Nemaline myopathy

Genetics

-ACTA1, NEB, TNNT1, TPM2, TPM3; rare: CFL2, KBTBD13, KHLH41

-AR or AD

Clinical findings/Dysmorphic features

-Weakness, hypotonia, depressed or absent deep tendon reflexes

-Weakness usually most severe in face, neck flexors, proximal limb muscles

-Age of onset: severe congenital (neonatal) (16%), Amish NM, intermediate congenital (20%), typical congenital (46%), childhood-onset (13%), adult-onset (late-onset) (4%)

Etiology

-Incidence of 1:50,000 live births

Pathogenesis

-Ten different genes: 6 encode protein components of the muscle thin filament, 3 involved in the protein turnover in the muscle sarcomere via ubiquitin proteasome pathway

Genetic testing/diagnosis

-Muscle biopsy --> diagnostic hallmark is the presence of rod-like inclusions (nemaline bodies) in the sarcoplasm of skeletal muscle fibers with trichrome stain

-NEB sequencing: 50%; ACTA sequencing: 15-25% of NM (ACTA Del/dup analysis: Exon 55)

Others

-Walking prior to 18 months is predictive of survival