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# CORRELATION BETWEEN SPECIFIC HISTOLOGICAL AND ELECTROMYOGRAPHIC FINDINGS IN NEUROMUSCULAR DISORDERS

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SUMMARY — An attempt was made to find a correlation between specific electromyography (EMG) abnormalities with histological findings in muscle biopsies (MB) in 100 patients with neuromuscular disorders. Quantified EMG and MB with histochemistry was made in the same muscle, but on the opposite side, within a period of 3 weeks. The isolated findings of EMG and MB were analysed with a computer through a chi-square test. A statistical relation ($p<0.01$) was found between the isolated findings of MB and EMG in only 6.99% (39 in 558 attempts) of the abnormalities expected to occur in myopathy and denervation. Also was found 2.51% (14 in 558 attempts) of inconsistences with the current literature.

**Correlação entre anormalidades específicas da histologia e da eletromiografia em doenças neuromusculares.**

RESUMO — Estudo de 100 pacientes com doenças neuromusculares, procurando verificar a correlação entre anormalidades específicas da eletromiografia (EMG) com alterações histológicas da biópsia muscular (BM). Foi realizada EMG quantificada e BM com histoquímica do mesmo músculo mas em lados opostos, sendo os procedimentos realizados no máximo dentro do período de três semanas. As alterações isoladas da EMG e da BM foram analisadas pelo teste do chi-quadrado e auxílio de computador. Relação estatística adequada ($p<0.01$) foi encontrada entre os dados isolados da BM e EMG em somente 6,99% (39 em 558 testes) das anormalidades esperadas em miopatias e desinervações. Também foram encontradas 2,51% (14 em 558 testes) de inconsistências com os dados publicados atualmente, com referência à patogênese das alterações. Nos comentários é feita revisão da patogenia das principais alterações histológicas e eletromiográficas que podem confundir achados de miopatia com desinervações. Concluindo, os autores acreditam que os dados incompatíveis e a falta de relação da maioria dos dados pode ser decorrente do método utilizado, utilização inadequada de um dos métodos, tentativas de obter relações que os métodos não permitem ou a que os conceitos entre os achados eletromiográficos e histológicos devem ser revistos.

Electromyography (EMG) is an useful test to study the pathogenesis of processes which involve skeletal muscles, although it is not able to offer a nosological diagnosis [4,17]. On the other hand, the importance of muscle biopsy (MB) has been shown in recent years for evaluation of patients to define prognosis and to obtain a nosological classification [2,9,14,34]. Several attempts were made to correlate the specific data of EMG with that from MB in the last years [5,6,8,17,23,27,32,33] without obtaining satisfactory results. This is due to the use of different criteria for the

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evaluation, as well as different techniques of investigation. Buchthal & Kamieniecka [6], and Castaigne & col.[8] using histochemistry techniques were able to find some correlation between elements of EMG and MB, but still insufficient for a wider correlation.

In this investigation we intend to correlate some specific alterations of EMG with specific structural abnormalities of MB processed by fresh-frozen stains and by histochemistry, in cases with well defined pathology, using more rigid criteria.

## MATERIAL AND METHODS

The MB and EMG of 100 patients with neuromuscular disorders (25 cases of Duchenne muscular dystrophy, 14 cases of limb-girdle muscular dystrophy, 9 cases of facio-scapulo-humeral dystrophy, 10 cases of myotonic dystrophy, 10 cases of dermato-polymyositis, 10 cases of amyotrophic lateral sclerosis, 9 cases of infantile spinal muscular atrophy and 13 cases of peripheral neuropathies) were compared, using the criteria previously reported (*35*): 1. Disease with symmetrical involvement, identical in both sides of the body; 2. EMG and MB done in identical muscles (Degree 4 MCRM), but on the opposite side; 3. Exclusion of cases in which an EMG was done previously in both sides to avoid the «needle myopathy»; 4. The EMG done within a 3 week period (*25*); 5. The EMG should have been made with concentrical needle electrodes and should have quantitative analysis with data for insertion activity, spontaneous activity during muscle relaxation, average duration of potentials, average voltage of potentials, registration of the abnormal incidence (over 25%) of short and long polyphasic potentials, recruitment of effort and pattern of severe efforts (*35*); 6. The MB should have been adequate in quality and in number of muscle fibers, with fresh-frozen sections stained for haematoxylin-eosin and modified Gomori trichrome by Engel & Cunningham, as well as histochemical reaction for alkaline ATPases pH 9.4, acid ATPases pH 4.3 and 4.6, NADH-Tetrazolium reductase, non-specific esterase, succinic dehydrogenase, acid and alkaline phosphatase, according to techniques used in our laboratory (*34*). Information was obtained on: proliferation of connective tissue, adipose tissue infiltration, necrosis, phagocytosis, inflammatory infiltration, internal nuclei, fiber splitting, whorls, moth-eaten, snake coils, ring fibers, positive fibers and increased alkaline phosphatase in the interstice, positive fibers and increased acid phosphatase in the interstice, type I and II fiber atrophy, type I and II fiber hypertrophy, type I and II fiber predominance, type I and II fiber deficiency, dark angular atrophic fibers in the NADH-Tetrazolin reductase and non-specific esterase, targets, grouping, atrophy of groups or fascicles and perifascicular atrophy (*34*).

