Int. j. adv. multidisc. res. stud. 2026; 6(4):288-289

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

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

m.3243A>G Carriers Scheduled for Transplantation Require Thorough Examinations for Clinical and Subclinical Multisystem Involvement

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Letter to the Editor

We read with interest the article by Nilsen *et al*. about a 40-year-old man with MELAS syndrome (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) due to the m.3243A>G variant in the MT-TL1 gene, which manifested phenotypically as diabetes mellitus, hearing loss, and renal insufficiency [1]. Due to deteriorating renal function requiring peritoneal dialysis, a combined pancreas and kidney transplant was performed. Subsequently, the patient no longer required insulin and fully recovered from renal failure [1]. During a five-year follow-up, the patient tolerated immunosuppressive therapy with steroids, tacrolimus, mycophenolate, and mofetil without major adverse effects and without signs of transplant rejection [1]. The study is interesting, but some questions remain.

First, we disagree with the diagnosis of MELAS [1]. MELAS is diagnosed according to the Hirano criteria or the Japanese criteria [2, 3]. According to the Japanese criteria, MELAS is diagnosed when there are signs of encephalopathy associated with dementia or epilepsy, stroke-like episodes (SLE) in early childhood, and biochemical evidence of mitochondrial dysfunction, such as acidosis and the presence of ragged-red fibers (RRFs) in muscle biopsy [2]. According to the Hirano criteria, MELAS is diagnosed when SLE occurs before the age of 40 and there are seizures or dementia, lactic acidosis or ragged-red fibers, normal development in early childhood, recurrent headaches, or recurrent vomiting [3]. What were the results of the muscle biopsy, and has the patient ever had lactic acidosis or a SLE, the main feature of MELAS?

Second, although a high heteroplasmy rate was found in the muscle tissue, it is not stated whether the muscle was clinically affected and whether the histological, immunohistological, and biochemical examination of the biopsy provided evidence of mitochondrial myopathy [1]. In particular, it was not mentioned whether the Gomori trichrome stain showed ragged-red fibers (RRFs) or the succinate dehydrogenase stain showed ragged-blue fibers. Was the heteroplasmy rate also determined in other tissues, and was it also elevated there? Knowledge of possible muscle involvement is crucial, as steroids and tacrolimus can cause myopathies [4].

Third, it was not mentioned whether organs other than the ears, pancreas, and kidneys were affected [1]. Since mitochondrial diseases (MIDs) are generally multisystem diseases [5], it is conceivable that, in addition to the organs described, other organs were clinically or subclinically affected or became affected during the five-year follow-up period. In carriers of the m.3243A>G variant, symptoms additionally manifest particularly in the central nervous system, the eyes, the endocrine organs, the myocardium, the skeletal muscles, the gastrointestinal tract, the peripheral nerves, and the skin.

The fourth point concerns the authors' lack of information regarding "low immune status" [1]. Does this refer to vaccination status, a history of previous infectious or immune disorders, or the status of the cellular (e.g., monocytes, T or B lymphocytes) or humoral immune system (e.g., immunoglobulins)? Immune system involvement has already been described in some cases of MID [6].

The fifth point is that it is unclear as to why the patient did not receive antioxidants or vitamins as non-specific adjunctive therapy. Although there is no evidence of a general effect of these substances, case reports and studies suggest that some of them may have a positive effect. In particular, idebenone is known to alleviate visual disturbances in patients with Leber's hereditary optic neuropathy [7].

Overall, carriers of the m.3243A>G variant can not only develop symptoms of MELAS, but also require prospective investigations for multisystem diseases as well as histological, immunohistological, biochemical and genetic tests of the clinically affected tissues.

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: mtDNA, m.3243A>G, MELAS, Renal Failure, Diabetes

References
1. Nilsén V, Bojstedt J, Nordström J. Case Report: Simultaneous pancreas-kidney transplantation in MELAS: First reported case with 5-year follow-up. Front Transplant, Jan 22, 2026; 5:1737352. Doi: 10.3389/frtra.2026.1737352
2. Hirano M, Ricci E, Koenigsberger MR, Defendini R, Pavlakis SG, DeVivo DC, *et al*. Melas: An original case and clinical criteria for diagnosis. Neuromuscul Disord. 1992; 2(2):125-35. Doi: 10.1016/0960-8966(92)90045-8
3. Yatsuga S, Povalko N, Nishioka J, Katayama K, Kakimoto N, Matsuishi T, *et al*. Taro Matsuoka for MELAS Study Group in Japan. MELAS: A nationwide prospective cohort study of 96 patients in Japan. Biochim Biophys Acta, May 2012; 1820(5):619-624. Doi: 10.1016/j.bbagen.2011.03.015
4. Orlandi V, Campieri C, Mosconi G, D'Arcangelo GL, Feliciangeli G, Scolari MP, *et al*. Tacrolimus-associated myositis: A case report in a renal transplant patient. Transplant Proc, Apr 2004; 36(3):708-710. Doi: 10.1016/j.transproceed.2004.03.018
5. Donato S. Multisystem manifestations of mitochondrial disorders. J Neurol, May 2009; 256(5):693-710. Doi: 10.1007/s00415-009-5028-3
6. Van Portfliet JJ, Lei Y, Ramanathan M, Martinez CG, Wong J, Stodola TJ, *et al*. Caspase-11 drives macrophage hyperinflammation in models of Polg-related mitochondrial disease. Nat Commun, May 20, 2025; 16(1):4640. Doi: 10.1038/s41467-025-59907-8
7. Sanders FWB, Votruba M. Outcomes of idebenone therapy for Leber hereditary optic neuropathy in a cohort of patients from Wales. Eye (Lond), Nov 2025; 39(16):2952-2957. Doi: 10.1038/s41433-025-03993-x