Int. j. adv. multidisc. res. stud. 2026; 6(4):292-293

Received: 18-06-2026
Accepted: 28-06-2026

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

MERRF is a Mitochondrial Multisystem Disease and Manifests itself not only Through Generalized Epilepsy and Myoclonus

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Letter to the Editor

We read with interest the article by Roy *et al*. about a 30-year-old man with myoclonic epilepsy with ragged-red fiber (MERRF) syndrome due to the m.8344A>G variant in the MT-TK gene, exhibiting a heteroplasmy rate of 84% in blood lymphocytes. The patient presented exclusively with alternating focal status epilepticus [1]. He benefited from combination therapy with levetiracetam (LEV), lacosamide (LAC), phenobarbital (PB), and peramapanel (PER) [1]. The study is promising but requires further discussion.

First, we would like to note that we do not share the diagnosis of MERRF syndrome [1]. The presence of the m.8344A>G variant does not necessarily mean that a patient has MERRF. The m.8344A>G variant is phenotypically heterogeneous and can also manifest as MERRF plus, Leigh/MERRF overlap syndrome, LHON/MERRF overlap syndrome, MERRF/MELAS overlap syndrome, and external ophthalmoplegia [2]. A diagnosis of MERRF requires the presence of four canonical features: generalized epilepsy, myoclonus, ataxia, and ragged-red fiber myopathy [2]. Other features may include dementia, lipomatosis, stroke-like episodes (SLE), lactic acidosis, migraine, intellectual disability, psychiatric disorders, optic atrophy, polyneuropathy, retinopathy pigmentosa, hearing loss, diabetes, hypothyroidism, short stature, cardiomyopathy, arrhythmias, vomiting, motility disorders, or dysphagia [2]. Since the index patient did not meet the diagnostic criteria for MERRF, he should be reclassified as an m.8344A>G carrier with a non-syndromal mitochondrial disorder.

The second point concerns the reasons for the patient's initial treatment with valproic acid (VPA), clonazepam (CZP), and phenytoin (PB) [1]. Were these antiepileptic drugs (AEDs) actually combined or administered sequentially? It is important to document the time course of this treatment and the occurrence of adverse events. Phenytoin and VPA are known to be potentially mitochondrially toxic [3].

Thirdly, it is unclear why the patient received a combination of four AEDs (levetiracetam (LEV), clobazam (CLB), lacosamide (LAC), and carbamazepine (CBZ)) after the intensive care unit stay at the age of 30. In what order were these AEDs administered, and what were the reasons for this combination? The dosage of the AEDs and the occurrence of adverse events should also be reported. Myoclonus has been shown to respond best to CZP and LEV [4].

The fourth point concerns the nature of the cortical lesion shown in Figure 1, which was not further specified [1]. Is it an epiphenomenon of seizure activity or a so-called stroke-like lesion, which can occur not only in MELAS patients but also in MERRF patients [2]?

The fifth point concerns the mother of the index patient; however, it is not reported whether other family members were clinically affected [1]. Did the mother or another family member have epilepsy and carry the m.8344A>G variant? Knowing whether the condition is hereditary or de novo is crucial for genetic counseling and assessing the likely course of the disease.

In summary, MERRF should only be diagnosed if the diagnostic criteria are met. Seizures in MERRF patients should preferably be treated with non-mitochondrially toxic antiepileptic drugs.

Declarations
Ethical Approval: Not applicable.

Consent to Participation: Not applicable.

Consent for Publication: Not applicable.

Funding: None received.

Availability of Data and Material: All data are available from the corresponding author.

Completing Interests: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contribution: JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. SM: contributed to literature search, discussion, correction, and final approval.

Acknowledgements: None.

Keywords: MERRF, Mitochondrial Disorder, m.8344A>G, Epilepsy, Seizures

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