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Abstracts

Articles appearing in the August 2019 issue

Novel mutation in *HTRA1* in a family with diffuse white matter lesions and inflammatory features

Objective To investigate the possible involvement of germline mutations in a neurologic condition involving diffuse white matter lesions.

Methods The patients were 3 siblings born to healthy parents. We performed homozygosity mapping, whole-exome sequencing, site-directed mutagenesis, and immunoblotting.

Results All 3 patients showed clinical manifestations of ataxia, behavioral and mood changes, premature hair loss, memory loss, and lower back pain. In addition, they presented with inflammatory-like features and recurrent rhinitis. MRI showed abnormal diffuse demyelination lesions in the brain and myelitis in the spinal cord. We identified an insertion in high-temperature requirement A (*HTRA1*), which showed complete segregation in the pedigree. Functional analysis showed the mutation to affect stability and secretion of truncated protein.

Conclusions The patients' clinical manifestations are consistent with cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL; OMIM #600142), which is known to be caused by *HTRA1* mutations. Because some aspects of the clinical presentation deviate from those reported for CARASIL, our study expands the spectrum of clinical consequences of loss-of-function mutations in *HTRA1*.

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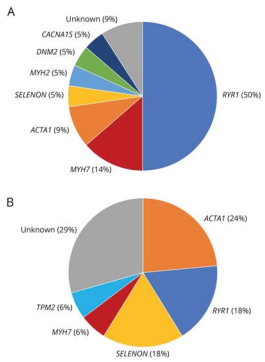
Congenital myopathies in the adult neuromuscular clinic: Diagnostic challenges and pitfalls



Objective To investigate the spectrum of undiagnosed congenital myopathies (CMs) in adults presenting to our neuromuscular clinic and to identify the pitfalls responsible for diagnostic delays.

Methods We conducted a retrospective review of patients diagnosed with CM in adulthood in our neuromuscular clinic between 2008 and 2018. Patients with an established diagnosis of CM before age 18 years were excluded.

Results We identified 26 patients with adult-onset CM and 18 patients with pediatric-onset CM who were only diagnosed in adulthood. Among patients with adult onset, the median age at onset was 47 years, and the causative genes were *RYR1* (11 families), *MYH7* (3 families) and *ACTA1* (2 families), and *SELENON*, *MYH2*, *DNM2*, and *CACNA1S* (1 family each). Of 33 patients who underwent muscle biopsy, only 18 demonstrated histologic abnormalities characteristic of CM. Before their diagnosis of CM, 23 patients had received other diagnoses, most commonly non-neurologic disorders. The main causes of diagnostic delays were mildness of the symptoms delaying neurologic evaluation and attribution of the symptoms to coexisting comorbidities, particularly among pediatric-onset patients.

Conclusions CMs in adulthood represent a diagnostic challenge, as they may lack the clinical and myopathologic features classically associated with CM. Our findings underscore the need for a revision of the terminology and current classification of these disorders.

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Q Niu, X Wang, M Shi, Q Jin. 2015;1;e20. doi.org/10.1212/NXG.0000000000000017