MYASTHENIA GRAVIS: A CLINICAL STUDY OF ONE-HUNDRED PATIENTS

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Abstract-One hundred myasthenic patients were prospectively studied. The ratio of female to male was approximately 1.12. Disease onset was most common in the third decade. The incidence of disease onset after age 50 was significantly higher in men. The most common presenting symptoms were ocular, seen in 76% of patients. In several cases, disease presentations were atypical, with symptoms such as weakness of chin or jaw, or dysphonia. In 31% of cases, the symptoms remained confined to ocular problems for two years or more. Accompanying disease states were present in 5% of patients. Twenty-two percent had a myasthenic crisis, which was more common in women. Thirty-three patients underwent thymectomy. The most common thymus histopathology was hyperplasia (75.7%). Thymoma was observed in six cases (18.1%). Four patients died during the study period. Acta Medica Iranica 33(1&2): 103-105; 1995

Key words: myasthenia gravis; neuromuscular junction; myasthenic crisis; thymus; thymectomy; plasmapheresis

INTRODUCTION

Myasthenia gravis (MG) is the most common disorder of neuromuscular transmission, caused by an antibody-mediated attack upon nicotinic acetylcholine receptors. It is characterized by a fluctuant weakness of certain voluntary muscles. It is a disease of worldwide distribution, that no study has to date suggested marked geographic differences in the incidence, prevalence, or clinical aspects of the myasthenia gravis (1). In the present study a prospective study was done and certain epidemiological characteristics of Iranian myasthenic patients were determined.

PATIENTS AND METHODS

One hundred and fifteen patients from a private neurologic clinic and the neurology ward of a university hospital in Tehran were observed for six years (1986-1992). Fifteen patients were omitted from the study because of inaccuracy concerning the age of disease onset and the presenting symptom(s).

Data were obtained and analyzed for the following: sex, age of disease onset, presenting symptom(s), disease severity (mild, moderate, severe), disease type (neonatal, congenital, ocular, generalized), response to tension test, accompanying diseases, incidence of crisis, tracheotomy, ICU admissions, plasmapheresis, thymectomy, and the thymus histopathology.

The presenting symptoms were categorized in the following way: 1) Ocular symptoms, by ptosis and diplopia (together or alone), 2) Bulbar symptoms, defined as weakness of the muscles innervated by the fifth, seventh, ninth, and tenth cranial nerves (such as weakness of chin or jaw, difficulty in speech or swallowing, fluid regurgitation through nose, weakness of the orbicularis oris muscle, dysphonia, myopathic facies, etc), 3) Proximal and distal weakness of the upper and lower extremities, 4) Ocular and bulbar symptoms, combined, 5) Ocular symptoms with weakness of extremities, 6) Combination of ocular and bulbar symptoms, with weakness of extremities, 7) Weakness of neck muscles, and 8) Generalized weakness and/or fatigue.

Severity of the disease was classified according to the degree of disability caused by it (2,3). The term"mild" was applied when the patient's life style and activities were not affected. With "moderate" disease, activities were limited, while the patient was still able to pursue his/her career. "Severe" disease rendered the patient unable to continue his/her activities or occupation. Patients with a history of myasthenic crisis were also designated to have severe disease.

RESULTS

Fifty-three patients were female, and the remaining 47, male. In three brothers the disease had neonatal onset. Overall, the most common age of disease onset was between 20 and 29 years (Table 1). The majority of patients were presented with purely ocular symptoms (n=60). In thirty-one patients the symptoms were solely

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ocular for at least two years. The prevalence of different presenting symptoms and symptom complexes are presented in Tables 2 and 3. Forty-six patients had mild disease; 28, moderate; and 28 were afflicted by severe disease. Four patients had a family history of MG. In five instances, MG was accompanied by other disease states such as hypothyroidism, epilepsy, polymyositis, and rheumatoid arthritis.

Twenty-two patients had a myasthenic crisis during the period of this study. The prevalence of crisis by age and sex is presented in Table 4.

Of the 22 patients who developed a crisis, 13 where thymectomized in the course of the disease. The thymus was histopathology specified as "thymus hyperplasia" in 8 patients, and thymoma was present in the remaining 5.

Twenty-three patients received plasma exchange therapy, 12 for the treatment of myasthenic crisis, and 11 for the treatment of severe conditions, who were resistant to other treatment modalities, or after thymectomy.

Twenty-four patients had ICU admission during this period; 4 were admitted after thymectomy and 20 for myasthenic crisis. Two patients in crisis were not admitted to the ICU, and died. A tracheotomy procedure was done on 10 patients.

During the study, 33 patients underwent thymectomy. The results of the histopathological analysis are shown in Table 5. Four patients died in the course of the disease (three died after a crisis).

Table 1. Age of onset in male and female patients.

Age of onset	Male	Female	Sum
Neonatal period	3	0	3
1-11 months	3	2	5
1-9 years	2	3	5
10-19 years	7	13	20
20-29 years	11	13	24
30-39 years	4	15	19
40-49 years	8	6	14
50 years & older	9	1	10
Sum	47	53	100

Table 2. Prevalence of presenting symptoms.

