Natural history of McArdle disease: a single centre study of a cohort of 220 patients

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Abstract

McArdle disease is caused by recessive mutations in *PYGM* gene. The condition is considered to cause a 'pure' muscle phenotype with symptoms including exercise intolerance, inability to perform isometric activities, contracture, acute rhabdomyolysis. However, studies aiming to describe extra-muscular manifestations are rare. In this study we extensively describe phenotypic and genotypic features of a large cohort of people with McArdle disease, all attending the Highly Specialized McArdle Disease and Related Disorders service at the National Hospital for Neurology and Neurosurgery, London.

We retrospectively assessed case records of 220 patients with a confirmed diagnosis of McArdle disease between 2011-2019 and report data relating to genotype and phenotype, including frequency of rhabdomyolysis, fixed muscle weakness, gout and unexpected comorbidities inclusive of retinal and thyroid disease.

Data from 197 patients are presented (23 were excluded due to lack of sufficient data). Seven previously unpublished *PYGM* mutations are described. Exercise intolerance and episodic rhabdomyolysis were the most common symptoms. Fixed muscle weakness was present in 41.6% of subjects with a median age of 60 years. Unexpectedly, ptosis was observed in 28 patients (14.2%). Hyperuricemia was a common finding (44.7%), complicated by gout in 25% of cases. Thyroid dysfunction was described in 14.7% of subjects, hypothyroidism being the most prevalent finding. 20.8% of our entire cohort underwent ophthalmology evaluation for pattern retinal dystrophy: of these, pattern retinal dystrophy was detected in 36.6% of subjects and 46.7% of these cases were symptomatic.

In addition to fixed muscle weakness, ptosis was a relatively common finding. Surprisingly, dysfunctions of thyroid and retina were relatively frequent comorbidities. Further studies are needed to better clarify this association, although our finding may have important implication for patients management.