Muscular Dystrophies: What the radiologist should know

J. Carmen Timberlake, MD; Kristina Siddall, MD; Christopher Bang, DO; Marat Bakman, MD; Gwy Suk Seo, MD; Johnny UV Monu, MD

Department of Imaging Sciences
University of Rochester Medical Center, Rochester, NY
Muscular Dystrophies: Introduction

- The muscular dystrophies are
  - a group of inherited, progressive muscle disorders
  - caused by mutations in genes encoding proteins required for normal muscle function.

- Biopsy reveals fiber degeneration
  - this manifests clinically as weakness.
Muscular Dystrophies: Introduction

• Role of imaging in diagnosis and management
  – Historically, diagnosis and evaluation of disease progression depend on clinical, pathologic, and biochemical parameters.
  – Imaging has not been used for primary diagnosis or for routine follow-up evaluation.
  – MRI, however, has a potential role in the work up, management, and study of muscular dystrophies
Muscular Dystrophies: Introduction

Teaching points:

1. Review of spectrum of muscular dystrophies.
2. Review patterns of inheritance, pathophysiology of disease, clinical manifestations, and clinical management.
3. Review radiologic findings in muscular dystrophies, with emphasis on MRI.
4. Explore potential role of MRI in evaluation, management, and scientific investigation of muscular dystrophies.
Muscular Dystrophies: Classification by physiology

- Disruption of the dystrophin-glycoprotein complex
  - DMD/BMD
  - CMDs (most)
  - LGMDs (some)

- Disruption of gene expression or chromosomal organization
  - FSHD
  - EDMD
  - Oculopharyngeal dystrophy
  - Myotonic dystrophy

Muscular Dystrophies: Classification

• The classification of muscular dystrophies continues to evolve with advances in understanding of their molecular genetics.
• Subdivisions of the major clinical categories are defined by their molecular features.
• Imaging features are not a component of established classification schema.
Muscular Dystrophies: Classification

- On the next slide is an overview of the major subtypes of muscular dystrophies. Click on highlighted links for more detailed information, including what is known about their patterns of specific muscle involvement and sparing.

- Description of major categories
  - Limb Girdle Muscular Dystrophies: Heterogeneous group of diseases characterized by proximal muscle weakness
  - Congenital Muscular Dystrophies: Diseases characterized by muscular weakness in early infancy (typically obvious at birth) and elevated CK in neonatal period (normalizes by 6-10 wks)
  - Other Muscular Dystrophies: Heterogeneous group of diseases, which do not fit into the above two major categories
## Muscular Dystrophies: Major Subtypes

### LIMB GIRDLE MDs (LGMDs)
- **Dystrophinopathies** – prototypes of LGMDs  
  - Duchenne MD  
  - Becker MD  
- **Autosomal dominant LGMD**  
  - LGMD1A through 1C  
- **Autosomal recessive LGMD**  
  - LGMD2A through 2J

### CONGENITAL MDs (CMDs)
- **CMD without major brain malformation**  
  - Merosin-absent CMD  
  - CMD  
  - CMD with rigid spine disease  
  - Ullrich myopathy  
- **CMD with major brain malformation**  
  - Fukuyama CMD  
  - Muscle-eye-brain disease  
  - Walker Warburg syndrome

### OTHER MDs
- **Table 1:**  
  - Facioscapulohumeral MD  
  - Emery Dreifuss syndrome  
- **Table 2:**  
  - Oculopharyngeal MD  
  - Myotonic Dystrophies
Muscular Dystrophies: Diagnosis

Mainstays of diagnosis:

• Clinical features

• Genetic testing
  – Myopathies with commercially available genetic testing include:
    • DMD/BMD
    • LGMD2B
    • Oculopharyngeal MD
    • DM1 and DM2
  – Additional genetic testing may be available through research laboratories

• Muscle biopsy with immunohistochemical staining
Muscular Dystrophies: Imaging

• Plain film
  – secondary features demonstrated
**Duchenne MD:** Severely hypoventilatory lungs. Respiratory failure is a common cause of death in Duchenne MD.
Duchenne MD: Gracile bones. Near translucent soft tissues (see arms) due to fatty replacement of muscles.
**Congenital MD:** Scoliosis. Contractures. Hyperlordotic lumbar spine due to loss of muscle tone. Gracile bones.
Muscular Dystrophies: Imaging

