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The Author Reply: Mitochondrial Ophthalmoplegia Is Not Only due to mtDNA Deletions

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We have read the comments on our study by Dr. Finsterer. We thank Dr. Finsterer for these important points and agree that there is a shortcoming in our current study.

It is well-known that mitochondrial diseases are a heterogeneous group of disorders, and they often show important differences in phenotype and severity. Generally, classification of a syndrome or disease relies on accurate clinical, biochemical, and genetic information and may be based on either genotype or phenotype. Drawing a clear line to classify mitochondrial diseases, however, can be difficult since there is significant overlap among them:[1,2] The diagnostic criteria for Kearns Sayre syndrome have not yet been completely established, as is the case with other mitochondrial diseases. Meanwhile, Leigh disease, a representative mitochondrial disease, has subclasses, such as Leigh syndrome and Leigh-like disease.[3]

Our study was retrospective in nature, and it has some limitations. Because of the rarity of the study disease, the size of our study population was small, which could have given the impression of a study not sufficient enough to make generalized interpretations. However, I would like to stress to readers that mitochondrial diseases are very rare, such that data on these diseases are limited to a degree that makes the research thereof extremely difficult.[4,5] Despite the lack of copious amounts of data, however, the fact that mitochondrial disease is heterogenous calls for the establishment of better classification and further studies to generalize its homogeneous aspects.

Confirmative diagnosis of pediatric patients with mitochondrial diseases by genetic diagnostic testing is very important. Over the past decade, technologies have continuously evolved and have enabled the use of sequencing as a clinical tool with better accessibility. However, in actual clinical settings, it is not easy to consistently apply confirmatory genetic diagnostic testing to all patients. Therefore, we tried to come up with common diagnostic criteria that could be applied objectively to all pediatric patients, and we wanted to emphasize the importance of gene study when evaluating phenotypes of a certain syndrome, such as Kearns Sayre syndrome.[6] Nonetheless, further studies on phenotypes and genotypes, including mtDNA and nuclear DNA, of a variety of different syndromes should be attempted in the future.

We do agree and understand Dr. Finsterer's view on these points, and there is no question that a properly controlled, multicenter study or analysis with larger sample would be ideal. Again, we sincerely appreciate Dr. Finsterer's inspiring and insightful comments on this study.

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