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Letter to Editor

What the eye tells about mitochondrial disorders

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Abstract:

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LETTER TO THE EDITOR

With interest we read the review article by Kisilevsky *et al.*, about the ophthalmologic involvement in mitochondrial disorders (MIDs) (Kisilevsky, E. *et al.*, 2019). The review has a number of limitations and raises concerns.

We do not agree that ophthalmologic involvement only occurs in syndromic MIDs, as indicated in table 1 (Kisilevsky, E. *et al.*, 2019). Since non-syndromic MIDs are more frequent than syndromic MIDs, ocular involvement is, most likely, also more frequent in non-syndromic MIDs. This issue needs to be discussed and highlighted as non-syndromic MIDs are more difficult to diagnose and require contributions from all professions being involved in the management of MID patients, including the ophthalmologist, for accurate detection. Thus, if the ophthalmologists detects abnormalities indicating a MID, other specialists should be contacted and involved.

We also do not agree that ophthalmologic involvement in syndromic MIDs only occurs in Leber's hereditary optic neuropathy (LHON), mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), chronic progressive external ophthalmoplegia (CPEO), Kearns-Sayre syndrome (KSS), and autosomal dominant optic atrophy (DOA) (Kisilevsky, E. *et al.*, 2019). Missing in this list is Leigh syndrome (Åkebrand, R. *et al.*, 2016; & Pesenti, F. *et al.*, 2018), maternally inherited deafness and diabetes (MIDD) (Qian, C. X. *et al.*, 2017; & Tripathy, K. *et al.*, 2020), autosomal recessive cardiomyopathy and ophthalmoplegia (ARCO) (Mojon, D. 2001), mitochondrial neuropathy, gastro-intestinal encephalopathy (MNGIE) syndrome (Mojon, D. 2001), myoclonic epilepsy with ragged-red fibers (MERRF) with retinal neuronal loss (Najjar, R. P. *et al.*, 2019), and particularly neuropathy, ataxia, and retinitis pigmentosa (NARP) syndrome (Lemoine, S. *et al.*, 2018).

Furthermore, ophthalmologic involvement in MIDs is broader than described in the review. Missing in the review is astigmatism, an ophthalmologic abnormality recognised in several MIDs (Åkebrand, R. *et al.*, 2016; & Pesenti, F. *et al.*, 2018). Other ophthalmologic abnormalities not addressed in the review are retinal pseudocysts, as has been reported in patients with (MIDD) (Tripathy, K. *et al.*, 2020), macular cystoid change, as has been described also in MIDD patients (Qian, C. X. *et al.*, 2017), hemianopia particularly in MELAS with a stroke-like lesion (SLL), the morphological equivalent of a stroke-like episode (SLE) on MRI, in an unilateral occipital distribution (Krysko, K. M., & Sundaram, A. N. 2017), and abnormal mitochondria in the ciliary body epithelium of LHON patients (Hayashi, N. *et al.*, 2000). Missing is also that SLEs may occur even in the optic nerve (Finsterer, J. 2019).

There may be involvement of the autonomic nerves in MIDs why these patients may also manifest with pupillary dysfunction or impaired secretion of the tear-fluid. It is conceivable that reduced production of

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tear fluid may result in sicca syndrome and that pupillary dysfunction may lead to photosensitivity. However, increased photosensitivity may be also due to epileptogenic activity in the occipital region in MIDs patients (Ohtsuka, Y. *et al.,* 1993).

Missing is that optic atrophy is a frequent manifestation of various syndromic and non-syndromic MIDs and not only occurs in LHON and DOA. Optic atrophy has been also reported in MERRF (Mancuso, M. *et al.,* 2013), Leigh syndrome (Maalej, M. *et al.,* 2018), MIDD (Taban, M. *et al.,* 2006), and non-syndromic MIDs (Del Dotto, V. *et al.,* 2019; & Wei, X. *et al.,* 2020).

We do not agree that the extra-ocular eye muscles belong to the visual pathway, as indicated in the abstract, and that involvement of the extra-ocular eye muscles has to be regarded as an ophthalmologic but rather as a neuromuscular abnormality.

Overall, this review is ambitious but has a number of limitations, which require discussion. The number and types of ophthalmologic abnormalities in MIDs are much broader than anticipated and more syndromic MIDs and particularly the non-syndromic MIDs need to be mentioned when ophthalmologic involvement is thematised.

Method If Reference Search

References were search via PubMed using appropriate search terms. Additionally, appropriate papers were taken from references lists in papers matching with the topic.

