Case Report

Long-Term Clinical Outcome after Extended Thymectomy Combined Postoperative High-Dose Steroid Therapy for Juvenile Myasthenia Gravis

Masato Kanzaki, MD,[1,2] Tetsuya Obara, MD,[1] Susumu Sasano, MD,[2,3] Yoshio Hikawa, MD,[4] and Takamasa Onuki, MD[2]

Myasthenia gravis (MG) is considered to be an autoimmune disorder of neuromuscular transmission and is rare in childhood. We report 3 juvenile MG (JMG) cases of extended thymectomy (ETMX) combined postoperative high-dose steroid therapy. All patients developed MG symptoms under the age of 14 years and were given cholinergic drugs and had generalized MG: the Myasthenia Gravis Foundation of America classification II was present in 1 case and classification III was in 2. All patients were taking pyridostigmine before surgery; none was treated with prednisone preoperatively. All patients performed the ETMX combined postoperative high-dose steroid therapy. Muscle weakness of extremities and bulbar symptoms improved in all patients, but not all exhibited an unstable phase in their clinical course as a result of combined therapy. There was no postoperative morbidity or mortality. All patients had follicular lymphoid hyperplasia without thymoma. Follow-up for more than 5 years has shown one to be in complete remission and the others to have improved symptoms. Although our results are inconclusive because we used only a few JMG patients, the ETMX combined postoperative high-dose steroid therapy appeared to provide a better chance of remission or control of symptoms. (Ann Thorac Cardiovasc Surg 2008; 14: 119–122)

Key words: myasthenia gravis, thymectomy, juvenile myasthenia gravis, steroid therapy

Introduction

Myasthenia gravis (MG) is a rare autoimmune disorder occurring in 0.5 to 5.0 per 100,000 people. Particularly, childhood or adolescent-onset MG accounts for 11% to 24% of all patients with MG.[1,2)] It affects neuromuscular transmission to the muscle nicotinic acetylcholine receptor (AChR).[3)] The autoantibodies associated with MG are directed at the AchR in the neuromuscular junction and lead to a functional and numeric AChR decrease.[4)] Therapeutic options for patients with MG include medical therapy with anticholinesterase inhibitors, such as pyridostigmine, or immunosuppressive medications, such as corticosteroids and azathioprine, plasmapheresis or intravenous immunoglobulin, and surgical treatment by thymectomy (TMX). There is considerable controversy with regard to the various combinations of these therapies and their sequence of use.

We present 3 juvenile MG (JMG) cases of extended thymectomy (ETMX) combined postoperative high-dose steroid therapy.

Case 1

A 12-year-old male presented an onset of both eyelid ptosis and diplopia. AchR antibodies were present at 8.9

From Departments of [1]Thoracic Surgery and [4]Anesthesiology, Tokyo Metropolitan Fuchu Hospital, Fuchu; [2]Department of Surgery I, Tokyo Women's Medical University School of Medicine, Tokyo; and [3]Department of Respirology, Tokyo Metropolitan Tama Cancer Detection Center, Tokyo, Japan

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Address reprint requests to Masato Kanzaki, MD: Department of Thoracic Surgery, Tokyo Metropolitan Fuchu Hospital, 2–9–2 Musashidai, Fuchu 183–8524, Japan.

nmoL/L (reference range: 0.00–0.30 nmol/L). He experienced 2 months of worsening dysphagia and was starting to take pyridostigmine in daily doses of 180 mg. Moreover, the diagnosis of MG was based on the association of clinical signs of fluctuating weakness of voluntary muscles with fatigability and at least two of the following criteria: unequivocal improvement i.v. edrophonium/i.m. neostigmine injection; electrophysiological signs of abnormal neuromuscular transmission, such as a decrement of more than 10% in compound muscle action potential on low-rate supramaximal repetitive nerve stimulation or prolonged jitter on single fiber electromyography, detectable serum anti-AChR antibody (Ab). The preoperative severity of the disease was classified according to the Myasthenia Gravis Foundation of America (MGFA) clinical classification. The preoperative MGFA class was III. One month when dysphagia appeared later, he underwent an ETMX and was extubated at the end of the procedure. There were no complications, including a myasthenic crisis. The resected thymus weighed 46 g, and follicular lymphoid hyperplasia was without thymoma. About 4 weeks after surgery, steroid therapy was performed by administering 80 mg/body of prednisone on alternate days, followed by its being gradually tapered off. The muscle weakness of extremities and bulbar symptoms has improved, and 7 years has now passed. The eyelid ptosis remains, and the patient is taking pyridostigmine in daily doses of 60 mg.

Case 2

A 12-year-old male presented an onset of diplopia and had coexisting Hashimoto's thyroiditis. He was not elevated AchR antibody titer of 0.30 nmoL/L. The diagnosis of MG was in the same fashion as with case 1. The reoperative MGFA was class II. He was administered pyridostigmine (180 mg/day). Nine months after the onset of diplopia, he underwent an ETMX and was extubated at the end of the procedure. The postoperative course was uneventful. The resected thymus weight was 63 g, and a histopathologic examination showed that the thymus was undergoing follicular lymphoid hyperplasia without thymoma. About 4 weeks after surgery, steroid therapy was performed by administering 80 mg/body of prednisone on alternate days and tapering off gradually. His symptom improved after combined therapy. He had been taking pyridostigmine for 3 years and achieved drug-free remission about 4 years after combined therapy. Seven years has now passed since he underwent surgery.

