Motor Neurone Disease

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Introduction

MOTOR NEURONE DISEASE is a chronic progressive disorder characterised by atrophy and fasciculation of the somatic musculature due to degenerative changes of motor neurone at all levels — from the motor cerebral cortex down to the anterior horn cells at the spinal cord.

The disease is subdivided into four main clinical types or groups depending upon the sites of maximal stress of the pathological processes. These are:

(1) Progressive spinal Muscular Atrophy or PMA (Aran-Duchenne's disease),
(2) Amyotrophic Lateral Sclerosis or ALS (Charcot's disease),
(3) Progressive Bulbar Paralysis or PBP (Duchenne's disease), and
(4) Infantile spinal Progressive Muscular (Werdnig-Hoffman's disease).

In this country, motor neurone disease has not been fully studied and the purpose of the present paper is to present a clinical study of 13 cases of this uncommon condition, found over a 7-year period at one medical unit in Singapore.

Materials and Methods

From January 1964 to December 1970, all patients diagnosed as Motor Neurone Disease at Medical Unit II, Outram Road General Hospital, Singapore were included in this study. The criteria for diagnosis of this disease were based on (1) a classical history and clinical picture, (2) the presence of loss of motor power, progressive atrophy of muscles and visible fasciculations at the sites of involvement, (3) compatible neurological signs, such as the presence of pyrimidal signs in ALS, (4) a rapid progressive clinical course, (5) electromyographic and muscle biopsy evidences of neurogenic muscle degeneration, and (6) exclusion of all other known causes, systemic or local. Not included were peroneal muscular atrophy (Charcot-Marie-Tooth disease), Kugelberg-Welander disease, Fazio-Londe's disease, Holmes' disease and other rare spinal muscular atrophies.

The cases are then classified into the four clinical types:— (1) Progressive Muscular Atrophy (PMA), (2) Amyotrophic Lateral Sclerosis (ALS), (3) Progressive Bulbar Paralysis (PBP) and (4) Infantile Spinal Muscular Atrophy or Werdnig-

Hoffman's disease — according to the criteria described by various other workers, (Baker, 1955; Brain, 1962, Walton, 1964).

From time to time, the patients were seen at the outpatients and reassessed neurologically. Drugs were given merely for symptomatic relief. In case of death, an autopsy was requested.

Results

The significant data of the 13 cases of Motor Neurone found during the 7-year period in one medical department were as follows: —

(A) SEX Males — 8 cases Females — 5 cases

(B) RACE Chinese — 11 cases Malay — 1 case
Indian — 1 case

(C) AGE OF ONSET AGE 0 — 9 1 case
„ 10 — 19 1 „
„ 20 — 29 2 cases
„ 30 — 39 2 „
„ 40 — 49 2 „
„ 50 — 70 5 „

(D) FAMILY HISTORY Nil.

(E) CLINICAL TYPES
(1) Progressive Muscular Atrophy 5 cases
(2) Amyotrophic Lateral Sclerosis 6 „
(3) Progressive Bulbar Atrophy 1 case
(4) Infantile spinal muscular atrophy 1 case

Fig. 1: 'Guttering' and 'clawing' of the hands from wasting of the intrinsic muscles.

Fig. 2: Marked wasting of the thenar and hypothenar muscles.

DETAILED STUDY OF EACH CLINICAL TYPE

(1) PROGRESSIVE MUSCULAR ATROPHY

(Total — 5 cases)

There were 4 males and one female in this group and their ages ranged from 20 years to 63 years with 3 cases in the sixth decade. Four were Chinese and one, an Indian. None had family history. Duration of symptoms prior to first seen was 8 months, 9 months, 12 months, 4 years and 5 years. The earliest sites of lower motor neurone involvement were the muscles of the upper limbs in 2 cases, lower limbs in another 2, and in the fifth case, the upper and lower limbs were affected simultaneously.

In the majority of cases, the disease spread from one limb girdle to another and finally involved the bulbar muscles within a few years. There was apparent clinical arrest of spread in one patient over a 2-year period. The classical sypmtoms and signs were present in all patients — viz., weakness, stiffness and clumsiness of movements of the fingers, hands, shoulders or legs, accompanied by progressive wasting and fasciculations of the affected muscles. Thus, in 4 patients, atrophy of the small muscles of the hands — the thenar and hypothenar eminences, the interossei and the lumbricals — resulted in "guttering" and "clawing" of the affected hands (Figures 1 & 2). The deltoids and other muscles of the fifth cervical nerves were next involved, producing a rounded shoulder posture and forward drooping of the head. Severe lower leg involvement in one patient resulted in bilateral footdrop and a steppage gait on walking.

