dystrophy phenotype, with strong family history, and a novel truncating variant identified in *LMNA*. Functional protein studies would contribute to confirm the pathogenicity of this variant.

http://dx.doi.org/10.1016/j.nmd.2019.06.153

EP.24

Recessive mutations in CAV3 - a new differential diagnosis of early-onset neuromuscular disorders

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Dominant *CAV3* mutations account for a very wide phenotypical spectrum, including limb girdle muscular dystrophy (LGMD), rippling muscle disease (RMD), distal myopathy or asymptomatic hyperCKemia. Very few recessive cases have been reported to date with mild clinical features. Here we report a 19-month-old male presenting antenatally with reduced foetal movements from 36/40 and possible polyhydramnios. Family history had been unremarkable except for a history of speech and language delay in 2 siblings. He was delivered by elective Caesarean section at 38 weeks gestation. He was hypotonic at birth and was given facial oxygen and started on intravenous antibiotics until sepsis had been excluded. He quickly established spontaneous breathing and breast feeding. He was re-admitted to hospital when he was 2 months old with bronchiolitis when he was noted to have generalized hypotonia pronounced axially, with significant head lag and scarce antigravity movements in his legs. There was bilateral talipes but there were no other contractures. DTR were difficult to elicit. He was not dysmorphic and did not have any facial weakness or ophthalmoplegia. CK was elevated up to 7398 IU/L. Brain MRI and cardiac evaluation were normal. His muscle biopsy showed abnormal variation in fibre size, increase in internal nuclei, necrosis and regeneration with modest endomysial chronic inflammation. Molecular analysis revealed a homozygous *CAV3* mutation (c.10_17delGAAGAGCA; p.Glu4Hisfs*17) in trans. Further muscle biopsy IHC studies revealed complete caveolin-3 deficiency. Subsequently the patient achieved independent sitting at the age of 8 months, crawled from 1 year and walked independently at 18 months. No rippling of muscle was noted on further examination. This report expands the genetic and clinico-pathological spectrum of *CAV3*-associated disease, and suggests that recessive *CAV3* mutations ought to be considered in the differential diagnosis of early-onset neuromuscular disorders.

http://dx.doi.org/10.1016/j.nmd.2019.06.154

EP.25

A limb girdle muscular dystrophy phenotype with mutations in *ISPD* and *TTN*

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We report a 9-year-old girl presenting with high serum creatine kinase associated with mild motor weakness and mutations in two genes responsible for heterogeneous neuromuscular diseases. She was referred to our hospital at the age of 7 years due to high serum creatine kinase (CK) and mild difficulty in running and climbing stairs. Neurological examination revealed mild sural hypertrophy and mild weakness at the pelvic girdle with positive Gowers' sign. Her developmental milestones were normal and mild walking and running difficulties were recognized at 2 years of age. Her parents were first cousins of Turkish origin and there was no history of neuromuscular disease in the family. Muscle biopsy revealed a dystrophic process with reduced alpha-dystroglycan staining. Cranial MRI was normal. Next generation sequencing revealed homozygous possibly pathogenic mutations in *ISPD* (exon 5, c.1114_1116del) and a pathogenic heterozygous mutation in *TTN* (intron 11, c.1800+1G>A) genes. *ISPD* mutations are known to cause alpha-dystroglycanopathy, while the TTN mutation is known to cause LGMDR10, dilated cardiomyopathy, Salih myopathy, early respiratory failure and tibial muscular dystrophy. Her motor performance has been non-progressive and she is still able to run at age 9. Her CK ranges from 630 to 3279 IU/L (N: <150 IU/L). Neither cardiac nor respiratory involvement is present so far. This is another case of co-existence of mutations in two separate genes related to neuromuscular diseases and emphasizes the importance of comprehensive genetic investigations in terms of genetic counseling and follow-up related to specific organ involvement.

http://dx.doi.org/10.1016/j.nmd.2019.06.155

EP.26

Phenotype may predict the clinical severity of facioscapulohumeral muscular dystrophy

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The precise classification of FSHD is crucial for deepening the understanding of disease as well as the efficient diagnosis and follow-up. We aimed to explore the difference of clinical severity in FSHD patients classified by the Comprehensive Clinical Evaluation Form (CCEF). Totally 54 Chinese FSHD1 patients, diagnosed by molecular combing or southern blot, were classified by CCEF, proposed by the Italian Clinical Network for FSHD. All patients were evaluated by structured questionnaire, as well as the manual muscle test (MMT), FSHD clinical score (CS), Ricci score (CSS), 6-minute walking test (6MWT) and motor function measure (MFM). Kruskal-Wallis test was used to analyze the difference of clinical characteristics between subgroups. There were 26 males and 28 females, whose average age was 33.15 years old and age of onset was 10.43, with the D4Z4 repeat number of 4.54 on average. According to the CCEF, there were 16 patients belonging to category A1, 22 of A2, 4 of A3, 1 of category B1 and B2 respectively, and 10 of category D1. The patients of category A1 was younger, with a lower mean age at onset, shorter disease duration, smaller D4Z4 repeat number and more severe clinical disability in CS, MMT and MFM, showing a statistical significance between category A1, A2 and A3. The tendency of CSS and 6MWT was coherent with other clinical outcome measures but without statistical significance. In addition, 6 patients of category D1 displayed pes cavus, while the other 4 showed myotonic phenomenon. Patients with different FSHD phenotypes may have different clinical severity. The patients with severer facial involvement may have faster disease progression and worse motor functions. And the level of facial impairment could be a predictor to patients' clinical severity. In Chinese patients, pes cavus was the commonest atypical sign, especially in heavily involved patients.

http://dx.doi.org/10.1016/j.nmd.2019.06.156

EP.27

Sporadic late-onset nemaline myopathy: an unusual case misdiagnosed as immune-mediated necrotizing myopathy

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Sporadic late-onset nemaline myopathy (SLONM) is a rare acquired, late-onset myopathy with progressive limb and axial muscle weakness and atrophy, histologically characterized by nemaline rods in muscle fibres. It has