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Letter to Editor

ND3 variant m.10197 not necessarily causes reversible LHON

Josef Finsterer

Krankenanstalt Rudolfstiftung, Messerli Institute, Veterinary University of Vienna, Vienna, Austria, Europe

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***Corresponding author:** Josef Finsterer, Krankenanstalt Rudolfstiftung, Messerli Institute,Veterinary University of Vienna, Vienna, Austria, Europe. E-mail: fifigs1@yahoo.de, Tel. +43-1-71165-72085

Correspondence

We read with interest the article [1] about a 48 years old female with chronic alcoholism and Leber's hereditary optic neuropathy (LHON) due to the variant m.10197 in the ND3 gene who became symptomatic three months after discontinuation of hormone replacement therapy with etonogesterol 0.12mg/d and ethinyl estradiol 0.012mg/d [1]. Vision markedly improved after resuming hormone replacement therapy in addition to starting idebenone 300mg/d, vitamin C, and after reducing alcohol consumption [1]. We have the following comments and concerns.

Key words: optic atrophy; retinal ganglion cells; visually evoked potentials; electro-retrinography; mtDNA; oxidative phosphorylation; antioxidants.

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The main shortcoming of the study is that it remains unclear which of the four measures applied can be truly made responsible for visual recovery. Since all four measures were applied simultaneously, it cannot be decided if it was the hormones, idebenone, vitamin-C, or the reduction of alcohol consumption. It is also possible that it was a combination of two or more of these measures. Since visual impairment can also recover spontaneously in LHON patients [2], it is also conceivable that visual recovery occurred spontaneously and was only accidentally time-related to the initiation of the drugs applied. We should also know if the reported patient regularly received drugs other than estrogens, idebenone, and vitamin-C. Were steroids applied time-related to the application of estrogens, idebenone, and vitamin-C?

Concerning the genetic cause of LHON in the presented patient, we should be informed which base-pairs were exchanged by the mutation. Since the m.10197 variant has been most frequently reported together with the G>A substitution [3], we should know if the same substitution was also found in the presented patient. Though LHON mutations usually occur in the homoplasmic form, we should be informed about the amount of heteroplsamy concerning the detected variant. It is also worthwhile if the variant was inherited from the mother or not. Furthermore, the pathogenicity of the variant needs to be confirmed.

Since the patient was previously misdiagnosed as multiple sclerosis and received steroids without effect, we should be

informed upon which investigations the diagnosis “multiple sclerosis” was established. The diagnosis “multiple sclerosis” is particularly curious as the cerebral MRI of the index case was reported as having been normal [1]. Were latencies of visually evoked potential normal or prolonged and was the N75 / P100 amplitude normal or decreased?

Since LHON can be a multisystem disease not only affecting the retinal ganglion cells and the optic nerve [4] either already at onset or during the disease course, we should be informed if the patients was prospectively investigated for affection of organs other than the eyes. Particularly, we should know if the central nervous system, ears, endocrinological organs, heart, bone marrow, arteries, kidneys, or the peripheral nervous system were affected or not.

Overall, this interesting case could be more meaningful if the exact nature of the causative mutation and heteroplasmy rates were provided, if the effect of the applied drugs would be more extensively discussed, if the patient was prospectively investigated for multisystem disease, and if it was explained why the patient was initially diagnosed with optic neuritis.

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