The data were analysed by grouping the abnormalities (variables) in tables of 2x2 (abscence or normal and presence or abnormal, indifferent to the intensity they occur), and applying the chi-square test (*29*) to detect possible relationships. To avoid some inconveniences when a small number of cases is being analysed, a correction for the continuity was applyed (*28,31*). When it was impossible to apply the chi-square test, Fischer's test was used (*28*). The tests were done using a S.P.S.S. Package (Statistical Package for the Social Sciences) (*22*), using a D.E.C. 1090 computer.

## RESULTS

558 chi-square tests were done to correlate the MB findings with the EMG abnormalities of all patients (Table 1). A statistical correlation ($p<0.01$) was found in 53 occasions (9.50%). To help the analysis, the correlations were grouped according to the higher significance level of histological and EMG data. These last ones were divided according to our expectations to occur in primary muscle disorders (myopathies), denervation (muscle involvement secondary to disease in the nerves and motor neurons), potentials which occur in both processes and potentials incompatible or unknown in relation to the current literature (Table 2).

In 39 occasions (6.99%) the data agreed with the pathogenesis currently accepted. There was a relationship among: 29 (5.19%) of the histological and EMG findings commonly found in the characterization of myopathies; 4 (0.72%) in the characterization of denervation; and 6 (1.06%) with unespecific data which occurs in both processes. There were 14 (2.51%) statistically significant relations ($p<0.01$) which were incompatible in relation to current literature.

High statistically relation was obtained ($p<0.001$ to 0.01) with the majority of EMG data found in primary myopathies (decreased potentials duration, excess of short duration polyphasic potentials, increased effort recruitment, BSAP pattern and reduced potentials

| Histological Alteration | Electromyographic Alterations | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Increased insertion activity | Fibrillation | Fasciculation | Positive waves | High frequency discharges | Myotonia | Average duration potentials | | Average potentials voltage | |
| | | | | | | | Decreased | Increased | Decreased | Increased |
| Connective tissue proliferation | • | ** | *** | ** | NS | NS | ** | NS | NS | * |
| Adipose tissue infiltration | NS | • | ** | ** | NS | NS | *** | NS | • | * |
| Necrose | NS | *** | ** | NS | NS | NS | • | • | NS | • |
| Phagocytosis | NS | ** | ** | NS | NS | NS | ** | NS | NS | • |
| Difuse inflammatory infiltration | NS | NS | NS | • | NS | NS | NS | NS | NS | NS |
| Perivascular inflam. infiltration | NS | NS | NS | NS | NS | NS | NS | NS | NS | • |
| Internal nuclei | • | * | *** | • | NS | NS | NS | * | NS | ** |
| Basophilic fibers | * | • | • | NS | NS | NS | NS | NS | *** | NS |
| Splitting | NS | ** | * | * | NS | NS | * | NS | NS | • |
| Whorls | NS | NS | • | • | NS | NS | * | NS | NS | NS |
| Motheaten | NS | NS | * | NS | NS | NS | NS | NS | NS | NS |
| Snake coils | * | NS | NS | NS | NS | NS | NS | — | NS | NS |
| Ring fibers | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Acid phosphatase - Positive fibers | NS | NS | • | NS | NS | NS | • | NS | • | NS |
| Acid phosphatase - Increased interst. | NS | * | ** | NS | NS | NS | ** | NS | NS | * |
| Alkaline phosphatase - Positive fibers | • | * | ** | • | NS | NS | * | NS | NS | • |
| Alkaline phosphatase - Incre. interst. | NS | • | * | NS | NS | NS | ** | NS | NS | * |
| Type I fiber atrophy | NS | * | NS | * | NS | NS | NS | NS | • | NS |
| Type II fiber atrophy | NS | NS | NS | NS | NS | NS | NS | NS | * | * |
| Type I fiber hypertrophy | NS | NS | NS | NS | • | NS | NS | NS | NS | NS |
| Type II fiber hypertrophy | NS | • | NS | • | NS | NS | NS | NS | NS | NS |
| Type I fiber predominance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Type II fiber predominance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Type I fiber deficiency | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Type II fiber deficiency | NS | NS | NS | NS | NS | NS | NS | — | NS | NS |
| Dark angular fibers - NADH Reductase | NS | • | * | * | NS | NS | * | NS | NS | * |
| Dark angular fib. - Non esp. esterase | NS | NS | *** | • | NS | NS | ** | • | • | • |
| Targets | NS | NS | ** | NS | NS | NS | • | NS | NS | *** |
| Fiber type grouping | NS | NS | NS | NS | NS | NS | * | NS | NS | NS |
| Group or fascicles atrophy | NS | * | NS | NS | NS | NS | NS | * | NS | NS |
| Perifascicular atrophy | NS | NS | NS | NS | NS | NS | NS | — | NS | NS |

