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Letter to the Editor

Survival and outcome in MELAS not only depends on onset and disease duration

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Letter to the Editor

We read with interest the article by Zhang et al. about a retrospective investigation of 138 Chinese MELAS patients, of whom 126 carried a mtDNA mutation and of whom 121 underwent face-to-face or telephone follow-up [1]. We have the following comments/concerns.

The study has several shortcomings, which weaken the reliability of the results. First, the heteroplasmy rate for any of the mtDNA mutations detected was not provided in any of the tissues. Heteroplasmy rates may be correlated with the severity of the phenotype and with the progression and outcome of a mitochondrial disorder (MID) due to a mtDNA mutation [2].

Second, the authors do not mention in how many of the 121 patients the follow-up was carried out face-to-face or by a telephone interview. Telephone interviews have the disadvantage that the information provided by the patient or the caregiver cannot be verified, that the patient usually cannot prepare for the interview, and that no clinical exam or instrumental investigations can be carried out. For example, if the patient reports a stroke-like episode (SLE) this needs to be confirmed by imaging. A SLE is characterised by a stroke-like lesion on cerebral MRI (cMRI) [3]. Thus, a SLE has a morphological equivalent which needs to be demonstrated to diagnose a SLE. Recently, a new method has been proposed to diagnose SLEs on MRI. The method relies on the measurement of the oxygen extraction fraction (OEF), defined as the ratio of blood oxygen that a tissue takes from the blood flow to maintain function and morphological integrity [4]. How can cortical blindness be assessed by a telephone interview? How to know the cause of death if patients were followed only by telephone interviews?

Other factors determining the phenotype and not investigated in the study by Zhang et al. are the haplotype, polymorphisms, the current medication, and the environment. For example, some antiepileptic drugs (AEDs), such as valproic acid, phenytoin, carbamazepine, and phenobarbital are well-known for their mitochondrion-toxic discard, [5]. We should be informed how many of the patients required AEDs and in how many of them mitochondrion-toxic AEDs were given. Since 12 of the 28 patient dying during follow-up deceased from seizures or status epilepticus during a SLE, it is essential to know if intractability of seizures was due to usage of mitochondrion-toxic AED. Concerning the haplotypes, it is conceivable that a longer survival time in the current study compared to an American study [6] could be attributed a different haplotype.

We do not agree with the statement in the introduction that there is no effective pharmacological or dietary intervention available for MELAS patients [1]. On the contrary, a lot can be done for epilepsy, ptosis, migraine, cardiac abnormalities, and gastro-intestinal and hormonal compromise in MELAS patients [7]. With regard to this statement, the authors should provide information about the current medication in their patients and how many were on a ketogenic diet, which has been shown to be highly effective in mitochondrial epilepsy [8]. As mentioned by the authors, there is also frequently cardiac involvement in MID, requiring appropriate measures, such as heart failure therapy, antiarrhythmic pharmacotherapy, implantation of pacemakers, CRT systems, or implantable cardioverter defibrillators. There is also the possibility to offer heart transplantation in case of intractable heart failure.

Overall, this interesting study could be more meaningful by providing additional genetic data, information about the medication, and by following-up patients face-to face not miss important information. Survival curves may look completely different if these shortcomings would have been accomplished.

Conflict of interest

There are no conflicts of interest.

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Author contribution

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References

[1] Z. Zhang, D. Zhao, X. Zhang, H. Xiong, X. Bao, Y. Yuan, Z. Wang, Survival analysis of a cohort of Chinese patients with mitochondrial encephalomyopathy with lactic

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acidosis and stroke-like episodes (MELAS) based on clinical features, J. Neurol. Sci. 385 (2018) 151–155.
[2] T. Howes, C. Madden, S. Dasgupta, S. Saeed, V. Das, Role of mitochondrial variation in maternally inherited diabetes and deafness syndrome, J. Laryngol. Otol. 122 (2008) 1249–1252.
[3] J. Finsterer, Stroke and stroke-like episodes in muscle disease, Open Neurol. J. 6 (2012) 26–36.
[4] S. Xie, MR OEF imaging in MELAS, Methods Enzymol. 547 (2014) 433–444.
[5] J. Finsterer, Toxicity of antiepileptic drugs to mitochondria, Handb. Exp. Pharmacol. 240 (2017) 473–488.
[6] P. Kaufmann, K. Engelstad, Y. Wei, R. Kulikova, M. Oskoui, D.M. Sproule, V. Battista, D.Y. Koenigsberger, J.M. Pascual, S. Shanske, M. Sano, X. Mao, M. Hirano, D.C. Shungu, S. Dimauro, D.C. De Vivo, Natural history of MELAS associated with mitochondrial DNA m.3243A > G genotype, Neurology 77 (2011) 1965–1971.
[7] J. Finsterer, P.S. Bindu, Therapeutic strategies for mitochondrial disorders, Pediatr. Neurol. 52 (2015) 302–313.
[8] E. Paleologou, N. Ismayilova, M. Kinali, Use of the ketogenic diet to treat intractable epilepsy in mitochondrial disorders, J Clin Med 6 (6) (May 26, 2017), https://doi.org/10.3390/jcm6060056 (pii: E56).

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