- **U/S**
  - proposed as a noninvasive screening technique in children with neuromuscular disease
  - evaluation of muscle echogenicity (fatty infiltration), muscle thickness
  - limited anatomic detail
Muscular Dystrophies: Imaging

• **CT**
  - evaluation of relative fatty infiltration of muscle and muscle thickness
  - good anatomic detail
  - use of ionizing radiation may be a disadvantage, particularly in children
Duchenne MD: (Advanced stage, same patient as slide showing severely hypoventilatory lungs). Diffuse fatty infiltration of muscles of the abdomen and pelvis.
Duchenne MD: Fatty infiltration of gluteal muscles.
Muscular Dystrophies: Imaging

- **MRI**
  - modality of choice due to its superior soft tissue contrast
  - typically T1W, axial images only
  - to improve efficiency, a limited number of selected slices through pelvis, thigh, calf, arm may be obtained
  - evaluation of atrophy, hypertrophy, pseudohypertrophy
Muscular Dystrophies: Imaging

• MRI
  – T1W for evaluation of relative fatty infiltration
  – T2W for evaluation of edema-like changes (has not been widely used)
  – contrast enhanced studies are not required
  – limited use of other features, such as MR spectroscopy and diffusion weighted imaging
Muscular Dystrophies: MRI

Becker MD: T1W axial MR images of (a) pelvic girdle, (b) upper thigh, and (c) upper arms. Note pattern of fatty infiltration of proximal muscles with relative sparing of gracilis and sartorius of the upper thigh and extensor compartment of the upper arms.
Fascioscapulohumeral MD: Axial T1W MR images of pelvic girdle, upper thigh, and lower thigh from 3 different patients (a-c). Note differences in severity of fatty infiltration and asymmetry of involvement between right and left limbs.
Fascioscapulohumeral MD: Patient A

Severe involvement of
- hamstrings (left > right)
- vastus medialis (right > left)
- rectus femoris

Once again, relative sparing of
- sartorius

Presentation material is for education purposes only. All rights reserved. ©2006 URMC Radiology
Fascioscapulohumeral MD: Patient B

- Fatty infiltration of rectus femoris
- Lesser degree of involvement of vastus medialis compared to Patient A
- Marked fatty infiltration of left hamstrings
Fascioscapulohumeral MD: Patient C

Fatty infiltration of **hamstrings** and **vastus medialis**

Severe fatty infiltration of most muscles of the limb girdle and upper thigh with relative sparing of the **sartorius** and **gracilis** muscles.
Fascioscapulohumeral MD:
Patient A

Mild disease with mild fatty infiltration of biceps brachii
Fascioscapulohumeral MD:
Patient B

Mild upper extremity disease with mild fatty infiltration of deltoids
Fascioscapulohumeral MD:
Patient C

Fatty infiltration of lateral head of triceps

Fatty infiltration of deltoid
Muscular Dystrophies: Imaging Trends Past and Present

• Grading system
  – MR grading system for Duchenne MD proposed by Liu et al, Radiology 1993

• Muscle compositional analysis
  – Study of age-related changes in composition in diseased muscle in boys with Duchenne MD by Marden et al, Skeletal Radiology 2005

• Differentiation among MD subtypes
  – Numerous papers by Mercuri et al describing comparative muscle involvement in EDMD, CMD (rigid spine phenotype and Ullrich phenotype), LGMD2A, published 2002-2005
  – Differentiating LGMD2I from other LGMDs by Fischer et al, J Neurol 2005
Muscular Dystrophies: Imaging Future

• Potential for MRI in diagnosis of muscular dystrophies:
  – Biopsy planning, limitation of false negative biopsies
  – Distinguishing conditions with similar clinical phenotypes
  – Using pattern of muscle involvement to inform genetic/biochemical work up
  – To assess if muscle grossly normal or abnormal in cases of confusing clinical presentation in patient with suspected neuromuscular disease

• Potential for MRI in management of muscular dystrophies:
  – Marker for disease progression
  – Marker for response to therapy

• Potential for MRI in research/clinical trials:
  – Marker for disease response to therapy
  – Tool for better understanding pathophysiology of disease – expanded use of T2W, MR spectroscopy and diffusion weighted imaging
Muscular Dystrophies: Conclusions

• MR imaging reveals a fascinating variation in pattern of muscle involvement and relative sparing among and within the subtypes of muscular dystrophies.

