eNeurologicalSci 4 (2016) 30–33

Contents lists available at ScienceDirect

eNeurologicalSci

journal homepage: http://ees.elsevier.com/ensci/

Characterization of patients with ocular myasthenia gravis — A case series

Arnon Karni [a,*], Ali Asmail [a], Vivian E. Drory [c], Hadar Kolb [a], Anat Kesler [b]

[a] Neuroimmunology Clinic, Tel Aviv Sourasky Medical Center, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[b] Neuro-ophthalmology Unit of the Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[c] Neuromuscular Service of the Department of Neurology, Tel Aviv Sourasky Medical Center, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ARTICLE INFO

Article history:
Received 23 March 2016
Accepted 23 April 2016
Available online 25 April 2016

Keywords:
Ocular myasthenia gravis
Generalized myasthenia gravis
Anti acetyl choline antibody
Thymoma
Thymic hyperplasia

ABSTRACT

Ocular myasthenia gravis (OMG) is sometimes difficult to diagnose and is probably both under-diagnosed and misdiagnosed. We studied the epidemiological parameters, relevant serology, electromyographic (EMG) findings, and the relationship between OMG and thymoma, thymus hyperplasia and other autoimmune disorders compared to generalized MG (GMG) in a case control study of 133 patients with MG (32 patients with OMG and 101 patients with GMG). The proportion of OMG among all MG patients was relatively high (24.1%). It affected more males than females and its onset was at an older age. Although anti-AChR Ab was detected in fewer OMG patients compared to GMG patients, the rate of positive serology in OMG patients was higher than previously reported. Male OMG patients had a higher positive serology rate than female OMG patients. OMG patients tended to have less supportive EMG evidence of neuromuscular disorder. Female OMG patients had higher rates of thymus hyperplasia and higher rates of other autoimmune disorders than males.

Diagnosing MG in patients with solitary ocular manifestation may be difficult due to lower rates of paraclinic supportive tests. Awareness of the characteristics of OMG is important in order to avoid delayed or misdiagnosis of MG and to prevent avoidable iatrogenic complications.

1. Introduction

Myasthenia gravis (MG) is an autoimmune disease against the post-synaptic components of the neuromuscular junction (NMJ) of the striated skeletal muscle. The disease is mediated by antibodies (Ab) against the acetylcholine receptor (AChR) in the majority of the patients [1,2] and in some patients by Ab against muscle specific kinase (MuSK) that play a role in AChR clustering or Ab against low-density lipoprotein receptor-related protein 4 (LRP4) that forms a complex with MuSK [3]. The disease manifestation includes muscular weakness that tends to fluctuate. Some patients have ocular weakness (ptosis and/or ophthalmoparesis) as the only symptom of the disease along its entire course, and they are designated as having ocular MG (OMG), while the majority of the patients also have weakness of extraocular muscles and they are designated as having generalized MG (GMG) [4]. The reasons for the predilection of MG to involve ocular muscles are not entirely clear, but they appear to be related to the facts that the extraocular muscles have less prominent synaptic folds, fewer postsynaptic AChRs and smaller motor units, in addition to being subject to high-firing frequencies [5].

About 90% of individuals who have the ocular form for more than 2 years will remain in the OMG subgroup [6]. The age at onset, serology, association with thymus pathology or with other autoimmune disorders and response to therapy may differ in patients with OMG from those with GMG [7]. Since fewer OMG patients have detectable anti-AChR Ab in their sera compared to GMG patients, it is more difficult to diagnose seronegative patients with only ocular manifestations as having MG. In this observational case control study, we sought to study the epidemiology, and the clinical, serology, and electromyographic (EMG) characteristics of individuals diagnosed as having OMG and to compare those parameters with those patients with GMG.

2. Methods

2.1. Study design and participants

We retrospectively reviewed all files of patients diagnosed as having MG who attended the Neuro-immunology Clinic at the Tel Aviv Medical Center, Tel Aviv, Israel from January 1, 2006 until December 31, 2014.

Abbreviations: OMG, ocular myasthenia gravis; SP, seropositive; SN, seronegative; AChR, acetyl choline receptor; MuSK, muscle specific kinase; RSEMG, repetitive stimulation electromyography; SFEMG, single fiber electromyography.

* Corresponding author at: Department of Neurology, Tel Aviv Sourasky Medical Center, 6 Weitzman St., Tel Aviv 6423906, Israel.
E-mail address: arnonk@tlvmc.gov.il (A. Karni).

http://dx.doi.org/10.1016/j.ensci.2016.04.005

Table 1
Gender and age at myasthenia gravis onset.

a	GMG n = 101	OMG n = 32	*P* value
Females: males	54:47	11:21	0.047
Age at onset (years, mean ± SD, range)	55.2 ± 20.9, 15–90 y	60.1 ± 13.6, 31–80 y	0.136
Age at onset > 50 years (%)	55.4%	78.1%	0.038
b	Females	Males	*P* value
Age at OMG onset (years, mean ± SD, range)	55.0 ± 16.8, 33–80 y	62.5 ± 11.5, 31–78 y	0.221
Age at GMG onset (years, mean ± SD, range)	50.5 ± 23.0, 15-84 y	60.9 ± 16.9, 21–90 y	0.014

Abbreviations: GMG, general myasthenia gravis; OMG, ocular myasthenia gravis; SD, standard deviation.

