

Myoclonic Epilepsy with Ragged-Red Fibers due to the Variant m.8344A>G may manifest Subclinically in Multiple Organs

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In a recent article, Najjar *et al.* reported three patients with myoclonic epilepsy with ragged-red fibers (MERRF) syndrome due to the variant m.8344A>G in the tRNA(Lys) gene, who all presented with subclinical neuroretinal loss and optic atrophy.^[1] We have the following comments and concerns.

MERRF is a diagnosis based on the presence of four canonical phenotypic features, which are myoclonic, generalized epilepsy, ataxia, and myopathy with ragged-fibers on muscle biopsy.^[2] Patient 1 had generalized epilepsy but no other clinical features of MERRF.^[1] Patient 2 had myoclonus and ataxia but no other features of MERRF.^[1] Patient 3 had generalized epilepsy, ataxia, and myoclonus, but it is unclear if he underwent muscle biopsy. How many of three patients underwent muscle biopsy and in how many of those undergoing muscle biopsy were ragged-red fibers detected?

Since MERRF patients may variably present with a plethora of phenotypic features in addition to the canonical items concerning organs other than the brain and the muscle,^[2,3] we should be informed if the three patients were prospectively investigated for involvement of the ears, endocrine organs, heart, gastrointestinal tract, and skin.^[2,4]

MERRF syndrome is genetically heterogeneous. Among the 26 variants so far reported in association with MERRF, only 22 were recently classified as pathogenic after application of the modified Yarham score.^[2] The m.8344A>G variant accounts for 80% of the MERRF cases, and 10% of the cases are attributable to the variants m.8356T>C, m.8363G>A, and

m.8361G>A.^[3] Thus, MERRF is a MT-TK disease in about 90% of the cases.^[2]

The heteroplasmy rate in patient 1 was 65% (blood), and it was 55% (blood) and 63% (urine) in patient 3. For patient 2, no heteroplasmy rate was provided. Since levels of the m.8344A>G variant were low and since heteroplasmy rates in blood, muscle, and urinary sediment do not predict the phenotype and are similar in asymptomatic carriers and symptomatic individuals,^[3] it would be interesting to know if any of the first-degree relatives also carried the m.8344A>G variant and how many of these relatives manifested clinically or subclinically. Since MERRF is maternally transmitted in the majority of the cases, it is of particular interest if the 3 mothers carried the variant and at which heteroplasmy rates.

..Patient 3 had generalized epilepsy but obviously did not receive treatment with antiepileptic drugs (AEDs).^[1] Which was the reason for not prescribing AEDs to patient 3? In patient 1, ubidecarenone, and in the patient 3, ubidecarenone and L-carnitine were given for epilepsy. Both drugs have no antiepileptic effect. Which was the rationale for prescribing these compounds as an AED regimen?

In conclusion, this case series could be more meaningful if supplementary information about the clinical presentation and the genetic background of first-degree relatives would have been provided, if the reason for choosing the AED regimen would have been provided, and if the index cases would have been prospectively investigated for clinical or subclinical involvement of organs other than the brain, eyes, or muscles.

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