Glutaric Aciduria Type I : A Case Report

S SINGH, V CHOWDHURY, R DIXIT, A PRAKASH, A AGARWAL

Ind J Radiol Imag 2006 16:4:723-726

Key words : Glutaric Aciduria Type I, Aminoaciduria

Introduction

Aminoacidopathics and aminoacidurias are autosomal recessive enzymatic defects that affect the amino acid (AA) metabolic pathways. Because amino acids are essential for formation of proteolipids (key components of myelin) defects in amino acid metabolism result in failure of myelin formation or failure to maintain otherwise normally formed myelin.

Deficiency of a specific enzyme (aminoacidopathy) causes accumulation of the affected amino acid that is often excreted in the urine (aminoaciduria). Examples of aminoacidopathics include phenylketonuria, maple syrup urine disease, methylmalonic acidemia and glutaric aciduria type I.

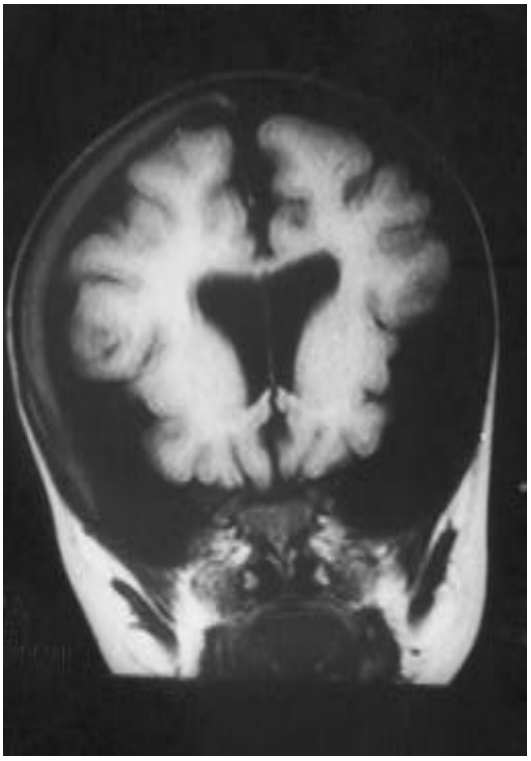

Fig. 1. FLAIR coronal MR image revealing wide CSF spaces anterior to the temporal lobes with temporal lobe hypoplasia , bilateral frontoparietal subdural effusions and atrophy .

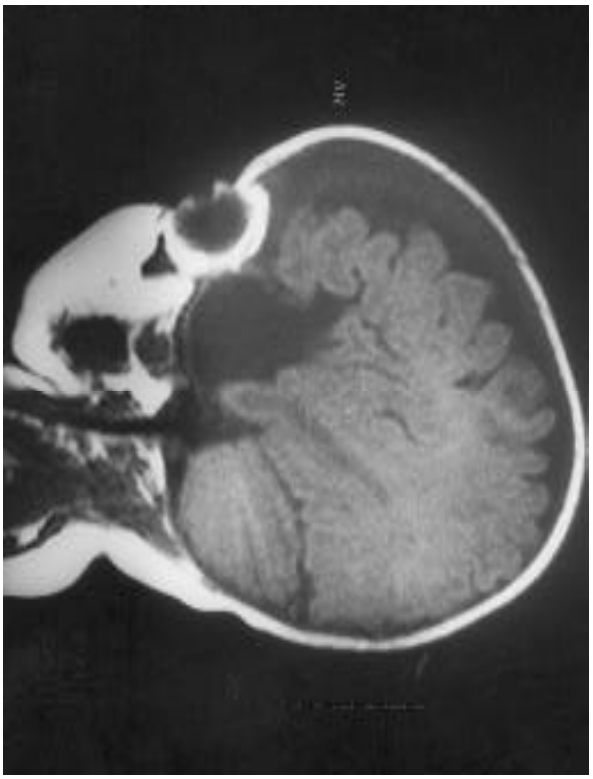

Fig. 2. Sagittal T1W MR image revealing bilateral subdural effusions in the fronto parietal regions and prominent CSF spaces.

