Sarcouncil Journal of Medicine and Surgery

ISSN(Online): 2945-3534

Volume- 03| Issue- 08| 2024

Letter to the Editor **Received:** 05-06-2024 | **Accepted:** 25-07-2024 | **Published:** 21-08-2024

Before Neovascular Glaucoma Can Be Assigned to the m.3243A>G Variant, Alternative Causes Must Be Ruled Out

Josef Finsterer

MD, PhD, Neurology Dpt., Neurology & Neurophysiology Center, Vienna, Austria, Orcid: 0000-0003-2839-7305

Keywords: mtDNA, m.3243A>G, MELAS, glaucoma, neovascularisation.

LETTER TO THE EDITOR

We read with interest the article by Khanna *et al* on a 48-year-old female with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome due to the m.3243A>G variant, phenotypically presenting with hypoacusis, diabetes, arterial hypertension, hyperlipidemia, cataract, macular dystrophy, and glaucoma due to neovascularisation in the anterior chamber and the retina [Khanna, S. *et al*., 2024]. Uncorrected visual acuity was 20/200 OD and 20/50 OS and intraocular pressure was 21 mm Hg OD and 11 OS [Khanna, S. *et al*., 2024], Florid iris neovascularization (OU), mild nuclear sclerotic cataracts, disc neovascularization OS, macular atrophy OU, arteriolar attenuation, dot blot haemorrhage OU, and outer retinal atrophy occurred [Khanna, S. *et al*., 2024]. Despite injection of aflibercept and placement of a glaucoma tube shunt, pallor developed in the right eye [Khanna, S. *et al*., 2024]. The study is impressive, but several points require discussion.

The first point is that the diagnosis of MELAS is not supported. MELAS is usually diagnosed according to the Japanese criteria [Yatsuga, S. *et al*., 2012] or the Hirano criteria [Hirano, M. *et al*., 1992]. According to the Japanese criteria, MELAS is diagnosed when there are signs of encephalopathy associated with dementia or epilepsy, early life stroke-like episodes (SLEs), and biochemical evidence of mitochondrial dysfunction, such as lactic acidosis and the presence of ragged-red fibres (RRF) on muscle biopsy [Yatsuga, S. *et al*., 2012]. According to the Hirano criteria MELAS is diagnosed when SLEs occur before age 40 and there are seizures or dementia, lactic acidosis or ragged-red fibres, normal early development, recurrent headache, or recurrent vomiting [Hirano, M. *et al*., 1992]. Based on these criteria, the index patient should not be diagnosed with MELAS syndrome, but rather with a diagnosis of maternally inherited diabetes and deafness (MIDD) plus.

The second point is the statement that all children of a sister of the index patient tested positive for MELAS [Khanna, S. *et al*., 2024]. We should know whether this means that all these children carried the m.3243A>G variant, that they had a MELAS phenotype, or that they had both the mutation and a suitable phenotype.

The third point is that the index patient was not systematically evaluated for multisystem disease. Since carriers of m.3243A>G variants usually manifest with multisystem disease [Giannese, D. *et al*., 2023], it would have been imperative to examine the index patient for subclinical manifestations of the mutation in organs other than the eyes or ears. The most commonly affected organs in m.3243A>G carriers are the brain, endocrine organs, heart, intestines, and the skeletal muscle. Since a sister died at an early age [Khanna, S. *et al*., 2024], we should be informed whether this patient died of cardiac, cerebral cause, or other causes and whether she was subjected to an autopsy. Knowing the cause of early death in this family is essential to assess the risk in living family members carrying the variant and to take appropriate measures to reduce the risk of sudden death.

The fourth point is optic atrophy in m.3243A>G carriers may not only be due to glaucoma but may also be an inherent feature of the phenotype [Scarcella, S. *et al*., 2023].

In summary, the excellent study has limitations that should be addressed before drawing final conclusions. Clarifying the weaknesses would strengthen the conclusions and could improve the study. Before neovascular glaucoma can be assigned to the m.3243A>G variant, alternative causes must be thoroughly ruled out.

REFERENCES

1. Khanna, S. & Smith, B. T. "Neovascular Glaucoma in MELAS syndrome." *American*

***Corresponding Author:** Josef Finsterer

DOI- https://doi.org/10.5281/zenodo.13367706

Journal of Ophthalmology Case Reports, 34 (2024): 102064.
2. Yatsuga, S., Povalko, N., Nishioka, J., Katayama, K., Kakimoto, N., Matsuishi, T., Kakuma, T., Koga, Y. & Taro Matsuoka 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.
3. 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.
4. Giannese, D., Montano, V., Lopriore, P., Nesti, C., LoGerfo, A., Caligo, M. A., Dal Canto, F., Pasquinelli, G., Bonadio, A. G., Moriconi, D., Siciliano, G. & Mancuso, M. "A multisystem mitochondrial disease caused by a novel MT-TL1 mtDNA variant: A case report." *Journal of Neuromuscular Diseases*, 10.1 (2023): 119-123.
5. Scarcella, S., Dell'Arti, L., Gagliardi, D., Magri, F., Govoni, A., Velardo, D., Mainetti, C., Minorini, V., Ronchi, D., Piga, D., Comi, G. P., Corti, S. & Meneri, M. "Ischemic optic neuropathy as first presentation in a patient with m.3243A>G MELAS classic mutation." *BMC Neurology*, 23.1 (2023): 165.

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

Cite this article as:
Finsterer, J. "Before neovascular Glaucoma Can Be Assigned to the m.3243A>G Variant, Alternative Causes Must Be Ruled Out." *Sarcouncil Journal of Medicine and Surgery* 3.8 (2024): pp 37-38.

Publisher: SARC Publisher