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Glutaric Aciduria Type I Diagnosed After Poliovirus Immunization: Magnetic Resonance Findings

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Glutaric aciduria type I is an uncommon inborn error of metabolism. It is a serious disease, often with a fatal outcome. Magnetic resonance imaging findings and the clinical course of monozygotic twin females with glutaric aciduria type I who were admitted with acute encephalopathic crisis symptoms 3 days after immunization for poliovirus are presented in this report. Magnetic resonance imaging findings revealed hyperintensity in the putamen, head of the left caudate nucleus, and globus pallidus, periventricular white matter (on T_2-weighted images), arachnoid cysts in bilateral temporal regions, and enlargement of the sylvian fissures. Glutaric aciduria type I should be included in the differential diagnosis of patients with acute encephalopathic crisis occurring shortly after poliovirus immunization. Typical magnetic resonance findings guide urinary organic acid analysis in these patients. **© 2002 by Elsevier Science Inc. All rights reserved.**

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Introduction

Glutaric aciduria type I is an uncommon and severe inborn error of metabolism with an autosomal recessive mode of inheritance. Glutaric aciduria type I occurs due to the deficiency of glutaryl CoA dehydrogenase, which is a mitochondrial enzyme involved in the degradation of lysine, hydroxylysine, and tryptophan, resulting in increased levels of glutaric acid [1]. The demonstration of elevated excretion of glutaric and 3-hydroxy-glutaric acids in the urine by organic acid analysis and the enzyme deficiency in cultured skin fibroblasts or lymphocytes are the basic laboratory manifestations of glutaric aciduria type I [2,3].

The disease may not be diagnosed by routine metabolic screening [4]. Early detection of glutaric aciduria type I is important in the prevention of acute brain damage [5]. The patients may die during the first decade of life if untreated [3]. Acute encephalopathy, macrocephaly, or gradual neurologic deterioration, including hypotonia, progressive dystonia, or choreoathetosis and tetraplegia could be the initial presentations of the patients [6]. Typical magnetic resonance findings, which are usually observed after clinical onset of the disease, include frontotemporal atrophy with bat wing-like middle cranial fossa, disturbance of myelination, and signal changes in the caudate nucleus, globus pallidus, and putamen [3].

Case Report

The polio vaccine had been administered to healthy 14-month-old monozygotic twin females. They were hospitalized because of high fever, diarrhea, vomiting, and limitation in motion of the right hand and arm 3 days after vaccination. In both patients, neurologic examination revealed hypotonicity of right upper and lower extremities and absence of deep tendon reflexes on the right side. Other system examinations were normal. Magnetic resonance imaging disclosed marked dilatation of the sylvian fissures as a "bat wing;" arachnoid cysts in temporal regions; bilateral linear-shaped hyperintensity in the putamen, head of the left caudate nucleus, and globus pallidus; and delayed myelination of the deep white matter on T_2-weighted images (Fig 1A, B, and C).

The severity of neurologic findings was different in each of the patients. In one of the twins there was much more hypotonicity, and she could not support her head.

Urinary organic acid analysis by gas chromatography and mass spectrometry revealed glutaric aciduria type I. Laboratory investigations disclosed marked excretion of glutaric acid (in one of the twins, 7,310 nmol/mol creatinine; in the other, 2,710 nmol/mol creatinine) and 3-hydroxy-glutaric acid in the urine.

