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Assessment of the phenotype genotype variability and correlation in m.3243A>G mutation carriers requires prospective studies

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With interest we read the article by Dvorakova et al. about phenotypic characteristics and genotype/phenotype correlations in 50 m.3243A>G mutation carriers [1]. We have the following comments and concerns.

The main disadvantage of this study is its retrospective design, implying that not all patients were investigated according to the same protocol. Accordingly, frequencies of clinical and laboratory manifestations are inaccurate. Asymptomatic or mild abnormalities may have been missed.

A second limitation is the variable length of follow-up periods, ranging between 1 and 19 y in asymptomatic patients [1]. Highly variable onset in symptomatic patients suggests that follow-up duration was also highly variable in this group, a further reason why various manifestations occurring during follow-up may have gone undetected.

A third point of concern is the number of erroneous descriptions: myopathy, SLEs, and rhabdomyolysis are not symptoms; ptosis and CPEO are not ocular manifestations but due to myopathy; an axonal lesion may be seen on nerve conduction studies but not on EMG; a stroke-like-lesion, the MRI correlate of a SLE, is not ischemic in nature but usually metabolic with increased DWI and increased ADC; [2] heart failure is a clinical diagnosis and may or may not go along with decreased EF.

Furthermore, the study lacks information about the family history and treatment. How many were under antiepileptic or cardiac drugs, were taking cocktails of vitamins, cofactors, or antioxidants, were under a ketogenic diet? Was disease progression different between those under treatment and those without?

Two patients became symptomatic during follow-up since they were diagnosed before onset [1], contradicting the statement that none of the asymptomatic patients became symptomatic.

Overall, this interesting study may profit from supplementary data and clarification of a number of issues as outlined above. A prospective follow-up investigation of the 50 patients could provide more reliable data about the genotype/phenotype correlation and outcome of this cohort.

Conflict of interest

There are no conflicts of interest.

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References

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