Mild degrees of dysarthria, dysphonia and dysphagia were detected in three patients but none had respiratory distress. All showed tongue wasting and fasciculation of varying severity (Figure 3). In advanced cases (2), flexion contracture of limbs and 'clawing' of the toes were observed (Figure 4). Mental disturbance was not found and none had any evidence of pyrimidal tract lesions although the deep tendon reflexes were brisk in the severely wasted muscles. In two cases, the tendon jerks were abolished in the atrophied extremities. Sensory

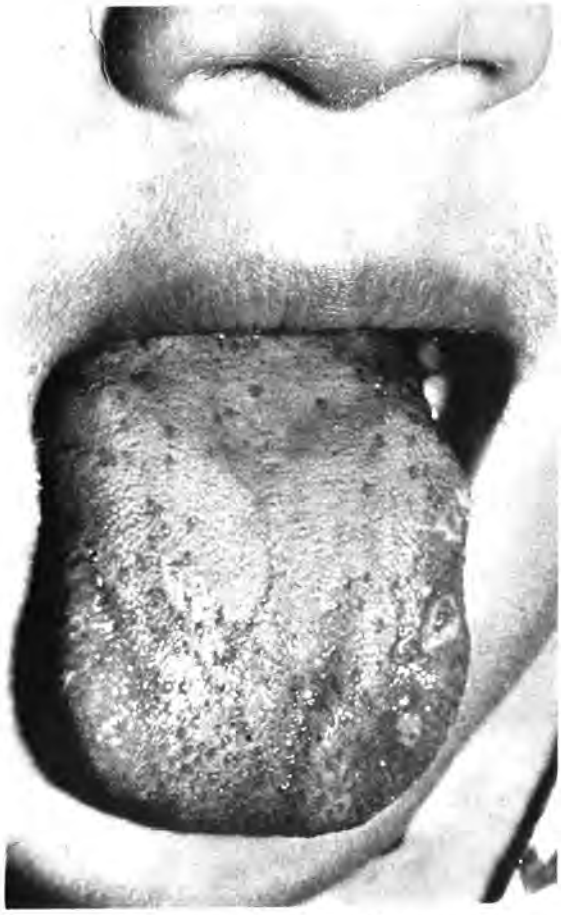

Fig. 3: Wasting and fasciculation of the tongue.

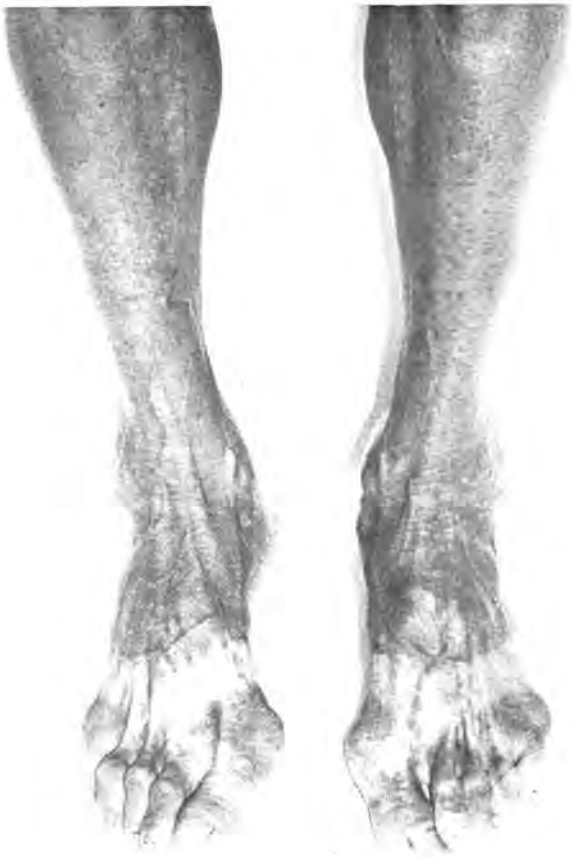

Fig. 4: Wasting of the feet with 'clawing' of the toes.

loss was not found and most of the haematological and biochemical tests — including serum aldolase, serum creatinine phosphokinase, serum transaminases — were all within normal limits. In 3 cases, the cerebrospinal fluid protein was raised over 60 - 90 mg per 100 ml, but other components of the fluid were normal. Electromyograms in 5 cases and muscle biopsies in 3 cases revealed a neurogenic type of muscular degeneration.