*Table 1 — Results of the statistical analysis (Chi-Square test) between specific alterations of muscle biopsy and electromyographic abnormalities. NS, Non significant; •, $p < 0.015$; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; —, Insuficient number of cases for statistical analysis.*
*Continues next page.*

| Histological Alteration | Electromyographic Alterations | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Polyphasic potentials | | Effort pattern | | | | Effort recruitment | |
| | Short. dur. | Long dur. | BSAP | SMUP | MUP | GMUP | Diminished | Increased |
| Connective tissue proliferation | *** | NS | *** | * | NS | NS | NS | *** |
| Adipose tissue infiltration | *** | * | *** | • | NS | NS | NS | * |
| Necrose | *** | • | ** | • | NS | NS | • | • |
| Phagocytosis | *** | • | ** | • | NS | NS | • | • |
| Difuse inflammatory infiltration | NS | NS | NS | NS | NS | NS | NS | NS |
| Perivascular inflam. infiltration | NS | NS | NS | NS | NS | NS | NS | NS |
| Internal nuclei | *** | NS | • | NS | NS | NS | NS | NS |
| Basophilic fibers | ** | NS | * | • | NS | — | ** | NS |
| Splitting | *** | • | ** | NS | NS | NS | NS | • |
| Whorls | ** | ** | NS | NS | NS | NS | NS | • |
| Motheaten | * | • | NS | NS | NS | NS | NS | NS |
| Snake coils | NS | * | NS | — | NS | — | NS | NS |
| Ring fibers | NS | • | NS | NS | NS | NS | NS | NS |
| Acid phosphatase - Positive fibers | ** | NS | • | NS | NS | NS | NS | NS |
| Acid phosphatase - Increased interst. | *** | NS | ** | NS | NS | NS | • | • |
| Alkaline phosphatase - Positive fibers | ** | NS | * | NS | NS | NS | NS | NS |
| Alkaline phosphatase - Incre. interst. | ** | * | NS | • | NS | NS | • | NS |
| Type I fiber atrophy | ** | • | ** | • | • | NS | NS | ** |
| Type II fiber atrophy | * | ** | * | NS | NS | NS | NS | NS |
| Type I fiber hypertrophy | • | • | • | NS | • | NS | NS | NS |
| Type II fiber hypertrophy | * | NS | * | NS | • | NS | NS | NS |
| Type I fiber predominance | NS | NS | NS | NS | NS | NS | NS | NS |
| Type II fiber predominance | NS | NS | NS | NS | NS | NS | * | • |
| Type I fiber deficiency | NS | NS | NS | — | NS | — | NS | NS |
| Type II fiber deficiency | NS | NS | — | — | NS | — | NS | NS |
| Dark angular fibers - NADH Reductase | ** | NS | NS | NS | NS | NS | • | NS |
| Dark angular fib. - Non esp. esterase | ** | NS | NS | NS | NS | NS | • | NS |
| Targets | *** | NS | NS | NS | NS | NS | • | NS |
| Fiber type grouping | NS | NS | — | — | NS | NS | • | NS |
| Group or fascicles atrophy | NS | NS | — | — | NS | NS | NS | — |
| Perifascicular atrophy | NS | NS | — | NS | — | — | — | NS |

