Table e-2. Distinguishing features of muscular dystrophies

Designation	Protein	Chromosome	Inheritance	Common patterns of weakness	Distinguishing clinical features	Distinguishing EMG and muscle biopsy features	Complications
X-linked muscular dystrophies							
EDMD-X1	Emerin	Xq28	XR	HP	Contractures invariably present early in the disease course		Cardiac conduction abnormalities
EDMD-X2	FHL1	Xq27.2	XR	LG, HP or SP, DM	Foot drop; extremity contractures and neck contractures common	Myofibrillar myopathy or reducing bodies	Severe respiratory failure in many patients
Becker muscular dystrophy	Dystrophin	Xp21	XR	LG	Calf hypertrophy	Mosaic appearance of dystrophin on immunohistochemistry in affected woman	Dilated cardiomyopathy in 4% to 70% depending on disease duration
Limb-girdle muscular dystrophies (LGMDs)							
LGMD1A	Myotilin	5q22.3-31.3	AD	LG, DM	Onset > 40 years, foot drop, asymmetric muscle weakness and atrophy	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
LGMD1B	Lamin A/C	1q11-21	AD	LG, HP, DM	Early humeroperoneal weakness, limb contractures		Cardiomyopathy and conduction system disease
LGMD1C	Caveolin-3	3p25	AD	LG	Rippling muscles, percussion-induced rapid contractions, prominent muscle		

					cramps and calf hypertrophy		
LGMD1D	DNAJB6	6q23	AD	LG, DM	Onset > 40 years, foot drop	Myofibrillar myopathy, rimmed vacuoles, myotonic or pseudomyotonic discharges	
LGMD1E	Desmin	2q35	AD	LG, HP, DM	Onset < 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
LGMD2A	Calpain-3	15q15.1-21.1	AR	LG	More common in patients with British, Southern or Eastern European, or Brazilian ancestry; scapular winging, absence of calf hypertrophy	Inflammatory changes on some biopsies	
LGMD2B	Dysferlin	2p13	AR	LG, DM (Miyoshi phenotype)	Calf atrophy, inability to stand on toes		Left ventricular hypertrophy or reduced ejection fraction in rare patients
LGMD2C	γ-Sarcoglycan	13q12	AR	LG	Age of onset 2-23 years; macroglossia, ankle contractures, and scoliosis		Severe ventilatory muscle weakness has been reported in up to one-third of patients
LGMD2D	α-Sarcoglycan	17q12-21.3	AR	LG			

LGMD2E	β-Sarcoglycan	4q12	AR	LG			
LGMD2F	δ-Sarcoglycan	5q33-34	AR	LG	Early age of onset, 4 to 10 years		Early respiratory muscle involvement
LGMD2G	Telethonin	17q11-12	AR	LG		Rimmed vacuoles	Cardiac involvement, type unspecified
LGMD2H	E3-ubiquitin-ligase (TRIM32)	9q31-33	AR		Hutterite descent	Many small vacuoles usually more prominent in type II fibers	
LGMD2I	Fukutin-related protein (FKRP)	19q13	AR	LG	Northern European ancestry, scapular winging, calf hypertrophy, early cardiorespiratory involvement		Dilated cardiomyopathy and respiratory dysfunction common
LGMD2J	Titin	2q31	AR	LG	Finnish and French populations	Rimmed vacuoles	
LGMD2K	POMT1	9q31	AR	LG			
LGMD2L	Anoctamin-5	11p14.3	AR	LG, DM (Miyoshi phenotype)	Calf atrophy, inability to stand on toes		
LGMD2M (fukutin)	Fukutin	9q31-33	AR		Early age of onset, 4 months to 4 years		Some muscle biopsies with prominent inflammatory changes
LGMD2N	POMT2	14q24	AR	LG			
LGMD2O	POMGNT1	1p32	AR	LG			
LGMD2P	α-Dystroglycan	3p21	AR	LG			

LGMD2Q	Plectin	8q24.3	AR	LG	History of epidermolysis bullosa; pyloric atresia seen in other forms of plectinopathies, although not in LGMD2Q		
Myofibrillar myopathies							
Myotilinopathy (LGMD1A)	Myotilin	5q22.3-31.3	AD	LG, DM	Onset > 40 years, foot drop, asymmetric muscle weakness and atrophy	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
Desminopathy (LGMD1E)	Desmin	2q35	AD	LG, HP, DM	Onset < 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
Titinopathy (HMERF)	Titin	2q31	AD	LG	Finnish and French populations	Rimmed vacuoles, myofibrillar myopathy	Autosomal dominant, early respiratory failure
BAG3	BCL2-associated athanogene 3	10q25.2-q26.2	AD	LG, DM	Onset < 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
Filamin C (Williams distal myopathy)	Filamin C	7q32.1	AD	LG, DM	Onset > 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
αB-Crystallin	αB-Crystallin	11q21-23	AD	LG, DM	Early or late onset, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic	Cardiomyopathy, respiratory muscle weakness