Case 3

A 14-year-old male presented an onset of diplopia. The diagnosis of MG was in the same fashion as with the previous 2 cases. He was taking pyridostigmine in daily doses of 180 mg. Two months later a muscle weakness of the extremities developed. Therefore his daily dose of pyridostigmine was increased to 240 mg. He progressed to bulbar symptoms, such as dysphagia. The preoperative MGFA was class III. Twenty months later diplopia appeared, and he underwent an ETMX; he was extubated at the end of the procedure. The postoperative course was uneventful. A histopathologic examination revealed thymic follicular hyperplasia. About 4 weeks after surgery, steroid therapy was performed by administering 100 mg/body of prednisone on alternate days followed by a gradual tapering off. When he changed oral medication to pyridostigmine (180 mg/day) from prednisone, intolerable side effects (nausea, cramping, and diarrhea) appeared. Therefore he has been using long-term steroid therapy, and every other 5 mg dose of prednisone is followed by a gradual tapering off. Eighteen years has now passed since he underwent surgery.

The case profiles are detailed in Table 1.

Discussion

MG is an autoimmune disease resulting from autoantibodies being produced against the AChR at the motor endplate, causing a defect in neuromuscular transmission.

Medical management consists of maintaining anticholinesterase inhibitors, such as pyridostigmine for symptomatic relief and immunosuppression, and such as corticosteroids azathioprine and tacrolimus to treat the underlying autoimmunity. Severe forms of MG require surgical TMX. Considerable controversy exists with regard to the various combinations of these therapies and their sequence of use. Recently, perioperative high-dose prednisone has been used because it provides clinical benefits during the perioperative period. Although it is only a matter of opinion, the reason why we do not use preoperative steroids is because of the belief that steroids disturb wound healing such as sternal dehiscence, superficial wound dehiscence, and superficial wound suppuration.[5–8] However, the rate of infectious complications after transsternal TMX does not increase, even if preoperative high-dose steroids are used.[9] Although indications for perioperative steroids are different between our strategy and the strategy of others, whether or not the goal of

Table 1. Clinical features

Patient	Sex	Age at onset (years)	Duration of symptoms (months)	Age at thymectomy (years)	Preoperative severity*	Postoperative severity*	Outcome therapy	Final	Follow-up (years)
1	M	12	5	12	III	I	MI	PY	7
2	M	12	9	13	II	–	R	None	7
3	M	14	20	15	III	I	MI	PS	18

*The Myasthenia Gravis Foundation of America clinical classification. R, remission; MI, marked improvement; PY, pyridostigmine; PS, prednisone.

treatment strategy for MG is that patient complete remission.

From January 1987 to December 2004, a total of 165 patients with MG, including 9 teenagers, were experienced at our hospital. Therapeutic management followed the same rationale for all patients. First, anticholinesterase inhibitors were used as needed to improve the symptoms; next, all patients with MG were subjected to ETMX combined postoperative high-dose steroid therapy in our hospital. About 4 weeks after ETMX, excepting and 8 postoperative myasthenic crises that were received high-dose steroid therapy immediately, the patients were treated with prednisone, 1.5–2 mg/kg (max 100 mg/body), a regimen that gradually was changed to every-other-day medication and finally a gradual reduction of dosage. The quantity of prednisone must be guided by the patient's clinical response. When symptoms of MG were stable, prednisone reduced it by 5 mg every two months. When a symptom showed instability or exacerbation after steroid reduction, the patient was forced to increase the quantity of prednisone dosages. Furthermore, when the amount of prednisone became 30 mg on alternate days, the patient started taking 180 mg of pyridostigmine every day. Both prednisone and pyridostigmine were tapered off very slowly, a process that may require months or years. All patients had no early or late morbidity. Especially, such side effects as growth disorder caused by hypercatabolism of protein did not appear in all JMG cases. Alternate-day dosing is encouraged to lessen adverse side effects and should be tapered off to the lowest effective dose. In our experience, the effective maintenance dose has been determined as the smallest dose of prednisone that allows the patient to maintain maximal improvement, and the long-term results of combined therapy justify the potential morbidity.

Moreover, a myasthenic crisis was conformed on 9 patients preoperatively. These patients were hospitalized for the initiation of steroid therapy. TMX was performed with the use of prednisone, and because clinical symptoms were stable, this was followed by its use being gradually tapered off.

The role of TMX in the management of adult MG is widely accepted. Most clinicians recommend surgery over medical treatment for severe generalized disease refractory, though controversy exists as to efficacy, appropriate timing, and immunologic safety in JMG.[4,10] It is difficult to predict JMG prognosis. Some patients undergo spontaneous remission after a period of months or years. Others have a permanent disease extending into adult life, and long-life immunomodulating therapy is often required. No deleterious consequences after the removal of the thymus in children have been reported.[11–14] Some authors report good results after surgery in prepubertal children; others describe a lower remission rate in younger patients than in older ones, or they even advise caution regarding TMX in very young children because of the possibility of spontaneous remission.[1,11–17] Long-term follow-up has shown one patient to be in complete remission requiring no medication, and the others to have improved symptoms. Other series have reported remission rates ranging from 10% to 40%.[3,4,10,15,16,18] Although our results are inconclusive because only a few patients, our JMG patients, can be treated satisfactorily, the ETMX combined postoperative high-dose steroid therapy appeared to provide a better chance for remission or control for symptoms.

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