

Clinical Profiles of Thai Patients with Ocular Myasthenia Gravis in Siriraj Hospital

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Ninety-six patients with ocular myasthenia gravis (OMG) seen at Siriraj Hospital during 1994 to 2004 were retrospectively reviewed. There were 59 female (61.5%) and 37 (38.5%) male patients with mean ages of 39.5 and 33.8 years, respectively. Patients presented with initial symptoms of only ptosis in 46.9%, only diplopia in 13.5% and both ptosis and diplopia in 39.6%. However, diplopia alone is uncommon in childhood OMG. Fifteen percent developed systemic symptoms within two years of diagnosis. Thyroid function test was abnormal in 27.5% of investigated patients. Most abnormalities were hyperthyroidism. Thymoma associated with OMG is a rare condition. Most purely OMG patients can control the disease by pyridostigmine, prednisolone or immunosuppressive drugs.

Keywords: Ocular myasthenia gravis, Ptosis, Diplopia, Pyridostigmine, Generalized myasthenia gravis

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Ocular myasthenia gravis (OMG) is considered as an acquired autoimmune disorder that involves abnormal neuromuscular transmission. The clinical symptoms of these patients are levator weakness, manifested by ptosis or extraocular muscle weakness, manifested by diplopia⁽¹⁾. Moreover, clinical results also show that some patients may develop systemic symptoms later.

The authors' previous study found that initial symptoms of both ptosis and diplopia were a significant factor associated with insensitivity to pyridostigmine therapy⁽²⁾, unlike other studies^(3,4) which revealed that diplopia alone was associated with insensitivity to pyridostigmine. The possible reason for this might be from the difference in characteristics and natural history of OMG between Asian and Caucasian patients. However, there have only been a few studies in Thailand which studied and reported about Thai OMG patient data⁽⁵⁾. Thus the present study was designed to evaluate clinical profiles of Thai patients with OMG in Siriraj Hospital.

Material and Method

The medical records of patients with a diagnosis of OMG during the period 1st January 1994 to 31st December 2004 were selected from the databases of the Out Patient Department of the Department of Ophthalmology, Siriraj Hospital. The authors also included the patients from their previous study⁽²⁾. The present study was approved by the Institutional Review Board of Siriraj Hospital. All medical records were retrospectively reviewed. The diagnosis of OMG was determined primarily by history and clinical presentation, including muscle fatigability limited to the extraocular muscle or the levator palpebrae superioris. Patients with a diagnosis of OMG were confirmed by positive response to an anticholinesterase test (neostigmine test or edrophonium test)^(6,7) or clinical response to pyridostigmine administration.

The patients were excluded from the present study if they were diagnosed as generalized myasthenia gravis (GMG) within one month after diagnosis. Proximal muscle weakness, dysphagia, dysarthria, dysphonia and respiratory difficulties were all considered signs of GMG.

General patients data were recorded including age, sex, initial symptoms to the first visit (only ptosis, only diplopia or combined ptosis and diplopia), the presence of systemic involvement after one month

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follow-up, associated thyroid disease, associated other autoimmune disease, presence of abnormal thymus gland (by computer topography and pathological section) and treatment. Initial symptoms of combined ptosis and diplopia were defined as the patients who had both ptosis and diplopia which presented within 1 month after developing symptoms of OMG.

Patients were divided in two groups according to the age of onset of OMG. The first group consisted of patients who were younger than 12 years old at age of onset (group I). The second group consisted of patients who were 12 years and older (group II).

Results

There were a total of 96 patients who met the inclusion criteria. Diagnosis of OMG was confirmed by a positive response to anticholinesterase test in 85 patients (88.5%). Eleven patients (11.5%) were established by the clinical response to pyridostigmine therapy. Fifty-nine patients were female and 37 patients were male (1.6: 1). The age at onset ranged from two to 78 years (mean 37.3 years) and mean follow-up was 3.6 years (range 2-30 years). There were 16 patients in group I and 80 patients in group II. The clinical characteristics and associated disease are summarized in Table 1.

Female to male ratio was 9:7 (1.3:1) in the first group and 5:3 (1.7:1) in the second group. Mean age at onset was 4.1 years in group I and 43.9 years in group II. During the first visit, the most common initial clinical presentation of all patients was ptosis (n = 45, 46.9%). Thirty-eight (39.6%) patients presented with both ptosis and diplopia and 13 patients (13.5%) presented with diplopia only. Results also showed that the most common initial clinical presentation of patients in group I was both ptosis and diplopia. Conversely, the most common initial clinical presentation of patients in group II was only ptosis without diplopia.

