptional case was called back by the referring physician, on the 3rd postoperative day, while perfoming well in the surgical ward. Unfortunately, this case developed respiratory problems that needed prolonged ventilatory support. This is the only post operative death.

Patients were observed in the surgical ward for their performances, mostly for the symptoms of muscular weakness. The patients was considered dischargeable once the muscular weakness was stabilised, whether it was a remission or improvement regardless of medication, The patient were to come for follow up commencing in the 2nd week after being discharged. Adjustment of medication in relation to muscular response was done by either of us. Patients who showed no satisfactory response to the maintenance treatment, and additional immunosuppressive seemed necessary, were referred to Rajvithi Hospital for initialisation of the drug. Evaluation of response of the operation was concluded when the clinical muscular weakness was stabilised. The patients who had to be on maintenance medication were told to come to the surgical outpatient clinic and regularly seen by us. Once remission had been ascertained, no regular follow up was further appointed.

Clinical response to thymectomy were graded as "early remission" if medical treatement could be totally withdrawn within 3 months postoperatively, as "late remission" if the withdrawal was enable later than the 4th month. "Improved in status" signified

Table 1 Showing 15 patients included in this review.

No.	Year	Age	Sex	Onset in month	Clinical class
1	1974	22	F	2	2a
2	1975	18	F	1	2b
3	1979	25	F	2	2b
4	1979	42	M	12	3
5	1982	32	F	3	2b
6	1986	35	F	8	3
7	1986	30	F	12	2b
8	1990	25	F	1	2b
9	1991	52	F	3	3
10	1992	22	F	1	2b
11	1992	45	M	99	3
12	1992	37	F	84	2b
13	1992	32	F	6	2b
14	1994	30	F	1	2b
15	1994	19	F	1	2a

Table 2 Clinical Classification of Myasthenia Gravis, After Osserman.

Group	Muscle Involvement
I Ocular	Ocular only, ptosis, diplopia
II Generalised	
a. Mild	Ocular frequent, gradual spread to skeletal and bulbar. No respiratory involvement.
b. Moderate	Frequent ocular, gradual onset, more severe skeletal and bulbar. Some dysarthria, dysphagia and mastication problems. No respiratory involvement.
III Acute fulminating	Rapid onset, severe bulbar and skeletal. Early respiratory involvement. High percentage of thymomas.
IV Late severe	Severe symptoms about two years after most Group II symptoms.

Table 3 Result of thymectomy in relation to duration of the disease, clinical staging and pathological finding.

Result of Operation	Number of patients	Subtotal number of patient by Duration in months				Subtotal number of patient by Clinical stages			Subtotal number of patient by Pathological finding		
		1 to 3	3 to 6	6 to 12	> 12	Stage 2a	State 2b	Stage 3	Normal	Hyperplasia	Thymoma
Early remission	8	8	0	0	0	2	5	1	1	7	0
Late remission	2	0	1	1	0	0	2	0	0	2	0
Status improvement	1	1	0	0	0	1	0	0	0	1	0
No improvement	3	0	0	0	3	0	2	1	0	2	1
Death	1	0	0	1	0	0	0	1	0	0	1
Total	15	9	1	2	3	2	10	3	0	12	2

for patients who fatigability was less while the medication was maintained. For those who showed no muscular improvement despite of preoperative dosage of medication were classified as "not improved".

Result

There were 15 patients ranging from age 18 to 52, mean = 31, SD = 9.86, (table 1). The commonest age ranges were early twenties and early thirties. There were 13 females out of the total 15, (86.7 %). The two males were 42 and 45 years of age. Most patients were seen early within a year of onset, 12 out of 15 (80%), while the other 3 patients came late at 24, 66 and 84 months. Nine patients, 60%, were moderately generalised in severity (IIb) while first seen. Four patients were in severely generalised class (III), while 2 patients were in mildly generalised class (IIa). Table 2 shows the clinical classification after Osserman.[2]

Clinical improvement, brought about by thymectomy, was obtained in 11 patients, (table 3). Three patients were not benefited by the operation, i.e. no improvement was obtained. There was 1 postoperative death. A female patient of 35 who had been recovering in the surgical ward under daily 180 mg. of pyridostigmine bromide. She was transferred back to the referring medical unit in the 4th postoperative day. We were informed that she developed crises and succumbed on the 20th day to pulmonary complication. Another late death was a man of 42 who was operated on 1979. He had been on pyridostigmine maintenance of 180 to 240 mg per day. Unability to afford leaded to therapeutic uncompliance, he had episodes of myasthenic crises. The last crisis, at the end of the 2nd postoperative year, was a serious unsalvageable respiratory failure.