The MG diagnosis was determined by history, physical examination, single-fiber EMG (SFEMG), repetitive-stimulation EMG (RSEMG), edrophonium testing and Ab serology of anti-AChR Ab or anti-MuSK Ab. In addition to compatible history and physical examination findings, the diagnosis of MG was established when at least 1 of the 3 following types of tests was supportive for MG: serology, SFEMG and/or RSEMG, and edrophonium assessments, as well as when other possible diagnoses were ruled out.

Included in the study were 133 patients diagnosed as having MG with disease duration of more than 2 years. The patients were categorized into 2 groups, OMG and GMG. All the patients underwent serology tests for anti-AChR Ab (tested by radioimmunoassay), and those who were negative were also tested for anti-MuSK Ab (tested by radioimmunoassay). All the serological assays were done in the same laboratory. They all underwent SFEMG and all GMG patients underwent also RTEMG that were done at the time of investigation for the possible diagnosis of MG. Some of them also underwent edrophonium test. All the study patients had either a chest computerized tomogram or a magnetic resonance imaging scan of the chest, and those that were detected with suspected thymic tissue underwent thymectomy. The pathology results determined whether there is thymic hyperplasia, thymoma or non thymic tissue.

2.2. Data analyses

The study was approved by the local Helsinki Committee. The significance of differences between groups was examined by Student's *t*-test for parametric parameters and by the Chi-Square test or Fisher Exact test for non-parametric parameters. Data are presented as mean ± standard deviation for age at the time of disease onset or as the number of patients for the other studied variables.

3. Theory

We hypothesized that as compared to patients with GMG, patients with OMG differ in epidemiology and electromyography features as well as in the rates of association with thymic pathology and with other autoimmune disorders.

4. Results

4.1. Rate of OMG

One-hundred and thirty-three MG patients (66 females and 67 males) were included in the study. Of them, 101 patients had GMG and 32 had OMG. We compared epidemiological parameters, serological results, EMG findings and the association with thymus hyperplasia and thymoma as well as with any other existing autoimmune disorders between the OMG patients and the GMG patients. OMG was diagnosed in 24.1% of our study cohort, and tended to occur more in males (n = 21) than in females (n = 11), unlike the trend in GMG which occurred in fewer males (n = 46) than females (n = 55), $P = 0.047$.

4.2. Age of OMG onset

The age at disease onset tended to be older among the OMG patients (60.1 ± 13.6 years) compared to the GMG patients (55.2 ± 20.9 years, $P = 0.136$). A higher proportion of OMG patients was older than 50 years at disease onset (n = 25, 78.1%) compared to GMG patients (n = 56, 55.4%, $P = 0.038$) (Table 1a). There were gender differences in the age at MG onset: there was a trend towards a difference in the OMG group (females: 55.0 ± 16.8 years, males: 62.5 ± 11.5 years, $P = 0.221$), while the difference between the females (50.5 ± 23.0 years) and males (60.9 ± 16.9 years) reached a level of significance ($P = 0.014$) in the GMG group (Table 1b). An age of onset until 50 years was found in 36.4% of females vs. 14.3% of males in the OMG patients and in 52.7% of the females and 26.1% of the males in the GMG patients.

4.3. Rates of thymic involvements

No significant differences were found in the rates of thymoma, thymus hyperplasia and non-thymus pathology between the OMG patients (2, 3 and 27 patients, respectively) and the GMG patients (6, 22 and 73 patients, respectively) (Table 2a). Thymus hyperplasia was found only among females (3 out of 11 patients) in the OMG group ($P = 0.029$). There was a similar trend in the occurrence of thymus hyperplasia in the GMG patients (16 out of 55 female patients vs. 6 out of 46 male patients, $P = 0.051$) (Table 2a). Thymoma and thymus hyperplasia were more common in the GMG patients with age at disease onset ≤ 50 years (6 and 18 patients, respectively) than in the GMG patients with age at disease onset > 50 years (none with thymoma and 4 patients with hyperplasia, $P = 0.007$ and $P < 0.001$, respectively). There was no difference in the occurrence of thymoma or thymus

Table 2
The relation of thymus pathologies with clinical manifestations of myasthenia gravis and gender.

a	GMG n = 101	OMG n = 32	*P* value
Thymoma	6	2	1.00
Thymus hyperplasia	22	3	0.188
b	Females	Males	*P* value
Thymus hyperplasia in OMG	3/11	0/22	0.029
Thymus hyperplasia in GMG	16/55	6/46	0.051
c	Age at onset ≤50 years	Age at onset >50 years	*P* value
Thymomas in OMG	1/7	1/25	0.395
Thymomas in GMG	6/46	0/55	0.007
Thymus hyperplasia in OMG	2/7	1/25	0.113
Thymus hyperplasia in GMG	18/46	4/55	>0.001

Abbreviations: GMG, general myasthenia gravis; OMG, ocular myasthenia gravis.