Limb-Girdle Muscular Dystrophy

Genetics

-Genes: CAPN3 (Calpain 3), FKRP (Fukutin related protein), LMNA (Lamin-A/C), SGCA/B/D/G (alpha/beta/delta/gamma-sarcoglycan), DYSF (Dysferlin)

-Mainly AR, some AD

Clinical findings/Dysmorphic features

-AR Sarcoglycan-LGMD: proximal limb weakness, difficulty running/walking, calf hypertrophy, onset age 3-15 (68% of childhood onset, 10% adult onset)

-AR Calpain-LGMD: proximal limb weakness, difficulty running and walking, calf atrophy, onset 2-40 yrs (10-30% AR LGMD)

-AR Dysferlin-LGMD: problems running/walking, foot drop, distal and/or pelvic weakness, transient calf hypertrophy, onset 17-23 yrs

Etiology

-1 in 14,500 to 1 in 123,000 individuals

Pathogenesis

-Sarcoglycanopathies: disruption of dystrophin-dystroglycan complex

-Calpainopathy: impairment of calpain proteolytic activity results in sarcomere remodeling by promoting ubiquitin-mediated degradation of sarcomeric proteins

-Dysferlinopathy: disruption of muscle membrane repair machinery is responsible for dysferlin-deficient muscle degeneration in dysferlin-null mice

Genetic testing/diagnosis

-Inc. serum CK, dystrophic changes on muscle biopsy, sarcoglycan protein staining

-Gene sequencing (80-99%)

Others

-Supportive care to promote mobility and ambulation

-Monitor for respiratory and orthopedic complications and for cardiomyopathy