Case Report

A 8 month old male was referred to the paediatrics neurology clinic because of macrocephaly. At birth the head circumference was 38 cm and showed rapid growth during the first 4 months of life. There was a history of regression of milestones, motor delay, dystonia, dysarthria and dyskinesia. The child was subjected to an MR examination. FLAIR coronal MR images revealed wide CSF spaces anterior to the temporal lobes with temporal lobe hypoplasia and bilateral frontoparietal subdural effusions (Fig. 1). Sagittal T1W MR image also revealed

From the Department of Radiodiagnosis, Maulana Azad Medical College and associated Lok Nayak Hospital, Jawahar Lal Nehru Marg, New Delhi-110002

Request for Reprints: Dr. SAPNA SINGH, 212, SFS FLATS, PHASE IV, ASHOK VIHAR, DELHI - 110052

Received 18 October 2006; Accepted 20 November 2006

the prominent CSF spaces and subdural effusions (Fig. 2). Diffuse white matter signal abnormality, bilateral high signal in the putamen and caudate nucleus, dilated sylvian fissures and open opercula was seen on the axial T2W MR scans (Fig. 3). Inversion recovery sequence also revealed widely open opercula and dilated sylvian fissures (Fig. 4).

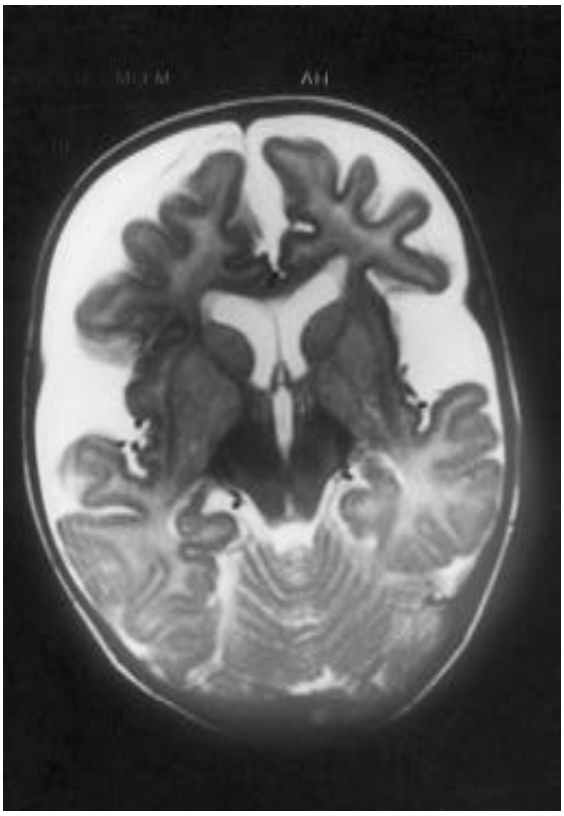

Fig. 3. Axial T2W MR images revealing dilatation of the sylvian fissures and open opercula. High signal intensity seen in bilateral caudate nuclei and putamen. High T2 signal is also seen in the deep subcortical white matter.

Based on these findings a diagnosis of glutaric aciduria type I was considered which was confirmed by urinary organic acid analysis by gas chromatography mass spectroscopy which revealed a marked excretion of glutaric acid(Fig 5).

Discussion

The organic acidurias comprise a relatively rare group of disorders involving protein synthesis, primarily related to synthesis in the mitochondrion [1]. The two of most importance are proprionic aciduria and methylmalonic aciduria. Glutaric aciduria type I is not actually an organic aciduria but rather a disorder of lysine metabolism. It has similarities in clinical presentation and on imaging to organic acidurias. These conditions are autosomal recessive. Oxidative metabolism is often inhibited secondary to metabolic acidosis and leads to cell death.

