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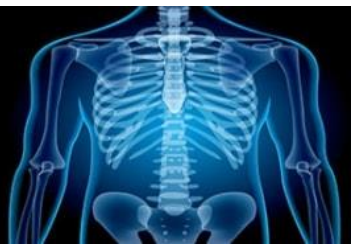

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Neuroimaging hallmarks of glutaric acidemia type 1: Early recognition through the "bat-wing" sign in an infant with seizures

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Abstract
Background: Glutaric acidemia type 1 (GA1) is a rare autosomal recessive neurometabolic disorder that can present with devastating neurological sequelae if not recognized early. We present a case highlighting the characteristic neuroimaging findings that enabled prompt diagnosis and treatment initiation.
Case Presentation: A 10-month-old female presented with new-onset seizures and developmental regression. Neurological examination revealed axial hypotonia, appendicular hypertonia, and delayed motor milestones. Magnetic resonance imaging (MRI) demonstrated pathognomonic features including bilateral widened opercula with "bat-wing" configuration of the sylvian fissures, symmetric basal ganglia signal abnormalities with restricted diffusion, and extensive white matter changes. These imaging findings, combined with elevated urinary glutaric acid levels, confirmed the diagnosis of GA1. The patient was immediately started on a low-protein diet with L-carnitine and riboflavin supplementation.
Conclusion: Recognition of characteristic neuroimaging patterns in GA1, particularly the "bat-wing" sign, is crucial for early diagnosis before irreversible striatal injury occurs. This case emphasizes the importance of MRI in the diagnostic workup of infants presenting with seizures and abnormal neurological findings.

Keywords: Glutaric acidemia type 1, GA1, neurometabolic disorder, MRI

Introduction
Glutaric acidemia type 1 (GA1) is an autosomal recessive disorder caused by a deficiency of glutaryl-CoA dehydrogenase (GCDH), affecting the metabolic pathway of lysine, hydroxylysine, and tryptophan [1]. The condition has an estimated incidence of 1 in 100, 000 newborns and typically manifests between 3 and 36 months of age, often precipitated by intercurrent illness [2, 3]. Without early recognition and treatment, affected children develop irreversible striatal injury leading to severe dystonia and movement disorders [1, 2].
The neuroimaging features of GA1 are distinctive and can precede clinical symptoms, making radiological recognition critical for early intervention [3, 4]. We present a case of a 10-month-old infant whose characteristic MRI findings led to prompt diagnosis and treatment of GA1, potentially preventing catastrophic neurological deterioration.

Case Report
A 10-month-old female infant presented to the emergency department with a 2-day history of focal seizures characterized by right-sided tonic-clonic movements lasting 2-3 minutes. The seizures occurred in the context of a mild upper respiratory infection with low-grade fever. Her parents reported progressive irritability and decreased activity over the preceding month.
The patient was born at term following an uncomplicated pregnancy and delivery. Birth weight was 3.2 kg with a head circumference at the 75th percentile. Early developmental milestones were appropriate until 7 months of age, when parents noticed she was no longer able to sit without support and had stopped babbling.

Clinical Examination
On examination, the infant was irritable but consolable. Head circumference was 47 cm (>95th percentile). Neurological examination revealed axial hypotonia with poor head

control and appendicular hypertonia. Deep tendon reflexes were brisk bilaterally with ankle clonus. No papilledema was noted on fundoscopy. The remainder of the systemic examination was unremarkable.

Laboratory Investigations

Initial laboratory studies including complete blood count, electrolytes, glucose, and ammonia were within normal limits. Metabolic workup revealed markedly decreased free carnitine levels (8 µmol/L; normal: 25-50) and elevated C5-dicarboxylic carnitine on acylcarnitine profile [1]. Urine organic acid analysis demonstrated significantly elevated glutaric acid (850 mmol/mol creatinine; normal: <10) and 3-hydroxyglutaric acid, confirming the biochemical diagnosis of GA1 [1, 2].

Neuroimaging Findings

MRI of the brain revealed striking abnormalities characteristic of GA1:

1. **Sylvian Fissure Abnormalities:** Bilateral widened opercula with dilated sylvian fissures demonstrating the pathognomonic "bat-wing" configuration (Figure 1A). This finding represents underopercularization with expansion of cerebrospinal fluid (CSF) spaces [3, 4].
2. **Basal Ganglia Changes:** Bilateral symmetric T2/FLAIR hyperintensity involving the globus pallidus and putamen (Figure 1A and B). Diffusion-weighted imaging showed restricted diffusion within these structures, indicating acute metabolic injury [3]. The caudate nuclei showed mild T2 hyperintensity with mild volume loss.
3. **White Matter Abnormalities:** Diffusely increased T2 signal and decreased T1 signal throughout the deep white matter, particularly affecting the periventricular regions and optic radiations bilaterally. These changes reflect the metabolic stress and early demyelination associated with GA1 [4, 5] (Figure 1C).
4. **CSF Space Expansion:** Widened extra-axial CSF spaces, particularly prominent in the anterior temporal regions (Figure 1D) and perimesencephalic cisterns. Mild dilatation of the ventricular system (Figure 1E) was noted without evidence of obstructive hydrocephalus [3, 4].
5. **Additional Findings:** Trace bilateral frontal subdural hemorrhages were identified (Figure 1F). These are recognized complications of GA1 due to the stretching of bridging veins [3].