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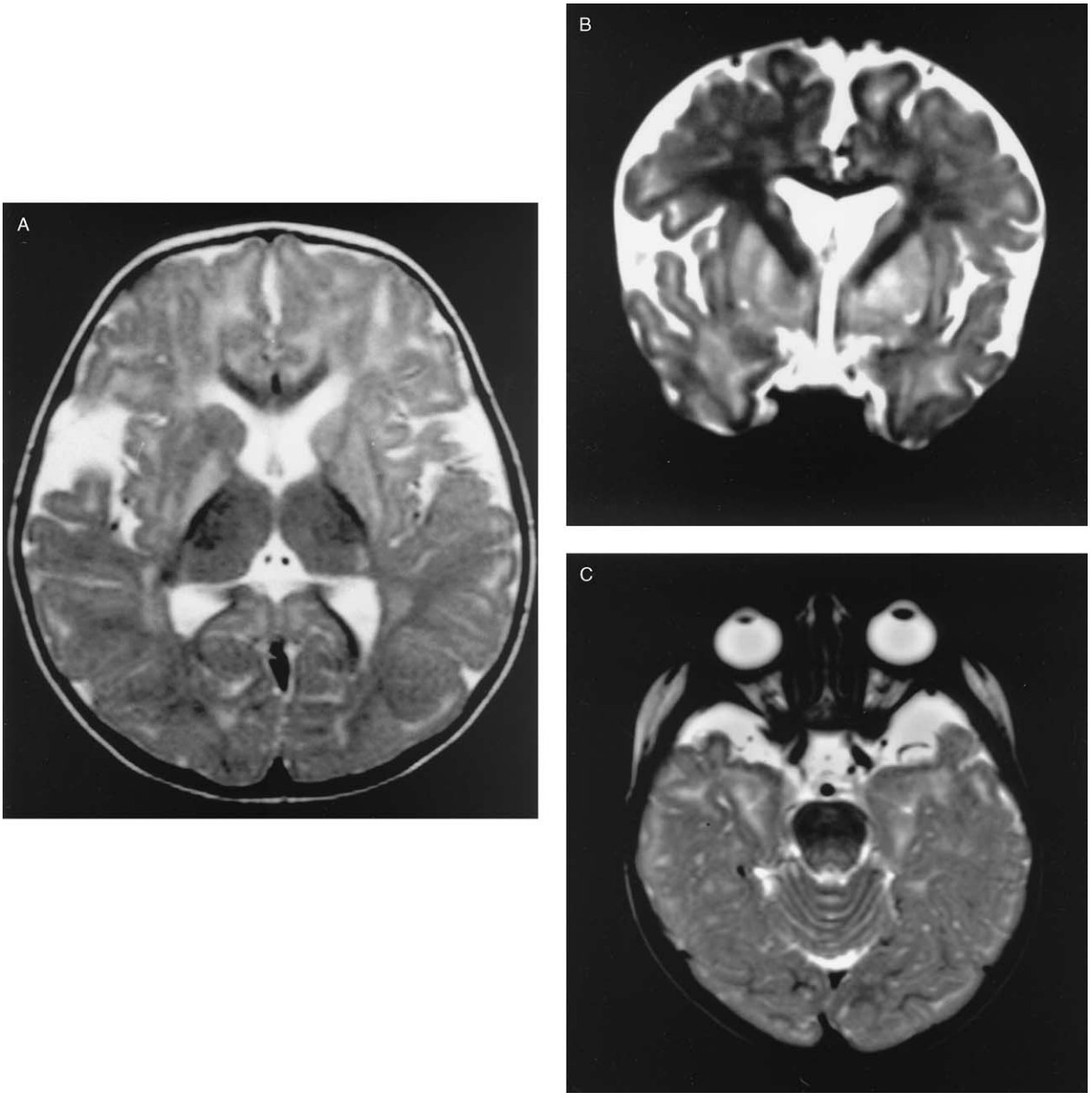

Figure 1. Monozygotic twin females, 14 months of age, with glutaric aciduria type I. (A) Axial T_2-weighted image (TR = 4531 ms, TE = 100 ms) reveals involvement of both the putamen (with more evidence in the left side), globus pallidus, and head of the left caudate nucleus. There is also marked dilatation of the right sylvian fissure. (B) Coronal T_2-weighted image (TR = 4500 ms, TE = 100 ms) demonstrates bilateral hyperintensities in the putamen and globus pallidus. (C) Axial T_2-weighted magnetic resonance image (TR = 4531 ms, TE = 100) reveal fluid collections of temporal regions, consistent with bilateral arachnoid cysts.

