Original article

Role of EMG in Congenital Hypotonia with Favorable Outcome

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Abstract. *Background:* Since hypotonia is the phenotype of several clinical conditions that do not always lead to a favorable outcome, prompt diagnosis is important. Congenital Hypotonia with Favorable Outcome (CHFO), an underestimated condition, should be rapidly differentiated from other more serious hypotonic states by means of simple, effective and only slightly invasive instrumental diagnostic examinations. *Aim:* We analyzed the electromyographic data of a group of patients with CHFO and compared them with data taken from their muscle biopsies to evidence the utility of the electromyographic study (EMG) in this condition. *Methods:* We performed EMG, nerve conduction study (NCS) and muscle biopsy on 41 subjects with a diagnosis of CHFO (age range 9 months to 12 years, mean age, 6.7 years). *Results:* No specific EMG findings were observed. Muscle biopsy was normal in all subjects, and we obtained concordance between biopsy and EMG in 85% of the subjects (35/41). *Conclusion:* A normal EMG examination helps investigators to exclude several neurological diseases characterized by hypotonia and it can provide valuable complementary information to confirm the clinical diagnosis of CHFO. (www.actabiomedica.it)

Key words: Benign congenital hypotonia, electromyography, children, muscle biopsy

Introduction

Muscle hypotonia often requires a neuropediatric consultation. Hypotonia is the phenotype of several clinical conditions (1, 2) that do not always lead to a favorable outcome. Thus it is important to make an immediate and prompt diagnosis with the help of instrumental examinations. However, we should keep in mind that some conditions have a favorable outcome. Consequently, an invasive diagnostic procedure, such as muscle biopsy, could be avoided: in particular this examination is totally unremarkable in congenital hypotonia with favorable outcome (CHFO) (3). It thus becomes essential to diagnose these subjects, above all, on the basis of exclusion, by means of their clinical history, the observation of clinical evolution and some exams. Furthermore, CHFO, that has an incidence of 13.4–15.5% (4), is still widely underdiagnosed, at least in our experience. In fact, it is difficult to diagnose both because motor disturbance is slight and improves over time and because laboratory examinations (serum muscular enzymes) and muscle biopsy are normal. In the present study the EMG data of a cohort of patients with CHFO were analyzed.

Methods

This longitudinal study was perfomed on hypotonic subjects referred to the Department of Child and Adolescent Neuropsychiatric Science of the University of Rome, "La Sapienza", from 1985 to 2000. We included all subjects with CHFO, fulfilling these criteria: (1) early hypotonia, usually since birth; (2) active movements of the limbs and normal tendon reflexes; (3) normal or mild motor retardation impro-

ving later on; (4) normal muscle enzymes. We used the following exclusion criteria, already described (3): (1) children with delayed cognitive development and/or abnormal thyroid function; (2) children with a history of hypoxic-ischemic insult; (3) children without a full investigation for muscle diseases (muscle serum enzyme activities, EMG, motor and sensory nerve conduction study, muscle biopsy with histological, histochemical and electron-microscopic studies). On the basis of these parameters, 41 children (25 males and 16 females, age range 9 months - 12 years), with typical features of CHFO, were selected. None of them presented genetic disorders, such as Prader-Willi syndrome, Down syndrome, and Ehler-Danlos syndrome. Muscle serum enzyme activity and needle muscle biopsy with histological, histochemical and electron-microscopic studies were performed in all cases. At least 1 EMG and 1 NCS examination were carried out before the muscle biopsy in all subjects according to the recommended protocol for the "floppy infant" used in our EMG laboratory (5). This protocol involves:

1) the study of at least 1 sensory and motor nerve in the arm and leg, usually the median and sural sensory nerves, and the median and peroneal motor nerves;
2) needle examination of at least 2 muscles in the arm and leg, usually sampling of 1 proximal and 1 distal muscle for each limb. Of course, more muscles are examined if anterior horn cell disease is suspected according to the EMG criteria proposed by Lambert (6);
3) repetitive nerve stimulation studies (from 1 to 50 Hz) are performed in the presence of a) ptosis or ophthalmoparesis; b) myopathic electromyography; c) low amplitude compound muscle action potentials (CMAPs); d) a clinical history suggestive of neuromuscular transmission disorder.

We classified the electromyographic findings, analysed with a flexible gestalt approach (7, 8), into 4 categories: 1) *myopathic* with early recruitment: significant presence of small amplitude polyphasic motor unit potentials and low amplitude recruitment with normal NCS; 2) *suggestive but not diagnostic of myopathy*: mild increment of short and polyphasic units with recruitment of low amplitude and normal NCS; 3) *non-specific changes*: minimal focus or scattered needle examination changes consisting in the presence of occasional polyphasic motor unit potentials of short duration and small amplitude with normal NCS; 4) *Normal.*

Quantitative electromyographic techniques were not used (9). All but 1 subject underwent needle muscle biopsy of the vastus lateralis muscle. In 1 subject, the deltoid muscle was sampled because it seemed weaker. Each specimen was cut into 2 samples for histological, histochemical and electron-microscopic studies (3). The first sample was snap frozen and cryostatic sections were submitted for morphologic and histoenzymatic studies (ATPase, NADH, SDH and acid phosphatase), the second one was fixed in buffered glutaraldehyde solution for electron microscopy.

