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Clinical Study

Clinical features and impact of myasthenia gravis disease in Australian patients

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ABSTRACT

We performed a community-based survey of 165 Australian patients with a physician-confirmed diagnosis of myasthenia gravis (MG). MG is an autoimmune disease of the neuromuscular junction causing fatiguable muscle weakness. Patients with early onset MG (<40 years of age) were more frequently female (22 males, 60 females) whereas patients with late onset MG (>40 years of age) were more frequently male (50 males, 28 females; $p < 0.001$). Triggering and exacerbating factors included physical and emotional stress, infections, surgery or trauma, seasonal changes and medications. The co-occurrence of other immune-related diseases was reported by 54% of patients. The median MG quality of life (QOL) score was 92 (range: 24–186). The factor most strongly associated with poor QOL was depression. Only 40.6% of patients were working at the time of the survey and of these, almost half had required sick leave due to MG in the past 12 months. A further 39.4% had stopped work due to MG and 19.4% having to change occupation. Full-time or part-time care was required by 29% of patients and government financial support was received by 52.7%.

1. Introduction

Myasthenia gravis (MG) is an autoimmune disease characterized by fatiguable muscle weakness. MG is mediated by antibodies, usually against the acetylcholine receptor (AChR) [1]. However, T cell immunity also plays an important role in the pathogenesis of the disease [2]. Weakness can affect the ocular, bulbar, trunk and limb muscles, and weakness due to MG can range in severity from mild ocular muscle weakness to severe weakness affecting respiratory muscles [3].

Epidemiological studies have reported the prevalence of MG to be to be about 100 to 200 per million [4,5]. In Australia, a review of prescriptions for pyridostigmine was used to study the occurrence of MG and the prevalence was estimated at 117 per million and incidence at 24.9 per million [6]. There have been no reports of the clinical features of MG in Australia. We have conducted a community-based survey of patients with MG and now report the clinical features including the diagnosis, treatment and triggers for onset of disease and the recorded association with other autoimmune diseases.

The effect of MG on quality of life (QOL) has been explored using generic measures like short form health surveys (SF-36) as well as MG-specific scores [7–10]. QOL with MG has been found to correlate with disease severity as measured by the Myasthenia Gravis Foundation of America score, and has been found to be useful in clinical trials [11–13]. A disease-specific, 60 question quality of life questionnaire (MG-QOL60) has been found to be superior to the generic SF-36 in MG patients [10,13]. The impact of MG has not been studied in Australian patients so we aimed to assess the impact of disease in a cohort of Australian patients with MG using MG QOL, questions about depression, and psychosocial and financial impacts.

2. Methods

2.1. Survey of patients

This study was approved by the Ethics committee of the Royal Brisbane and Women's Hospital. All patients gave informed consent. Patients with MG were recruited in a survey performed in collaboration the Myasthenia Gravis Association of Queensland. A total of 303 patients were approached. The patients were asked to complete a 37 page survey document. Questions asked included

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demographic data, symptoms of MG, possible triggers for disease, exacerbating factors, occurrence of other autoimmune diseases and treatment, and the MG-QOL60 questionnaire. A score ranging from 0 to 240 was calculated with higher scores indicating worse QOL [10]. The participants were also asked to provide confirmation of their diagnosis by their treating neurologist including data regarding confirmatory testing. The survey document is available in a supplementary file (Supp. Fig. 1).

Of 198 responses, 165 were used for this analysis with 33 patients being excluded due to lack of information regarding confirmatory tests such as seropositivity to AChR/muscle-specific receptor tyrosine kinase (MuSK) antibodies, repetitive nerve stimulation, single fibre electromyography and positive tensilon test, or due to incomplete responses.

2.2. Statistical analyses

Data was entered into Excel and Access files (Microsoft Corp., Redmond, WA, USA). Data was analysed using SPSS Statistics (version 21; IBM Corporation, Armonk, NY, USA) and Excel. Chi-squared testing was used for statistical significance when comparing groups. To assess factors impacting on QOL, we split our cohort by comparing patients in the first quartile (good QOL: $\leqslant 65$) with the fourth quartile (poor QOL: $\geqslant 125$). We performed Fisher's exact tests to assess the influence of various factors on QOL with Bonferroni correction for multiple tests.

