VIDEO-ASSISTED COMPLETION THYMECTOMY IN REFRACTORY MYASTHENIA GRAVIS

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Thymectomy is an effective surgical therapy complementing the medical care of patients with myasthenia gravis. Residual thymic tissue is present in 64% up to 70% of patients showing partial improvement or no response after thymectomy.¹ Either it is due to a remnant of the original gland missed during the operation or it develops from ectopic thymic tissue.^{2,3} Completion thymectomy, carried out by the extended transsternal^{2,3} or the maximal transsternal-transcervical⁴ approaches, has been advocated after unsuccessful transcervical thymectomy. Video-assisted thymectomy is being investigated in the belief that this procedure may also allow a complete removal of the thymus and the anterior mediastinal and lower cervical perithymic adipose tissue.^{5,6} We have adopted the video-assisted approach as a less invasive modality to reoperate on patients with nonthymomatous refractory myasthenia who did not undergo extended thymectomy initially.

Between December 1995 and December 1996, four patients with myasthenia gravis, three women and one man with a mean age of 41 years, underwent video-assisted completion thymectomy. The mean duration of myasthenia gravis before the initial operation was 21 months, ranging from 12 to 38 months. The initial operation was transcervical thymectomy performed by one of the authors (T.C.M.) in three patients and sternal-splitting thymectomy performed in a different institution in one. No patient underwent extended thymectomy originally. The mean interval between operations was 120 months, ranging from 72 to 180 months. Informed consent was obtained from all patients. They were given the main information regarding the different approaches and the possible complications. Worthy of note, results of preoperative computed tomography and magnetic resonance imaging were deemed negative or inconclusive regarding the identification of residual or ectopic thymus. Three patients had elevated serum titers of antibody to the acetylcholine receptor, and all had a positive edrophonium test and characteristic decreasing responses to low-frequency repetitive nerve stimulation. At admission, ev-

Fig. 1. Potential sites of ectopic thymic tissue that are dissected through the left thoroscopic approach.

ery patient was completely disabled. Three patients were receiving large doses of pyridostigmine bromide (mean dose 560 mg/day) in combination with prednisone (mean dose 45 mg/d), and one patient was receiving prednisone and azathioprine (Table I). All attempts to taper medication were unsuccessful because of increased fatigue. Three patients were receiving long-term maintenance plasma exchange with a mean of 6.25 cycles/year (Table I). Each patient underwent four exchange cycles over the last two preoperative weeks to stabilize the clinical condition and reduce postoperative morbidity. Adjuvant pneumomediastinum was always induced within the last 24 hours to facilitate the subsequent visualization of the thymic tissue and the dissection maneuvers.⁵ The operation was performed after double-lumen intubation by a four-trocar access and with the patient lying in a 45-degree off-center position. Thymectomy routinely included en bloc removal of the residual thymus, if present, or all of the mediastinal-lower cervical perithymic adipose tissue (Fig. 1). Thymic

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Supported by a grant from MURST 60%.

Received for publication August 26, 1997; accepted for publication Sept. 3, 1997.

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J Thorac Cardiovasc Surg 1998;115:252-4

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0022-5223/98 \$5.00 + 0 12/54/85820

Table I. *Clinical data*

Variable	Case 1	Case 2	Case 3	Case 4
Thymic tissue location	Anterior mediastinal fat	Aorto-pulmonary window	Anterior mediastinal fat	Anterior mediastinal fat
Thymic tissue characteristics	Ectopic microscopic	Ectopic microscopic	Ectopic gross	Residual left lower horn
Weight of removed tissue (gm); fat $\pm$ thymus	20	28	16	27
Follow-up (mo)	19	17	13	11
Prednisone* (mg/day)	50 $\rightarrow$ 20	20 $\rightarrow$ 20	50 $\rightarrow$ 20	60 $\rightarrow$ 20
Pyridostigmine* (mg/day)	240 $\rightarrow$ 240	—	480 $\rightarrow$ 240	960 $\rightarrow$ 480
Azathioprine* (mg/kg/day)	—	3 $\rightarrow$ 3	—	—
Plasma exchange* (cycles/yr)	5 $\rightarrow$ 5	—	10 $\rightarrow$ 0	10 $\rightarrow$ 0
Osserman class*	IIB $\rightarrow$ I	IIB $\rightarrow$ IIB	IV $\rightarrow$ IIA	IV $\rightarrow$ I
Outcome	Improvement	No change	Improvement	Improvement

*Comparison of the preoperative/postoperative data.