In the early remission group of 8 patients, 2 were discharged without anticholine esterase drug being given, while the six others needed pyridostigmine bromide for 1 to 3 months. There were 2 late remissions. The status improvement case was a lady of 30, who needed less pyridostigmine to maintain her daily choir. She has been on 60 mg. Mestinon® twice daily for 8 years. Three patients who were not benefited from the thymectomies, 2 have been on continuous pyridostigmine and azathioprine.

Relation of the outcomes to clinical features of the disease and pathological appearance of the thymus was notable. In 8 patients who attained early remission, the operations were performed within 3 months of the onset of myasthenia gravis. The thymus glands were normal or hyperplastic. In three patients who were not benefited from thymectomies, the operations were done at 12, 24, and 84 months after the onset. There were 2 thymomas, both of which presented in patients who did not recover. Three out of 4 patients presented with the disease severity of grade III show no improvement after thymectomies.

Discussion

The incidence of myasthenia gravis was generally cited at 2-6 per million population annually.[6] A recent study in western Denmark, from 1975 to 1989, showed an annual incidence of 5 per million ; and a point prevalence, as of January

1,1990, of 78 per million.[3] While relating epidemiological data is not available, 310 cases of the disease were accountable in 8 reports in Thailand from 1984 to 1994. One hundred and six thymectomies were done for the lot. Among those, 2 large and well documented series of 55 and 42 cases, in which 35 and 34 thymectomies respectively were performed.[11,12] Apparently myasthenia gravis is not so rare in Thailand. However, thymectomy as an option of curing the disease, has been limitedly performed .

Thymectomy has gained widespread acceptance in the treatment of myasthenia gravis. It is the consensus that thymectomy should be carried out in all patients with generalised myasthenia gravis between the ages of puberty and at least 55.[13] Total thymectomy is the operative procedure of choice and have been shown to brought about the improvement in 70% of patients with operative mortality of 0 to 4.85%.[7,8,9,10,12] Plasmapheresis, a relatively simple adjunct perioperative management, allows optimal clinical improvement and permits the surgeon to discontinue anticholinesterase medication if they have been in use. This, in turn, permits a less complicated postoperative course.[14] It is doubted that the therapeutic regimen of myasthenia gravis is still philosophical in this country ; that is, depends on the physician who first sees the patient. And yet, plasmapheresis has not been adopted in the process.

While the thymus gland plays a central part to the disease process, and its removal may be clinically beneficial, its role remains to a large degree undefined. Some relationship seems clear in view of the high incidence of pathology of the thymus gland in myasthenia gravis. However, 10% of thymus glands examined from patients with myasthenia gravis are normal.[15] Not all patients with myasthenia gravis are benefited from the operation. Factors influencing outcomes are age, sex, duration of disease, stage of disease, histological characteristics of the thymus and duration of follow-up on outcome.[8] Moreover, as the disease is self remitting in its nature ; and that remission may take place years after the operation by itself. An analysis in 400 patients operated during 1974-1983, and prospectively followed up for five years after surgery concluded that : in those patients where stabilised remission occurred within the first year after surgery, was more likely to be ascribed to thymectomy than merely reflect the natural course of the disease.[10]

Conclusion

Fifteen patients were operated on for myasthenia gravis in Ratchaburi Hospital during 1974 to 1994. Complete removal of the thymus gland through a median sternotomy was applied in all. Improvement was obtained in 11 patients (73.3%). Among those were 8 early remission (53.3%), 2 late remission (13.3%), and 1 improvement in status (6.6%). There was 1 post operative death and 1 late death at the end of the 2nd year. We believe that there could have been more patients not brought to surgical attention. In conjunction with improved perioperative management, more patients with myasthenia gravis will be benefited from thymectomy.

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