Sarcouncil journal of Medical sciences

ISSN(Online): 2945-3526

Volume- 03| Issue- 08| 2024

Letter to the Editor **Received:** 02-07-2024 | **Accepted:** 22-07-2024 | **Published:** 21-08-2024

MELAS Patients and their Relatives Must Be Examined Carefully

***Josef Finsterer*[2], *and Sounira Mehri*[1]**

[1]*Md, PhD, Neurology & Neurophysiology Center, Vienna, Austria, ORCID: 0000-0003-2839-7305*

[2]*Biochemistry Laboratory, LR12ES05 "Nutrition-Functional Foods and Vascular Health", Faculty of Medicine, Monastir, Tunisia, ORCID 0000-0002-2221-7193*

Keywords: mtDNA, heteroplasmy, MELAS, stroke-like episode, seizure.

LETTER TO THE EDITOR

We read with interest the article by Zijun *et al*. about a 52-year-old female (height 158cm, weight 42kg) with mitochondrial encephalopathy lactic acidosis and stroke-like episode (MELAS) syndrome that manifested only by hypoacusis and short stature for 40 years [Zijun, L. *et al*., 2024]. She experienced her first stroke-like episode (SLE) at age of 52, which was characterised by visual impairment, auditory agnosia, severe lactic acidosis, and occipital epileptiform discharges [Zijun, L. *et al*., 2024]. The study is impressive, but some points require discussion.

The first point is that the heteroplasmy rate of 6% is extremely low and does not explain the phenotype. Was heteroplasmy in the muscle also determined after biopsy? Since muscle biopsy suggested myopathy and was therefore clinically affected by the mtDNA variant, it can be assumed that the heteroplasmy rate was higher than in blood lymphocytes.

Surprisingly, cerebrospinal fluid (CSF) glucose levels were elevated. Was there any evidence that the patient had diabetes? Was urine glucose level elevated? Was the HbA1c value increased above 6.5? It is important to provide an explanation for the elevated CSF glucose level as MELAS is often associated with diabetes [Seidowsky, A. *et al*., 2013].

The patient had a negative history of epilepsy and did not exhibit convulsions on admission or during hospitalisation [Zijun, L. *et al*., 2024]. In contrast, the EEG showed frequent epileptiform discharges in the occipital regions bilaterally [Zijun, L. *et al*., 2024]. The discrepancy between the negative seizure history and the abnormal EEG should be clarified. Is it possible that the patient had unwitnessed seizures? Was she living alone when the SLE developed? It is crucial to know whether the patient had seizures before onset of the SLE, as one hypothesis is that all SLEs are triggered by seizures [Finsterer, J. *et al*., 2023]?

Another point is that no ophthalmologic examination was reported [Zijun, L. *et al*., 2024]. We should know whether the patient underwent ophthalmological examination and whether it was normal or not. Visual disturbances in MELAS are common and can occur during a SLE or independently of SLEs. Visual impairment during SLEs is most commonly due to SLE and manifests as hemianopia. Visual impairment outside of SLEs may be due to cataracts, glaucoma, optic atrophy, or retinopathy [Romano, F. *et al*., 2022]. Is it conceivable that the index patient's visual impairment was a manifestation of occipital seizures?

Another point is that no family history was provided. Was the causative variant inherited from the mother or did it occur sporadically? To assess whether the index patient has inherited the disease or whether it occurred sporadically, a thorough family history and extensive examinations of other first-degree relatives are mandatory. In particular, we should know whether other first-degree relatives also carried the mtDNA variant, regardless of whether they were clinically affected or not. mtDNA variants are inherited in 75% of cases [Poulton, J. *et al*., 2017], making it very likely that MELAS was also inherited in the index patient.

A last limitation is that neither the Hirano nor the Japanese criteria [Hirano, M. *et al*., 1992; Yatsuga, S. *et al*., 2012] have been used to diagnose MELAS. Has the patient fulfilled both criteria?

In summary, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. MELAS should be diagnosed not only on

***Corresponding Author:** Josef Finsterer

DOI-https://doi.org/10.5281/zenodo.13367368

the phenotypic appearance, but also based on documentation of a pathogenic mtDNA variant with a heteroplasmy rate high enough to justify the diagnosis.

REFERENCES

1. Zijun, L., Xu, Y., Yujia, Y. & Zhiqiang, X. "Elderly onset of MELAS carried an M.3243A >G mutation in a female with deafness and visual deficits: A case report." *Clinical Case Reports*, 12.3 (2024): e8438.
2. Seidowsky, A., Hoffmann, M., Glowacki, F., Dhaenens, C. M., Devaux, J. P., de Sainte Foy, C. L., Provot, F., Gheerbrant, J. D., Hummel, A., Hazzan, M., Dracon, M., Dieux-Coeslier, A., Copin, M. C., Noël, C. & Buob, D. "Renal involvement in MELAS syndrome - a series of 5 cases and review of the literature." *Clinical Nephrology*, 80.6 (2013): 456-463.
3. Finsterer, J. & Mehri, S. "Seizure phenomenology in MELAS." *Seizure*, 111 (2023): 223-224.
4. Romano, F., Cozzi, M., Staurenghi, G. & Salvetti, A. P. "Multimodal retinal imaging of m.3243A>G associated retinopathy." *American Journal of Ophthalmology Case Reports*, 26 (2022): 101411.
5. Poulton, J., Finsterer, J. & Yu-Wai-Man, P. "Genetic Counselling for Maternally Inherited Mitochondrial Disorders." *Molecular Diagnosis & Therapy*, 21.4 (2017): 419-429.
6. Hirano, M., Ricci, E., Koenigsberger, M. R., Defendini, R., Pavlakis, S. G., DeVivo, D. C., DiMauro, S. & Rowland, L. P. "MELAS: an original case and clinical criteria for diagnosis." *Neuromuscular Disorders*, 2.2 (1992): 125-135.
7. Yatsuga, S., Povalko, N., Nishioka, J., Katayama, K., Kakimoto, N., Matsuishi, T., Kakuma, T. & Koga, Y. for MELAS Study Group in Japan. "MELAS: a nationwide prospective cohort study of 96 patients in Japan." *Biochimica et Biophysica Acta*, 1820.5 (2012): 619-624.

Source of support: Nil; **Conflict of interest:** Nil.

Cite this article as:
Finsterer, J. and Mehri, S. "MELAS Patients and their Relatives Must Be Examined Carefully." *Sarcouncil journal of Medical sciences* 3.8 (2024): pp 08-09.

Publisher: SARC Publisher