• While overlap and variations in these patterns preclude widespread use of MR in diagnosis of muscular dystrophies, investigators are finding gaps in traditional diagnostic methods into which MRI may fall and become useful.

• Furthermore, MRI may become useful as a marker for disease progression, response to therapy, and as a tool for better understanding the pathophysiology of disease.
The most intriguing question remains:

– Why is one muscle affected and its neighbor spared?

– Perhaps information gained through MR imaging of the muscular dystrophies will help guide investigators to the answer(s) to that question.
References

# Dystrophinopathies

<table>
<thead>
<tr>
<th>Name</th>
<th>Genetics</th>
<th>Genetic Location</th>
<th>Protein</th>
<th>Clinical Features</th>
<th>Muscles Affected</th>
<th>Muscles Relatively Spared</th>
<th>Other Imaging Features</th>
<th>Genetic overlap with</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duchenne MD</strong></td>
<td>XLR</td>
<td>Xp21</td>
<td>Dystrophin</td>
<td>Complete or near complete absence of dystrophin protein</td>
<td>Early: Gluteus maximus</td>
<td>Sartorius</td>
<td>Edema-like signal on T2W tends to precede fibrofatty infiltration seen on T1W</td>
<td>Isolated cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 1:3500 live male onset @ 2-3 yrs</td>
<td>Adductor magnus</td>
<td>Gracilis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• onset then upper extremities</td>
<td>Gastrocnemii</td>
<td>Semitendinosus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• wheelchair by 12 yrs</td>
<td></td>
<td>Semimembranosus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• death late teens/20s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• respiratory failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• arrhythmia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• primary cardiomyopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• progressive scoliosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• mental retardation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Earlier:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Later:</td>
<td>Quadriceps</td>
<td>Sartorius</td>
<td>Edema-like signal on T2W tends to precede fibrofatty infiltration seen on T1W</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Rectus femoris</td>
<td></td>
<td>Gracilis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Biceps femoris</td>
<td></td>
<td>Semitendinosus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Sartorius</td>
<td></td>
<td>Semimembranosus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Gracilis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Semitendinosus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Semimembranosus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Edema-like signal on T2W tends to precede fibrofatty infiltration seen on T1W</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Isolated cardiomyopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Becker MD</strong></td>
<td>Same</td>
<td>Same</td>
<td>Same</td>
<td>Decreased quantity of abnormal or normal MW dystrophin</td>
<td>Similar to DMD</td>
<td>Similar to DMD</td>
<td>Similar to DMD</td>
<td>Similar to DMD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 1:30K live male later onset than DMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• ambulatory 15+ yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• survive &gt; 30 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• less severe mental retardation, contractures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• preserved neck flexor strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• +/- more severe cardiac disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key: MD (muscular dystrophy); MW (molecular weight)
### Limb-girdle Muscular Dystrophies (LGMDs) – Autosomal Dominant Subtypes

<table>
<thead>
<tr>
<th>Name</th>
<th>Genetics</th>
<th>Genetic Location</th>
<th>Protein</th>
<th>Clinical Features</th>
<th>Muscles Affected</th>
<th>Muscles Relatively Spared</th>
<th>Other Imaging Features</th>
<th>Genetic overlap with</th>
</tr>
</thead>
</table>
| LGMDs in general | | | | • Variable age onset  
• AR – typically childhood onset  
• AD – typically adult onset  
• Slowly progressive  
• Weakness predominantly affecting hip girdle  
• +/- neck flexor and extensor involvement  
• +/- mild facial weakness  
• Extraocular muscles spared  
• Preferential weakness biceps  
• Distal muscles preserved  
• Low back pain  
• Intellect normal  
• Cardiac – rarely  
• Can be confused with DMD/BMD – but intellect normal in LGMDs | | | | |
| LGMD1A | AD | 5q31 | Myotilin | | | | | |
| LGMD1B | AD | 1q11-21 | Lamin A/C | • Cardiac involvement | | | | AD-EDMD  
Dunnigan-type familial partial lipodystrophy  
Dilated cardiomyopathy and cardiac conduction system defect |
| LGMD1C | AD | 3p25 | Caveolin-3 | • +/- Cardiac involvement | | | | Rippling muscle syndrome  
Hyper-CK-emia |