REFERENCES

1. Åkebrand, R., Andersson, S., Seyedi Honarvar, A. K., Sofou, K., Darin, N., Tulinius, M., & Grönlund, M. A. (2016). Ophthalmological characteristics in children with Leigh syndrome–A long-term follow-up. *Acta ophthalmologica*, *94*(6), 609-617.
2. Del Dotto, V., Ullah, F., Di Meo, I., Magini, P., Gusic, M., Maresca, A., ... & Macao, B. (2019). SSBP1 mutations cause mtDNA depletion underlying a complex optic atrophy disorder. *The Journal of clinical investigation*, *130*(1),108-125.
3. Finsterer, J. (2019). Stroke-like episode of the optic nerve. Can J Ophthalmol. pii: S0008-4182(18)31080-9. doi: 10.1016/j.jcjo.2018.10.019.
4. Hayashi, N., Geraghty, M. T., & Green, W. R. (2000). Ocular histopathologic study of a patient with the T 8993-G point mutation in Leigh's syndrome. *Ophthalmology*, *107*(7), 1397-1402.
5. Kisilevsky, E., Freund, P., & Margolin, E. (2019). Mitochondrial disorders and the eye. Surv Ophthalmol. pii: S0039-6257(19)30288-7. doi: 10.1016/j.survophthal.2019.11.001.
6. Krysko, K. M., & Sundaram, A. N. (2017). Recurrent alternate-sided homonymous hemianopia due to mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS): A case report. *Neuro-Ophthalmology*, *41*(1), 30-34.
7. Lemoine, S., Panaye, M., Rabeyrin, M., Errazuriz-Cerda, E., de Camaret, B. M., Petiot, P., ... & Guebre-Egziabher, F. (2018). Renal involvement in neuropathy, ataxia, retinitis pigmentosa (NARP) syndrome: a case report. *American Journal of Kidney Diseases*, *71*(5), 754-757.
8. Maalej, M., Kammoun, T., Alila-Fersi, O., Kharrat, M., Ammar, M., Felhi, R., ... & Fakhfakh, F. (2018). Cytochrome C oxydase deficiency: SURF1 gene investigation in patients with Leigh syndrome. *Biochemical and biophysical research communications*, *497*(4), 1043-1048.
9. Mancuso, M., Orsucci, D., Angelini, C., Bertini, E., Carelli, V., Comi, G. P., ... & Tonin, P. (2013). Phenotypic heterogeneity of the 8344A> G mtDNA "MERRF" mutation. *Neurology*, *80*(22), 2049-2054.
10. Mojon, D. (2001). Eye diseases in mitochondrial encephalomyopathies. *Therapeutische Umschau. Revue therapeutique*, *58*(1), 49-55.
11. Najjar, R. P., Reynier, P., Caignard, A., Procaccio, V., Amati-Bonneau, P., Mack, H., & Milea, D. (2019). Retinal Neuronal Loss in visually asymptomatic patients with myoclonic epilepsy with ragged-red fibers. *Journal of Neuro-Ophthalmology*, *39*(1), 18-22.
12. Ohtsuka, Y., Amano, R., Oka, E., & Ohtahara, S. (1993). Myoclonus epilepsy with ragged-red fibers: a clinical and electrophysiologic follow-up study on two sibling cases. *Journal of child neurology*, *8*(4), 366-372.
13. Pesenti, F., Doucet, E., Morin, C., & Falcao, M. (2018). Ophthalmic manifestations in patients with Leigh syndrome, French Canadian type. *Ophthalmic genetics*, *39*(6), 725-727.
14. Qian, C. X., Branham, K., Khan, N., Lundy, S. K., Heckenlively, J. R., & Jayasundera, T. (2017). Cystoid macular changes on optical coherence tomography in a patient with maternally inherited diabetes and deafness (MIDD)-associated macular dystrophy. *Ophthalmic genetics*, *38*(5), 467-472.
15. Taban, M., Cohen, B. H., Rothner, A. D., & Traboulsi, E. I. (2006). Association of optic nerve hypoplasia with mitochondrial cytopathies. *Journal of child neurology*, *21*(11), 956-960.
16. Tripathy, K., Sarma, B., & Mazumdar, S. (2020). Outer retinal tubulation and inner retinal pseudocysts in a patient with maternally inherited diabetes and deafness evaluated with optical coherence tomography angiogram. *Indian Journal of Ophthalmology*, *68*(1), 250-253.
17. Wei, X., Du, M., Li, D., Wen, S., Xie, J., Li, Y., Chen, A., Zhang, K., Xu, P., Jia, M., Wen, C., Zhou, H., Lyu, J., Yang, Y., & Fang, H. (2020). Mutations in FASTKD2 are associated with mitochondrial disease with multi-OXPHOS deficiency. Hum Mutat. doi: 10.1002/humu.23985