

Three case series involving progressive motor deficit

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ABSTRACT

The muscular dystrophies are a group of inherited, non-inflammatory disorders, consisting of progressive muscle wasting, without peripheral or central nerve involvement. We present a series of three cases involving progressive motor deficit and their different evolutions. The first case is about a 57-year-old female patient, without a significant family medical history, presenting for progressive motor deficit involving the shoulder and pelvic muscles, started at the age of 20-year-old, when she was diagnosed with a sporadic form of limb-girdle muscular dystrophy. The second case is about a 27-year-old male, diagnosed with muscular dystrophy at the age of 15. The third case is about a 43-year-old male admitted for frequent falls and weakness of the limbs, mainly distal, started 10 years ago. He was diagnosed with myotonic dystrophy. Although there is still no treatment for muscular dystrophies, the pathology is under investigation in clinical trials.

Keywords: muscular dystrophy, myotonic dystrophy, Steinert's disease, motor deficit

Abbreviations:

MD – muscular dystrophy

LGMD – limb-girdle muscular dystrophy

DAG – dystrophin-associated glycoproteins

CK – creatine kinase

LDH – lactate dehydrogenase

EMG – electromyography

ENG – electroneurography

EMA – European Medicines Agency

INTRODUCTION

The muscular dystrophies are a group of inherited, non-inflammatory disorders consisting of progressive muscle wasting, without peripheral or central nerve involvement. A definite fiber degeneration can be observed, without morphologic aberrations. The incidence of MD varies, Duchenne being the most common, with an inheritance pattern of 1 case per 3,500 live male births (1). Other types of MD are less common, LGMD occurring in only 1.3% of the MD patients.

The MD are a result of pathologic genetic coding of the proteins from the structure of the skeletal muscle fiber. There are multiple proteins involved

in the complex interactions of the muscle membrane and the extracellular environment (2). For sarcolemal stability, dystrophin and dystrophin-associated glycoproteins (DAGs) are some of the most important elements (3). The dystrophin gene is located on the short arm of chromosome X, near the p21 locus and codes for the large protein Dp427, which contains 3,685 aminoacids (4). The size of the protein is responsible for its susceptibility to sporadic mutations. Dystrophin associates with actin at the N-terminus and DAG complex at the C-terminus, forming a complex that interacts with laminin in the extracellular matrix.

The lack of dystrophin (Duchenne MD) leads to cellular instability, with progressive leakage of in-

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Article History:

Received: 23 November 2016

Accepted: 12 December 2016

tracellular components, resulting in high levels of creatine kinase. Less active forms of dystrophin may still function as a sarcolemmal anchor, but they allow some leakage of intracellular substance (classic Becker MD).

The other types of muscular dystrophies are caused by alterations in the coding of one of the DAG complex proteins. Gene defects in these proteins can lead to alterations in cellular permeability. Because of the different mechanism of action and location within the body, there can be associated effects.

The MD can be classified according to the inheritance pattern: X-linked – Duchenne, Becker, Emery-Dreifuss, Autosomal dominant – facioscapulohumeral, oculopharyngeal, limb girdle (LGMD1), Autosomal recessive – limb girdle (LGMD2).

The symptomatology onset can occur from birth to over 50 years old, the patients presenting, most often, progressive, symmetrical, proximal limb muscular atrophy (or in some cases pseudohypertrophy), spine curvature disorders. They can complain of frequent falls, respiratory difficulties, contractures and pain in the involved muscles. The cardiopulmonary involvement can be present from the beginning of the disease. The life expectancy in MD patients can vary from 20 years (Duchenne) to an almost normal life span (facioscapulohumeral MD).

CASE PRESENTATIONS

We present a series of three cases involving progressive motor deficit and their different evolutions.

The first case is about a 57 year old female patient, hypertensive, dislipidemic, with a personal medical history of untreated type II diabetes for about 4 years, without a significant family medical history, admitted for progressive motor deficit involving the shoulder and pelvic muscles. The symptomatology started at the age of 20, with weakness of the right shoulder muscles, followed 2 years later by weakness of the left shoulder muscles, manifested by difficulties in the abduction of the upper limbs over the head level. Lately, at the age of 30 the motor deficit also involved the pelvic muscles, the patient affirming difficulties in rising from a seated position, in climbing and descending stairs.

Objective examination at the admission date: thorax deformed by kiphoscoliosis, scapular protrusion (scapula alata) – the right side being more affected than the left, muscle wasting involving the biceps brachii, triceps brachii, supraspinatus and

infraspinatus muscles, quadriceps femoris, without deep or superficial sensitivity impairment, without cranial nerves involvement, normal deep tendon reflexes (Fig. 1).



FIGURE 1. Case 1 of progressive motor deficit.