tissue was identified at histologic examination by the presence of Hassal's corpuscle or after immunohistochemical staining with cytokeratin and T-cell markers. The therapeutic effect of completion thymectomy was established for each patient by comparing the preoperative clinical status with the status at the most recent follow-up examination. Completion thymectomy was performed by the left video-assisted approach in three patients and by the right approach in one patient because of diffuse pleural adhesions on the left side. Mean operative time was 136 minutes, ranging from 90 to 210 minutes. In all the patients thymic remnants were found below the left innominate vein. Mean weight of the removed tissue was 22.7 gm (Table I). No operative deaths nor major morbidity occurred. Mean hospital stay was 3.25 days (range 2 to 5 days). Mean follow-up was 15.0 months (Table I). Postoperatively, one patient required further plasma exchange treatment because of a myasthenic crisis, which occurred at 6 months. At the most recent follow-up examination, although no patient was in complete remission, three had significant improvement in bulbar and limb function, needing substantially lower doses of corticosteroids and anticholinesterase drugs (Table I). Both patients who had removal of the gross thymic tissue improved after completion thymectomy.

Standard transcervical and transsternal thymectomy have been implicated as possible causes of incomplete thymectomy.²⁻⁴ In these cases completion thymectomy carried out by the extended transsternal^{2,3} or maximal transsternal-transcervical approaches⁴ proved effective in ameliorating the effects of refractory myasthenia gravis.

Similarly we noted that video-assisted completion thymectomy provided clinical improvement in three of four patients. In our experience clinical improvement clearly correlated with the reoperation, because symptoms eased soon after the operation and the improvement persisted during the follow-up period. We have always intentionally performed an extended dissection of the residual thymus and adipose perithymic tissue, and we have found residual thymic tissue in all our patients.

We believe that the video-assisted approach might be considered a reliable alternative to the transsternal or

the combined approach for a number of reasons. First, it is minimally invasive, which however does not seem to compromise either a complete anatomic thymectomy or a wide dissection of the anterior mediastinal and lower cervical adipose tissue. Second, patients with chronic refractory myasthenia are often receiving high doses of steroids, which exposes them to an increased risk of wound healing problems if the transsternal approach is used. Third, the transsternal reexploration of the anterior mediastinum after transcervical or transsternal thymectomy might be particularly demanding because dense adhesions might be found at the site of the innominate vein. On the other hand, the surgical reexposure of the anterior mediastinum can be facilitated by using a different route, such as the transpleural route. Finally, the magnified video imaging may allow better visualization of the vascular and nervous structures and may help reduce the risk of injuring them during the dissection maneuvers. To date the combined transsternal-transcervical thymectomy represents the gold standard in terms of extent of dissection and removal of ectopic thymic tissue in patients with myasthenia.⁴ However, many patients and neurologists are reluctant to accept it because of its invasiveness and because its superiority over other approaches has not yet been demonstrated. This initial experience suggests that completion thymectomy is not a contraindication for the video-assisted approach, which might prove as effective as open approaches. The role of the video-assisted thymectomy is evolving and seems to hold unsuspected potentiality. More detailed studies based on a wider accrual of patients and longer follow-up are needed to confirm these findings.

REFERENCES

1. Husain F, Ryan NJ, Hogan GR, Gonzalez E. Occurrence of invasive thymoma after thymectomy for myasthenia gravis: report of a case. *Neurology* 1990;40:170-1.
2. Masaoka A, Monden Y, Seike Y, Tanioka T, Kagotani K. Reoperation after transcervical thymectomy for myasthenia gravis. *Neurology* 1982;32:83-5.
3. Miller RG, Filler-Katz A, Kiprov D, Roan R. Repeat thymec-

- tomy in chronic refractory myasthenia gravis. *Neurology* 1991; 41:923-4.
4. Jaretzki A, Penn AS, Younger DS, Wolff M, Olarte MR, Lovelace RE, et al. "Maximal" thymectomy for myasthenia gravis: results. *J Thorac Cardiovasc Surg* 1988;95:747-57.
 5. Mineo TC, Pompeo E, Ambrogi V, Sabato AF, Bernardi G, Casciani CU. Adjuvant pneumomediastinum in thoracoscopic thymectomy for myasthenia gravis. *Ann Thorac Surg* 1996;62: 1210-2.
 6. Mack MJ, Landreneau RJ, Yim AP, Hazelrigg SR, Scruggs GR. Results of video-assisted thymectomy in patients with myasthenia gravis. *J Thorac Cardiovasc Surg* 1996;112:1352-60.

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