Pediatric Neurology Part III: Chapter 141. Progressive muscular dystrophies (Handbook of Clinical Neurology)

Jamel Chelly, Isabelle Desguerre

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Infancy- or childhood-onset muscular dystrophies may be associated with profound loss of muscle function, affecting ambulation, posture, cardiac and respiratory functions, while those of late onset may be mild and associated with slight weakness or fatigability induced by effort. In addition to the distribution of muscle weakness, symptoms, and course of the disease, the diagnosis of muscular dystrophy is usually ascertained by histological findings. There is connective tissue proliferation in the perimysium and endomysium, variation in muscle fiber size, cytoarchitectural alterations of myofibers such as internal nuclei, myofibrillar whorls, and fiber splitting and lobulation, but, most of all, degeneration and regeneration of myofibers. Causes of muscular dystrophies characterized by muscle weakness and wasting are heterogeneous and include dysfunction of diverse genetic pathways and genes encoding proteins of the plasma membrane, extracellular matrix, sarcomere, and nuclear membrane components. Duchenne and Becker muscular dystrophies are prototypes illustrating advances in the field of myology. Limb-girdle muscular dystrophies (LGMDs) are clinically and genetically heterogeneous, some with autosomal dominant (LGMD1) and others with autosomal recessive (LGMD2) inheritance. Neither clinical and genetic grounds nor biopsy patterns are specific enough to distinguish them, but two common denominators are: (1) weakness and wasting predominating in pelvic and shoulder girdle muscles, with occasional involvement of the myocardium; and (2) necrosis and regeneration of myofibers. While identification of genetic causes and molecular diagnosis are increasingly improved, especially with the advent of new generation sequencing technologies, optimized care, information for the family, and prevention, including genetic counseling and prenatal diagnosis, require multidisciplinary follow-up with genetic, pediatric, and psychological involvement.

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