Paraclinical: CK-233UI/L, LDH-358UI/L, cholesterol – 332 mg/dL, glucose-108 mg/dL, glycosylated hemoglobin – 6.45%. The electromyography objectified the presence of a myopathy at the scapulo-humeral and pelvic muscles. The quadriceps muscle biopsy revealed mild muscular dystrophy. Taking into consideration the clinical and paraclinical aspects of this case, we put the diagnosis of limb-girdle muscular dystrophy – sporadic form.

The second case is about a 27 year old male, diagnosed with muscular dystrophy at the age of 15. He is admitted for painful contractions and motor deficit of the scapulo-humeral and pelvic muscles. From the family medical history, we mention the mother (deceased at 55 year old due to a respiratory complication) and two brothers (from the total of seven) diagnosed with muscular dystrophy.

Objective clinical examination: underweight (BMI-16.6), scapulae alatae, muscle wasting of the biceps and triceps brachii (Fig. 2), supraspinatus and infraspinatus, trapezius, serratus anterior, rhomboideus major and quadriceps femoralis muscles, impossibility of lifting the upper limbs over the shoulder level, but with normal distal strength and impossibility of rising from seated position (Gower's sign), without swallowing impairment, deep or superficial sensitivity loss, walk possible without assistance for short distances (up to 100m).

The laboratory/ancillary examinations revealed: CK-859UI/L, normal EKG and chest radiography. Deltoid muscle biopsy revealed moderate muscular dystrophy. The patient was diagnosed with an inherited form of LGMD.



FIGURE 2. Case 2 of progressive motor deficit.

The third case is about a 43 year old male, with a personal medical history of hepatitis B virus infection (2002), very few data regarding the family medical history (he was adopted), an uncle (that he never met) deceased at approximately 45 year old from an unknown chronic disease. The patient was admitted for frequent falls and weakness of the limbs, mainly distal. The symptomatology started 10 years ago and aggravated during the last 4 years.

Objective clinical examination: symmetrical muscle atrophy of the limbs, mainly distal, facial muscle wasting with incomplete eyelid occlusion, absence of the forehead folds, impossibility of rising the eyebrow, shuffled gait, myotonic phenomenon (Fig. 3).

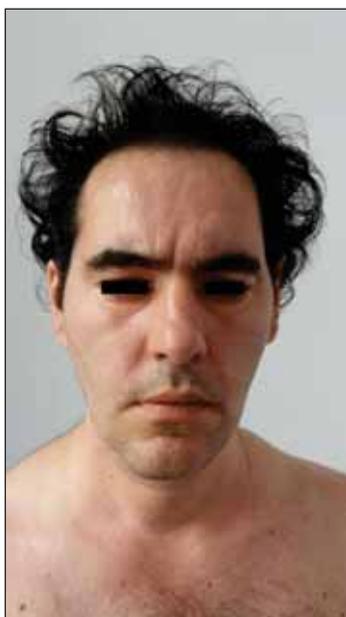


FIGURE 3. Case 3 of progressive motor deficit.

Laboratory/Ancillary examination results revealed: CK-259UI/L, TGO-28UI/L, TGP-56UI/L, normal EKG and spirometry. The EMG shows myotonic discharge with normal ENG. The muscle biopsy objectifies a muscular dystrophy. Considering the clinical and paraclinical aspects of the case we diagnosed the patient with Steinert's disease.

DISCUSSION AND CONCLUSIONS

We have to take into consideration the diagnosis of muscular dystrophy even in patients without a family history of MD, in up to one third of the cases the gene involved being subject to a sudden abnormal change (spontaneous mutation) (5).

The evolution of a patient diagnosed with MD can be very variable even in the same group (the first and the second cases presented being diagnosed with LGMD), due to a high heterogeneity. The limb-girdle muscular dystrophy group consists of two subgroups (8 forms of autosomal dominant LGMD1A to LGMD1H and 24 forms of autosomal recessive LGMD2A to LGMD2X) (6).

Although there is still no treatment for MD, the pathology is under intense investigation in clinical trials. In gene therapy, healthy immature myoblasts are introduced into the diseased muscles, which then fuse and stimulate dystrophin to reverse the degeneration that occurs in the affected muscles (7).

In 2011, there was performed a meta-analysis of all clinical trials using creatine monohydrate supplements in neuromuscular disorders. In patients with dystrophinopathies and type II myotonic myopathy, a modest but significant increase in maximum voluntary contraction versus placebo can be observed (8).

One study demonstrated that the Ataluren treatment increases the expression of full-length dystrophin protein in human and mouse primary muscle cells containing the premature stop codon mutation for Duchenne muscular dystrophy and rescues the striated muscle function (9). Although in 2010 the preliminary results of a 2b phase of a clinical trial for Duchenne MD showed no significant improvement in the six minute walk distance after 48 weeks of trial, the medication was approved by EMA in 2014. In November 2016, the selling company announced the agreement on pricing and reimbursement terms in Romania.

Conflict of interest: none declared
Financial support: none declared

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