Int. j. adv. multidisc. res. stud. 2022; 2(5):708-709

Received: 01-10-2022
Accepted: 11-10-2022

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

MELAS in children does not differ from MELAS in adults

Josef Finsterer
Neurology & Neurophysiology Center, Vienna, Austria

Corresponding Author: **Josef Finsterer**

We read with interest the article by Seed *et al*. on a retrospective study of three pediatric patients with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome and a literature review of 114 pediatric patients with MELAS [1]. The three patients had seizures and MRI lesions that were not confined to a vascular territory. Among the 114 patients from the literature, seizures were the most common phenotypic manifestation of stroke-like episodes (SLEs) and heteroplasmy was higher in tissues other than blood [1]. It was concluded that the threshold for investigating MELAS should be low in children with suspicious neurological symptoms and invasive investigations or further genetic studies should be initiated in these children if tests for the variant m.3243A>G are negative [1]. The study is attractive but raises concerns that should be discussed.

A limitation of the study is that the methods section does not mention how MELAS was diagnosed [1]. We should know whether the Japanese or the Hirano criteria were used. It should also explain why MELAS overlap syndromes were excluded from the assessment and the criteria based on which 40 patients were not diagnosed as MELAS.

Patient-2 had an abnormal muscle biopsy with subsarcolemmal accumulated and proliferated mitochondria and a high heteroplasmy rate in muscle but was classified according to table 1 without myopathy. This discrepancy should be clarified.

According to the abstract, one of the three patients required a muscle biopsy [1]. However, the main text describes a muscle biopsy in two patients. This discrepancy should be resolved.

Patient-1 was described as having normal development but with short stature and hearing loss. We should know when these anomalies were first detected.

With regard to the tissue that is more suitable for determining heteroplasmy rates, it should be mentioned that urinary epithelial cells usually have higher heteroplasmy rates than blood lymphocytes [2]. Patient-1 had a heteroplasmy rate of 58% [1]. We should be told what tissue was examined and whether heteroplasmy was also determined in other tissues and with what result.

The phenotype of an mtDNA-related mitochondrial disorder (MID) is not only determined by heteroplasmy rates, but by a number of other factors, such as mtDNA copy number, polymorphisms, and secondary damage of the causative mtDNA variant [3]. We should know whether these aspects have been taken into account.

Regarding patient-1, it should be explained why there was an eye deviation and a head tilt [1]. We should know whether this was due to palsy of cranial nerve IV (Bielschowsky sign) or to dystonia (torticollis), a clinical manifestation previously described in MELAS [4].

Patient-1 had focal seizures [1]. We should know if the patient was receiving anti-seizure drugs (ASDs), what type of ASDs, and at what dosage. Did the epileptogenic focus correspond to one of the cerebral lesions described on MRI?

The mother of patient-1 did not carry the m.3243A>G variant [1]. We should know whether the variant was classified as sporadic in the index patient or whether family members other than the mother were clinically or genetically affected.

MELAS patients often show dysmorphism [5], which can already be detected at birth. We should know whether dysmorphism was evaluated as a phenotypic feature of MELAS among the 114 cases from the literature and the three cases from the author's department.

MELAS often manifests as a multiorgan disease [6]. We should know the most common phenotypic characteristics of the 114 patients collected from the literature.

Missing are the findings about magnetic resonance spectroscopy. We should know whether there was cerebral lactic acidosis or not.

Overall, the interesting study has some limitations and inconsistencies that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study.

Acknowledgements

Funding: No funding was received.

Author contribution: JF: design, literature search, discussion, first draft, critical comments, final approval.

Disclosures: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Compliance with Ethics Guidelines: This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Keywords: MELAS, mtDNA, m.3243A>G, Myopathy, Heteroplasmy

References

1. Seed LM, Dean A, Krishnakumar D, Phyu P, Horvath R, Harijan PD. Molecular and neurological features of MELAS syndrome in paediatric patients: A case series and review of the literature. Mol Genet Genomic Med. 2022: 26:e1955. Doi: 10.1002/mgg3.1955.
2. De Laat P, Koene S, Van den Heuvel LP, Rodenburg RJ, Janssen MC, Smeitink JA. Clinical features and heteroplasmy in blood, urine and saliva in 34 Dutch families carrying the m.3243A > G mutation. J Inherit Metab Dis. 2012; 35(6):1059-1069. Doi: 10.1007/s10545-012-9465-2
3. Finsterer J. Secondary manifestations of mitochondrial disorders. J Zhejiang Univ Sci B. 2020; 21(7):590-592. Doi: 10.1631/jzus.B2000010.
4. Sudarsky L, Plotkin GM, Logigian EL, Johns DR. Dystonia as a presenting feature of the 3243 mitochondrial DNA mutation. Mov Disord. 1999; 14(3):488-91. Doi: 10.1002/1531-8257(199905)14:3<488:aid-mds1017>3.0.co;2-4.
5. McPherson E, Zabel C. Mitochondrial mutation in a child with distal arthrogryposis. Am J Med Genet A. 2006; 140(2):184-185. Doi: 10.1002/ajmg.a.31041.
6. El-Hattab AW, Adesina AM, Jones J, Scaglia F. MELAS syndrome: Clinical manifestations, pathogenesis, and treatment options. Mol Genet Metab. 2015; 116(1-2):4-12. Doi: 10.1016/j.ymgme.2015.06.004.