Key: AD (autosomal dominant), AR (autosomal recessive), CMD (congenital muscular dystrophy), MD (muscular dystrophy)
## Limb-girdle Muscular Dystrophies (LGMDs) – Autosomal Recessive Subtypes

<table>
<thead>
<tr>
<th>Name</th>
<th>Genetics</th>
<th>Genetic Location</th>
<th>Protein</th>
<th>Clinical Features</th>
<th>Muscles Affected</th>
<th>Muscles Relatively Spared</th>
<th>Other Imaging Features</th>
<th>Genetic overlap with</th>
</tr>
</thead>
</table>
| LGMDs in general | | | | • Variable age onset  
• AR – typically childhood onset  
• AD – typically adult onset  
• Slowly progressive  
• Weakness predominantly affecting hip girdle  
• +/- neck flexor and extensor involvement  
• +/- mild facial weakness  
• Extracranial muscles spared  
• Preferential weakness biceps  
• Distal muscles preserved  
• Low back pain  
• Intelect normal  
• Cardiac – rarely  
• Can be confused with DMD/BMD – but intellect normal in LGMDs | | | |
| LGMD2A | AR | 15q15-21 | Calpain 3 | Thigh:  
• Early involvement of posterior thigh muscles  
• In young ambulatory patients:  
  • Adductors  
  • Semimembranosus  
• In patients with restricted ambulation:  
  More diffuse involvement of posterior lateral muscles of the thigh and vastus intermedius | Thigh:  
• Vastus intermedius  
• Vastus lateralis  
• Sartorius  
• Gracilis | Pattern at thigh level different and more extensive than AD EDMD  
General pattern of muscle atrophy | |
| LGMD2B | AR | 2p13 | Dystrophin | Calf:  
• Soleus  
• Medial head gastrocnemius | Calf:  
• Lateral head of gastrocnemius | Pattern at calf level similar to AD EDMD | |
| LGMD2C | AR | 13q12 | Gamma-Sarcoglycan | • Cardiac involvement | | | Myotonic myopathy  
Distal myopathy | |
| LGMD2D | AR | 17q12-21 | Alpha-Sarcoglycan | • +/- Cardiac involvement | | | | |
| LGMD2E | AR | 4q12 | Beta-Sarcoglycan | • Cardiac involvement | | | | |
| LGMD2F | AR | 5q33-34 | Delta-Sarcoglycan | • Cardiac involvement | | | | |
| LGMD2G | AR | 17q11-12 | Telethonin | • Cardiac involvement | | | | |
| LGMD2H | AR | 9q31-34 | TRIM32 | | | | | |
| LGMD2I | AR | 19q13.4 | Fukuyama-related protein | Thigh:  
• Predominant involvement of adductor magnus and posterior thigh muscles  
• More involvement of anterior compartment than LGMD2A  
• Hypertrophy of sartorius and gracilis | | Muscle hypertrophy common (compared to atrophy in LGMD2A)  
CMD 1C | |
| LGMD2J | AR | 2q31 | Titin | Calf:  
• Variable with predominantly posterior compartment involvement  
• No significant differential involvement between medial and lateral head of gastrocnemius (in comparison to LGMD2A) | | | Tibial MD | |

