Distal Myopathies

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KEYWORDS

• Distal myopathy • Welander myopathy • Myoshi myopathy • Nonaka myopathy
• Laing myopathy • Markesbery-Griggs myopathy • Udd distal myopathy
• Myofibrillar myopathy

KEY POINTS

- Except for hand extension weakness in Welander myopathy, the classic distal myopathies manifest as distal leg weakness beginning in early or late adult life.
- Myoshi myopathy, manifesting as calf muscle weakness and atrophy after a hypertrophic phase, is allelic to LGMD2B, because both diseases are caused by mutation in the gene encoding for dysferlin.
- Patients with myofibrillary myopathy present in the third to fifth decade with distal myopathy, frequent cardiomyopathy, and pathologic evidence of myofibrillary degradation.
- Mutation in genes encoding for αBC, desmin, myotilin, ZASP, filamin C, BAG3, and SEPN1 are responsible for myofibrillary myopathies.
- Myotonic dystrophy is the most common adult muscular dystrophy; early in the disease, wrist and finger extensors and ankle dorsiflexors are weaker than proximal muscles.

APPROACH

In approaching patients with distal weakness, we have to consider disorders affecting motor neurons, peripheral nerves, neuromuscular junction, or muscle[1] and the reader is referred for a full discussion to the article an the approach to muscle disease elsewhere in this issue by Barohn and colleagues. Some myopathies with pattern 2 have predominantly distal presentations, including distal muscular dystrophies, myofibrillar myopathies, myotonic dystrophy type 1, and some forms of hereditary inclusion body myopathies (hIBM). Pattern 3 or scapuloperoneal pattern has proximal arm and distal leg involvement. In the presence of facial weakness, fascioscapulohumeral (FSH)

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muscular dystrophy is considered likely. Emery-Dreifuss muscular dystrophy is usually associated with contractures and cardiac involvement. Late onset acid maltase deficiency can rarely have a scapuloperoneal presentation as well. Pattern 4 consists of distal arm involvement and proximal leg weakness, as is typical for the sporadic inclusion body myositis (IBM), in which there is prominent finger flexor, wrist flexor, and knee extensor weakness. Pattern 5 is associated with ptosis and ophthalmoplegia and includes patients with oculopharyngeal dystrophy and mitochondrial myopathy.

The presence of rimmed vacuoles (**Box 1**) significantly helps to further narrow down these diagnostic possibilities. Welander myopathy is nearly always in cases from Scandinavia and presents with distal hand involvement. The Markesbery-Griggs and Udd types are autosomal dominant (AD) late onset distal leg myopathies caused by mutations in the genes encoding Z-band alternatively spliced PDZ-motif-

Box 1
Muscle disorders with rimmed vacuoles on biopsy

IBM

h-IBM

- h-IBM2 or Nonaka type distal myopathy (GNE)
- IBMPFD[a] (VCP)
- h-IBM3 (myosin heavy chain IIa)[a]

Distal muscular dystrophies

- Welander type[a]
- Markesbery-Griggs type (ZASPopathy)[a]
- Udd type (titinopathy)[a]

MFM

- Myotilinopathy (LGMD1A)[a]
- ZASPopathy[a]
- Desminopathy[a]
- Filaminopathy[a]
- Bag3-opathy[a]
- αB-crystallin[a]
- SEPN1

Other muscular dystrophies/myopathies

- Reducing body myopathy (FHL1-opathy)
- Emery-Dreifuss (emerinopathy, laminopathy[a])
- LGMD2G (telethoninopathy)
- Oculopharyngeal muscular dystrophy (PABP2-GCG triplet)[a]
- Oculopharyngodistal muscular dystrophy
- Pompe disease (acid maltase deficiency)
- Danon disease (LAMP-2)
- X-linked myopathy with excessive autophagy (VMA21)

[a] Autosomal dominant.