MYASTHENIA GRAVIS – A CLINICAL SURVEY IN MALAYSIA

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SUMMARY

A retrospective study of 62 cases of myasthenia gravis in Malaysia is reviewed. It shows an apparent prevalence among the ethnic Chinese compared with the Malay and Indian. The incidence of male and female and their average age of onset are similar. Unlike the western figure, among those with age of onset less than 20 years, both sexes are equally affected. The symptomatology, morbidity and mortality and incidence of thymoma are the same as those reported elsewhere.

INTRODUCTION

Although myasthenia gravis is known to occur universally, with no known endemic area, socio-economic predilection, occupational or known exposure correlation - "indeed nothing of a specific epidemiologic nature" (Bundey, 1972), an impression has been created that in this country very few patients with myasthenia gravis have been encountered (Spillane's Tropical Neurology). There is a need to alter this view by presenting patients with this interesting disease seen in the University Hospital, Kuala Lumpur, Malaysia.

MATERIAL AND METHOD

All patients with confirmed mysthenia gravis admitted to the University Hospital from its inception in 1968 were included in the study. Confirmations were made on clinical presentation supplemented by pharmacologic response to tensilon (edrophonium hydrochloride) and neurophysiological tests. All revelent data were obtained from the case notes. Most of the patients have been seen by either one of the authors.

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RESULTS

Incidence

A total of 62 cases were seen from 1968 to 1979, giving an average of 5.16 new cases every year. During the same period the hospital had an average admission of 19,787 cases per year giving an incidence of 2.6 cases per 10,000 admissions.

Race and Sex

Among the 62 cases the number of Chinese, Malay and Indian patients were 44, 10 and 8 respectively. The average racial composition of patients in the medical ward was 45% Chinese, 23% Malays and 28% Indians. After adjusting for the racial difference of the admission, the likelihood of the different races in contracting the illness is Chinese : Malay : Indian — 3.41 : 1.5 : 1. The sex ratio of the patients within each racial group is as shown in Table I.

TABLE I
INCIDENCE OF MYASTHENIA GRAVIS ACCORDING TO THE RACES

Sex	Chinese	Malay	Indian	Total
Male	20	6	4	30
Female	24	4	4	32

Age of onset

The age at which patients were seen with this condition ranged from 1 to 72 years in our series. The average age of onset was 30.2 years. When this was broken down according to sex; in males it was 30.5 years and for females 29.9 years. The age of onset for the various ethnic races were Chinese : Malay : Indian — 32.4 : 20.3 : 30.5 years. A breakdown of the incidence of various ages of onset within their sex is shown in Figure 1.

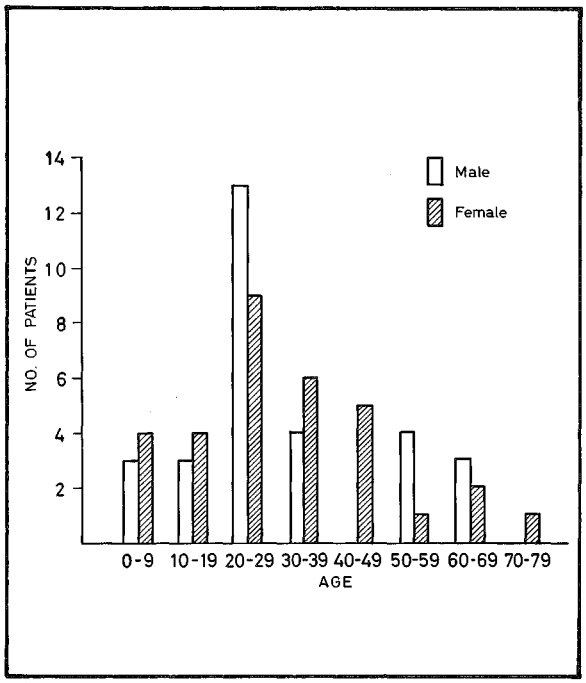

Fig. 1. Distribution of Age of Onset

Clinical Classification

Table II gives the details of the number of patients grouped according to the modified clinical classification of Osserman and Genkins (1971). In the juvenile group, three patients had their onset of the disease before the age of 2 years while another four after the age of two years. Only patients with the onset of disease less than 10 years are included under the juvenile group (Table II).

Table III gives the racial breakdown of patients group according to the clinical classification.

