Hereditary myopathies

Francesco Muntoni

University College Institute of Child Health
& Great Ormond Street Hospital
London WC1N 1EH
United Kingdom

Francesco Muntoni: disclosures

Duchenne Muscular Dystrophy

Clinical trials

- CI of 4 antisense oligonucleotides clinical trials with Sarepta.
- PI of Sarepta Phase III AAVrh74 microdystrophin
- CI of MDUK/Genethon AAV8 microdystrophin

Natural history studies

- PI of the MDUK funded UK North Star DMD network; and AFM funded iMDEX natural history study
- PI of D-Brain, dystrophin restoration in *mdx* brain, funded by Sarepta

Spinal Muscular Atrophy

- PI of Biogen antisense oligonucleotide nusinersen Phase III study
- PI of Novartis AAV9 phase II and III trials in SMA I
- PI of Roche risdiplam Jewelfish study

Natural history studies

- PI of the Biogen and MDUK funded UK North Star DMD network; and AFM funded iMDEX natural history study

Myotubular Myopathy

- PI of Astellas AAV8 MTM1 gene natural history and gene therapy trial

- **Other financial disclosures**
- Member of Dyne Therapeutics SAB
- Ad-hoc SAB participation for Novartis, Biogen, Dynacure, Roche, Sarepta therapeutics, Lilly, Edgewise

Structure of the lecture

- Congenital myopathies are rare and genetically heterogenous with overlapping clinical features
- Some clinical findings are very helpful to suspect a congenital myopathy, including the presence of facial, axial and respiratory muscle weakness
- In the past muscle biopsy was always indicated to reach a final diagnosis
- While muscle biopsies still play an important role, muscle imaging techniques (muscle MRI and ultrasound) and next generation sequencing techniques now play a major role in the diagnostic pathway

Learning objectives

- Most relevant clinical signs
- Differential diagnosis
- Conditions associated with involvement of organs other tan skeletal muscle
- Diagnostic algorithm
- Management and standards of care
- Therapeutic options

References

- Ogasawara M, Nishino I. A review of major causative genes in congenital myopathies. J Hum Genet. 2023 Mar;68(3):215-225
- Ginestre C, Laporte J. Therapeutic approaches in different congenital myopathies. Curr Opin Pharmacol, 2023
- Radke J, Stenzel W, Goebel HH. Recently Identified Congenital Myopathies. Semin Pediatr Neurol. 2019 Apr;29:83-90.
- Jungbluth H, Muntoni F. Therapeutic Aspects in Congenital Myopathies. Semin Pediatr Neurol. 2019 Apr;29:71-82.
- Carlier RY, Quijano-Roy S.. Myoimaging in Congenital Myopathies. Semin Pediatr Neurol. 2019 Apr;29:30-43.
- Pelin K, Wallgren-Pettersson C.. Update on the Genetics of Congenital Myopathies. Semin Pediatr Neurol. 2019 Apr;29:12-22
- Gonorazky HD, Bönnemann CG, Dowling JJ. The genetics of congenital myopathies. Handb Clin Neurol. 2018;148:549-564.
- Jungbluth H, Treves S, Zorzato F, Sarkozy A, Ochala J, Sewry C, Phadke R, Gautel M, Muntoni F. Congenital myopathies: disorders of excitation-contraction coupling and muscle contraction. Nat Rev Neurol. 2018 Mar;14(3):151-167.
- Wang CH, Dowling JJ, North K et al. Consensus statement on standard of care for congenital myopathies. J Child Neurol. 2012 Mar;27(3):363-82.