Int. j. adv. multidisc. res. stud. 2024; 4(2):1519-1520

Received: 08-04-2024
Accepted: 15-04-2024

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

Multimodal Cerebral Imaging is required to Detect Stroke-like Lesions in *NDUFS8* Mutation Carriers

Josef Finsterer
Department of Neurology, Neurology & Neurophysiology Center, Vienna, Austria

DOI: https://doi.org/10.62225/2583049X.2024.4.2.2723
Corresponding Author: **Josef Finsterer**

We read with interest Gowda *et al*'s article on a 17-months-old female with mitochondrial disorder (MID) due to the variant c.304C>T in *NDUFS8* [1]. The *NDUFS8* variant manifested phenotypically with developmental delay, generalised hypotonia, quadrispasticity, lactic acidosis, leucoencephalopathy, stroke-like episodes (SLEs), and hypertrophic cardiomyopathy complicated by heart failure [1]. The patient benefited from a mitochondrial cocktail and heart failure treatment [1]. The study is impressive, but several points require discussion.

The first point is that only a limited number of MRI modalities (T1, T2, diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) have been performed [1]. To characterise a stroke-like lesion (SLL), which represents the morphological equivalent of a SLE, it is imperative to perform additional MRI modalities that typically characterise SLL [2]. These include perfusion-weighted imaging (PWI), oxygen-extraction fraction (OEF), magnetic resonance angiography (MRA), and magnetic resonance spectroscopy (MRS) [2]. SLLs are typically hyperintense on PWI but hypointense on OEF MRI [2]. MRA is usually normal but MRS typically shows a lactate peak and a reduced N-acetyl aspartate (NAA) peak. Perfusion single photon emission computed tomography (SPECT) can show hyperperfusion, but fluordeoxy glucose (FDG) positron emission tomography (PET) can show hypometabolism [3]. Another typical feature of SLLs is their dynamic expansion up to a nadir and their regression after reaching this nadir. SLLs can terminate as normal brain, or as structural lesion in the form of white matter lesions, cysts, focal atrophy, laminar cortical necrosis, or as toenail sign [2].

The second point is that cerebrospinal fluid (CSF) studies are not mentioned even though the patient had cerebral disease [1]. It is of particular interest to know whether CSF lactate was elevated or not.

The third point is that it was not mentioned whether the patient suffered from myopathy or not [1]. Since MIDs often manifest with myopathy [4], we should know whether needle electromyography (EMG) recorded on weak muscles was abnormal (myogenic, neurogenic, non-specific). Normal creatine-kinase, as in the index patient, does not rule out myopathy.

A fourth point that electroencephalography (EEG) recordings have not been reported [1]. Since the patient presented with dullness, had SLE, and SLEs often manifest with seizures, we should know whether the electroencephalography (EEG) recordings showed epileptiform discharges or not. In particular, non-convulsive status epilepticus (NCSE) should be excluded.

A fifth point is that cerebral vasculitis is unlikely as a differential diagnosis of MID because SLLs are not limited to one vascular territory and therefore do not correspond to a vascular lesion.

A sixth point is that the statement that MELAS does not manifest with respiratory chain complex deficiencies is not supported. Usually, biochemical studies in MELAS show multiple respiratory chain defects, as previously reported [5]. However, MELAS may manifest with a single respiratory chain defect if it is due to a nuclearly encoded mitochondrial gene [6].

In summary, the excellent study has limitations that should be addressed before drawing final conclusions. Clarifying the weaknesses would strengthen the conclusions and improve the study. Documentation of SLL in non-syndromic MID due to a pathogenic variant in *NDUFS8* requires multimodal MRI, MRA, MRS, and FDG-PET.

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: NDUFS8 Gene, Stroke-like Episode, Mitochondrial Disorder, Stroke-like Lesion, Multimodal MRI

References

1. Gowda VK, Bylappa AY, Kinhal U, Srinivasan VM, Vamyanmane DK. Mitochondrial Complex I Deficiency Masquerading as Stroke-Like Episode Clinically and as Alexander Disease Radiologically Following Chicken Pox. Ann Indian Acad Neurol. 2023; 26(6):977-979. Doi: 10.4103/aian.aian_339_23
2. Finsterer J. Characteristics of stroke-like lesions on cerebral imaging. Ideggyogy Sz. 2023; 76(1-2):5-10. Doi: 10.18071/isz.76.0005
3. Kim JH, Lim MK, Jeon TY, Rha JH, Eo H, Yoo SY, *et al*. Diffusion and perfusion characteristics of MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episode) in thirteen patients. Korean J Radiol. 2011; 12(1):15-24. Doi: 10.3348/kjr.2011.12.1.15
4. Hu C, Li X, Zhao L, Shi Y, Zhou S, Wu B, *et al*. Clinical and molecular characterization of pediatric mitochondrial disorders in south of China. Eur J Med Genet. 2020; 63(8):103898. Doi: 10.1016/j.ejmg.2020.103898
5. Arpa-Gutiérrez FJ, Cruz-Martínez A, Campos-González Y, Gutiérrez-Molina M, Santiago-Pérez S, Pérez-Conde MC, López-Pajares MR, Martín-Casarrubias MA, Rubio-Muñoz JC, del Hoyo P, Arpa-Fernández A, Arenas-Barbero J. Enfermedades de la cadena respiratoria mitocondrial. Evaluación y variabilidad en 52 pacientes Mitochondrial respiratory chain diseases. Evaluation and variability in 52 patients. Rev Neurol. 2005; 41(8):449-454.
6. Wang W, Sun Y, Lin Y, Xu X, Zhao D, Ji K, *et al*. A novel nonsense variant in MT-CO3 causes MELAS syndrome. Neuromuscul Disord. 2021; 31(6):558-565. Doi: 10.1016/j.nmd.2021.02.020