*Table 1 (cont.) — Results of the statistical analysis (Chi-Square test) between specific alterations of muscle biopsy and electromyographic abnormalities.*

| Histological Alterations | Electromyographic abnormalities usually found in: | | | |
|---|---|---|---|---|
| | Myopathies | Denervation | Non-specific | Inconsistent-Unknown |
| $p < 0.001$ (***) | | | | |
| Connective tissue proliferation | Short polyphasics<br>Increased recruitment<br>BSAP pattern | | | Fasciculation |
| Adipose tissue infiltration | Decreased pot. duration<br>Short polyphasics | | | |
| Necrose | Short polyphasics | | Fibrillation | |
| Phagocytosis | Short polyphasics | | | |
| Internal Nuclei | Short polyphasics | | | Fasciculation |
| Basophilic fibers | Decreased voltage | | | |
| Splitting | Short polyphasics | | | |
| Acid phosphatase - Increased interstice | Short polyphasics | | | |
| Dark angular fibers - Esterase non-esp. | | Fasciculation | | |
| Targets | | Increased voltage | | Short polyphasics |
| $p < 0.01$ (**) | | | | |
| Connective tissue proliferation | Decreased pot. duration | | Fibrillation<br>Positive waves | |
| Adipose tissue infiltration | BSAP pattern | | Positive waves | Fasciculation |
| Necrose | BSAP pattern | | | Fasciculation |
| Phagocytosis | Decreased pot. duration<br>BSAP pattern | | | Fasciculation<br>Increased voltage |
| Internal nuclei | | | | |
| Basophilic fibers | Short polyphasics | | | Decreased recruitment |
| Splitting | BSAP pattern | | Fibrillation | |
| Whorls | Short polyphasics | | | Long polyphasics |
| Acid phosphatase - Positive fibers | Short polyphasics | | | |
| Acid phosphatase - Increased interstice | Decreased duration<br>BSAP pattern | | | Fasciculation |
| Alkaline phosphatase - Positive fibers | Short polyphasics | | | |
| Alkaline phosph. - Increased interstice | Decreased pot. duration<br>Short polyphasics | | | Fasciculation |
| Type I fiber atrophy | Short polyphasics<br>Increased recruitment<br>BSAP pattern | | | |
| Type II fiber atrophy | | Long polyphasics | | |
| Dark angular atrof. fibers - NADH TR | | | | Short polyphasics |
| Dark angular fib. - Esterase non-spec. | | | | Decreased pot. duration<br>Short polyphasics |
| Targets | | Fasciculation | | |

*Table 2 — Results of the statistical analysis between the specific alterations of electromyography and histology. Relation to Pathogeny.*

voltage) and specific histological alterations found in myopathies (connective tissue proliferation, adipose infiltration, necrosis, phagocytosis, internal nucleus, basophilic fibers, fiber splitting, whorls, acid phosphatase positive fibers, increased acid phosphatase in the interstice, alkaline phosphatase positive fibers, increased activity in alkaline phosphatase in the interstice and type I fiber atrophy). In the same level of significance, little EMG correlations attributed to denervation were found (fasciculation, increased voltage and excess of long polyphasic potentials) with a few specific histological data for denervation (dark atrophic angular fibers in the unespecific esterase and type II fiber atrophy) (Table 2).

Several EMG findings (fasciculation, increased voltage, decreased recruitment and excess of long polyphasic potentials), which are considered an indication of denervation, obtained a significant statistical relation with some histological abnormalities which occurs frequently in primary myopathies (connective tissue proliferation, adipose tissue infiltration, necrosis, phagocytosis, internal nuclei, basophilic fibers, whorls, increased activity of acid and alkaline phosphatase in the interstice). Also the presence of excess short polyphasic potentials and decreased potentials duration, considered elements of primary muscle involvement, obtained a significant statistical relation with histological data commonly found in denervation such as target fibers, dark angular atrophic fibers in NADH-Tetrazolium reductase and unespecific esterase.

