

Opinion

LHON Patients Require Therapy, Family Investigations, and Long-Term Follow-Up

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COMMENT

In a recent article Bouzidi *et al.*, reported about two Moroccan pedigrees with Leber's hereditary optic neuropathy (LHON) both carrying the mtDNA variant m.11778G>A (pedigree-I and pedigree-II) (Bouzidi, A. *et al.*, 2020). We have the following comments.

The current standard treatment of LHON is idebenone (900mg/d) (Lyseng-Williamson, K. A. 2016). We should know if affected probands in either pedigree received the drug, in which dosage, for how long, and it should be reported if the compound had a beneficial effect or not.

Spontaneous remission of visual impairment has been occasionally reported in m.11778G>A carriers (Stone, E. M. *et al.*, 1992). We should know if the authors observed spontaneous improvements during disease trajectory in any of the affected probands in either pedigree. It would be also interesting to know for how long the affected patients underwent follow-up investigations after diagnosis.

In pedigree-I probands III.5 and III.6 entered into a consanguineous marriage (Bouzidi, A. *et al.*, 2020). At least one of their 3 children was affected (Bouzidi, A. *et al.*, 2020). We should know if both

parents carried the causative variant and if the son was more severely affected than other family members of this pedigree or not.

Since LHON is not only a disorder of the retinal ganglion cells, but manifests occasionally also in other organs, such as the central nervous system, ears, endocrinological organs, heart, bone-marrow, arteries, kidneys, and the peripheral nervous system (Finsterer, J., & Zarrouk-Mahjoub, S. 2016), we should know if LHON patients of either pedigree were prospectively investigated for clinical or subclinical multisystem involvement, which has prognostic implications.

A number of family members of pedigree-I carried the variant but did not become clinically manifest. It should be discussed if reduced penetrance in these probands was due to low heteroplasmy rate, high mtDNA copy number, or variable exposure to triggering agents, such as hormones, or tobacco.

In conclusion, the interesting study could be even more meaningful if supplementary data were provided and if unsolved issues were discussed.

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