Headache, Cataract, and Unilateral Visual Loss: Unusual Features of DARS2 Variants in LBSL

Abstract:
Headache is an unusual phenotypic feature of LBSL. Since migraine-like headache is a frequent feature of MIDs. Unusual is also congenital cataract. Though congenital cataract has not been reported in association with LBSL, it is quite likely that it was a feature of the mitochondrial disorder (MID) since MIDs frequently go along with cataract in early ages.

Keywords: myasthenia, seronegativity, acetylcholin-receptor antibodies, depression, quality of life, immunosuppression.

CORRESPONDENCE

With interest we read the article by Cavusoglu et al., (2018) about a 12yo male with congenital cataract bilaterally, right-sided visual loss, recurrent frontal headache since age 9y; paraspasticity, T2-hyperintensities of the corporis and genu callosum, posterior limb of internal capsule, inferior cerebellar peduncles, and mesencephalic portion of nucleus-V (Cavusoğlu, D. et al., 2018). Spinal MRI revealed T2-hyperintensities of the corticospinal tract, the spino cerebellar tracts, and the dorsal columns (Cavusoğlu, D. et al., 2018). MRS revealed a lactate peak (Çavuşoğlu, D. et al., 2018). Based on these findings leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) was suspected and confirmed by documentation of the variant c.455G>T (p.C152F)(p.Cys152Phe/c.228-21_228-20delTTinsC in DARS2 (Çavuşoğlu, D. et al., 2018). We have the following comments and concerns.

Headache is an unusual phenotypic feature of LBSL. We should know how headache was classified (tension-type, migraine, migraine-like, cluster). Since migraine-like headache is a frequent feature of MIDs (Finsterer, J., & Zarrouk Mahjoub, S. 2018), we should know if headache was regarded as a feature of LBSL or a second trouble independent of LBSL. It should be also mentioned how headache was treated and if it was effective.

Unusual is also congenital cataract. Though congenital cataract has not been reported in association with LBSL, it is quite likely that it was a feature of the mitochondrial disorder (MID) since MIDs frequently go along with cataract in early ages (Liao, S. L. et al., 2003; & Choi, B. O. et al., 2008). Cataract has been also reported in patients carrying IARS2 mutations (Vona, B. et al., 2018). As DARS2, IARS2 encodes a tRNA-synthetase required for charging of tRNAs with their cognate amino acid for translation.

Missing in this report is an extensive family history and genetic work-up of first-degree relatives. Thus, it remains unclear if the DARS2 variant in the index case occurred spontaneously or was inherited. We should know if any of the first-degree relatives was clinically affected or not.

Bladder dysfunction in the form of a spastic bladder is an occasional feature of LBSL (Cheng, F. B. et al., 2013). We should know if the index patient presented with bladder dysfunction and if steroids were beneficial as has been previously reported (Vona, B. et al., 2018).

Some of the LBSL patients present with double vision, spontaneous nystagmus, cognitive impairment (Cheng, F. B. et al., 2013), or developmental delay (Yahia, A. et al., 2018). We should know if any of these features were also found in the index patient or not.

Extensive involvement of the spinal cord may not only occur in LBSL but has been also reported in other MIDs due to impaired aminotransferase (Toldo, I. et al., 2018), such as ISCA2.
Unexplained remains visual loss of the right eye. We should know if visual loss was due to complications from cataract surgery, affection of the optic nerve, or affection of the post-chiasmatic visual pathways. We should be informed about ophthalmologic investigations and the results of the visually-evoked potentials.

Overall, this interesting case could profit from resolution of some shortcomings, such as more detailed description of headache and congenital cataract, provision of an extensive family history, assessment of bladder function, comparison with rare features previously reported, and explanation of the unilateral visual loss.

REFERENCES