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Phenotypic, Biochemical, and Genetic Spectrum of Patients with Leigh-Syndrome

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LETTER TO THE EDITOR

In a recen article, Lee et al. reported about the phenotype, genotype, therapy, and outcome of 39 patients with Leigh-syndrome (LS) [1]. In 32 of the patients a complex-I defect was identified and 11 patients carried a mtDNA mutation [1]. The outcome ranged widely but was worse among those with early-onset LS [1]. We have the following comments and concerns.

Three patients with stroke-like episodes (SLEs) were reported [1]. In which cerebral territory did they occur? Were they preceded or accompanied by seizures? Did the clinical manifestations of the SLE completely resolve? Which type of treatment was applied? L-arginine, citrulline, or steroids? Were there residual lesions on cerebral MRI? Did these patients receive antiepileptic drugs? How many required a long-term antiepileptic drug treatment and was the prognosis of those with epilepsy (n=12) worse than of those without epilepsy (n=27)?

Three children had hemiparesis [1]. Which was the cause of hemiparesis? Was it due to a SLE, ischemic stroke, intracerebral bleeding, seizures, migraine, or mass lesion? Were these the 3 patients with ischemic lesions on cerebral MRI at follow-up? Was hemiparesis accompanied by spasticity or hypotonia? Did any of the included patients have a history of migraine?

One patient with cranial nerve involvement was reported [1]. Which cranial nerve was involved? Was cranial nerve involvement unilateral or bilateral? Which was the outcome of cranial nerve affection?

Though LS is frequently associated with failure to thrive, only 8% presented with this feature and only 12% had developed dysphagia. How to explain the low rate of dysphagia at diagnosis? Did any of the patients require tube feeding? How many required a percutaneous endoscopic gastrostomy (PEG)?

Hypertrophic cardiomyopathy (hCMP) is the type of CMP most frequently reported in LS patients [2,3]. Interestingly, 5 patients had CMP [1]. Which type of CMP was detected, dilated CMP, hCMP, restrictive CMP, arrhythmogenic right ventricular dysplasia, non-compaction, or Takotsubo syndrome? How many of them developed heart failure or ventricular arrhythmias?

Affection of the respiratory muscles requiring ventilatory support can be a phenotypic feature of MIDs [4]. Did the two patients with apnea require ventilatory support? Which was the cause of respiratory insufficiency? Central or muscular or was it due to heart failure from CMP or pulmonary disease?

Therapeutic options for LS are limited to symptomatic and supportive measures [5]. Which type of treatment for LS was administered? Did the patients receive cocktails comprising vitamins, cofactors, and anti-oxidants? Did those who did not progress during follow-up (n=10) receive another therapy compared to those with a progressive course (n=28)?

Was there a correlation between the severity of clinical features and the extension of abnormalities on MRI? Did all those who progressed over the 4 years of mean follow-up also progress on cerebral MRI?

Overall, this interesting study provides new insights into the phenotypic, biochemical and genetic spectrum of LS. It could be further improved by provision of more detailed data as outlined above. The prognosis of LS patients seems to be more favourable than so far anticipated.

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