Discussion

Glutaric aciduria type I was first described by Goodman in 1975 [7]. Glutaric aciduria type I often remains undiagnosed or misdiagnosed, or the diagnosis is made late, usually more than 20 months after the initial neurologic presentation, in the course of the disease. Patients with glutaric aciduria type I likely have a greater tendency to become infected because of decreased immunity [4].

Neuroimaging Findings

Imaging findings in glutaric aciduria type I include large frontotemporal cerebrospinal fluid spaces, frontotemporal atrophy with bat wing-like middle cranial fossa, bilateral temporal arachnoid cysts, and hyperintensity in the basal ganglia (most commonly the putamen) and periventricular white matter. The white matter changes may not be observed early in course of the disease [6,8].

Dilatation of sylvian fissures is an important imaging finding [9]. The severity of symptoms, such as dystonia or choreoathetosis, correlates with the degree of enlargement of fissures in the bilateral frontotemporal region around sylvian fissures [2]. In our cases, there were bat wing appearances caused by dilatation of sylvian fissures. In the twin with more severe neurologic findings, dilatation of the sylvian fissures and the size of temporal arachnoid cysts were more prominent.

The pathogenesis of the frontotemporal atrophy is unknown. The possible factor may be the diminished cerebrospinal fluid reabsorption. The reason for the small appearance of the temporal lobes could be atrophy or primary hypoplasia [3]. It is suggested that arachnoid cysts in symptomatic patients with GA-1 would form after the rapid occurrence of frontotemporal atrophy, which in turn leads to alterations in CSF flow in the subarachnoid spaces and to fluid accumulation as occurs in communicating arachnoid pouches [4].

Magnetic resonance imaging is important and preferable in evaluation of myelination and the basal ganglia pathologies [3]. The hyperintensities in the basal ganglia are characteristic of mitochondrial disorders. There is mild to moderate nerve cell loss in the pallidum and in the putamen with gliosis. The caudate nucleus demonstrates no nerve cell loss in early infancy, although it shares the same developmental origin with putamen. This finding suggests that the putamen may be the first region affected in glutaric aciduria type I. The marked neuronal loss, astrogliosis, and hypervascularity are the events during the degeneration of the putamens [9]. Magnetic resonance imaging findings suggest that the abnormal metabolites in glutaric aciduria type I are toxic mainly to the extrapyramidal tract in the central nervous system [2]. There was bilateral involvement of putamen, head of left caudate nucleus, and globus pallidus in our patients.

At 12 months of age, most patients with glutaric aciduria type I were reported to have an acute encephalopathic crisis and loss of motor skills [6]. It is reported that glutaric aciduria type I may present acutely, sometimes after a mild infection, mimicking viral or immune-mediated encephalitis [4]. In addition, a patient with glutaric aciduria type I diagnosed after immunization for poliovirus has been reported by Nagasawa et al. [2]. This patient had vomiting and diarrhea followed by unconsciousness and seizures, which occurred shortly after vaccination for poliovirus. Dystonia and athetosis also were present. Findings in our patients were revealed to be related to the involvement of the pyramidal system and were diagnosed as immunization-related encephalopathy inducing clinical manifestation of latent glutaric aciduria type I. To our knowledge, this is the first report of monozygotic twins with glutaric aciduria type I diagnosed after an acute encephalopathic crisis shortly after immunization.

Early diagnosis and treatment seem to be crucial for the outcome of these patients [3]. The early detection of glutaric aciduria type I is important in the prevention of acute brain damage [5]. Dietary control, consisting of low protein, riboflavin, and carnitine before the onset of neurologic symptoms might allow normal neurologic development. Treatment should be initiated in the asymptomatic stage after testing the patient for glutaric aciduria type I [3,4].

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