KUGELBERG-WELEANDER SYNDROME OR MUSCULAR DYSTROPHY? — A FAMILY STUDY

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SYNOPSIS

Three young boys in an extended family were first seen in their first decade for proximal muscle weakness without sensory loss. The patients were diagnosed as Duchenne muscular dystrophy for over 10 years. The diagnosis is now reviewed and these cases are shown to suffer from a benign childhood variant of motor neuron disease called Kugelberg-Weleander syndrome or benign proximal spinal muscular atrophy. The similarities between the two conditions are many, including age of onset, proximal muscle weakness, heredofamilial, male preponderance, raised muscle enzymes and normal nerve conduction studies. Denervation atrophy however can be established by the presence of fasciculations, a well chosen muscle biopsy or more simply and accurately by electromyography.

INTRODUCTION

It is increasingly recognised that motor neuron disease has numerous clinical variants and simulates many other diseases. In children, Wohlfart, Kugelberg and Weleander were the first to clearly describe a distinct variant affecting proximal muscles (Wohlfart et al, 1955; Kugelberg et al, 1954). This entity clinically simulates Duchenne type of muscular dystrophy in affected male children. Because of this recognition we reviewed the diagnosis of Duchenne muscular dystrophy in an extended family in which three male members were affected (Fig. 1).

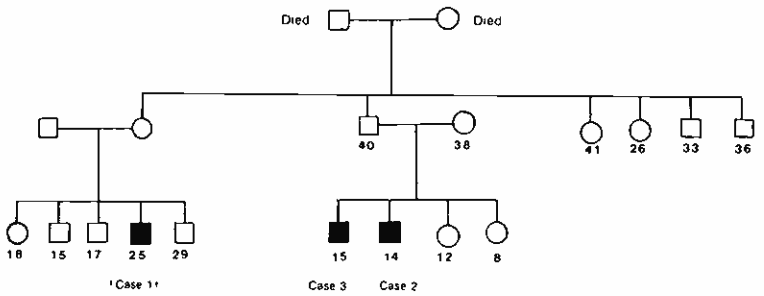

Figure 1 — Family Tree

CASE REPORTS

Case 1 (Fig. 2)

The patient, a 25 year old Chinese male, was first seen in 1957 at the age of 2 years for inability to sit up or walk. Weakness was mainly proximal and reflexes were diminished without sensory loss. Muscle enzymes were raised. He was diagnosed as Duchenne type of muscular dystrophy and placed in the Singapore Cheshire Home because of family neglect.

When re-examined this year he was markedly deformed with slight wasting and fasciculations of the tongue. Neck muscles were weak. In the trunk and limbs all muscles were affected, the proximal more severely than the distal. Intelligence was normal.

Nerve conduction studies were normal. Electromyographic studies of the deltoid, supraspinatus and biceps were not helpful due to severe involvement of these muclses. The thenar muscles, however, showed definite denervation pattern.

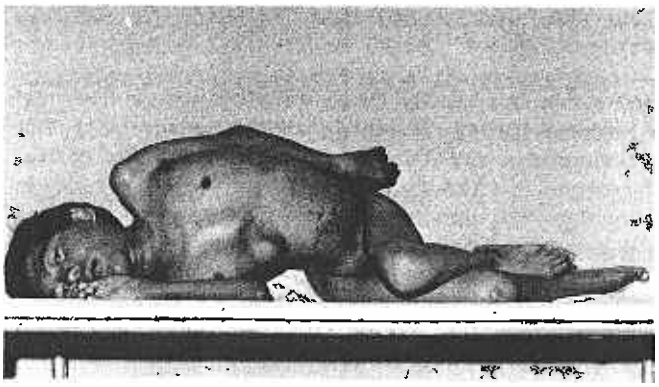

Figure 2, Case 1

Case 2 (Fig. 3)

The patient, a 14 year old Chinese male, was first seen at the age of 3 years because of inability to walk although initially he could do so normally. On examination he had severe weakness of the pelvic girdle muscles and to a lesser extent the shoulder girdle muscles. He demonstrated the Gower's sign. Serum aldolase was markedly elevated although phosphokinase was normal. Muscle biopsy was reported as consistent with a muscular dystrophy. He was diagnosed as Duchenne type of muscular dystrophy and was institutionalised in the Singapore Red Cross Home until today.

