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Correspondence

Genotype/Phenotype Issues of *CARS2* Variants

Letter to the Editor:

I read with interest the article by Samanta et al. about a 13-year-old girl with a *CARS2* variant manifesting with epilepsy, intellectual decline, autism spectrum disorder, global cerebral atrophy, cerebral ischemia of the left hemisphere, and gastric tube dependence.[1] She developed supra-refractory status epilepticus despite phenobarbital, levetiracetam, valproic acid, phosphenytoin, and benzodiazepines. Occipital lobectomy was only temporarily effective. I offer a few comments and concerns.

Since the patient developed supra-refractory status epilepticus and since there are individuals with mitochondrial epilepsy who exclusively responded to a ketogenic diet,[2] it would be interesting to know whether the diet was considered and whether it was effective. Another therapeutic option for seizures in mitochondrial disorders is the application of steroids.[3] Steroids can help to repair the blood-brain barrier, which may be damaged by glycolytic by-products resulting from seizure activity.[3] Damage of the blood-brain barrier may be responsible for the vasogenic edema typical of the stroke-like episodes.

A second point for discussion is the nature of the left-hemispheric lesion on magnetic resonance imaging.[1] It would be interesting to know whether the diffusion-weighted hyperintense lesion hyperintense, isointense, or hypointense on apparent diffusion coefficient maps, whether there was hyper- or hypoperfusion of the damaged areas on perfusion-weighted imaging, and whether the lesion showed dynamic progression or regression over time on follow-up magnetic resonance imagings. If the lesion is considered a stroke-like lesion and not as ischemic, progression or regression should have been documented and L-arginine should have been tried in addition to a non–mitochondrion-toxic antiepileptic regimen. At least in single cases, L-arginine had a beneficial effect on epilepsy.[4]

If the lesion was truly ischemic, what was the cause? Was the stroke regarded as atherothrombotic or embolic? The cardiovascular risk profile and the secondary prophylaxis should be specified. Supposing it was embolic, we should know if there was atrial fibrillation, severe heart failure, noncompaction, or macroangiopathy of the extracerebral arteries. Since the myocardium is frequently affected in mitochondrial disorder,[5] it would be useful to know the result of the cardiological evaluation. This is crucial with regard to the outcome, since antiarrhythmic treatment, heart failure therapy, or anticoagulation are options. The report would profit from discussing alternative therapeutic options for mitochondrial epilepsy, the nature of the cerebral lesions, and the results of the cardiologic investigations.

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