Int. j. adv. multidisc. res. stud. 2025; 5(4):497-498

Received: 28-06-2025
Accepted: 08-07-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

Supra-refractory status epilepticus in MERRF requires the exclusion of a stroke-like episode

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DOI: https://doi.org/10.62225/2583049X.2025.5.4.4638
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The article by Baysal *et al*. about a 38-year-old woman with myoclonic epilepsy with red fibers (MERRF syndrome) due to the mtDNA variant m.8344A>G in *MT-TK* is excellent [1]. The patient presented with myoclonus and seizures that developed into focal and generalized status epilepticus and even supra-refractory status epilepticus (SRSE), despite receiving various antiseizure medications (ASM) since the onset of the disease [1]. SRSE was successfully treated by implantation of a vagus nerve stimulator (VNS), which significantly reduced seizure frequency, frequency and intensity of status epilepticus, but also the intensity and frequency of myoclonus [1]. The report suggests some reflections.

First, specific parameters of the m.8344A>G variant were not reported [1]. These include heteroplasmy rate, mtDNA copy number, mtDNA polymorphisms and haplotype. Since all of these parameters influence, at least in part, the phenotypic expression of the mutation, and since SRSE has not been previously reported in MERRF, it is crucial to determine them in order to establish the correlation between genotype and phenotype. These parameters may also be useful for evaluating disease progression and outcome and for genetic counseling.

Second, only T2 images of the cerebral MRI were presented [1]. To assess whether the T2 hyperintesnity in the right middle cerebral artery territory is truly a postictal phenomenon or actually a stroke-like lesion (SLL), the morphological correlate of a stroke-like episode (SLE), a multimodal MRI with DWI, ADC, SWI, STIR, OEF and PWI sequences, magnetic resonance angiography (MRA) and magnetic resonance spectroscopy (MRS) are required. Since MERRF can manifest phenotypically with SLEs [2] and since seizures are a common complication or trigger of SLLs [3], it would have been useful to provide at least a description of these modalities that can be used to characterize SLLs [3].

Third, the patient had a lumbar puncture at the age of 26, which was reported as non-informative [1]. Since MERRF can manifest with lactic acidosis in serum or CSF [4], it would be interesting to know if the patient's lactate was determined at that time. Lactic acidosis can be an indicator of mitochondrial disorders (MID) in general, as oxidative phosphorylation is often impaired in MID patients [4]. Lactic acidosis in the CSF can also be documented by MRS in the form of a double lactate peak and a reduced NAA peak [5]. Lactic acidosis in the cerebrospinal fluid could be a driver for seizure activity.

Fourthly, no explanation was given as to why the patient used a wheelchair [1]. Was this initiated as a protective measure to prevent falls during a seizure or during myoclonus storms, was this due to muscle weakness in the lower limb muscles, or was this due to other causes? MERRF is characterized by a myopathy with ragged-red fibers. Did the patient have this cardinal manifestation of the syndrome?

Fifth, the patient has received potentially mitochondrial toxic drugs such as propofol, valproic acid or zonisamide [6]. Is it conceivable that the persistence of myoclonus and seizures was due, at least in part, to the potentially toxic effects of some ASMs? Was there an improvement in seizure frequency and intensity when the potentially mitochondrial toxic drugs were discontinued?

In summary, implantation of a VNS in MERRF with intractable seizures can obviously be beneficial, but the triggers of seizure activity need to be identified and appropriately eliminated.

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. JGM: contributed to literature search, discussion, correction, and final approval.

Acknowledgements: None.

Keywords: SRSE, MERRF, Epilepsy, Myoclonus, Anti-Seizure Medications

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