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Case Report

Another Differential Diagnosis of Leukoencephalopathy in a Young Adult: 3-Hydroxy-3-Methylglutaryl- CoA Lyase Deficiency

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Abstract

3-Hydroxy-3-methylglutaryl-CoA lyase deficiency (OMIM 246450), an inborn error of leucine degradation, characterized by recurrent episodes of hypoglycemia, metabolic acidosis, and, often, hyperammonemia, but no ketosis. We report on an 18-year-old caucasian young man with seizures, recurrent metabolic disturbances, and severe leukoencephalopathy. The diagnosis was made by analysis of amino acids in urine and serum and was confirmed by demonstration of the deficient enzyme in cultured skin fibroblasts. The patient improved clinically on oral L-carnitine substitution. This treatable condition can remain unrecognized in adults and should be considered a potential cause of leukoencephalopathy.

Keywords: *Leucine Inborn Error; Leukoencephalopathy; L-Carnitine Treatment*

Introduction

3-Hydroxy-3-methylglutaryl-CoA lyase deficiency (OMIM 246450), is a rare genetic disease of leucine metabolism (Figure 1) with recessive autosomal hereditary pattern. This inborn disease is characterized by recurrent episodes of hypoglycemia, metabolic acidosis, and, often, hyperammonemia, but no ketosis [1].

Case Report

An 18-year-old white man was referred for investigation, bringing a brain MRI showing periventricular white matter lesions without enhancing (Figure 2). The patient had mild mental retardation, recurrent episodes of non ketotic hypoglycemia and seizures since birth.

Metabolic acidosis, hyperammonemia associated with elevation of serum liver enzyme levels were found. The urinary organic acid analysis showed increased amounts of 3-Hydroxy-3-methyl-glutaryl CoA, 3-Methylglutaconic, 3-Methylglutaric and 3-Hydroxy-isovaleric acid. The diagnosis was confirmed by demonstration of the deficient enzyme in cultured skin fibroblasts and genetic study. (E37X homozygous HMGCL gene mutation on chromosome 1p36.1). The patient obtained clinical improvement with oral L-carnitine supplementation.