Most of the patients received vitamins and anabolic agents like intramuscular Deca-Durabolin or oral Winstrol, but they showed no clinical responses. By the end of December 1970, 3 patients were still alive after having the disease for 7, 4 and 3 years. One could not be traced as he had left the country, and one succumbed to bronchopneumonia after having survived the disease for 3 years. Unfortunately, an autopsy of this patient was not obtained.

(2) Amyotrophic Lateral Sclerosis

(Total — 6 cases).

In this group of 3 males and 3 females, the ages of onset of disease were 19, 32, 44, 46, 56 and 60. All were Chinese. Duration of symptoms prior to first seen were 5 months, 7 months, 12 months, 2 years, and $2\frac{1}{2}$ years. Family history was not found. Sites of initial involvement of the disease were: upper limbs — 2 cases, lower limbs — 2 cases, and both limbs — one case. In 5 patients of this group, the lesions spread from one site to another and then became generalised after a short period of 3 months to 5 years. The condition remained fairly static, however, in one case after a 2-year follow-up. As in the previous clinical group, weakness and wasting with visible fasciculation of the affected muscles were observed in the early stages. The tongue was commonly affected and

clawing of the hands and toes were present in three advanced cases.

In addition to the above-mentioned features, signs of corticospinal and corticobulbar tracts degeneration were found — e.g. exaggerated jaw reflex, hyperactivity of the deep tendon jerks of the upper and lower limbs, clonus of patellae and the ankles, marked spasticity of the muscle tone, presence of pathological reflexes such as the Babinski responses, snout reflex, Hoffman's sign, Wartenburg's signs and so forth. Bulbar symptoms were found in 4 cases and one developed respiratory muscle paralysis. In one patient, however, the classical signs of ALS were masked by the predominance of the lower motor neurone involvement and the diagnosis was only revealed at the autopsy. Aching limbs were complained in one case but sensory changes in this patient as well as the other 5 patients were absent. Pseudobulbar lesions with impaired emotional control was encountered only in one case.

Most of the laboratory investigations were essentially normal and these included muscle enzymes, E.C.G., E.E.G. and radiological studies. E.M.G. and muscle biopsies in 4 patients showed neurogenic type of muscular atrophy. At the end of 1970, 5 out of 6 patients in this group were still alive having survived the disease for 4 years, (2 cases), 3 years (1 case) and 2 years (2 cases). The only death was the patient who developed respiratory paralysis after suffering from the disease for 2 years. In all cases, treatment was nonspecific and included drugs like vitamins, anabolic agents and so forth.

(3) PROGRESSIVE BULBAR PARALYSIS

(1 case)

In this distinct clinical entity, the muscles involved were mainly restricted to the motor nuclei of the brain stems and the course is rapidly progressive with an early fatality. One such case was found. He was a Malay man, aged 60, with progressive bulbar involvement of the tongue, orbicularis oris, palatal and pharyngeal muscles and later, the cranial nerves of the fifth, seventh and eleventh. Marked wasting and fasciculation of these muscles were seen. The patient deteriorated so rapidly within a short three-week period that he became gravely ill and was taken back home by his relatives prior to his imminent death. Other causes like basilar artery thrombosis, brain stem tumours, nasopharyngeal carcinoma, cervial myelopathy, myasthenia gravis and other diseases were excluded.

(4) INFANTILE SPINAL PROGRESSIVE MUSCULAR ATROPHY (WERDNIG-HOFFMAN'S DISEASES)

One case was found in this series. She was a 13-year-old Chinese girl with generalised weakness and marked muscle atrophy since early infancy. Proximal muscles were first affected, followed rapidly by the spread of the disease to the distal portions of the extremities as well as the trunk and tongue. Fasciculation was seen at these sites. Tendon jerks were generally absent in the wasted limbs and marked flexion contractures of the limbs were observed. E.M.G. and muscle biopsy confirmed the neurogenic origin of the muscle atrophy, but other laboratory tests yielded no significant findings. She was given symtomatic treatment, and on occasions she had a course of antibiotics for the chest infection. To date, she was alive but bedridden, totally incapacitated and requires institutional care.

Discussion

In this region, Motor Neurone Disease has not been fully investigated. Hence the present study, though small in the total number of cases, nevertheless demonstrates some interesting points in certain aspects of the disease.

