Answers, Discussion and Teaching Points for *Myopathies with Contracture*

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ABSTRACT

The two videos show physical examination of two patients with contractures. The answers are at the end of this file along with further discussion as to how to approach a case of muscle contracture and myopathy, as well as teaching points.

Keywords: *Contractures, Neuromuscular, Myopathy.*

Questions:

Q1/ A 34-year-old man who walked on his toes as a child and had Achilles tendon surgery. As he grew older, he developed weakness of the triceps and knee flexors and extensors. He had two healthy brothers and no family history of muscle disease. Examination findings are shown in the video number 1. CPK was: 477 IU/L, Electromyography (EMG) showed mixed long and short duration MUAPs in the tested proximal muscles. (see video 1)

Cardiac involvement is typically a feature of the following myopathy:

A. Oculopharyngeal muscular dystrophy (OPMD)
B. Emery-Dreifuss muscular dystrophy (EDMD)
C. Facioscapulohumeral muscular dystrophy (FSHD)
D. Collagen VI myopathies

Q2/ A 32-year-old woman who walked on tiptoes at age 5 years for which she had an elongation of the Achilles tendon bilaterally. She had one healthy sister and no family history of muscle disease. She developed a fixed mild proximal legs weakness since childhood. CPK level was slightly elevated and EMG was myopathic. Physical findings are shown in video 2.

Contractures are common in the following myopathies:

A. Limb Girdle muscular dystrophy type 2 B (LGMD2B)
B. Myotonic dystrophy
C. Bethlem myopathy
D. FSHD

Discussion:

It is important to differentiate between metabolic contractures, a feature of some metabolic myopathies which are painful, occur during exercises and are electrophysiologically silent, and myopathic contractures which limit passive stretch ability of a muscle to its proper length due to fibrosis. While most advanced myopathies are associated with contractures due to fibrosis, the development of contractures while the muscles are still functional, is a feature of only a few myopathies.

Contractures are an important diagnostic clue, especially, most of the contractures-associated myopathies carry no other specific features (normal or mild CK elevation, myopathic EMG and muscle biopsy). Such differentiation is important to select the right genetic testing and to facilitate the identification of some fatal myopathies due to cardiac arrhythmias which can be prevented by a defibrillator and or a pacemaker. Toe walking during childhood is an important sign of contracture of the calf muscles and many patients undergo surgical repair of the Achilles tendon for it. Such a finding should prompt a search for other contractures and a family history of muscle disease or sudden death.

There are two major groups of myopathies with contractures:

1. Bethlem myopathy: this is characterized by:
   - It is caused by Collagen VI mutations in one of the three collagen VI genes COL6A1, COL6A2 and COL6A3
   - Mutations cause two main types of muscle disorders: Ullrich congenital muscular dystrophy, an autosomal recessive disease with a severe phenotype, and a mild to moderate phenotype, Bethlem myopathy which is usually autosomal dominant.
   - Clinically, this group is characterized by muscle and connective tissue involvement, including weakness, joint laxity and contractures, and abnormal skin findings. Bethlem myopathy is proximal and contractures are characteristically distal, affecting finger flexors and to a lesser extent, they affecting ankles and elbows.
   - Although considered benign, 10% of patients need nocturnal respiratory support and 2/3 of patients require a walking aid after age 50 years.
   - Cardiac involvement is rare.

2. Emery-Dreifuss muscular dystrophy (EDMD): this is characterized by:
    - Early contractures, often before any significant weakness, of elbows, Achilles tendons, and post-cervical muscles
    - Slowly progressive muscle wasting and weakness with a distinctive humero-peroneal distribution (i.e. proximal in the upper limbs and distal in the lower limbs) early in the course of the disease.
    - Cardiac conduction defects (ranging from sinus bradycardia, prolongation of the PR interval on electrocardiography to complete heart block). Cardiomyopathy may also supervene. Thus, affected individuals may die suddenly from heart block, or develop progressive cardiac failure.
    - Responsible mutations affect Emerin and Lamin A and C genes. There are two main modes of inheritance; X-linked (Emerin) and autosomal dominant (Lamin). Rare autosomal recessive inheritance has also been described. EDMD can be also caused by mutation of FHL1 and SYNE genes.

Teaching points:

1. Toe walking history should prompt a search for contractures of other joints and family history of muscle disease or sudden death.
2. If contractures are out of proportion to weakness, consider EDMD
3. If finger flexors are contracted, consider Bethlem myopathy
4. Cardiac monitoring is essential for all EDMD patients.

Reference:

Walters RJ Contractures and muscle disease. Practical Neurology 2016;16:258-263.

Answers:

Answer 1:

B-Blood genetic testing revealed a heterozygous pathogenic mutation in Lamin A (LMNA) gene, confirming EDMD

Answer 2:

C- Blood genetic testing revealed a Heterozygous De Novo Pathogenic mutation of Collagen 6A2 (COL6A2) gene confirming Bethlem myopathy.