NEUROPATHY IN MYOTUBULAR OR CENTRONUCLEAR MYOPATHY

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In 1966 Spiro, Shy and Gonatas [12] described a congenital myopathy in a 12-year-old boy whose muscle biopsies revealed small myofibers with centrally located nuclei that were surrended by a clear area. Histochemically the central region of the myofibers showed disturbed enzymatic activity and ultrastructurally the nuclei were associated with myelin figures, glycogen granules and mitochondriae. The authors called this condition "myotubular myopathy" because the muscle fibers resembled the myotubes seen in early fetal life.

Since then several reports have appeared in the literature generally regarding the syndrome as myopathic (Ortiz de Zárate and Maruffo [7], 1970; Sher, Rimalovski, Athanassiades and Aronson [9], 1967; Kinoshita and Cadman [4], 1968; Bethlen, van Wijngaarden, Mumenthaler and Meijer [1], 1970; Schochet, Zellweger, Ionasescu and McCormick [8] 1972; Campbell, Rebeiz and Walton [2] 1969), though neuropathic features, namely distal atrophy (Ortiz de Zárate et al. [7] 1970; Spiro et al. [12] 1966; Sher et al. [9] 1967; Schochet et al. [8] 1972), hypo or arreflexia (Ortiz de Zárate et al. [7] 1970; Spiro et al. [12] 1966; Kinoshita et al. [4] 1968, Schochet et al. [8] 1972; Engel, Gold and Karpati [3], 1968), electromyographic fibrillation potentials (Spiro et al. [12] 1966; Bethlem et al. [1] 1970, Engel et al. [3] 1968) and histological muscle fibers grouping (Spiro et. al. [12] 1966, Engel et al. [3] 1968) have been also described in this entity.

These studies clearly indicate the need for a quantitative investigation of motor unit function in this "myopathy". Recently we have described some electrophysiological methods which enables estimates to be made of the number and sizes of motor units in the small muscles of the foot (McComas, Fawcett, Campbell and Sica [5], 1971) and hand (Sica, McComas, Upton and Longmire [11], 1974) and in the soleous muscle (Sica, Sanz and McComas, umpublished results).

The application of these techniques to the study of this condition provided electrophysiological evidences that neuropathic changes do occur.

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MATERIAL

The patient submitted to investigation was a 34-year-old white man who clinically and histologically proved to suffer from centronuclear or myotubular myopathy as he was published by Ortiz de Zárate and Maruffo [7] elsewhere with such diagnosis (Case 1, A. K.).

METHODS

The methods employed for studying the number and sizes of motor units and impulse conduction in motor nerve fibers have been described elsewhere (McComas et al. [5], Sica et al. [11]) as well as the technique employed for repetitive stimulation of the motor nerve fibres (Sica and McComas [10]).

For sensory conduction velocity recordings were made with two chlorided silver discs each one cm in diameter spaced three cm appart in a plastic holder. Except for the sural nerve, all recordings were made of orthodromically conducted impulses. The limbs were warmed with an infra-red lamp prior to study and the ambient temperature was mantained at about 25°C.

For the studies of the of the extensor digitorum brevis muscle a total of 45 healthy subjects below the age of 60 served as controls. For the thenar muscles 67 control muscles were employed, for hypothenar 80 and for soleus 75.

For the sensory studies 55 subjects acted as controls.

RESULTS

The most important finding was a definite reduction of the number of functional motor units in the left thenar, left hypothenar, left extensor digitorum brevis and right soleus muscles. The reduction in the motor unit estimates was associated with normal sizes of the surviving motor units (Table 1).

	Number of motor units		Mean motor unit size (uv)	
Thenar	47	(> 220)	32	(11-47)
Hypothenar	23	(> 250)	19	(14-70)
Soleus	77	(> 540)	18	(16-38)
E. D. B.	2	(> 122)	15	(11-43)
	Motor conduction velocities (m/s)		Distal latencies (ms)	
Median nerve	68	(50-71)	3.5	(< 4.6)
Ulnar nerve	52	(51-72)	3.3	(< 3.5)
	Sensory conduction velocities (m/s)		Amplitude of sensory compound action potential (uv)	
Median nerve	1st. digit	46 (42-67)	27	(> 12)
	2nd. digit	58 (44-65)	21	(> 14)
	3rd. digit	58 (44-61)	27	(> 15)
	4th. digit	56 (46-64)	12	(> 9)
Ulnar nerve	4th. digit	52 (47-65)	10	(> 8)
	5th. digit	56 (41-61)	17	(> 9)
Radial nerve	Thumb	50 (42-59)	15	(> 12)
Sural nerve		48 (42-58)	18	(> 9)

Table 1 — Values of number of motor units and conduction velocities in patient A. K. Normal values are given in brackets.

Motor and sensory nerve conduction velocities as well as amplitudes of sensory action potentials were well within normal limits in the upper and lower limbs (Table 1).

A decremental response in the thenar muscles evoked potential to repetitive median nerve stimulation at the wrist was observed in this patient. There were no differences between the amplitudes of the first and last evoked potential when tested with one second train of supramaximal stimuli at frequencies of 3 or 10 Hz; however at 50 Hz 80% decrease was evident.

Conventional electromyographic studies were done in proximal and distal muscles of the upper and lower limbs. A mixed to interference pattern was recorded in all them, the individual potentials were mainly of reduced duration and amplitude in proximal muscles, whilst in the distal groups they were mainly poliphasic and of increased amplitude.

Neither fibrillations nor positive sharp waves were observed. No myotonic discharges were recorded.

DISCUSSION

The above observations suggest that the disease is neurogenically determined and support Engel et al. [3] (1968) earlier postulation who made the assuption that the pathological process might be due to "functional deficiency of maturational factor from the motor nerves".

In terms of the "sick" motoneurone hypothesis (McComas, Sica and Campbell [6], 1971) the entity might be interpreted as due to an inability of the skeletomotor neurone to drive or to maintain the muscle fiber in a complete mature state, establishing a defective relationship between its axon and the muscle fibers which would account for a later functional denervation.

As most of the cases reported in the literature show a progressive downhill course, it is sensible to assume that the whole motoneuronal population is "sick", this situation could explain the lack of increased size of the remainer functional units for they would be unable to branch their axons or grow new axonal sprouts; it can also explain the decremental muscle response to high repetitive stimulation as impaired neuromuscular transmission is other feature which characterizes the "sick" motoneurone.

If Engel et al. [3] assumption that the defect in the relationship between the muscle fibers and their innervation should be produced early in the development of the muscle, before the 20th fetal week, it can be postulated that by then most of the motoneurones should be already ill.

SUMMARY

A detailed electrophysiological study has been made of the extensor digitorum brevis, thenar, hypothenar and soleus muscles in one patient with myotubular or centronuclear myopathy. The main finding was a noticeable reduction in the population of active motor units in all the investigated muscles. The remainer units showed normal sizes. The experimental observations have been interpreted in terms of a neuropathic process.

RESUMEN

Un estudio electrofisiológico detallado fué hecho en los músculos extensor corto de los dedos, de la eminencia tenar, de la eminencia hipotenar y soleo en un paciente con el diagnóstico de miopatía miotubular o centronuclear. El hallazgo principal fué una notoria reducción en el número de unidades motoras activas en todos los músculos investigados, en tanto que las unidades remanentes mostraron tamaño conservado. Las observaciones hechas se han interpretado como favoreciéndo la génesis neurógena en el desarrollo de este proceso.

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