3. Results

3.1. Patient group

Responses were received from 198 patients. In 172 of these, clinical confirmation of diagnosis combined with positive results of a confirmatory test was provided by the treating physician (Table 1). A further seven patients were excluded as they had not completed the questionnaire. This left 165 patients for analysis, as shown in Table 2. Of these, 138 (81.8%) were seropositive for AChR antibodies and 6 (3.6%) were MuSK antibody positive with the remainder being seronegative. The majority of the patients were born in Australia (n = 126; 76%), with the remainder originating from middle and western European countries (n = 26; 15.7%). Due to the method of recruitment, the majority (n = 92; 73%) are currently living in Queensland with the remainder living in other Australian states, mainly New South Wales (18%). The genetic background was reported to be largely Caucasian.

3.2. Age of onset and age at diagnosis

The mean age ± standard deviation (SD) of disease onset was 47.4 ± 19.7 years and the mean age at diagnosis was 50.8 ± 18.4 years. There were 82 patients, 22 men and 60 women, with early onset myasthenia gravis (EOMG; onset less than 50 years;) and 78 patients, 50 men and 28 women, with late onset myasthenia gravis (LOMG; $p < 0.001$). The distribution of age of onset is shown in Figure 1. The age of onset peaked at shortly after

Table 1
Diagnostic tests used in myasthenia gravis patients (multiple answers possible per patient)

Test	Patients, n (%)
Repetitive nerve stimulation	60 (36.3)
Single fibre electromyograph	21 (12.7)
Tensilon test	52 (31.5)
Ice pack test	14 (8.5)

Table 2
Clinical characteristics of the 165 myasthenia gravis patients surveyed

Variable	Patients, n (%)
Sex	
Male	72 (41.9)
Female	93 (54.1)
Antibody status	
AchR Positive	138 (83.6)
MusK positive	6 (3.4)
Other autoantibodies	3 (1.8)
Antibody negative	21 (12.8)
Supportive therapy at any time	
Ventilation	35 (21.2)
Feeding tube	27 (16.4)
Both	21 (12.7)
In remission	36 (21.8%)

AChR = acetylcholine receptor, MuSK = muscle-specific receptor tyrosine kinase.

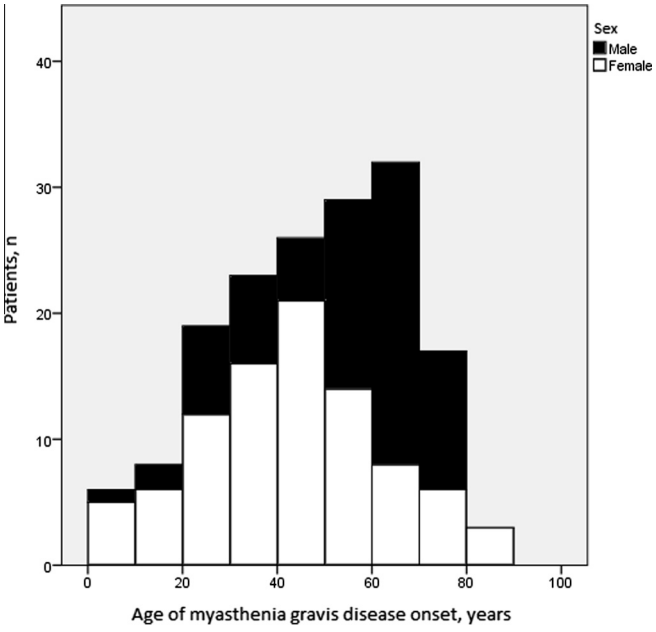

Fig. 1. Histogram of age of myasthenia gravis onset in men and women from this study cohort. The age of onset peaked at shortly after 40 years for women and men were more commonly affected at a later stage of life (peak 60–65 years).

Table 3
Initial symptoms and current symptoms identified by myasthenia gravis survey respondents (multiple answers were allowed per patient)

Symptom	Initially, n (%)	Last 12 months, n (%)
Weak eyelids	111 (67.2)	81 (49.1)
Double vision	100 (60.6)	66 (40.0)
Arms weakness	92 (55.7)	100 (60.6)
Weak legs	87 (52.7)	96 (58.2)
Weakness neck	53 (32.1)	47 (28.5)
Weakness face	78 (47.2)	59 (35.8)
Speech	90 (54.5)	71 (43.0)
Chewing	82 (49.6)	62 (37.6)
Swallow	78 (47.2)	61 (37.0)
Breathing	57 (34.5)	69 (41.8)
Fatigue	98 (59.3)	109 (66.1)
Balance	43 (26.0)	60 (36.4)
Pelvic floor weakness	41 (24.8)	70 (42.4)
Cough incontinence	30 (18.1)	57 (34.5)
Feeding tube	8 (4.8)	5 (3.0)
Ventilator	12 (7.2)	12 (7.3)