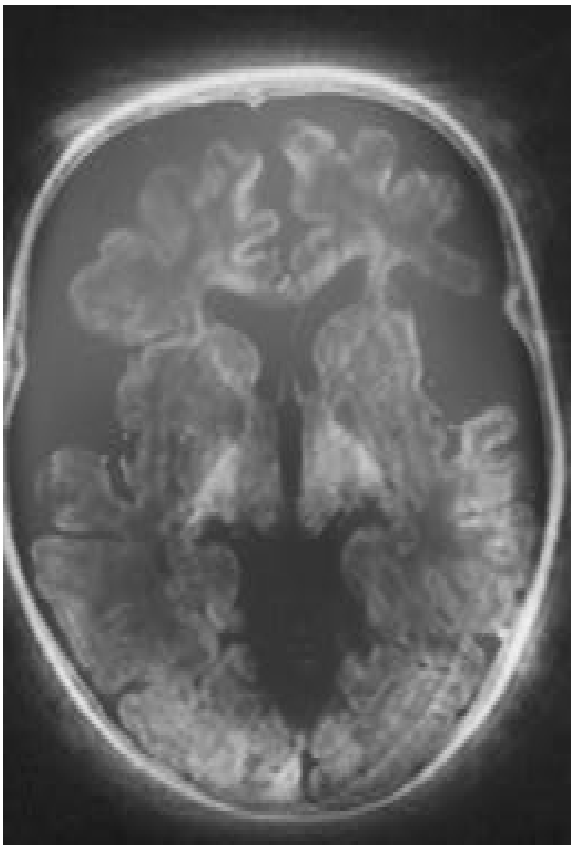

Fig. 4. Inversion recovery sequence revealing the severe widening of the sylvian fissures - bat wing appearance and wide open opercula.

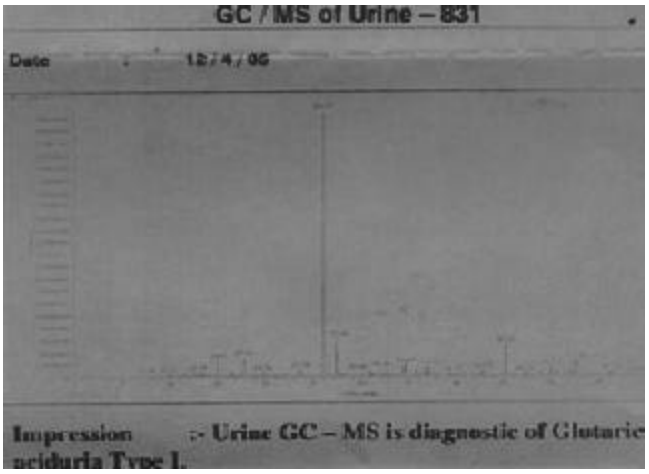

Fig 5 Urine organic acid analysis by gas chromatography mass spectroscopy revealed a marked excretion of the glutaric acid.

There are two clinical presentations, both occurring early in infancy or in the neonatal period. The most common is a progressive encephalopathy beginning in the first 3 to 4 months of life and consists of hypotonia developmental delay, seizures, choreoathetosis, dystonia or dysmetria. This constellation of symptoms, once started can rapidly progress [2]. Macrocephaly may be an early sign before other neurologic alteration.

The second presentation consists of an acute encephalopathy that might be confused with hypoxic or ischaemic encephalopathy especially in the neonatal period. Seizures, metabolic decompensation (ketoacidosis), vomiting and lethargy often accompany this acute presentation. It is rapidly progressive and leads to death in the acute phase if undiagnosed.

Glutaric acidemia is classified as type I or II depending on the specific enzymatic defects. In glutaric acidemia type I there is a deficiency in the flavin adenine dinucleotide dependent glutaryl - COA dehydrogenase which involves the metabolism of several amino acids including lysine, hydroxylysine and tryptophan. This deficiency leads to an accumulation of glutaric and other amino acids in serum and tissues. GA-I adversely affects mitochondrial activity and preferentially involves the basal ganglia.

The most striking finding on brain imaging is the presence of very wide CSF spaces anterior to the temporal lobes and within the sylvian fissures. Widening of the sylvian fissures is a very characteristic finding in glutaric acidemia type I [3]. The anomaly may range from a complete lack of operculation with gross hypoplasia of the temporal lobes to widening of sylvian fissures in proportion to the prominence of other extra cerebral CSF spaces. It has been suggested that bilateral temporal fluid collections may be caused by arachnoid cysts of the temporal fossa [4]. Extra cerebral fluid collections other than those anterior to the temporal lobes include subdural collection or bilateral frontoparietal subdural hematomas [4].