## COMMENTS

Lang & Partanen [21] and Desmedt & Borenstein [11] using special techniques in primary myopathies show that it is possible to find late potentials in the EMG (45 to 60 ms), belonging to the same motor unit. These potentials seems to originate from the recently reinervated fibers after the focal necrosis through the axons sprouting process [11]. This "emergency" colateral reinervation cannot conduct the electrical stimuli at its normal speed, causing a delay in the depolarization of the muscle fibers and originating the late potentials. These late potentials, when near its original potentials, become indistinguishable from the long polyphasic potentials in the regular EMG. This is the reason why in myopathies with a high degree of necrosis, is possible to find an increased duration of the potentials in the later phase and decreased duration in the initial phase [21]. Also this helps to explain why there is some delay in the progression of the asthenia in patients, even with the existence of important histological alteration [11]. The long latency, jitter and disynchronization probably are produced by the motor unit under regeneration, involving several factors such as slow conduction through the regenerated axon sprouting, ectopic motor end plate, failure of the neuromuscular transmission and muscle fiber atrophy [3]. During the denervation process the motor unit increases in size because of the denervated fibers of other units which were added through the sprouting processes [13,19,20].

The histological diagnosis of denervation depends on several elements, such as group fiber atrophy, fiber type grouping, dark atrophic angular fiber in the NADH-Tetrazolium reductase and unespecific esterase and targets fibers [2,14,15,18,34].

Histological alterations which commonly occur in myopathies, have been described in denervation processes, such as poliomyelitis [12,18]. A suggestion is made that in poliomyelitis cases [12], several years after the initial outbreak, the regenerated and reinervated muscle fibers from other motor units, have a very slight trophic support. This trophic support in critical levels barely permits the normal survival of the fibers, leaving them very vulnerable to trauma, minor injury or ischemia, with subsequent necrosis [12]. The histological reaction to muscle fiber necrosis is almost identical, not only to primary muscle diseases but also to neurogenic ones, with the presence of phagocytosis, connective tissue proliferation, adipose tissue infiltration and the presence of internal nucleus in the fiber under regeneration. The increase of alkaline and acid phosphatase in the interstitial tissue would have the same meaning in the healing process, because both are related to the interstitial inflammatory reaction and the connective tissue proliferation [1,7]. It is also possible, in cases of denervation, to find moth-eaten fibers and fiber splitting, specially in chronic and progressive denervation disorders [18,26,30].

Hausmanowa-Petrusewicz & Jedrzejowska [17] believed that the fibrillation and positive waves correspond to muscle fibers under regeneration and to isolated fragments of those fibers secondary to segmental necrosis, but were not able to obtain

statistical correlations. The same happened with the proliferation of connective tissue and spontaneous potentials, high frequency discharges and necrotic fibers in chronic lesions, reduction of muscle fibers and decreased in the average duration of the potentials, ring fibers and high frequency discharges. Some of the above findings were demonstrated experimentally, specially the relationship between fibrillation with necrosis and segmentation of muscle fibers [10]. Petajan & Thurman [23], were able to demonstrate in denervation cases, correlation between potentials of long duration, increased amplitude, long polyphasic and decreased recruitment in EMG with grouping and grouped atrophy of fibers. However, normal motor units were found and even with reduced duration with the same histological patterns [23]. Buchthal & Kamieniecka [6] obtained a correlation between an EMG and a MB with the increased of long duration polyphasics and signs of regeneration in patients with pseudo-hypertrophic muscular dystrophy of Duchenne, myotonic dystrophic and polymiositis. Castaigne and col.[8] obtained a statistic correlation between the EMG and MB with predominance of type I fibers and potentials of long duration and great amplitude.

In this study, typical myopathic alteration occurred in cases of denervation and vice versa. Not always necrosis and phagocytosis mean primary myopathies, as well as denervation elements do not mean abscence of inflammatory muscle reaction. This was reported in another study, when muscle necrosis and late potentials were found [24]. Also, Borenstein & Desmedt [3] showed in denervation cases that at the beginning the potentials are unique, similar to fibrillations; they become polyphasics of normal duration and reduced voltage; later they are transformed into long duration polyphasics, and can even present some late components. They say: "as a practical point, it is important to stress that abundant small, brief potentials recorded with the concentric needle are not necessarily indicative of a myopathic EMG pattern since they also occur in muscle after a severe nerve lesion" [3].

Concluding, we obtained only good statistic relation ($p<0.01$) among 39 of the isolated alterations in MB with the isolated data of EMG considered typical of myopathies or denervation, and 14 statistically significant relation of isolated alterations of EMG with isolated data of MB, which are incompatible with data known in the current literature. These incompatible data can be due to the method used, inadequate evaluation of one of the methods, trying to obtain a correlation of data which the methods did not allow, or the relationship concepts between the histological and electromyographical findings must be revised.

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