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Case Report

Imaging Contribution in Glutaric Aciduria Type 1 through a Case Report

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Abstract

Glutaric aciduria type 1 (GA-1) is an autosomal recessive inherited metabolic disorder resulting from a defect in glutaryl-CoA dehydrogenase, rarely asymptomatic, decompensation often occurs in early childhood, marked by dystonia-dyskinesia outcomes. Neuroimaging provides a diagnosis based on well-defined signs, features and provides a non-invasive evaluation of cerebral metabolism using magnetic resonance spectroscopy.

This article aims to highlight the typical radiological characteristics of GA-1 through a clinical case.

Keywords: *Glutaric Aciduria Type 1; Brain Magnetic Resonance Imaging; Spectroscopy*

Introduction

Glutaric aciduria type 1 is an infrequent neurometabolic disorder inherited in an autosomal recessive pattern, caused by a deficiency in the mitochondrial enzyme glutaryl-CoA dehydrogenase. This enzyme deficit leads to a cytotoxic impact on the brain, especially affecting the basal ganglia.

Distinctive imaging patterns suggest the diagnosis, include dilation of the sylvian fissures and subarachnoid spaces, occasionally accompanied by subdural hematomas, and abnormalities in striatal structures during episodes of decompensation. Magnetic resonance spectroscopy provides a non-invasive tool for assessing metabolic disturbances and the extent of brain damage. All these findings must be coupled with high levels of urinary and plasma glutaryl derivatives.

Case Report

A 4-month-old male infant presented to the pediatric emergency department with apyretic seizures. The anamnesis revealed no particular context, while the physical examination showed macrocephaly and tonic posture of all four limbs.

A non-injection CT scan was urgently performed which revealed a widened sylvian fissures and frontotemporal fluid spaces, leading to a "bat-wing" configuration, as well as a dilated mesencephalic and prepontine cistern. (Figure 1).

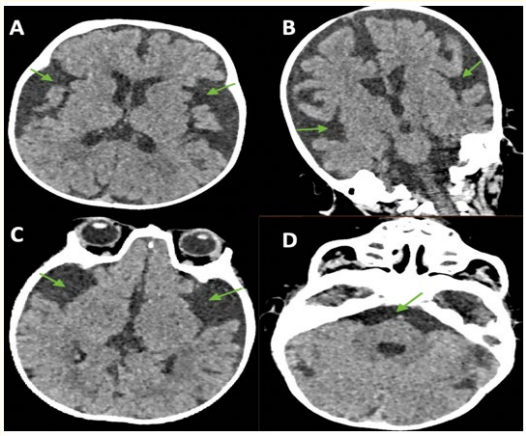

Figure 1: *Axial and coronal CT scan sections showing enlargement of lobe frontotemporal fluid spaces and sylvian valleys "Bat wing appearance" (A, B) enlarged CSF spaces anterior to the temporal (C), enlarged prepontine cistern.*

A brain MRI was undertaken after resolution of the seizures, which showed, in addition to the abnormalities described on CT, bilateral and symmetrical increased intensity signal in diffusion, with slight ADC restriction of the caudate nuclei, putamen, pallidum and cerebral peduncles, with no signal abnormalities on conventional sequences (T1, T2 and flair) (Figure 2).

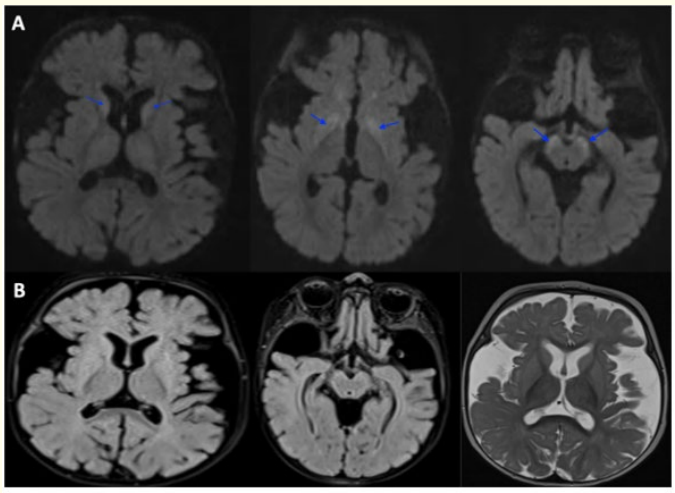

Figure 2: *(A) Axial b 1000 DWI image showing a bilateral and symmetric increased signal intensity in the caudate nuclei, lenticular nuclei and cerebral peduncles, without any signal abnormality in axial flair and T2 sequences (B).*

Spectroscopy showed a slight increase in choline, with a minimal decrease in NAA, a decrease in the NAA/Cr ratio and slight increases in the Cho/Cr ratio, without a peak in lactate (Figure 3).