When reviewed this year distal muscle function was still good. Mental function and cranial nerves were not affected. Fasciculations were present. Electromyogram of the supraspinatus, infraspinatus, deltoid and biceps showed large motor unit potentials with prolonged mean duration. Fasciculation potentials, fibrillation potentials and a pseudomyotonic pattern were recorded at rest. Interference pattern was discrete in all muscles sampled. Nerve conduction studies were normal. A review of the muscle biopsy showed that there was evidence of denervation atrophy.

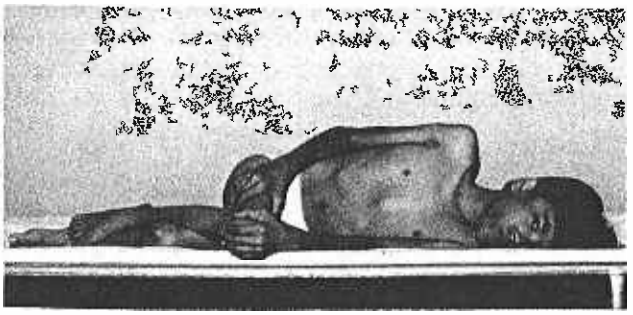

Figure 3, Case 2

Case 3 (Fig. 4 & 5)

The patient, a 15 year old Chinese male, brother of the 2nd patient and cousin of the first (Fig. 1), experienced weakness at the age of 6 years. His general practitioner and parents assumed he had a similar type of muscular dystrophy and consequently he was not investigated until now.

Weakness was mainly proximal, the lower limbs being more affected than the upper. Fasciculations were noted over the triceps, sternomastoids, and pectores major. Muscle enzymes were elevated. Muscle biopsy showed group atrophy, fibre type grouping and core-targetoid fibres suggesting the presence of denervation and re-innervation. Electromyography of various muscles showed definite denervation pattern.

Other family members were found to be normal clinically. There was no history of a consanguinous marriage.