Key: AD (autosomal dominant), AR (autosomal recessive), CMD (congenital muscular dystrophy), MD (muscular dystrophy)
<table>
<thead>
<tr>
<th>Name</th>
<th>Genetic Location</th>
<th>Protein</th>
<th>Clinical Features</th>
<th>Muscles Affected</th>
<th>Muscles Relatively Spared</th>
<th>Other Imaging Features</th>
<th>Allelic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMDs in general</td>
<td></td>
<td></td>
<td>• Hypotonic and weak at birth or early infancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Elevated CK at birth, which falls to normal range by 6-10 wks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Muscle bx c/w MD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Non- or slowly progressive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merosin-absent CMD</td>
<td>6q2</td>
<td>Merosin Alpha chain of laminin</td>
<td>• Normal IQ</td>
<td></td>
<td></td>
<td></td>
<td>Brain MRI: White matter abnormal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• +/- cardiac involvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMD</td>
<td>19q13.3</td>
<td>Fukutin-related protein</td>
<td>• Normal IQ</td>
<td></td>
<td></td>
<td></td>
<td>Brain MRI: Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Spine rigidity</td>
<td></td>
<td></td>
<td></td>
<td>LGMD2I</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Early restrictive lung disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rigid Spine Disease (RSMD1)</td>
<td>1p35-36</td>
<td>Selenoprotein N</td>
<td>• Normal IQ</td>
<td></td>
<td></td>
<td></td>
<td>Brain MRI: Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Spine rigidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Early restrictive lung disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Thigh: Variable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Sartorius, always and often severely affected (spared in Ullrich CMD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Postero-lateral muscles less affected compared to Ullrich CMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Thigh:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Rectus femoris</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Gracilis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ullrich myopathy</td>
<td>21q22.3 (COL6A1, A2)</td>
<td>Collagen VI</td>
<td>• Normal IQ</td>
<td></td>
<td></td>
<td></td>
<td>Brain MRI: Normal</td>
</tr>
<tr>
<td></td>
<td>2q37 (COL6A3)</td>
<td></td>
<td>• Very early contractures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Arthrogryposis (contracture of of ≥ 2 joints at birth)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Distal hyperlaxity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Flat feet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Thigh:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Diffuse involvement of all posterior and lateral muscles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Thigh:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Sartorius</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Gracilis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Adductor longus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Rectus femoris</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Signal increased at periphery of the muscle with relative preservation of the muscle belly on T1WI (not typically seen in Ulrich-like phenotype without collagen VI mutation)</td>
<td></td>
<td></td>
<td></td>
<td>Bethem myopathy – similar imaging features as Ulrich, but milder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Brain MRI:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Presentation material is for education purposes only. All rights reserved. ©2006 URMC Radiology
## Congenital Muscular Dystrophies (CMDs) – Subtypes with Major Brain Malformation

