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Letter to the Editor

### Not only Patients with LHON, but also Patients with LHON Plus Should be Treated with Coenzyme-Q or a Mitochondrial Cocktail

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#### Letter to the Editor

We were interested to read the article by Thaller *et al.* about a 27-year-old woman with generalized dystonia who later also developed Leber's hereditary optic neuropathy (LHON) due to the mtDNA variant m.14459G>A in ND6 <sup>[1]</sup>. Treatment with high-dose steroids and plasma exchange had no beneficial effect on either the visual impairment or the generalized dystonia, for which the patient had previously been treated with deep brain stimulation (DBS) and a dorsal root ganglion stimulator for lower leg pain <sup>[1]</sup>. The study is noteworthy, but several points should be discussed.

The first point is that the parents, particularly the mother, and other first-degree relatives were not genetically tested for the presence of the m.14459G>A variant <sup>[1]</sup>. Since mtDNA mutations are inherited through the maternal line in 75% of cases <sup>[2]</sup>, it is very likely that the mother was also a carrier of the causative variant, even though the variant may have remained subclinical.

The second point is that the patient had already been tested for mtDNA mutations in childhood, but the results were negative <sup>[1]</sup>. Surprisingly, mtDNA analysis at the age of 27 revealed the causative variant in ND6. What was the reason that the mtDNA variant was not detected in childhood? What technique was used to screen for mtDNA variants at that time? Was the index patient subjected to mtDNA sequencing or were they only screened for certain common mtDNA variants known to be associated with mitochondrial disorder (MID)? This discrepancy should be clarified.

The third issue is that CSF testing for lactate was reported as normal in childhood, but no mention was made that it was performed at age 27 <sup>[1]</sup>. As the patient had progressive MID with cerebral involvement, it is conceivable that CSF lactate was elevated on the second CSF examination. It is not reported whether the serum lactate was normal or elevated. Serum lactate can be high, particularly in cases of skeletal muscle involvement. Was there any evidence of striated muscle involvement in the index patient?

The fourth point is that cerebral involvement in MID is often associated with epilepsy, especially when patients also have a stroke-like episode (SLE) <sup>[3]</sup>. Was there any evidence of epilepsy or SLEs in the index patient? Was the EEG normal?

The fifth point is that apart from the administration of steroids and plasma exchange because of the suspected immunologic pathophysiology of optic neuropathy, the treatment applied after obtaining the results of mtDNA analysis was not reported <sup>[1]</sup>. Since LHON has been reported to respond positively to high-dose coenzyme-Q <sup>[4]</sup>, we should know whether the index patient received this type of treatment or not. Did the patient receive other antioxidants, vitamins or supplements or a specific mitochondrial cocktail for the therapeutic management of MID? Knowing the therapy used is crucial as it could have a positive impact on visual disturbances <sup>[4]</sup> or even dystonia <sup>[5]</sup>.

To summarize, this interesting study has limitations that affect the results and their interpretation. Addressing these limitations could strengthen the conclusions and support the message of the study. All open questions need to be addressed before readers uncritically accept the conclusions of the study. Not only patients with LHON, but also patients with LHON plus should be treated with coenzyme-Q or a mitochondrial cocktail.

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