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【 LETTERS TO THE EDITOR 】

Phenotypic Diversity of Myoclonus Epilepsy Associated with Ragged-red Fibers with an 8344A>G mtDNA Mutation

Key words: MERRF, mitochondrial myopathy, exercise intolerance, paroxysmal kinesigenic dyskinesia, mtDNA

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The Authors Reply Thank you for reading our case report (1) and providing important comments on the content. We have the following reply to your comments, with additional information included.

We encountered a patient with an 8344A>G mtDNA "myoclonus epilepsy associated with ragged-red fibers (MERRF)" mutation whose chief complaint was falling after starting running. Although this complaint was considered similar to the symptoms seen in cases of paroxysmal kinesigenic dyskinesia, we found that it was caused by slight weakness of the right quadriceps femoris muscle and exercise intolerance.

Regarding concerns about whether or not it is appropriate to diagnose our case with MERRF, we feel that this diagnosis is indeed appropriate. MERRF is a mitochondrial syndrome mainly characterized by myoclonus epilepsy, cerebellar ataxia, and RRF on a muscle biopsy. Mitochondrial syndromes, including MERRF, sometimes show clinical features that overlap with multiple other mitochondrial syndromes, and phenotypic diversity has been noted. Muscle weakness and exercise intolerance are reportedly present more frequently than myoclonus and seizure in a large cohort of patients with the 8344A>G MERRF mutation (2). In our case, a neurological examination showed cerebellar ataxia, and brain magnetic resonance imaging showed cerebellar atrophy, in addition to myopathy with RRF, which are the main features of MERRF (1). We believe that these findings are consistent with a case of MERRF.

Regarding other potential causes of leading exercise-induced falls including cardiac involvement, his pro-BNP levels were within the normal range, but we did not perform other investigations suggested in the editor's letter, such as echocardiography. However, we did have the patient walk up stairs rapidly and jump on one leg in order to confirm his muscle weakness and exercise intolerance (Supplementary material). Although he performed these exercises without a problem on the left side, he found them difficult to continue on the right side. Two years later, he was hardly able to jump on his right leg at all. These results implied that his complaint of exercise-induced falls had the same cause as that of laterality of mitochondrial disorders: weakness and exercise intolerance of his right quadriceps femoris muscle.

As you mentioned, detailed neurological investigations and genetic analyses of his mother or other first-degree relatives were not performed. This is an important point that would likely improve our understanding of this mutation, so we will consider performing such analyses in a future study.

We appreciate your comments. For the above-mentioned reasons, we feel it is not contradictory to diagnose this patient with MERRF and attribute his exercise-induced falls to weakness and exercise intolerance in his right quadriceps femoris muscle.

The authors state that they have no Conflict of Interest (COI).

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