The acute presentation is often accompanied by abnormal T2 signal in the caudate heads and putamen bilaterally [5]. Diffuse edema involving all the white matter might also be seen especially in conjunction with a transient macrocramia lasting several months. This eventually leads to diffuse volume loss involving both the white and gray matter.

Diffusion weighted MR imaging may reveal widespread restricted diffusion in the white matter and MR spectroscopy shows decreased NAA/Cr ratio compared with sex and age matched control.

Glutaric acidemia type II usually does not present with macrocrania and involves a defect in multiple acyl COA dehydrogenase (MAD). The neonatal form is X linked and typically presents as an acute encephalopathy at birth with rapid deterioration accompanied by hyperammonemia, metabolic acidosis and hypoglycemia. It might be associated with dysmorphic features and anomalies involving the kidneys (polycystic kidney disease). There may be an association with cortical dysmorphism or pachygyria that is similar to that found in peroxisomal disorder. Imaging pattern is consistent with acute edema and might be confused clinically with hypoxic ischaemic encephalopathy.

The differential diagnosis of metabolic disease with macrocrania includes Canavan's disease, glutaric aciduria type 1, Alexander's disease and Van der Knapp disorder and these need to be differentiated from each other. The signal abnormality in Canavan's disease is centripetal i.e. there is an early involvement of the subcortical white matter then spreads to involve the deep white matter [6]. The globus pallidus is invariably affected with relative sparing of the putamen and caudate nucleus. There is a relative sparing of the internal, external and extreme capsules. In contrast, in glutaric aciduria type I the putamen and caudate nucleus are usually affected. The involvement of brainstem is also more typical of Canavan's disease. MR spectroscopy in Canavan's disease is pathognomonic, there is a marked elevation of NAA for age.

Alexander's disease is a leukoencepathopathy, the infantile form is characterized by macrocephaly. This disorder is characterized by frontal predominance of white matter abnormalities with a fronto-dorsal progression and enhancement of the frontal horns may be seen on the post gadolinium scans [7]. In both Canavan's and Alexander's diseases widening of the extracerebral CSF spaces is not a feature.

Van der Knapp disorder, is a vaculoting leukoencephalopathy with subcortical cysts. Generally, there is no regional predominance, rather, there is a diffuse involvement of the white matter with marked swelling early in the course of the disease.

Thus the finding of very widely open opercula suggests glutaric aciduria type 1 and if combined with basal ganglia lesions is almost pathognomonic, especially in a child with macrocephaly [8].

REFERENCES

1. Kyllerman M, Steen G. Glutaric aciduria : a common metabolic disorder. Arch Fr Pediatr 1980; 37: 279.
2. Bergman I, Finegold D, Gartner JC et al. Acute profound dystonia in infants with glutaric acidemia. Pediatrics 1989; 83; 228-234.
3. Amir N, El-Peleg O, Shalev RS, Christensen E. Glutaric aciduria type I : Clinical heterogeneity and neuroradiological features. Neurology 1987; 37: 1654-1657.
4. Hald JK, Nakstad PH, Skjeldal OH, Stromma P. Bilateral arachnoid cysts of the temporal fossa in four children with glutaric aciduria type 1. Am J Neuroradiol 1991; 12: 407-409.
5. Altman NR, Rovira MJ, Bauer M. Glutaric aciduria type I : MR findings in two cases. Am J Neuroradiol 1991; 12: 966-968.
6. Brismar J, Brismar G, Gascon C, Ozand P. Canavan

disease : CT and MR imaging of the brain. Am J Neuroradiol 1990; 11: 805-810.
7. Pridmore CL, Baraister M, Harding B, Boyd SG, Kendall B, Brett E. Alexander's disease : clues to diagnosis. J Child Neurol 1993; 8: 134-144.
8. Brismar J, Ozand P. CT and MR of the brain in glutaric academia type I. A review of 59 published cases and report of 5 new patients. Am J Neuroradiol 1995; 16: 675-683.