Symptomatology

The incidence of their presenting symptoms at University Hospital is listed in Table IV.

Associated disorders

Three patients had non-toxic goitre, one had thyrotoxicosis. One patient each had epilepsy, diabetes mellitus, traumatic paraplegia, urethral calculus and retinal haemorrhage.

Thymus

A total of 27 thyrectomies were done, out of which one was malignant and 7 benign. Eighteen cases had normal thymic histology with varying degrees of hyperplasia. One patient had an atrophied thymus.

TABLE II
DISTRIBUTION OF CASES WITH CLINICAL CLASSIFICATION ACCORDING TO SEX

	Juvenile	Group I	Group IIA	Group IIB	Group III	Group IV
Male	3	9	6	7	4	1
Female	4	4	11	10	1	2
Total	7	13	17	17	5	3
%	11.3	24	27.4	27.4	8.06	4.8

TABLE III
DISTRIBUTION OF CASES WITH CLINICAL CLASSIFICATION ACCORDING TO RACES

Race	Juvenile	Group I	Group IIA	Group IIB	Group II	IV
Chinese	5	6	12	13	3	2
Malay	1	2	3	4	2	0
Indian	1	2	1	3	0	1

TABLE IV
INCIDENCE OF SYMPTOMATOLOGY AT PRESENTATION

Symptoms	No	%
Ocular Diplopia	36	58.1
Ptosis (bilateral)	45	72.6
Ptosis (unilateral)	8	12.9
Bulbar Dysarthria	30	48.4
Dysphagia	27	44
Chewing weakness	14	22.6
Dyspnoea	9	14.5
Skeletal generalised weakness	3	4.8
facial weakness	22	35.5
neck weakness	9	14.5
weakness of all extremities	27	43.5
one or two extremities	3	4.8
atrophy	1	1.6

Confirmatory Test

In 60 patients, positive tensilon test was demonstrated. The other two patients had positive response to neostigmine test. In 7 patients, 3/second repetitive stimulations were done on the median nerves. Out of these, four were positive. In general, the test was usually positive on those patients whose muscles tested showed clinical involvement. Tetanic stimulation was done in one patient which was positive.

Treatment and Outcome

Twenty six patients were given anticholinesterase inhibitors only. Four patients had steroid in addition. Twenty seven patients had thymectomies, 7 of these had thymectomy as well as steroid. The outcome is as shown in Table V. 'Remission' is said to occur when a patient becomes symptom-free or shows minimal sign without medication. Improvement denotes decreasing signs and symptoms in a patient while

TABLE V

FORMS OF TREATMENT WITH THEIR OUTCOME

Group	Remision	Improve-ment	No Change	Worse	Died	Total
Anti-cholinesterase inhibitors only	3	17	7	2†	2	31
Steroid	0	3	0	1	0	4
Thymectomy and steroid	0	5	1	0	1	7
Thymectomy	3	10	3	0	4	20

† These two patients showed initial improvement with anticholinesterase inhibitor but subsequently deteriorated at later follow up.

still requiring medication. It also includes patients whose symptoms and signs are the same, but the dosage of medication is less. 'No change' decribes patients who remain in status quo; 'worse' describes patients whose symptoms and signs deteriorate or who require higher doses of medication.

A total of 10 patients had a course of steroid. It varies from ACTH to gradually increasing dose of prednisolone (Seybold and Drachman, 1971). Five of these patients showed improvement with the steroid therapy. Two patients showed 'no change'. In the other three patients the improvement may be attributed to and contributed by thymectomy which were performed at the same time. One patient had inadequate follow-up.

Thymectomy was done in 27 patients. The indication for thymectomy varied from case to case. It was dependent on the physician directly looking after the patient. In no instance was thymectomy done on Group 1 patients. Majority of patients were operated on as patients had significant symptoms despite medications, or minimal symptoms achieved with very high dose of anticholinesterase inhibitors. Sixteen patients (59.3%) apparently benefitted from this procedure with either 'improvement' or 'remission'. In 2 other patients though they also improved, steroid was given at the same time as thymectomy. In 9 patients (33.3%) there was no apparent benefit. Among these patients, 5 (18.5%) died.