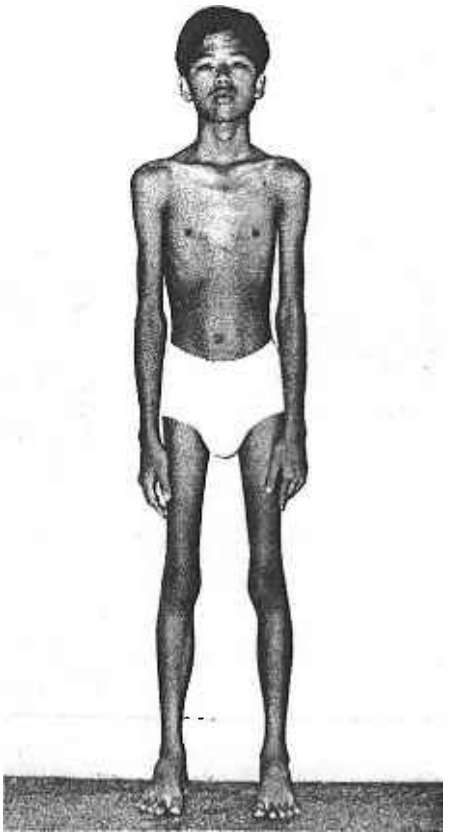

Figure 4, Case 3

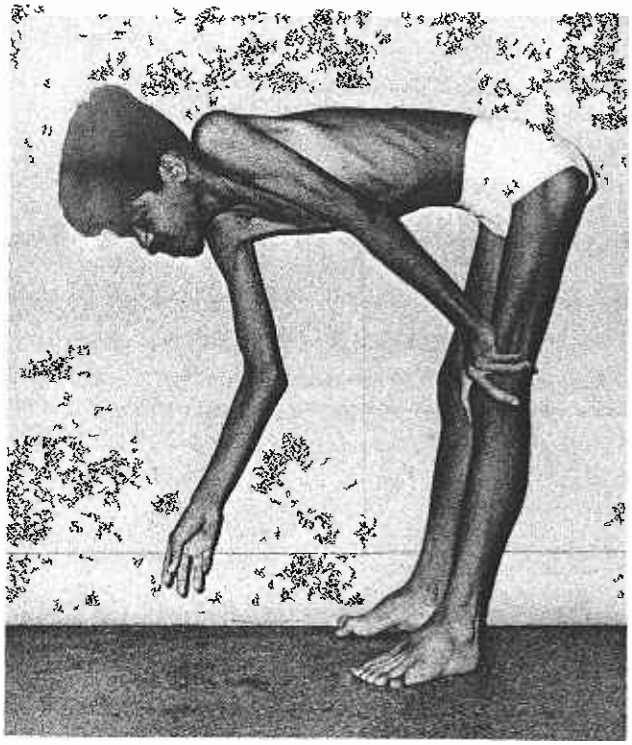

Figure 5 — Gowers' Sign Case 3

DISCUSSION

The three patients illustrate the initial diagnostic difficulties in distinguishing Kugelberg-Weleander syndrome from Duchenne muscular dystrophy. Two patients were examined and investigated more than 10 years ago and were diagnosed as Duchenne muscular dystrophy. The third patient was assumed to have the same condition through a sex-linked mode of inheritance.

In Kugelberg-Weleander syndrome (or proximal spinal muscular atrophy), however, autosomal dorminant, autosomal recessive and sex-linked modes of inheritance have all been reported (Tsukagoshi et al 1966, 1970). Generally there is a male preponderance (Brandt, S. 1950). Hence sex and mode of inheritance are not helpful distinguishing features. In this family the mode of inheritance is uncertain but autosomal dominance with variable penetrance and prediliction for males is a likely explanation.

In both conditions the disease starts in childhood. 50% of cases with proximal spinal muscular atrophy have symptoms starting from 3 to 18 years. However survival beyond beyond the 2nd decade is unusual for Duchenne muscular dystrophy but common for Kugelberg-Weleander syndrome. The mean age of death for the latter condition is about 50 years (Namba et al, 1970).

Distribution of muscle weakness is not helpful. Lower cranial nerves are involved in only about 20% of cases in Kugelberg-Weleander syndrome and involvement is usually mild (Kugelberg 1975).

Fasciculations occur in 50% of cases in Kugelberg Weleander syndrome and is an extremely helpful clinical sign. It is not present in muscular dystrophy. All the three patients reported above showed fasciculations.

Muscle enzymes, contrary to popular belief, are also elevated in this motor neuron disorder. Raised serum phosphokinase and aldolase merely reflect an increase in cell membrane permeability and over-activity of the ribosomes in ischaemic fibres. Half of patients with Kugelberg-Weleander syndrome have raised creatinine kinase (Kugelberg 1975).

Nerve conduction studies again is not of help as it is normal in both conditions. In proximal spinal muscular atrophy because the primary pathology is anterior horn cell degeneration followed by axonal degeneration, myelin remains intact for a long time. Conduction velocity decrements are noted only when secondary myelin damage sets in.

Electromyogram remains the simplest and most accurate way of differentiating denervation from primary muscle disease. However, severely atrophic and fibrotic muscles will also deceptively show myopathic patterns. Affected but still functioning muscles should be chosen (Kugelberg 1975). We documented insertional pseudomytonic bursts in one of our patients. This association is rare but reported (Amick et al 1966).

Muscle biopsy where carefully selected and read by an experienced histologist is extremely helpful. Enzyme histochemical studies will show group atrophy and fibre type grouping in Kugelberg-Weleander syndrome, suggesting denervation and re-innervation respectively. However, as demonstrated by Drachman, concomittant myopathic or dystrophic changes like fibre splitting, degeneration, myophagia, regenerative changes, and variable fibre size, may occur in this syndrome (Drachman et al 1967; Pearce, J et al 1966).

In conclusion, it is the benign nature of the illness, occasional involvement of lower cranial nerves, fasciculations, electromyogram and muscle biopsy that distinguishes these two conditions. The differentiation is not an academic exercise since in Kugelberg-Weleander syndrome more hope can be given to the patient and his family. Here a vigorous and active life is to be encouraged at all stages. Immobilization even for a few days has been shown to alter the benign course to a relentless, downhill trend.

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