L-2-Hydroxyglutaric Aciduria

Alternative Names
L-2-Hydroxyglutaric acidemia
L-2-Hydroxyglutaric Acidemia
L-2-hydroxyglutaricaciduria
D-2-hydroxyglutaricaciduria
L-2-HGA

WHO International Classification of Diseases
Endocrine, nutritional and metabolic diseases

OMIM Number
236792

Mode of Inheritance
Autosomal recessive

Gene Map Locus
14q22.1

Description
Organic acidurias are a group of inherited metabolic disorders characterized by increased urinary excretion of organic acids. These disorders may present with episodes of severe metabolic decompensation or exclusively with severe neurologic disease. L-2-hydroxyglutaricacidemia is a rare autosomal recessively inherited disorder from the latter category. The clinical phenotype is variable. Affected individuals show slowly progressive neurodegenerative disorder with cerebellar ataxia and mental retardation. Other finding such as pyramidal and extrapyramidal signs, seizures and macrocephaly can be observed. The MRI shows a spongiform encephalopathy and cerebellar atrophy. Laboratory finding include significant elevation of plasmatic and urinary levels of L2-hydroxyglutaric acid and lysine in plasma, urine, and cerebrospinal fluid (CSF), as well as elevated lysine in plasma and CSF.

Molecular Genetics
Identification of a gene for L-2-hydroxyglutaricacidemia using homozygosity mapping was recently made. Nine homozygous mutations including three missense mutations, two nonsense mutations, two splice site mutations and two deletions were identified in the a gene named Duranin, localized on chromosome 14q22.1. The gene encodes for a putative mitochondrial protein with homology to FAD-dependent oxidoreductases.

Epidemiology in the Arab World

Morocco
Duran et al. (1980) reported a 5-year-old boy of Moroccan (Berber) origin who had nonspecific mental and motor delay and growth deficiency. Tests indicated that he had a solitary, large, and persistent increase of L-2-hydroxyglutaric acid in the urine (3.3-7.6 mmol/l). The 2-hydroxyglutaric acid was found to have the L-configuration, as analyzed by capillary gas chromatography of the O-acetylated dl-(−)-2-butyl ester derivative. In addition, the child also presented with dystrophy. The EEG was not well differentiated and resembled that observed in 2-year-old children. Thchild had a severe anemia, but reacted well to iron supplements.

Tunisia
Larnaout et al. (1994) described three brothers from Tunisia, born to a consanguineous family, with a progressive neurological disorder associated with L-2-hydroxyglutaric aciduria. The oldest patient died at the age of 30 years. Pathological examination of his brain showed bilateral and diffuse spongiosis with notable cystic cavitations of the cerebral white matter without abnormal storage in neurons and glial cells.

References
Duran M, Kamerling JP, Bakker HD, van Gennip AH, Wadman SK. L-2-Hydroxyglutaric aciduria: an inborn error of

Contributors
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