Innovative Journal of Medical and Health Science

IJMHS 10 (06), 916–917 (2020) ISSN (O) 2277:4939 | (P) 2589:9341

Electrophysiology of LHON eyes may strongly depend on genetics, drugs, and multisystem involvement

Josef Finsterer, MD, PhD[⋆,†]

Krankenanstalt Rudolfstiftung, Messerli Institute, Austria

DOI: https://doi.org/10.15520/ijmhs.v10i03.2811

Accepted 01/06/2020; Received 25/05/2020; Publish Online 06/06/2020

Reviewed By: Dr Daniel V.
Department: Medical

Key words: neurology–SARS-Cov2–cerebrospinal fluid–brain–meningitis

Letter to the Editor

With interest we read the article by Wang et al. about a retrospective study of 13 Chinese patients with Leber's hereditary optic neuropathy (LHON) by means of optical coherence tomography (OCT), visually-evoked potentials (VEPs), and pattern- / multifocal electroretinography (p/mfERGfERG) [1]. The authors found disc hyperemia vs. optic atrophy, normal vs. reduced retinal nerve fibre layer (RNFL) thickness, and mild, subnormal mfERG responses vs. reduced mfERG responses in the early respectively chronic stages of the disease. We have the following comments and concerns.

A major shortcoming of the study is that it had a retrospective design and that thus reproducibility of the results or inter-observer variabilities were not tested.

Though LHON mutations frequently occur in the homozygous form or reach nearly homozygosity, we should know the heteroplasmy rates of the mutations presented in table 1. Additionally, severity of the phenotype may depend on the mtDNA copy number. Knowing heteroplasmy rates and mtDNA copy number is crucial as these parameters may strongly determine disease severity and disease trajectory [2].

LHON may not only affect the retinal ganglion cells but may show also involvement of other organs, such as the brain, the ears, the endocrine organs, or the heart (LHON plus) [3]. We should know how many of the included patients had pure LHON and how many LHON plus. This is crucial as it may strongly influence the disease course and progression, as some of these manifestations are accessible to treatment.

We do not agree with the notion that LHON is one of the most common mitochondrial disorders (MIDs). LHON is rare compared to Leigh syndrome, MELAS, PEO, and particularly to the non-syndromic MIDs. Non-syndromic MIDs (MIMODS) are the most frequent as many MIDs do not fit to any of the syndromic phenotypes.

The authors claim that localised central macula dysfunction more severe in chronic as compared to acute cases is a novel finding. However, macula dysfunction has been previously reported in the acute stage of LHON [4].

In some countries, idebenone has been approved as a therapeutic agent for LHON "patients", We should know how many of the 13 patients received idebenone and if the inves-tigations were carried out under treatment or without treat-ment. In this respect we should know the entire medications the patients were taking at the time of the investigations. Knowing current drug therapy is crucial as some of them may influence test results significantly. We also should know how many of the included patients benefited from idebenone and in how many it was ineffective.

From some of the LHON mutations it is known that spontaneous recovery may occur [5]. We should know if particularly in group 2 (chronic stage) spontaneous remission was observed.

Fluorescence angiography and OCT angiography may be supplementary for diagnosing LHON [6]. We should know if there was also a difference between the acute and chronic stage with regards to these investigations.

Interestingly, table 1 lists a patient (patient 2) who carried two LHON mutations in one gene. We should know if this particular patient was heterozygous for either variant or if this was simply an error.

In summary, the above mentioned shortcomings of the study need to be addressed before drawing conclusion as provided.

⋆ Corresponding author.
† Email: fifigs1@yahoo.de

Table 1. CNS and PNS disease caused by SARS-CoV2

CNS/PNS	Abnormality	Evidence level	Reference
CNS	Meningitis/encephalitis	Case reports	[1,2,4]
	Ischemic stroke	Case reports, RCS	[1,7, Li et al. 2020]
	Seizures	Case reports, RCS	[1,3,5]
	Headache	Case reports, RCS	[1]
	Cerebral bleeding	RCS	[Li et al. 2020]
	Sinus venous thrombosis	RCS	[Li et al. 2020]
	Optic neuritis	Murine, felline model	[Seah et al. 2020]
	Reduced alertness	RCS	[1, Wang et al. 2028, Chen et al. 2020, Yin et al. 2020]
PNS	Guillain Barre syndrome	Case report	[8, Sedaghat et al. 2020, Toscano et al. 2020, Zhao et al. 2020]
	MFS	Case report	[9]
	Polyneuritis cranialis	Case report	[9]
	Hyposmia/hypogeusia	Case reports, RCS	[1,9]
	Neuralgia	RCS	[1]
	Myalgia	Case report, RCS	[1, Fiorino et al. 2020]

MFS: Miller-Fisher syndrome, RCS: retrospective cohort studies

REFERENCES

[1] Kousal B, Kolarova H, Meliska M, Bydzovsky J, Diblik P, Kulhanek J, et al. Peripapillary microcirculation in Leber hereditary optic neuropathy. Acta Ophthalmologica. 2019;97(1):e71–e76. Available from: https://dx.doi.org/10.1111/aos.13817.

[2] Emperador S, Vidal M, Hernández-Ainsa C, Ruiz-Ruiz C, Woods D, Morales-Becerra A, et al. The Decrease in Mitochondrial DNA Mutation Load Parallels Visual Recovery in a Leber Hereditary Optic Neuropathy Patient. Frontiers in Neuroscience. 2018;12:61–61. Available from: https://dx.doi.org/10.3389/fnins.2018.00061.

[3] Asanad S, Meer E, Fantini M, Borrelli E, Sadun AA. Leber's hereditary optic neuropathy: Shifting our attention to the macula. American Journal of Ophthalmology Case Reports. 2019;13:13–15. Available from: https://dx.doi.org/10.1016/j.ajoc.2018.11.010.

[4] Wang M, Guo H, Li S, Wang G, Long Y, Meng X, et al. Electrophysiological and Structural Changes in Chinese Patients with LHON. J Ophthalmol. 2020;2020:4734276–4734276.

[5] Acaroğlu G, Kansu T, Doğulu ÇF. Visual Recovery Patterns in Children with Leber's Hereditary Optic Neuropathy. International Ophthalmology. 2001;24(6):349–355. Available from: https://dx.doi.org/10.1023/b:inte.0000006855.48323.f1.

[6] Finsterer J, Zarrouk-Mahjoub S. Leber's hereditary optic neuropathy is multiorgan not mono-organ. Clin Ophthalmol. 2016;10:2187–2190.

AUTHOR BIOGRAPHY

Josef Finsterer, MD, PhD Krankenanstalt Rudolfstiftung, Messerli Institute, Austria