neurogenetics (2019) 20:53–54
https://doi.org/10.1007/s10048-019-00566-5

LETTER TO EDITOR

PTCD3 mutations cause Leigh-like rather than Leigh syndrome

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Received: 7 January 2019 / Accepted: 23 January 2019 / Published online: 31 January 2019

Letter to the Editor:

With interest, we read the article by Borna et al. about a newborn female with intrauterine growth retardation, respiratory insufficiency, rigidity, myoclonus, psychomotor retardation, hypoacusis, optic atrophy, and symmetric cerebral T2-hyperintense lesions of the thalamus, caudate nucleus, putamen, cerebellar peduncles, and the ventral medulla, suggesting Leigh syndrome [1]. Upon exome sequencing, a causative compound heterozygous mutation in the *PTCD3* gene was detected [1]. We have the following comments and concerns.

We do not agree that the patient presented with Leigh syndrome. In addition to the typical symmetric, necrotic cerebral lesions, Leigh syndrome is clinically characterized by epilepsy, ataxia, hypotonia, failure to thrive, and lactic acidosis [2]. Contrary to hypotonia, the patient presented with rigidity. We should be informed if the extra-pyramidal manifestations were attributable to affection of the basal ganglia. Since the cerebellum was affected, we can expect ataxia. We should know if any of the classical features of Leigh syndrome were found in the index case.

The patient developed myoclonus shortly after cesarean section [1]. Since Leigh syndrome is frequently associated with epilepsy [3], we should know if myoclonus in the index case was associated with abnormal EEG recordings, such as generalized spikes, spike waves, or poly-spike waves. Myoclonus in mitochondrial disorders (MIDs) may not only be due to epilepsy, but may also be due to cerebellar or spinal cord dysfunction [4]. We should also be informed how myoclonus was treated, if myoclonus resolved upon clonazepam, piracetam, levetiracetam, topiramate, or zonisamide, antiepileptic drugs (AEDs) proposed for the treatment of myoclonic epilepsy in MID patients [personal communication].

According to figure 1, the shape of the head is asymmetric and skewed particularly on the left side with the impression that cerebral atrophy was asymmetric being more pronounced on the left side. Since Leigh syndrome may go along with dysmorphism [5], we should be informed if the index case presented with facial or other dysmorphism.

Growth retardation in patients with a MID is frequently due to involvement of the endocrine organs, including the pituitary gland. Thus, it should be discussed if the patient was systematically investigated for impairment of the pituitary, thyroid, adrenal, or parathyroid glands, the gonads, and the pancreas. In case serum level of the somatotropic hormone was reduced, it should be systematically looked for empty sella or a pituitary adenoma.

The elder sister of the index case carried the variant of the mother, why we should be informed if the elder sister manifested clinically with any of the typical phenotypic features of a MID.

Only scarce information about the treatment of the patient is provided, why we should be informed if antioxidants, vitamins, cofactors, or the ketogenic diet were beneficial. It is unclear and not comprehensible why the patient received clonazepam at 13 months of age for bronchitis [1].

Altogether, this study could be more meaningful if the clinical presentation of the index case and her first degree relatives would be more comprehensive, if the cause of myoclonus was clarified, and if the phenotype would be reclassified as Leigh-like syndrome.

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