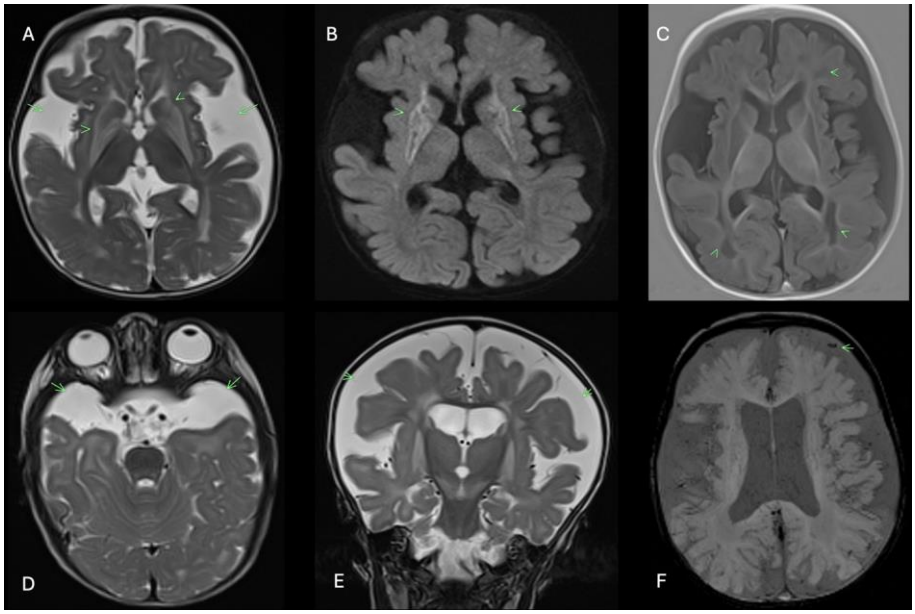

Fig 1: MRI imaging findings of Glutaric acidemia Type 1. (A) Axial T2-weighted image shows bilateral widened opercula with dilated sylvian fissures demonstrating the pathognomonic "bat-wing" configuration. (A and B) Axial T2-weighted and DWI show bilateral symmetric T2 hyperintensity involving the globus pallidus and putamen with restricted diffusion. The caudate nuclei showed mild T2 hyperintensity with mild volume loss. (C) Axial T1-weighted inversion recovery image shows diffusely decreased T1 signal throughout the deep white matter, particularly affecting the periventricular regions and optic radiations bilaterally (arrowheads). These changes reflect the metabolic stress and demyelination associated with GA1. (D) Axial T2-weighted image shows widened extra-axial CSF spaces, particularly prominent in the anterior temporal regions. (E) Coronal T2-weighted images show Mild dilatation of the ventricular system without evidence of obstructive hydrocephalus. (F). Trace bilateral frontal subdural hemorrhages were identified (arrow). These are recognized complications of GA1 due to the stretching of bridging veins.

Management and Follow-up

Following confirmation of GA1, the patient was immediately started on:

- Low-protein diet (1.5 g/kg/day) with lysine restriction
- L-carnitine supplementation (100 mg/kg/day in three divided doses)
- Riboflavin (200 mg/day)
- Emergency protocol for intercurrent illnesses with increased caloric intake

After 6 months of treatment, the patient showed stabilization of neurological symptoms with improved head control and reduced dystonic movements. Follow-up MRI at 16 months demonstrated interval decrease in basal ganglia T2 hyperintensity, though the white matter changes and sylvian fissure widening persisted [5].

Discussion

This case illustrates the critical role of neuroimaging in the early diagnosis of GA1. The combination of macrocephaly,

acute encephalopathy during a febrile illness, and characteristic MRI findings should prompt immediate metabolic investigation [1, 2].

The "bat-wing" appearance of the sylvian fissures is virtually pathognomonic for GA1 and results from frontotemporal hypoplasia with incomplete opercularization [3, 4]. This finding, present in over 90% of affected patients, can be identified even in presymptomatic infants and distinguishes GA1 from other causes of macrocephaly with white matter disease [4, 5].

The basal ganglia changes in our patient, particularly the restricted diffusion, indicated acute striatal injury coinciding with the metabolic decompensation triggered by intercurrent illness [3]. The preferential vulnerability of the striatum in GA1 relates to its high density of glutamatergic neurons and susceptibility to excitotoxic injury from accumulated glutaric acid and 3-hydroxyglutaric acid [1, 2].

Early diagnosis is paramount as dietary management and carnitine supplementation can prevent or minimize neurological sequelae if initiated before striatal injury occurs [1, 2, 5]. Countries with newborn screening for GA1 report significantly better neurological outcomes, with up to 80-90% of diagnosed infants remaining asymptomatic with appropriate management [2].

The differential diagnosis for the imaging findings includes other organic acidemias, mitochondrial disorders, and leukodystrophies. However, the combination of the "bat-wing" sign, symmetric basal ganglia involvement, and characteristic white matter changes strongly suggests GA1 [4, 5]. Additional imaging considerations in GA1 include the risk of subdural hematomas, which can occur spontaneously or with minimal trauma due to stretched bridging veins, potentially leading to misdiagnosis of non-accidental injury [3].

Long-term neuroimaging follow-up typically shows persistent sylvian fissure widening and white matter changes, even with successful treatment. However, early intervention can prevent progression of basal ganglia injury and the development of severe movement disorders [5].

Conclusion

This case emphasizes the importance of recognizing the characteristic neuroimaging pattern of GA1, particularly the "bat-wing" configuration of widened sylvian fissures, in infants presenting with seizures and neurological abnormalities. Early radiological diagnosis enables prompt initiation of dietary and medical management, potentially preventing irreversible striatal injury and severe dystonia. Radiologists play a crucial role in identifying these pathognomonic features, which can lead to life-changing early intervention in affected children.

Conflict of Interest

Not available.

Financial Support

Not available.

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