There were 15 patients (15.6%) who developed GMG. Five patients (31.3%) from group I developed GMG, while ten patients (12.5%) in group II developed GMG. By all means, patients had systemic symptoms and signs within 2 years after diagnosis of ocular myasthenia gravis.

Thyroid function test was investigated in 51 patients and it was found that 11 patients (21.6%) had hyperthyroidism and three patients (5.9%) had hypothyroidism. For patients in group I, 13 patients were investigated for thyroid function and it was found that one patient (7.7%) had hyperthyroidism and one patient (7.7%) had hypothyroidism. However, 38 patients in group II were investigated and it was

Table 1. Clinical characteristics and associated diseases of patients with ocular myasthenia gravis

	Group I (n = 16)	Group II (n = 80)	Total (n = 96)
Female/Male	9/7	50/30	59/37
Age (years)	4.1 (2-10)	43.9 (12-78)	37.3 (2-78)
Initial chemical presentation			
Ptosis	7 (43.75%)	38 (47.5%)	45 (46.9%)
Diplopia	-	13 (16.25%)	13 (13.5%)
Ptosis and diplopia	9 (56.25%)	29 (36.25%)	38 (39.6%)
Developed GMG	5 (31.3%)	10 (12.5%)	15 (15.6%)
Abnormal thyroid function			
Hyperthyroid	1/13 (7.7%)	10/38 (26.3%)	11/51 (21.6%)
Hypothyroid	1/13 (7.7%)	2/38 (5.3%)	3/51 (5.9%)
SLE	-	1	1
Abnormal thymus gland	3/8 (37.5%)	6/18 (33.3%)	9/26 (34.6%)
Thymoma	-	3	3
Lymphoid hyperplasia	2	1	3
Thymolipoma	1	-	1
Malignant thymoma	-	1	1

Group I: patients younger than 12 years old

Group II: patients 12 or older than 12 years old

SLE = systemic lupus erythematus

found that 10 patients (26.3%) had hyperthyroidism and two patients (5.3%) had hypothyroidism.

There was only one patient found with Systemic Lupus Erythematus (SLE). She was 40 years old and developed lupus nephritis.

Twenty-six patients underwent computed tomographic (CT) evaluation for thymus lesion. Nine patients (34.6%) were found to have abnormal thymus gland. From group I, CT scans were performed on 8 patients; three (37.5%) of these revealed abnormal thymus gland. CT performed on 18 patients in group II was abnormal in 6 patients (33.3%). Thymectomy was performed in eight patients from both groups. One patient was lost to follow-up before surgery. Pathological sections of these patients were thymoma in three patients. Three others demonstrated lymphoid hyperplasia. The last two patients were thymolipoma and malignant thymoma. Seven patients who had abnormal thymus gland developed GMG

All patients were treated with pyridostigmine. Forty-four patients (45.8%) did not respond to only pyridostigmine and were treated with other medications such as prednisolone, immunosuppressive treatment, thymectomy, extraocular muscle surgery, frontalis sling, and plasmapheresis. Clinical symptoms of 50 patients were improved to be normal or nearly normal. Clinical symptoms of 46 patients were improved but still exhibited some clinical defects.

Discussion

The present study revealed that overall OMG affected females more than males. It was the same finding in most studies of myasthenia gravis (MG)^(8,9). Whilst it showed nearly an equal number of males and females (9/7) in children younger than 12, the female to male ratio was 1.3 in childhood OMG. This result is the same as one previous study that recruited only children younger than 12⁽¹⁰⁾, while other studies which revealed a high female to male ratio (3-6/1) included children aged under 16^(11,12). The possible factors for the difference of female to male ratio may be from the difference in race, diagnostic criteria, and small number of patients. The other previous studies reported a higher incidence of MG in young women under 40 years old and men over 40^(1,8,9). To compare, the authors also divided the patients into prior and after 40 years old. The result showed no difference in gender between these two groups. The female to male ratios prior and after 40 years old were 1.25 and 2.1, respectively.