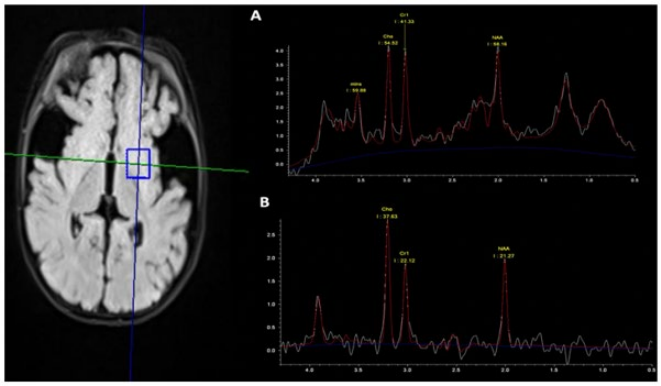

Figure 3: *Single-voxel hydrogen magnetic resonance spectroscopy (A: TE 35) and (B:TE 135) obtained through the left putamen nucleus, shows a decreased NAA (ratio NAA/Cr: 1.41), without a pic of lactate.*

Discussion

Glutaric acidemia type 1 is an inherited organic acidemia, transmitted in an autosomal recessive manner, resulting from a defect in the enzyme glutaryl-CoA dehydrogenase. This enzyme is necessary for the decomposition of the amino acids lysine, hydroxylysine, and tryptophan. It is a rare metabolic condition, with a prevalence of 1 per 100,000 people.

The clinical presentation can vary, but the typical pattern is macrocephaly in an asymptomatic infant, who then presents with encephalopathic crises in early childhood following an intercurrent illness (either an infection or an acute catabolic state), leading to acute striatal degeneration and, consequently, severe dystonia and dyskinesia.

The neuroimaging aspects of GA-1 are variable; in the early stages of the disease, brain imaging may show bilateral frontotemporal atrophy, a term that probably refers to the widening of the sylvian fissures, producing a "bat-wing" appearance, most often associated with enlargement of the basal cisterns, particularly the mesencephalic cistern [5-7], subdural hematomas may be present secondary to macrocephaly and enlargement of the pericerebral CSF spaces, leading to bleeding from the stretched cortical vessels [8].

After encephalopathic episodes, imaging reveals striatal damage; cranial CT is not a reliable technique for detecting such damage, particularly in the acute phase [9], in this case, MRI is more perforating, showing bilateral and symmetrical T2 and flair hypersignal signal abnormalities in the basal ganglia, namely in the caudate nucleus and lenticular nuclei, with atrophy in the sequelae stage [10]. Changes in the deep periventricular white matter have been described in patients with type 1 glutaric aciduria. In addition, signal changes in the corticospinal tracts of the cerebral peduncles and in the tegmental tract, as well as damage to the optic chiasma, have been reported in the literature [11,12].

Diffusion weighting is highly sensitive to changes in the state of water molecules in brain tissue, particularly during acute necrosis or cytotoxicity. Compared with conventional MRI sequences, it enables faster and more accurate detection of lesions in the basal ganglia. It is possible to have type I glutaric aciduria with abnormalities visible on diffusion that are not necessarily detectable on T2 and FLAIR sequences, which is the case with our patient. This could allow earlier identification of affected patients, leading to improved long-term outcomes with early therapeutic management of GA1 patients [4,13].

Magnetic resonance spectroscopy is an advanced diagnostic tool that allows non-invasive measurement of brain metabolites. In individuals with GA1, there's an observed decline in the N-acetylaspartate (NAA) signal, coupled with a reduction in the N-acetylaspartate/creatine ratio. NAA, pivotal as a marker for neuronal density and viability, indicates potential neuronal loss or disruption in neuronal metabolism upon its decline. in severe cases, loss of glutamate and the appearance of lactate peaks have been observed, glutamate is an important neurotransmitter and brain metabolite. The presence of increased lactate is indicative of a rise in anaerobic glycolysis, which may be the consequence of hypoxia or mitochondrial disruption, two potential pathological processes in GA1 [14-16].

Conclusion

In summary, neuroimaging techniques have greatly enhanced our knowledge and diagnostic approach to glutaric aciduria type I. MRI, and specifically diffusion-weighted imaging, offers a more comprehensive view of the extent of the disease that might be overlooked in conventional imaging. Additionally, magnetic resonance spectroscopy provides a deeper insight by detecting particular metabolic changes. Combined, these imaging modalities promote early management, which is essential in minimizing neurological damage and improving long-term prognosis for patients with glutaric aciduria type I.

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