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SCIENTIFIC LETTER

Drug Resistant Epilepsy (DRE) Secondary to 3-Hydroxy Acyl-CoA Dehydrogenase Deficiency (HADH) in Siblings

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To the Editor: Biallelic mutations in the *HADH* gene cause 3 alpha hydroxy acyl CoA dehydrogenase deficiency (HADH deficiency) [1]. We are reporting sibling pair presenting with refractory seizures.

A 13-y-old girl born to consanguineous parentage presented with seizures beginning from the age of 3 mo, delayed attainment of milestones, and ataxia. The seizures precipitated by fasting were refractory requiring multiple antiseizure medications (ASMs). Her younger sibling had seizures noted since the age of 3 d of life, progressed to clinical presentation as the elder sibling. On examination, weight: 29.4 kg (-2 to -3SD), height: 144 cm (-2 to -3SD) head circumference: 48.5 cm (<-3SD), spastic quadriparesis, and cerebellar signs were noted. Hypoglycaemia was documented in both siblings during episodes of seizures on few occasions. Tandem mass spectrometry showed elevated 3 hydroxy butyryl carnitine: 0.66 (Normal: 0-0.5). Urine for organic acids revealed mild elevation in lactate (24.58 mg/dl; 4.5–19.8 mg/dl), normal ammonia and blood gases with absence of urinary ketones. EEG revealed multifocal sharp waves; MRI of the brain was normal. Whole exome sequencing showed a novel homozygous frameshift deletion c.165_168delGGTA, p.Val56fs*41 in exon-2 of *HADH* gene. With diet modification of avoidance of fasting, having frequent meals as well as corn starch, there was significant decrease in frequency of seizures.

Mutations in the *HADH* gene present with hypoketotic hypoglycemia, failure to thrive, tone abnormalities, cardiac and hepatic involvement [2, 3]. Hypoglycemia in HADH deficiency is caused due to impaired beta oxidation and hyperinsulinism caused by loss of inhibitory effect of HADH on Glutamate dehydrogenase (GDH) [4]. Management involves avoiding episodes of fasting and stress. Treatment with diazoxide which reduces insulin secretion has shown variable response [4]. Awareness of this condition prevents antiseizures medications' side-effects in addition to specific management of this condition and for genetic counselling.

Declarations

Conflict of Interest None.

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