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Myoclonus of the Eyelids in MERRF Manifests as Eye Closure Sensitivity

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LETTER TO THE EDITOR

We read with interest the article by Nordli *et al*. on a 12-year-old boy with mild intellectual disability who had new-onset convulsions, staring spells and body twitching [Nordli, D. R. *et al*., 2024]. The initial EEG showed a normal background but evidence of eye closure sensitivity (transient (maximum 3s) generalized epileptiform discharges triggered by eye closure) [Nordli, D. R. *et al*., 2024]. Despite taking levetiracetam, the seizures persisted and the EEG showed a worsened gradient from anterior to posterior [Nordli, D. R. *et al*., 2024]. Investigation of the etiology of the syndrome revealed the *MT-TK* variant m.8344A>G with a heteroplasmy of 96% [Nordli, D. R. *et al*., 2024]. The study is excellent, but some points should be discussed.

The first point is that conspicuous family history was not used as an indicator for diagnosis [Nordli, D. R. *et al*., 2024]. A maternal great-aunt had epilepsy and the maternal grandmother had several strokes in her forties [Nordli, D. R. *et al*., 2024]. Assuming a common genetic cause for all these conditions, it could be concluded that they are inherited through the maternal line.

The second point is that a history of "multiple strokes" in the forties suggests that the maternal grandmother actually suffered from stroke-like episodes (SLEs) and not recurrent juvenile ischemic strokes. Were the grandmother's MRIs available and were they reviewed for the presence of stroke-like lesions (SLLs), the morphologic correlate of SLEs [Finsterer, J. *et al*., 2023].

The third point is that the index patient's mother has not been clinically or instrumentally tested. Since it is very likely that the causative mutation was inherited through the maternal line, and since heteroplasmy of this variant was high in the index patient, it is very likely that his mother was not only a carrier of this variant, but also manifested clinically with some or all of the features of MERRF.

The fourth point is that the cerebral imaging results were not reported. Since MERRF manifests in the central nervous system and the index patient had cognitive impairment and epilepsy [Velez-Bartolomei, F. *et al*., 2003], it is very likely that the brain morphology was abnormal. It is even conceivable that the index patient had developed SLE and that his seizures were in fact a manifestation of a stroke-like lesion (SLL), the morphologic equivalent of SLE.

The fifth point is that the patient had not been systematically and prospectively examined for multisystem disease. Since the involvement of organs other than the brain can dominate the phenotype and determine the outcome, it is imperative to know which other organs were also affected and to what extent.

There are also some other issues that should be addressed. We should know the serum levels of levetiracetam. It should be mentioned that MERRF is not only caused by tRNA variants but also by *POLG1* mutations [Van Goethem, G. *et al*., 2003]. It should also be added that phenotypic heterogeneity and severity of clinical presentation may depend not only on the degree of heteroplasmy, but also on mtDNA copy number, number of polymorphisms and nuclear background. It should also be emphasized that not only VPA is mitochondrion-toxic, but potentially also CBZ, PHT, barbituric acid and zonisamide [Finsterer, J. *et al*., 2017].

In conclusion, it can be said that this interesting study has limitations that relativize the results and their interpretation. Addressing these limitations could strengthen the conclusions and reinforce the message of the study. Eye closure sensitivity is a rare phenomenon in genetic epilepsy that probably represents myoclonus of the eyelids.

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