Compared with most countries of the world, this disease is rather uncommon in Singapore as an average of 2 new cases was found annually. About 3.3% of neurological admissions into United States hospitals were suffering from motor neurone disorders (Friedman and Freedman, 1950; Merritt, 1963) and in most countries of the world, an incidence rate of 1.4 and prevalence rate of 4 to 6 per 100,000 population per year were estimated to have this malady (Kurland, 1957; Marburg, 1911; Dana, 1925; Wohlfahrt, 1950). Our sex ratio of 2 males to 1 female is less than that found in other series where the males were affected three or four times as frequently as females (Merritt, 1963).

Majority of patients in this series had the first signs of the disease during middle age — between ages 30 to 70, as shown in other series, but younger patients were not uncommonly seen. Eleven cases were Chinese in this study, but the other races — Malays and Indians — were not totally exempted. None had a family history, a well-known fact that inheritance seldom plays an important part in the motor neurone disorder as contrasted with the muscular dystrophies. However, there is a high familial incidence of ALS associated with Parkinsonian-dementia complex in the Chamorro people residing in the island of

Guam, and a genetic factor was implicated. (Kurland & Mulder, 1955; Hirano et al., 1961).

Of the four main types of Motor Neurone Disease, we had 5 cases of PMA, 6 cases of ALS and one case each of PBP and Werdnig-Hoffman's disease. The last two conditions were rare and the first two were more common as found in other series reported from elsewhere. The difference in clinical patterns are attributed to the variation and different combinations of the nature and distribution of the motor neurone degeneration in the spinal cord, brain stem and the cerebral cortex. A survey of autopsy materials of Motor Neurone Disease in the literature revealed higher incidence of lesions in the cervical cord and medulla than that in the lumbar cord or cerebral cortex, thus explaining the increased frequency of ALS and PMA. (Dana, 1925; Friedman and Freedman, 1950; Hassin and Dublin, 1945; Arnold et al., 1953; Wohlfart & Swamk, 1941).

On the whole, the clinical pictures of the four types in this series were not significantly dissimilar to those described in the literature. Although the classical site of initial involvement was the upper limb, a number of patients in this series however, started with the lower limbs. Duration of symptoms prior to first seen were invariably short and in most instances, the disease spread rapidly to other sites and became generalised. Typical features, like loss of muscle power, wasting and progressive atrophy, fasciculations and other neurological signs, were observed in the all four clinical types of this series. The bulbar muscles were seldom affected and mental changes as well as the sphincteric functions were rarely disturbed.

In 3 patients with PMA, cerebrospinal fluid protein was elevated over 60 mg%, a not uncommon finding in this condition. (Merritt, 1963). One patient in the ALS group showed predominantly lower motor neurone signs masking the presence of a corticospinal tract lesion. However, the diagnosis of ALS was confirmed later at the autopsy. In this study, we were not able to have pathological verification of all the cases since most of the patients were still alive. The diagnosis were made mainly on clinical, histological and electromyographic grounds.

Of the 5 cases with PMA, 3 had survived from 3 to 7 years after the illness. One died of bronchopneumonia after having been bedridden by the disease for three years and one was not traced as he had left the country. Most cases with ALS were still alive after 2 to 4 years from the onset of the disease. Majority of them were physically incapacitated. Our only case with PBP presumably died at home soon after discharge from hospital. In the literature, most cases with PMA and ALS died within 3 years after the onset. The prognosis on the whole is poor. Walton (1956) noted that the survival of patients with Werdnig-Hoffman's disease rarely exceed 12 years, but our patient with this condition had survived more than 13 years now.

Numerous theories have been postulated as to the aetiologies of Motor Neurone Disease — e.g. genetic factor, inherited predisposition, infections, syphilis, poliomyelitis, trauma, lead poison, dietary deficiency, enzyme defects, etc. — but the cause is still unknown (Schwab, 1961; Ask-Upmark, 1961; Zilkha, 1962, McMenemy 1962, Fullmer et al., 1960; Cumings, 1962; Walton, 1964). Treatment of this disease, therefore, remained nonspecific. Polyvitamins, vitamin E, vitamin B 12, prostigmine, oral and intramuscular anabolic agents have been tried as in this and other series, but the course of the disease remained unaltered.

Summary

Thirteen cases of Motor Neurone Disease, found over a 7-year period in one Singapore medical unit, were studied. The majority of the cases were Chinese males in middle age with a short history of onset of the disease. Five patients were found to have Progressive Muscular Atrophy, 6 with Amyotrophic Lateral Sclerosis, and there were one case each with Progressive Bulbar Paralysis and Infantile spinal Muscular Atrophy.

The clinical features, investigations, course and treatment of these groups were presented and discussed.

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