Leigh Syndrome Should Not Be Diagnosed Exclusively Upon Cerebral MRI

Abstract:

Keywords: mtDNA, mitochondrion, Leigh syndrome, brain, imaging, MRI.

Letter to the Editor

We read with interest the article by Alves et al., 2020 about a retrospective study of 53 pediatric patients with Leigh syndrome of whom 125 cerebral MRIs were evaluated for imaging characteristics (Alves, C. A. P. F. et al., 2020). It was concluded that the study may help to identify imaging biomarkers for diagnosing Leigh syndrome (Alves, C. A. P. F. et al., 2020). We have the following concerns.

Despite pretending that all included patients fulfilled the diagnostic criteria for Leigh syndrome (Alves, C. A. P. F. et al., 2020), it is not mentioned which diagnostic criteria for Leigh syndrome respectively MELAS were applied. We should know if Leigh syndrome was diagnosed according to the Rahman criteria and MELAS according to the Japanese respectively Hirano criteria.

Though stroke-like episodes (SLEs) have been occasionally reported in Leigh syndrome, an amount of 34% (table 2), is excessively high. Stroke-like lesions (SLLs), the MRI equivalent of a SLE, typically progress in size and density, do not exclusively originate from the cortex, and are not restricted to a vascular territory (Hongo, Y. et al., 2019). SLLs cannot be diagnosed solely upon hyperintensities on T2/FLAIR and DWI but require confirmation by hyperperfusion on PWI/ASL and reduced oxygen-extraction on OEF-MRI. Furthermore, parenchymal/CSF lactate needs to be elevated. The high frequency of SLEs may result from misdiagnosing T2-/DWI hyperintensities as SLLs.

Several cerebral imaging abnormalities of Leigh syndrome have not been discussed. Not mentioned was basal ganglia calcification, recently described in a 9yo male with Leigh syndrome due to a ATP6 variant (Angural, A. et al., 2019).

Not described either was global cerebral atrophy. In a 7 months-old female with Leigh syndrome due to a variant in IARS2, global cerebral atrophy with infantile spasms was the dominant feature (Takezawa, Y. et al., 2018).

Since 57% had short stature, we should know if this was due to pituitary insufficiency or developmental delay. How often was an empty sella syndrome with hypopituitarism found?

The authors should explain the discrepancy between substantia nigra lesions in 75% of patients but dystonia/Parkinsonism in only 66% (Alves, C. A. P. F. et al., 2020). Since dystonia can be the major manifestation of ATP6 variant (Angural, A. et al., 2019).
Leigh-syndrome (Lera, G. et al., 1994) we should know how many had indeed dystonia and how many Parkinsonism, confirmed by SPECT.

Was hemiparesis in 15% of the patients due to contralateral, supratentorial or infratentorial SLLs, due to ischemic stroke, or due to a cervical spinal cord lesion?

The discrepancy between 34% SLEs in table 2 and 18.8% in the text requires clarification.

Overall, cerebral morphological abnormalities in Leigh-syndrome are more widespread than anticipated. There is a strong need to apply not only multimodal MRI but also other imaging techniques. Final conclusions cannot be drawn before discrepancies and shortcomings mentioned are solved.

REFERENCES