						discharges	
ZASP	Z-band alternatively spliced PDZ motif-containing protein	10q22.3-23.2	AD	LG, DM	Onset > 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
FHL1	Four-and-one-half LIM1 protein	Xq27.2	X-linked	LG, HP or SP, DM	Foot drop; extremity contractures and neck contractures common	Myofibrillar myopathy or reducing bodies	Severe respiratory failure in many patients
Hereditary inclusion body myopathy (hIBM)							
AR hIBM	Glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase (GNE)		AR	DM	Early adult onset, foot drop	Rimmed vacuoles	
AD hIBMPFD	Valosin-containing protein (VCP)		AD	LG, DM	Proximal and distal weakness; past or family history of frontotemporal dementia, Paget disease, motor neuron disease	Rimmed vacuoles, myotonic discharges	
hIBM3	MYHC-IIA		AD	LG	External ophthalmoplegia, joint contractures	Rimmed vacuoles, lobulated fibers, absent type IIA fibers	
Distal dystrophies/myopathies							
Welander distal myopathy	TIA1	2p13	AD	DM	Swedish/Finnish ancestry, late adult onset, index finger and wrist extensor weakness followed		

					by atrophy of hand muscles		
Udd distal myopathy	Titin	2q31	AR, AD	LG, DM			Some phenotypes with early respiratory failure or early dilated cardiomyopathy
Markesbery-Griggs	Z-band alternatively spliced PDZ motif-containing protein (ZASP)	10q22.3-23.2	AD	LG, DM	Onset > 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
Laing, hyaline body myopathy	MYH7, myosin heavy chain	14q11	AD	DM	Early adult onset, foot drop, neck weakness, disabling myalgias, calf hypertrophy		Cardiomyopathy
Williams distal myopathy	Filamin C	7q32.1	AD	LG, DM	Onset > 40 years, foot drop	Myofibrillar myopathy, myotonic or pseudomyotonic discharges	Cardiomyopathy, respiratory muscle weakness
Vocal cord and pharyngeal weakness with distal myopathy (VCPDM)	Matrin-3	5q31.2	AD	DM	Mean age at onset 45 years, foot drop and distal upper extremity weakness, dysphagia, dysphonia	Subsarcolemmal rimmed vacuoles	

Distal myopathy with Kelch-like homologue 9 mutations	Kelch-like 9	9p22	AD	DM			
Miyoshi myopathy type I, LGMD2B	Dysferlin	2p13	AR	DM (Miyoshi phenotype)	Calf atrophy, inability to stand on toes		Left ventricular hypertrophy or reduced ejection fraction in rare patients
Miyoshi myopathy type III, LGMD2L	Anoctamin-5	11p14.3	AR	DM (Miyoshi phenotype)	Calf atrophy, inability to stand on toes		
Nonaka myopathy, AR hIBM	Glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase (GNE)		AR	DM	Early adult onset, foot drop	Rimmed vacuoles	
Nebulin myopathy	Nebulin	2q21.2-q22	AR	DM	Early adult onset, foot drop	Nemaline rods	
Other dystrophies							
Bethlem myopathy	Collagen VI		AD	HP	Joint laxity, prominent calcanei, variable age of onset		
Ullrich myopathy	Collagen VI		AR	HP	Joint laxity, prominent calcanei, neonatal or congenital onset		
Selenoprotein N1 (rigid spine	Selenoprotein N1	1p36	AR	LG	Rigid spine, joint contractures,	Multiminicores, cores, Mallory bodies, type I	Restrictive lung disease

syndrome)*					generalized weakness	fiber predominance	
Muscular dystrophy with generalized lipodystrophy	Cavin-1/PTRF	17q21.2	AR	Distal dominant, generalized	Generalized lipodystrophy, myalgia, cramps, percussion-induced muscle mounding, hepatosplenomegaly, insulin resistance, acanthosis nigricans		Arrhythmias including prolonged QT syndrome, sudden cardiac death

Abbreviations: AD = autosomal dominant; AR = autosomal recessive; DM = distal muscular; EDMD = Emery-Dreifuss muscular dystrophy; hIBMPFD = hIBM with Paget disease and frontotemporal dementia; HMERF = hereditary myopathy with early respiratory failure; HP = humeroperoneal; LG = limb-girdle; PTRF = polymerase I and transcript release factor; SP = scapuloperoneal; XR = X-linked recessive.

*Rigid spine syndrome can also be caused by FHL1, BAG3, lamin A/C, and collagen VI mutations.

LGMD 2R and 2S were described after this systematic review was performed and hence are not discussed in this guideline.