Juvenile Myasthenia Gravis

There were seven patients in this group, three of them had their onset at younger than 2 years, and the other four older than two years. The sex ratio of male : female was 3 : 4. Three patients had only ocular manifestations. In one, the involvement was limited to the bulbar muscles. In three others, the involvement was generalised. In six of the patients the symptom could be described as mild. One patient however, died three years after the onset of symptoms. The racial composition of this group is Chinese : Malay : Indian is 5 : 1 : 1.

Mortality

Seven patients (11.3%] died during an average follow up of 2.6 years. The sex ratio in this group of patients was male : female = 3 : 4. The death in each clinical group was : one juvenile, three Group IIB, one Group III, one in Group IV.

DISCUSSION

Although it is not possible to extrapolate the average hospital admission of 5.16 case per year to the population at large, it is certainly not rare and probably not far from the figure of 1 in

40,000 to 1 in 20,000 as quoted for the western population (Simpson, 1960). Ethnically, Chinese and Malays are closely related when compared to Indians. It is thus interesting to note that Myasthenia Gravis is apparently more prevalent among the Chinese and Malay compared with Indian (Chinese : Malay : Indian = 3.4 : 1.5 : 1).

It is the experience of clinicians practising in this country that there is a prevalence among ethnic Chinese in developing systemic lupus erythematosus (White *et al.*, 1978) and thyrotoxicosis which are other examples of autoimmune disorders.

In western literature it is usually stated that females predominate (3.2) (Swab and Leland, 1953). The average age of onset is also younger for females, 26 years compared with 31 years for males (Simpson, 1960). In younger patients, females predominate. For those less than 20 years, female to male ratio is 4.5:1. For older patients the male predominated (Simpson, 1971). Our figures in contrast show that both sexes are affected equally and their age of onset is similar. Among those with age of onset of less than 20 years, both sexes are equally affected. However, male predominates in patients with onset of 50 years and above. Malay patients appear to have been the younger at the onset of the disease compared with the other two races.

The clinical groups correspond fairly closely to that given by Osserman and Genkins (1971). Fifty five per cent of our patients fall into Group II compared with 50% in the series of Osserman and Genkins (1971). The figures for the other groups compared to Osserman's figures given in bracket are as follows: Juvenile 11% (9%), Group I 24% (20%), Group III 8% (11%), Group IV 5% (9%].

Grob and Baltimore (1958) had emphasized the predominance of male among the group I patients. A study by Perlo *et al.* (1966) gave a similar finding. The present review corresponds to the above finding. The clinical grouping among the different races correspond to the overall pattern.

The frequent occurrence of bilateral ptosis, diplopia, dysarthria, dysphagia and generalised limb weakness during the initial presentation reflected the experience of others. The high incidence of all non-malignant thyroid disorders has been quoted as supporting the hypothesis of immune disorder in Myasthenia Gravis (Simpson, 1971). Our own figure for associated thyroid disorder is 4 cases (6.4%).

Our figures for associated thymoma is 12.9% which is within the range quoted by Castleman (10%) (Castleman, 1955), Keynes (1955) (15.4%). The association of germinal follices in relation to its response to thymectomy among our patients had been earlier reported by Leong *et al.* (1976).

As for the confirmatory procedure tensilon test has proved to be the most useful. McQuillen and Leone (1977) have high-lighted the many difficulties in proving the benefits of thymectomy. We have not tried to prove the efficiency of thymectomy but to show the outcome in our patients with various forms of therapy.

Bundey (1972) has argued for separating the juvenile cases into those with onset of less than 2 years and those of more than 2 years. The former group is likely to have autosomal recessive inheritance with mild disease. The latter group is similar in its features to the adult group. We have taken our juvenile group as those with onset of less than 10 years. None of our cases had a family history. Our patients in this group tend to have mild disease; 3 of the 7 patients in fact have symptoms confined to the eyes. The only mortality is unfortunate since the patient was well under medication but patient's mother discontinued his drugs when he developed a chest infection, and only came to seek medical attention after a delay of several days. The death is thus probably avoidable.

Among those who died, both sexes are similarly represented. There is a predominance of Chinese reflecting the greater proportion of Chinese that we see. Three out of seven patients were more than 50 years old with their onset of illness suggesting poorer prognosis among older patients. Of these three, two had thymoma.

Though the thymomatous patient is small its clinical picture is not at variance with others; an incidence of 10-15% with male predominance and at a later age of onset (Simpson, 1971). The prognosis is also poorer (Genkin, 1966; Keynes, 1954).

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