Statistical Analysis

χ^2 test and, if significant, Fisher's Exact test for 2 by 2 comparison was used to compare the distribution of categorical variables across groups.

Simple factorial ANOVA was performed to separately evaluate the effect of factor categories and, if significant, a multiple comparison by t test with Bonferroni correction.

P values <0.05 were considered significant.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) program, version 8.0 (10).

Results

We performed these examinations in all subjects with a mean age of 6.7 years. Muscle serum activity was normal in all cases. EMG examination was clearly normal in 25 children, suggestive but not diagnostic of myopathy in 6 of them, while only 10 evidenced non-specific changes (table 1). None of the subjects presented frank myopathic changes. Nerve conduction studies of motor and sensory nerves showed normal velocities, with CMAPs or sensory action potentials (SAPs) of normal amplitude in all subjects. All 6 patients with suggestive signs of myopathy at EMG exa-

Table 1. EMG – Muscle Biopsy correlation

EMG	Pts =41 (%)	Mean (mo/yr ± DS) Age	Muscle Biopsy
Myopathic	0	/	/
Suggestive in a myopathic sense	6 (14.6%)	18.3 mo ± 5.1 mo	Normal
Non-specific changes	10 (24.4%)	9.3 yr ± 3.4 yr	Normal
Normal	25 (61.0%)	7.3 yr ± 3.4 yr	Normal

Table 2. Demographic data

	Patients with suggestive EMG findings (N= 6)	Patients with non-specific EMG changes (N=10)	Patients with normal EMG findings (N=25)	P
Age				
Months ± DS	18.3 ± 5.1	112.5 ± 41.5	88.5 ± 41.5	<0.001[(1)]
Range	9-24	41-150	9-156	
Age (years)				
≤2 yr	6 (66,7%)	0	3 (33%)	<0.001[(1, 2)]
2-6 yr	0	2 (20%)	8 (80%)	
>6 yr	0	8 (36,4%)	14 (63%)	

[(1)] χ^2 test, p<0.001. Suggestive vs Normal, Suggestive vs Non-specific: χ^2 test; p=0.001 (Bonferroni correction for multiple comparisons); [(2)] Anova, p<0.001

mination were under 2 years of age when the examination was performed (table 2). Needle muscle biopsy was normal in all patients, and we obtained concordance between biopsy and EMG in about 85% of the subjects (35/41 = 85%). Concordance was total in all patients with normal EMG examinations.

Discussion and conclusions

When hypotonia is not correlated with brain dysfunction or is of unclear origin, clinicians often rely on EMG and NCS examination as well as muscle biopsy as specific diagnostic tools. While undoubtedly very useful, they are certainly invasive procedures for young children. However, at times, muscle biopsy may be deemed necessary: in this case, the decision for this procedure cannot be based only on clinical experience but also requires objective diagnostic support. In fact, if hypotonia is due to real myopathy, it might be a mistake not to perform a biopsy (11). EMG and NCS may be helpful to determine the use of muscle biopsy and/or DNA analysis and to identify the origin of the hypotonia (12). The aim of our study in patients with CHFO was to look for specific electromyographic abnormalities in order to obtain an early diagnosis without the need for muscle biopsy. In this regard, we are unaware of other studies reporting EMG and NCS findings in such a large group of patients with CHFO. In our patients, NCS never revealed motor or sensory velocity abnormalities, and CMAPs and SAPs were well-formed, even in the lower limbs where hypotonia was usually more evident. None of our subjects presented signs of denervation on needle examination. In 6 patients, the small amplitude of the interferential pattern and of the motor unit potentials were suggestive but not diagnostic of myopathy. Furthermore, all 6 children were under 2 years of age. We therefore believe that the false positive EMG reports were partially due to the technical difficulties in executing needle examination in often non-cooperative children. In fact, in accordance with other authors (13), we confirm that distinguishing the normally low amplitude and short duration motor unit potantials of a child from the motor unit potentials (MUPs) seen in myopathies might be particularly difficult, mainly in

children between 0 and 2-3 years of age. In 10 children, we observed non-specific EMG changes. Muscle biopsy was unremarkable in all of them.

EMG and NCS examinations are a useful diagnostic tool in CHFO in as much as when they are normal, they provide strong support for this diagnosis, given the high concordance between the normal EMGs and normal muscle biopsies observed in our cohort. However, since normal EMG and NCS do not exclude myopathy, we must carry out invasive procedures such as muscle biopsy in cases where the clinical course raises doubts concerning a positive outcome.

In conclusion, we emphasize that normal EMG and NCS provide valuable complementary information to confirm the clinical diagnosis of CHFO. Furthermore, we suggest that biopsy should be carried out on subjects in whom, after careful evaluation, signs of significant clinical improvement are not observed and the clinical diagnosis of CHFO begins to be dubious, even if the EMG and NCS do not indicate myopathic processes.

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