Skeletal Muscle Edema in Muscular Dystrophy: Clinical and Diagnostic Implications

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- Muscular dystrophy • MRI • Myoedema
- Neuromuscular disease

Numerous major forms of muscular dystrophy have been identified.[1] The type of muscular dystrophy influences the progression of muscle degradation and the pattern of muscle involvement (**Table 1**). An increasing number of defects in specific genes have been identified as the underlying cause of different forms of muscular dystrophy. Many of these genes encode for components of transmembrane and membrane-associated proteins that form a structural linkage between the F-actin cytoskeleton and the extracellular matrix in muscle. One example of this is the dystrophin–glycoprotein complex (DGC), an assembly of proteins that are organized into three subcomponents: the cytoskeletal proteins, sarcoglycans, and sarcospan.[2,3] Several of the subtypes of limb girdle muscular dystrophy (LGMD) arise from primary mutations in genes encoding components of this complex. At least four sarcoglycan subunits (α, β, γ, and δ subunits) are present in muscle, and mutations here also result in a form of muscular dystrophy. Alpha laminin-2 (LAMA2) is a basement membrane

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Table 1
Types of muscular dystrophy and general pattern of progression

Type	Typical Age of Onset	Muscles Affected
Myotonic	20–30 y	Facial, neck, forearm, cardiac
Duchenne	Childhood	Leg, pelvis, arm, shoulder, cardiac
Becker	11–25 y	Leg, pelvis, arm, shoulder, cardiac
Limb-girdle	Childhood to adulthood	Shoulder, hip
Facioscapulohumeral	15–40 y	Facial, shoulder, upper arm, leg
Congenital	Childhood	Generalized
Oculopharyngeal	40–50 y	Eyelid, facial, throat, tongue, proximal limbs
Distal (Miyoshi)	40–60 y	Forearm, hand, lower leg, feet
Emery-Dreifuss	10–25 y	Upper arm, lower leg, shoulder, facial, cardiac

Data from Muscular dystrophy: hope through research. Muscular Dystrophy: Hope Through Research. National Institute of Neurological Disorders and Stroke Web site. Available at: http://www.ninds.nih.gov/disorders/md/detail_md.htm. Accessed September 20, 2011.

protein and binds to β-dystroglycan. Mutations in the *LAMA2* gene result in another form of muscular dystrophy.[4]

Mutations in the dystrophin gene that result in a complete loss of dystrophin lead to the Duchenne muscular dystrophy (DMD) phenotype.[5] Mutations that cause reduced amounts of dystrophin or a truncated, dysfunctional form of dystrophin result in the Becker muscular dystrophy (BMD) phenotype. Mutations in components of the DGC complex are thought to lead to a loss of sarcolemmal integrity and render muscle fibers more susceptible to activity- or exercise-induced muscle injury. The mechanisms of muscle injury are relatively well characterized in the dystrophinopathies (ie, DMD/BMD). In others, the genetic basis has only recently been described and the mechanisms of injury are yet to be elucidated (eg, production of the protein DUX4 in facioscapulohumeral muscular dystrophy [FSHD]).[6] Furthermore, even though the genetic basis for a particular muscular dystrophy may be known, in some cases multiple genes or epigenetic modifications may modulate disease expression.

Despite the variation in the pattern and rate of muscular involvement, affected muscles follow a largely similar course of compromise in which the muscles begin to leak creatine kinase and take on excess calcium. The affected muscle fibers lose integrity, resulting in fiber degeneration and weakness. Ultimately, two primary paths result: shortening of the muscle fibers and tendons, leading to muscle atrophy; or replacement of muscle fibers with fat and connective tissue. Less affected or unaffected muscle groups may compensate with hypertrophy. During the course of muscle degeneration, multiple factors may modulate or influence the pathology seen, such as reversible injury, pseudohypertrophy (in which fat has replaced muscle to a degree that the tissue appears hypertrophied by gross examination), atrophy, and fatty replacement over time. These morphologic changes may be readily appreciated with MRI.

PROGRESSION OF MUSCLE CHANGE ASSESSMENT WITH IMAGING

In most forms of muscular dystrophy the muscle cell membrane (sarcolemma) is weakened, making it susceptible to contraction-induced damage and loss of homeostasis. Over time, the muscles become progressively weaker as they are replaced by fat and connective tissue. The rate of progression, severity of changes, and pattern of involvement