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Editorial

Inherited metabolic disorders presenting with epilepsy in childhood

Saadet Mercimek-Mahmutoglu*
Division of Clinical and Metabolic Genetics, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Epilepsy is one of the most common neurological disorders in childhood and its prevalence is 0.5–1%. About 30% of all childhood epilepsies are intractable to anti-epileptic medications. The most severe forms usually begin in infancy associated with global developmental delay or cognitive dysfunction, defined as epileptic encephalopathy. Epileptic encephalopathy caused by an inherited metabolic disorder is intractable to anti-epileptic medications, unless it is treated with a disease specific diet, vitamin, amino acid or cofactor supplementations.

Inherited metabolic disorders are individually rare, but their estimated collective prevalence is 1:1000. There are more than 100 inherited metabolic disorders presenting with epilepsy including disorders of amino acid metabolism, vitamin/cofactor responsive disorders, disorders of carbohydrate metabolism, disorders of energy metabolism, lysosomal storage disorder, peroxisomal disorders, mitochondrial disorders and primary neurotransmitter defects. The seizure type can vary from myoclonic, generalized tonic-clonic, generalized tonic, absences, infantile spasms, atonic and complex partial seizures. In one patient with one of the inherited metabolic disorders, there can be multiple seizure types in combination. The age of seizure onset is usually neonatal or early infantile period. According to age of seizure onset, the examples of the inherited metabolic disorders include: (1) neonatal period: e.g. pyridoxine-dependent epilepsy, pyridoxalphosphate dependent epilepsy, molybdenum cofactor deficiency, non-ketotic hyperglycinemia; (2) infantile period: e.g. glucose transporter 1 deficiency, mitochondrial disorders, neuronal ceroid lipofuscinosis, biotinidase deficiency, Menkes disease and congenital disorders of glycosylation and (3) early childhood: e.g. creatine deficiency disorders, lysosomal storage disorders. In various inherited metabolic disorders, disease specific therapy is successful to achieve good seizure control and improve long-term neurodevelopmental outcome.

Intractable epilepsy with global developmental delay or history of developmental regression warrants detailed metabolic investigations for the possibility of an underlying inherited metabolic disorder. Identification of a treatable underlying inherited metabolic disorder is crucial for the initiation of an effective treatment. For the inherited metabolic disorders with no specific treatment, confirmation of the diagnosis in the index case will enable prenatal diagnosis for the future pregnancies.

*Corresponding author: Dr. Saadet Mercimek-Mahmutoglu, Division of Clinical and Metabolic Genetics, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, 525 University Avenue, Suite 935, 9th Floor, Toronto, ON, M5 G 1X8, Canada. Tel.: +1 416 813 7654/Ext 201480; Fax: +1 416 813 5345; E-mail: saadet.mahmutoglu@sickkids.ca.