

Glutaric aciduria type 1: diagnosis and neuroimaging findings of this neurometabolic disorder in an Iranian pediatric case series

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Background: Glutaric aciduria type 1 is a rare congenital neurometabolic disorder with autosomal recessive inheritance. This disorder is caused by a defect in glutaryl-CoA dehydrogenase enzyme and presents with hypotonia, spasticity, rigidity, seizure, and neurodevelopmental delays.

Methods: The patients who were diagnosed as glutaric aciduria type 1 in the Neurology Department of Mofid Children's Hospital in Tehran, Iran, between 2002 and 2012, were included in our study. This disorder was confirmed by clinical manifestation, neuroimaging findings, and neurometabolic and genetic assessments from a laboratory in Germany. Our study was conducted to define the age, gender, past medical history, developmental status, clinical manifestations, and neuroimaging findings in 20 patients with glutaric aciduria type 1.

Results: Eighty-five per cent of the patients were offspring of consanguineous marriages. In this study, there was no pattern of macrocephaly at birth; however, 25% of patients had a larger head circumference than weight, but follow-ups showed that 50% of these patients had macrocephaly (greater than 95%). The patients were followed for approximately 5 years. This follow-up shows that the patients with early diagnosis had a more favourable clinical response to treatment. The serial neuroimaging was done in seven patients and five of them (71%) followed a particular pattern, as front temporal atrophy and widening of the Sylvian sulcus, then white matter and basal ganglia involvement, and subependymal cyst.

Conclusions: According to the results of this study, we suggest that early assessment and diagnosis of glutaric aciduria type 1 has an important role in the prevention of the disease progression and clinical signs.

KEYWORDS glutaric aciduria type 1, neurometabolic disorder, developmental delay, intellectual disability, early detection

Introduction

Glutaric aciduria type 1 is a rare neurometabolic disorder with characteristic clinical manifestation and neuroimaging. The disorder may present with brain atrophy in frontotemporal region, macrocephaly, acute encephalopathic episode, and acute dystonia (Superti-Furga and Hoffmann, 1997), which was triggered by fever, infection, and dehydration (Twomey *et al.*, 2003). This disorder is identified by detection of elevated glutaryl carnitine level in serum and glutaric acid and 3-hydroxy glutaric acid in urine (Serarslan *et al.*, 2008). Other manifestations of glutaric aciduria type 1 include hypotonia, motor delay, dystonia, dysarthria, and dyskinesia in the first year of life in macrocephalic patients (Brismar and Ozand *et al.*, 1995; Barić *et al.*, 1998).