

CASE REPORT

L-2-Hydroxyglutaric Aciduria is a Diagnostic Indicator of Leukodystrophy: A Case Report

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Abstract

L-2-Hydroxyglutaric aciduria is a rare autosomal recessive inherited neurometabolic disorder. It is characterized by slow progressive neurological dysfunction with cerebellar ataxia, pyramidal and extrapyramidal signs, intellectual decline, and seizures. Herein, we report a case of a 7-year-old boy from Tehran whose symptoms and signs indicated leukoencephalopathy with macrocephaly and motor delay.

Keywords: Regression; leukodystrophy; L-2-Hydroxyglutaric aciduria

Introduction

L-2-Hydroxyglutaric aciduria is a rare autosomal recessive inherited neurometabolic disorder. Since its first description by Duran in 1980, L-2-hydroxyglutaric aciduria has been reported in less than 100 patients (1). It is characterized by slow progressive neurological dysfunction with cerebellar ataxia, pyramidal and extrapyramidal signs, intellectual decline and seizures (2). White matter changes observed on magnetic resonance imaging (MRI) were highly suggestive of this disorder (1, 2). The condition is diagnosed by screening urine, blood, and/or cerebrospinal fluid for L-2-hydroxyglutaric acid (2, 3). Herein, we report a case of a 7-year-old boy whose symptoms and signs indicated leukoencephalopathy with macrocephaly and motor delay. The patient was diagnosed with L-2-hydroxyglutaric aciduria on the basis of urinalysis using gas chromatography and mass spectrometry (GC/MS).

Case Report

The patient was a 7-year-old boy from Tehran who had an unremarkable perinatal and postnatal history. The circumference of his head at birth was 35 cm. His parents were healthy and first cousins. The growth and development of the patient was almost normal during the first 5 years of his life. Thereafter, the parents noticed the child's diminished ability to stand up from a seated position. The child also showed a disturbed ability to paint. After a few months, he could not walk and run normally and fell down frequently. He had no seizures or abnormal movements such as tremor or dystonia. At presentation, the circumference of his head was 57 cm. He showed ataxic gait and a tendency to bend forward. He developed tremors during writing and painting. Neurologic examination revealed hyperreflexia in the upper and lower limbs, mild spasticity, and decreased muscle force. Although he showed obvious deterioration of motor function, his cognitive and linguistic skills were acceptable, and he had normal visual function.

His routine laboratory test findings were unremarkable, and the results of

electrophysiological study (electromyography [EMG]/ nerve conduction velocity [NCV] test) were normal. MRI of the brain revealed diffuse white matter changes that indicated leukodystrophy (Figure 1). Routine metabolic study revealed no remarkable findings; however, urinalysis for organic acids by using GC/MS revealed very high levels of L-2-hydroxyglutaric acid, indicating deficiency of 2-hydroxyglutarate dehydrogenase. On the basis of these findings, he was diagnosed with L-2-hydroxyglutaric aciduria.

Discussion

L-2-Hydroxyglutaric aciduria is a rare autosomal recessive inherited neurometabolic disorder (1). It is caused by mutations in a gene present on chromosome 14q22.1 that encodes for L-2-hydroxyglutarate dehydrogenase (1, 2). This flavin adenine dinucleotide (FAD)-linked mitochondrial enzyme catalyzes the irreversible conversion of L-2-hydroxyglutarate to alpha-ketoglutarate. In patients with L-2-hydroxyglutaric aciduria, L-2-hydroxyglutaric acid accumulates and is toxic for brain tissue. Accumulation of this acid and its subsequent effects lead to the development of leukoencephalopathy and increases the susceptibility to develop brain tumors (2, 3). L-2-hydroxyglutaric aciduria is commonly diagnosed in infancy and childhood (4). It is characterized by slow progressive neurological dysfunction, gait disturbance, ataxia, seizures, macrocephaly, and abnormal findings on MRI (2, 3, 5). In fact, macrocephaly, cerebellar signs, and MRI abnormalities that suggesting leukodystrophy, are diagnostic clues. Urinalysis for organic acids is necessary because organic aciduria is a probable cause of leukodystrophy (6). Recently, the gene responsible for this disorder has been mapped to chromosome 14q22.1 (7, 8). We suggest that urinalysis using GC/MS should be performed in patients with macrocephaly and leukoencephalopathy (8).

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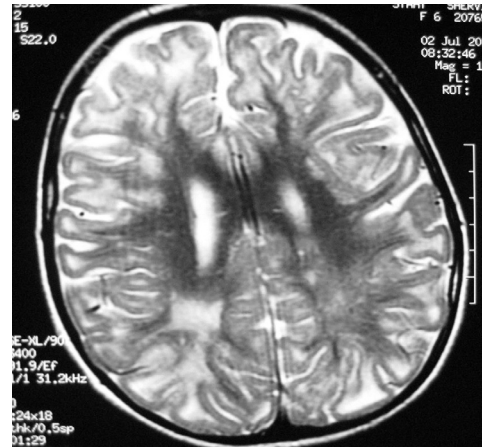


Fig 1. Axial T2-Weighted Magnetic Resonance Imaging (MRI) Scan of the Patient Showing Subcortical and Deep White Matter Changes

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