Presenting symptom	Number of patients
Ptosis	59
Diplopia	20
Weakness of extremities	9
Dysphonia	1
Fatigability of chin or jaw	9
Dysarthria	4
Dysphagia	6
Neck weakness	1
Generalized weakness/fatigue	10
Myopathic facies	2
Orbicularis oris weakness	2
Fluid regurgitation through nose	1

Table 3. Prevalence of presenting symptom complexes.

Presenting symptom complex	Number of patients
Ocular symptoms (O)	60
Bulbar symptoms (B)	14
Weakness of extremities (E)	6
O + B	8
O + E	2
O + B + E	6
Generalized weakness/fatigue	3
Neck weakness	1

DISCUSSION

One hundred MG patients were analyzed in a prospective study. The ratio of female to male patients was 1.12 (female = 53, male = 42). Three patients were afflicted by the congenital form of the disease, with disease onset in the neonatal period, and a favourable response to anticholinesterase medication. The parents of these three patients were closely related. In other studies, the most common age of disease onset in the congenital form of the disease was reported to be in the neonatal period as well (4,5,6).

Overall, the most prevalent age of disease onset was in the third decade. In women, disease onset was most common in the fourth decade, but in men, it was in the third decade. In > 50-y age group, there were nine men and only one woman. Therefore, according to this study, disease onset in the older age group was significantly more common in men. In other studies (2,5,7) disease onset in men was reported to be most common in the

Table 4. Prevalence of myasthenic crisis by age and sex.

Age	Female	Male	Sum
10-19y	2 (9%)	1 (4.5%)	3 (13.6%)
20-29y	5 (22.7%)	1 (4.5%)	6 (27.2%)
30-39y	7 (31.8%)	2 (9%)	9 (40%)
40-49y	2 (9%)	—	2 (9%)
> 50y	—	2 (9%)	2 (9%)
Sum	16 (72%)	6 (27.2%)	22(~100%)

Table 5. Results of thymus histopathology in thymectomized patients.

Histopathology	Number of patients
Hyperplasia	25
Thymoma	6
Normal	2

sixth and seventh decades, but this was not the case in our patients.

The most prevalent and presenting symptoms were ocular, manifested by ptosis and diplopia. In 60% of patients the presenting symptoms were solely ocular; in 16%, ocular symptoms were accompanied by other symptoms. Overall, ocular problems at presentation were observed in 76%. In preceding studies, 40-50% of cases were reported to present with ocular problems, although 90-95% eventually acquired them (4,8,9). In the present study, 14 patients (14%) presented with symptoms attributable to weakness of muscles supplied by the fifth, seventh, ninth, and tenth cranial nerves (bulbar symptoms). Nine of these patients presented with fatigue of chin and jaw muscles, and one with dysphonia. Fatigability of extremities and trunk was the first complaints in 12% of our patients, although in other studies, they were reported in 20-30% (5,6,8). The substantiality of fatigue as a discrete symptom of myasthenia gravis is controversial, however it was the sole presenting symptom in several patients. Fatigue may be attributed to weakness of the truncal musculature in association with gravis, or other systemic diseases (4,8,10).

Disease severity was classified as mild in 44%, moderate in 28%, and severe in the remaining 28% of patients, indicating that 56% of patients regarded their disease as limiting or disabling.

Accompanying disease states were present in 5% of patients. Thyroid diseases were seen in two cases, which have been reported in 3-18% of patients in other studies (1). Seizure disorders have been reported to occur in 2.3-3.5% of myasthenic patients (1,4). In the present series, only one patient was epileptic. Polymositis, another disease that has been observed in myasthenia (1,10), was seen in one case. Rheumatoid arthritis and hypo-parathyroidism were also seen in our patients.

Twenty - two percent of the cases had a crisis during their disease. The most common age of myasthenic crisis was in the fourth decade. Sixteen patients were female (72. 73%), and six were male (27. 27%). Apparently myasthenic crisis was more prevalent in females. The most important precipitating factor of crisis was infection.

Fifty - nine percent of the patients that had a crisis (n=13) were thymectomized during the course of the disease. In five cases (38%) the thymus histopathology was thymoma and in the remaining 8 (61.5%), hyperplasia was reported.

Plasmapheresis was performed in 23 patient, and tracheotomy in 10. The latter solely in crisis, whereas plamapheresis was undertaken to treat patients in crisis in only 12 cases. In the remaining 11, plasmapheresis was performed as a treatment of intractable and severe disease, and before or after thymectomy. Twenty - four patients were admitted to the ICU due to myasthenic crisis, or severe disease state.

Overall, 33 patients were thymectomized The most common histologic report was, hyperplasia' (n=25 or 75.7%), followed by 'thymoma' (n=6 or 18.1%), and 'normal' (n=2 or 6%). In other studies, hyperplasia and thymoma were observed in approximately 86% and 13% of the cases, respectively (4). In our series, patients with purely ocular disease were not thymectomized; furthermore, many of the patients did not approve to undergo surgery in spite of their physician's consent. Four patients died due to intractable respiratory infection in the ICU.

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