<table>
<thead>
<tr>
<th>Name</th>
<th>Genetic Location</th>
<th>Protein</th>
<th>Clinical Features</th>
<th>Muscles Affected</th>
<th>Muscles Relatively Spared</th>
<th>Other Imaging Features</th>
<th>Allelic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMDs in general</td>
<td></td>
<td></td>
<td>- Hypotonic and weak at birth or early infancy&lt;br&gt;- Elevated CK at birth, which falls to normal range by 6-10 wks&lt;br&gt;- Muscle bx c/w MD&lt;br&gt;- Non- or slowly progressive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fukuyama CMD</td>
<td>9q31-33</td>
<td>Fukutin</td>
<td>- Mild to moderate MR&lt;br&gt;- +/- eye involvement&lt;br&gt;- Almost exclusively Japanese population</td>
<td></td>
<td></td>
<td>Brain MRI: Cobblestone cortex, cerebellar and brainstem hypoplasia</td>
<td></td>
</tr>
<tr>
<td>Muscle-eye-brain disease</td>
<td>1p32</td>
<td>POMGnT1</td>
<td>- Severe MR&lt;br&gt;- Myopia&lt;br&gt;- Cataracts&lt;br&gt;- Ganglion cell and optic nerve atrophy&lt;br&gt;- Common in Finland</td>
<td></td>
<td></td>
<td>Brain MRI: Cobblestone cortex, pachygyria/agyria, cerebellar and brainstem hypoplasia, mild hydrocephalus</td>
<td></td>
</tr>
<tr>
<td>Walker-Warburg syndrome</td>
<td>9q34</td>
<td>POMT1, others</td>
<td>- Severe MR&lt;br&gt;- Retinal abnormality&lt;br&gt;- Myopia&lt;br&gt;- Cataracts&lt;br&gt;- Ganglion cell and optic nerve atrophy</td>
<td></td>
<td></td>
<td>Brain MRI: Cobblestone lissencephaly, severe hydrocephalus, abnormal white matter, polymicrogyria, cerebellar and brainstem hypoplasia, misline fusion, abnormal corpus collosum</td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td>Genetics</td>
<td>Genetic Location</td>
<td>Protein</td>
<td>Clinical Features</td>
<td>Muscles Affected</td>
<td>Muscles Relatively Spared</td>
<td>Other Imaging Features</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>----------</td>
<td>------------------</td>
<td>--------------------------</td>
<td>-------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>-------------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Fascioscapulohumeral MD</td>
<td>AD</td>
<td>4q35</td>
<td>Transcription repressor proteins</td>
<td>General: • Early weakness of the face, shoulder girdle, proximal arms • Increased incidence of hearing loss • Rarely, MR and seizures</td>
<td>Infant form: • Facial muscles • Later muscles of shoulder and hip girdle</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Classical form: • Onset 2nd-3rd decade • Slow progression • Normal lifespan</td>
<td>Thigh: • Facial muscles • Muscles of shoulders and upper arms • Hypertrophic extensor digitorum brevis</td>
<td>Deltoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Calf: • soleus</td>
<td></td>
</tr>
<tr>
<td>EDMD</td>
<td>XL (more common than AD)</td>
<td>Xq28</td>
<td>Emerin</td>
<td>• Indistinguishable from AD form • Childhood-onset weakness starting in the shoulder girdle and lower legs • Early contractures (especially elbows, Achilles tendons, neck) • Restrictive cardiomyopathy AV block • Isolated atrial paralysis is strongly suggestive of EDMD • Sudden death in 50% • +/- mild facial weakness • Female carriers may develop heart block, but do not typically have skeletal muscle weakness</td>
<td>Thigh: • Variable severity • XL with minimal involvement</td>
<td>Calf: • soleus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thigh: • AD form with moderate to severe involvement of • Vastus lateralis • Vastus intermedius • + adductor magnus</td>
<td>Abnormal distribution of body fat – accumulation of fat in the neck and abdomen and little fat in subcutaneous tissue of the limbs</td>
</tr>
<tr>
<td></td>
<td>AD</td>
<td>1q11-q23</td>
<td>Lamin A/C</td>
<td>• Indistinguishable from XL form in affected male</td>
<td>Thigh: • AD form with moderate to severe involvement of • Vastus lateralis • Vastus intermedius • + adductor magnus</td>
<td></td>
<td>Abnormal distribution of body fat – accumulation of fat in the neck and abdomen and little fat in subcutaneous tissue of the limbs</td>
</tr>
</tbody>
</table>

Key: XL (X-linked), AD (autosomal dominant), MR (mental retardation)
# Other Muscular Dystrophies

<table>
<thead>
<tr>
<th>Name</th>
<th>Genetics</th>
<th>Genetic Location</th>
<th>Protein</th>
<th>Clinical Features</th>
<th>Muscles Affected</th>
<th>Muscles Relatively Spared</th>
<th>Other Imaging Features</th>
<th>Allelic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oculopharyngeal MD</td>
<td>AD with complete penetrance</td>
<td></td>
<td>Poly (A) binding protein (gene transcription)</td>
<td>• Progressive ptosis, dysphagia&lt;br&gt;• +/- proximal and distal muscle weakness&lt;br&gt;• Onset mid-adulthood&lt;br&gt;• Onset asymmetric&lt;br&gt;• Usually slowly progressive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myotonic Dystrophies in general</td>
<td></td>
<td></td>
<td></td>
<td>• Multisystem disorders&lt;br&gt;• Clinically indistinguishable, except that most severely affected patients with DM1 have cognitive impairment&lt;br&gt;• Myotonia&lt;br&gt;• Cardiac conduction defects&lt;br&gt;• Premature cataracts&lt;br&gt;• Diabetes/insulin resistance&lt;br&gt;• Slowly progressive muscle weakness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM1 (type 1)</td>
<td>AD</td>
<td>19q13.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM2 (type 2)</td>
<td>AD</td>
<td>3q13.3-q24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key: XL (X-linked), AD (autosomal dominant), MR (mental retardation)