

Letter to the Editor

Retinal Vascular Abnormalities in LHON Due To the *ND1* Variant M.3460G>A

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In a recent article, Asanad *et al.*, reported about a 22 years old male with chronic alcoholism and Leber's hereditary optic neuropathy (LHON) due to the variant m.3460 in the *ND1* gene (Asanad, S. *et al.*, 2019). The patient showed retinal, capillary microangiopathy on optical coherence tomography angiography (OCTA) in the temporal and nasal peripapillary microvasculature (Asanad, S., *et al.*, 2019). We have the following comments and concerns.

Missing in this report is the exact nucleotide exchange of the m.3460 variant (Asanad, S., *et al.*, 2019). The most common nucleotide exchange is the substitution G to A in the *ND1* gene (Yu-Wai-Man, P., & Chinnery, P.F. 2000). However, we should know if this was also the case in the presented patient, since other substitutions may be conceivable as well.

Though primary LHON mutations, including the m.3460G>A variant, usually occur in a homoplasmic or near homoplasmic distribution (Yu-Wai-Man, P., & Chinnery, P.F. 2000), some exceptions from this rule have been reported (Adam, M.P., *et al.*, 1993-2019). Thus, we should be informed about the heteroplasmy rates of the m.3460 variant in the index case and his mother. This is of particular interest since the mother was asymptomatic without an explanation. Since heteroplasmy rates may correlate with the severity of the phenotype (Sun, Y., *et al.*, 2018), a heteroplasmy rate in the mother lower than that of her son could explain the different phenotypes. Another explanation could be that the mother was not described as alcoholic but this needs to be definitively confirmed.

LHON is frequently a disorder not restricted to the retina and the optic nerve, but also involves other organs, such as the brain, ears, endocrine organs, heart, bone marrow, arteries, kidneys, or the peripheral nervous system, either already at onset of the disease or later during the disease course (Howes, T., *et al.*, 2008). We should be informed if the index case or his mother were prospectively investigated for multisystem disease, and which were the results.

It should be also more extensively discussed if the capillary dropout in the temporal and nasal region was interpreted as primary or secondary. Primary degeneration of the ganglion cells and its axons may result in secondary degeneration of the vascular supply. On the other hand, there is primary mitochondrial vasculopathy manifesting as macro- or microangiopathy including the retinal vasculature (Finsterer, J., & Zarrouk-Mahjoub, S. 2016).

Today, LHON is treated with the antioxidant idebenone (Finsterer, J., & Zarrouk-Mahjoub, S. 2016). Thus, we should be informed if the patient received idebenone, in which dosage, and over which time. We would like to know if this type of treatment was effective or caused any side effects.

Overall, this interesting case could be more meaningful if the heteroplasmy rate of the m.3460 variant was provided, if the nucleotides substituted were provided, if the patient and his mother were prospectively investigated for multisystem involvement, and if the discussion about primary or secondary

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capillary dropout of the temporal and nasal region was broadened.

REFERENCES

1. Asanad, S., Meer, E., Tian, J.J., Fantini, M., Nassisi, M., & Sadun, A.A. (2019). Leber's hereditary optic neuropathy: Severe vascular pathology in a severe primary mutation. *Intractable Rare Dis Res*;8:52-5.
2. Yu-Wai-Man, P., & Chinnery, P.F. (2000). Leber Hereditary Optic Neuropathy. Oct 26 [updated 2016 Jun 23]. In:
3. Adam, M.P., Ardinger, H.H., Pagon, R.A., Wallace, S.E., Bean, L.J.H., Stephens, K., & Amemiya, A. (1993-2019). Editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1174/>.
4. Sun, Y., Lei, K., Xu, Z.L., & Geng, Y. (2018). [A study of clinical and genetic characteristics of a Leber hereditary optic neuropathy family with the heteroplasmic m.14484T>C mutation]. *Zhonghua Yan Ke Za Zhi*;54:526-34.
5. Howes, T., Madden, C., Dasgupta, S., Saeed, S., & Das, V. (2008). Role of mitochondrial variation in maternally inherited diabetes and deafness syndrome. *J Laryngol Otol*;122:1249-52.
6. Finsterer, J., & Zarrouk-Mahjoub, S. (2016). Leber's hereditary optic neuropathy is multiorgan not mono-organ. *Clin Ophthalmol*;10:2187-90.
7. Finsterer, J., & Zarrouk-Mahjoub, S. (2016). Mitochondrial vasculopathy. *World J Cardiol*;8:333-9.
8. Jurkute, N., Harvey, J., & Yu-Wai-Man, P. (2019). Treatment strategies for Leber hereditary optic neuropathy. *Curr Opin Neurol*;32:99-104.