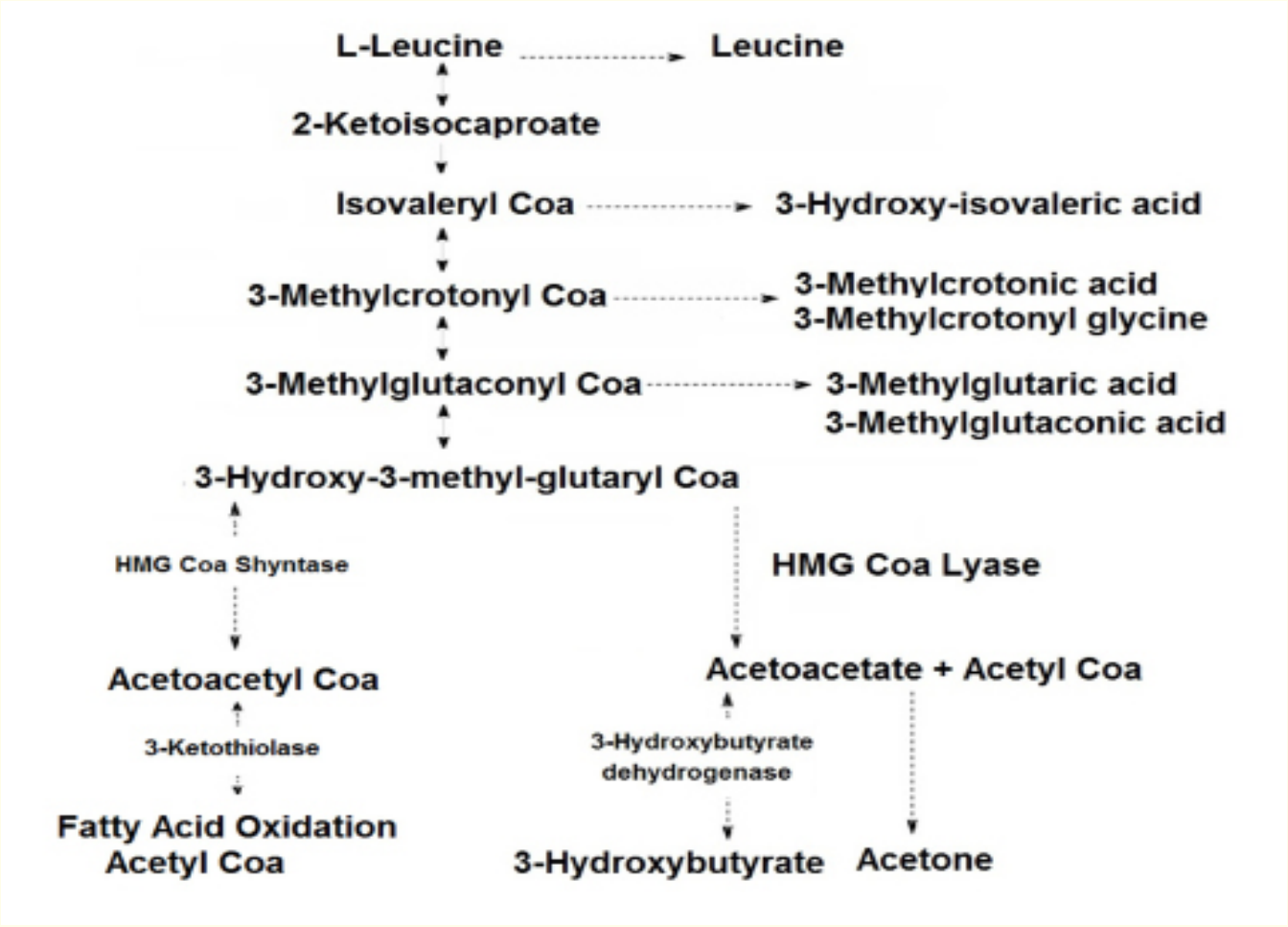

Figure 1: *Leucine metabolism.*

Discussion

3-Hydroxy-3-methylglutaryl-CoA lyase is mitochondrial enzyme that catalyzes the cleavage of 3-Hydroxy-3-methylglutaryl-CoA to form acetyl-CoA and acetoacetate. Hypoglycemia may occur due to failure to produce ketones and free fatty acids for oxidation. This enzyme deficiency also leads to an excessive production of acyl-carnitine which in turn is excreted by renal tract. Dietary supplementation with L-carnitine may avoid hypoglycemia. This is a treatable disease, but permanent neurological consequences can occur following hypoglycemic episodes in undiagnosed patients [2,3].

Early diagnosis and treatment with L-carnitine are important in the prevention of episodes of hypoglycemia and in secondary permanent neurological impairment.

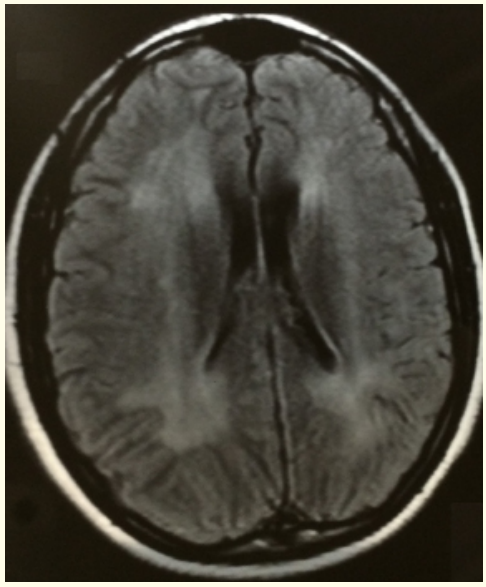

Figure 2: *Brain FLAIR-MRI- White matter lesions without enhancing.*

Conclusion

The presentation of this case warns to the possibility of 3-hydroxy-3-methylglutaryl-coa lyase deficiency in the differential diagnosis of young patients with leukoencephalopathy in young adults.

Author's Contribution

These authors contributed equally to the manuscript.

Author Disclosures

The authors have no conflicts of interest to declare.

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