As the authors know, 31-70% of patients with OMG developed systemic signs and symptoms of GMG later^(1,13). In the present study, the patients with OMG developed systemic signs and symptoms at a rate of 15.8% and this was more common in patients younger than 12 years old (31.3%) compared to the older group (12.5%). The presented children developed GMG at the similar rate as a previous study⁽¹²⁾. If that study selected only children younger than 12 years old, the incidence rate would be 22%. Other studies reported a lower incidence rate (8-15%)^(10,11). The differences of the developed GMG rate might be due to the differences in race, diagnostic criteria, severity of disease, early treated with immunosuppressive drugs⁽¹³⁾ and the natural history of the disease. Generalized signs and symptoms developed within two years of diagnosis. This result was exactly the same as that of Western countries. Therefore, patients in whom the disease had been confined to the ocular muscles for two or more years seem unlikely to progress to generalized disease.

The clinical presentations in OMG are ptosis, diplopia or both ptosis and diplopia. The results confirm the finding of the previous study that diplopia alone is uncommon in childhood OMG⁽¹²⁾.

There was a coexistence of myasthenia gravis with other autoimmune disorders. Patients with myasthenia gravis had a chance to develop thyroid disease of about 5-10%^(1,14). In the present study, 27.5% of investigated patients had abnormal thyroid function and most of these were hyperthyroidism. This was similar to the incidence of thyroid disease in a study of OMG patients⁽¹³⁾. Due to the nature of the authors' retrospective data, all OMG patients were not investigated. OMG patients may often have abnormal autoantibodies against the thyroid gland and showed concomitant disorder of thyroid function more often than GMG patients. Another autoimmune disease, SLE, was also found in only one patient.

Enlarged thymus gland by CT scans was found in the same rate as the previous study⁽¹²⁾. However, thymoma was rare in the present study (3%) and compatible with the previous studies (0-5%)^(12,13,15-17). Thymectomy was the treatment of choice in patients with GMG who had thymic enlargement. Pure OMG was usually not treated by thymectomy but any patients with thymoma required thymectomy⁽¹⁸⁾. Thymectomy for pure OMG is controversial but tends to improve symptoms in most cases because lymphocytes in the thymus gland appear to be responsible for the production of

acetylcholine receptor antibodies⁽¹⁾. Eight patients (8.3%) in the present study underwent thymectomy and most of them had systemic involvement.

Treatment in each myasthenia gravis patient varies and depends on the severity of the disease. Most pure OMG patients can control the disease through use of pyridostigmine, prednisolone and other immunosuppressive drugs.

This was a longitudinal study that observed patients characteristics of OMG in order to have sufficient data for applying more efficient clinical research in the future. However, the scope of the present study was limited only to patients at Siriraj Hospital. Further research should expand the scope of the study by comparing clinical profiles between Asian and Caucasian populations. OMG patients may have to be reevaluated in the future.

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Potential conflicts of interest

None.

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ลักษณะทางคลินิกของผู้ป่วย *ocular myasthenia gravis* ในโรงพยาบาลศิริราช

สุพินดา ลือมรศิริ, นิพนธ์ จิรภาไพศาล, วณิชชา ชื่นก่องแก้ว

การศึกษาย้อนหลังผู้ป่วย *ocular myasthenia gravis* (OMG) จำนวน 96 คน ที่มาตรวจที่โรงพยาบาลศิริราช ในช่วงปี พ.ศ. 2537 ถึงปี พ.ศ. 2547 โดยเป็นผู้หญิง 59 คน (61.5%) อายุเฉลี่ย 39.5 ปี และเป็นผู้ชาย 37 คน (38.5%) มีอายุเฉลี่ย 33.8 ปี อาการเริ่มต้นมีเพียงหนังตาตก 46.9% มีเพียงภาพซ้อน 13.5% และมีทั้งหนังตาตก และภาพซ้อน 39.6% โดยภาพซ้อนเพียงอย่างเดียวเป็นลักษณะที่พบไม่บ่อยในผู้ป่วยเด็กที่มี OMG ผู้ป่วยจำนวน 15% จะมีอาการทางร่างกายภายในเวลา 2 ปีหลังได้รับการวินิจฉัยว่าเป็นโรค OMG โดยพบความผิดปกติของต่อมไทรอยด์ 27.5% ส่วนใหญ่เป็น *hyperthyroidism* เนื่องจาก *thymoma* พบน้อยโดยผู้ป่วย OMG ส่วนใหญ่สามารถคุมอาการได้ด้วย *pyridostigmine*, *prednisolone* หรือ ยากดภูมิคุ้มกันต้านทานโรค
