Letter to the Editor

Leigh Syndrome Is Geno- And Pheno-Typically Heterogeneous

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With interest we read the article by Baskaran, D., & Hussain, N. (2020) about a 22 months-old female with Leigh-syndrome (LS) due to a variant in SURF1, phenotypically manifesting with classical features of the syndrome (Baskaran, D., & Hussain, N. 2020). We have the following comments and concerns.

A shortcoming of the study is that the causative SURF1 variant was not specified. Additionally, information if the variant occurred in the homo- or heterozygous form is missing.

Furthermore, we do not agree that LS is only caused by variants in genes encoding proteins responsible for the pyruvate-dehydrogenase complex, cytochrome-c oxidase, adenosine-triphosphate synthase subunit-6, or subunits of mitochondrial complexes (Baskaran, D., & Hussain, N. 2020). The spectrum of mutated genes causing LS is broader than mentioned in the introduction. Currently, mutations in about 75 different genes have been linked to LS (Fecek, C., & Samanta, D. 2020).

Missing in the report is the family history. Since LS due to SURF1 mutations is usually transmitted via an autosomal recessive or dominant trait (Danis, D. et al., 2018), we should know if other first-degree relatives were clinically affected or carried the variant. Of particular interest is the clinical presentation and genetic status of the mother and father of the index patient.

Unfortunately, no details about seizure type, seizure frequency, type of anti-seizure drug (ASD) treatment, compliance, and effect or side effects of the AED treatment have been provided. Knowing the exact AED treatment is crucial as it may determine the outcome of these patients.

LS is usually a multisystem disease, in which not only the brain but also the eyes, ears, endocrine organs, heart, the gastro-intestinal tract, the kidney, the bones, or the skin can be affected. The index patient obviously manifested in the brain (epilepsy, hypotonia, ataxia, failure-to-thrive), the endocrine system (hirsutismus), gastro-intestinal tract (vomiting, diarrhea, poor weight gain), the muscle (myopathy of limb and extra-ocular muscles), and other systems (dysmorphism, developmental delay). We should know if the patient was prospectively investigated for subclinical or mild involvement of other organs, such as the heart or the kidneys. Of particular interest is cardiac involvement since it may strongly co-determine the outcome of these patients (Jaksch, M. et al., 2001).

Overall, the case report presented by Baskaran et al., has a number of shortcomings, which should be met before drawing final conclusions. We should know the mutation load in the index patient, the genetic status of the parents or other first-degree relatives, and the results of prospective investigations of the heart. More information about epilepsy in the index patient is warranted.
REFERENCES


