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Subdural Hematoma in an Infant with Glutaric Aciduria Type 1: A Case Report on Conservative Management

Hematoma Subdural em Lactente com Acidúria Glutárica Tipo 1: Caso Clínico com Abordagem Conservadora

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ABSTRACT

Glutaric aciduria type 1 is an inherited metabolic disorder associated with subdural hematomas, possibly due to the widening of external cerebrospinal fluid spaces. We present the case of an infant with macrocephaly since birth, diagnosed with glutaric aciduria type 1 through newborn screening, who exhibited accelerated cephalic growth during follow-up. At eight months of age, cranial magnetic resonance imaging revealed bilateral subdural hematomas with intracranial mass effect. The infant displayed no signs of intracranial hypertension, history of trauma, or signs of abuse. Although surgical treatment was considered, a multidisciplinary discussion led to the decision to manage conservatively with close monitoring. The patient remained clinically stable, and imaging showed a clear reduction in the dimensions of the hematomas. This case highlights that conservative management can be an effective approach for large subdural hematomas with mass effect in glutaric aciduria type 1, provided there is no associated symptomatology, thereby avoiding the risk of metabolic decompensation.
Keywords: Amino Acid Metabolism, Inborn Errors; Brain Diseases, Metabolic; Glutaryl-CoA Dehydrogenase; Infant; Hematoma, Subdural/therapy

RESUMO

A acidúria glutárica tipo 1 é uma doença hereditária do metabolismo associada a hematomas subdurais, possivelmente devido ao aumento dos espaços subdurais. Apresentamos o caso de um lactente com macrocefalia desde o nascimento, com o diagnóstico de acidúria glutárica tipo 1 através do rastreio neonatal, que exibiu um crescimento acelerado do perímetro cefálico durante o seguimento. Realizou ressonância crânio-encefálica aos oito meses que revelou hematomas subdurais bilaterais com efeito de massa, sem sinais de hipertensão intracraniana, história de trauma ou sinais de maus-tratos. Embora se tenha considerado o tratamento cirúrgico, após discussão multidisciplinar optou-se pelo tratamento conservador com vigilância periódica. A criança manteve-se clinicamente estável e radiologicamente observou-se uma redução das dimensões dos hematomas. Este caso pretende salientar que o tratamento conservador pode ser uma opção eficaz nesta patologia na ausência de sintomatologia, mesmo na abordagem de hematomas subdurais de grandes dimensões com efeito de massa, evitando o risco de descompensação metabólica.
Palavras-chave: Encefalopatias Metabólicas; Erros Inatos do Metabolismo dos Aminoácidos; Glutaril-CoA Desidrogenase; Hematoma Subdural/tratamento; Lactente

INTRODUCTION

Glutaric aciduria type 1 (GA1, OMIM#231670) is an autosomal recessive inherited metabolic disorder caused by a deficiency of glutaryl-CoA dehydrogenase, leading to toxic levels of glutaryl-CoA, glutaric acid, and 3-hydroxyglutaric acid.[1,2] In Portugal, this disease has been identified through newborn screening (NBS) since 2006. Early diagnosis allows for the timely implementation of dietary management, particularly a low-lysine diet and a lysine-free, tryptophan-reduced and arginine-enriched amino acid mixtures along with carnitine supplementation to prevent and manage catabolic states, such as febrile illness and surgery, which can trigger acute encephalopathic crises (AEC) and result in irreversible striatal damage.[1-3] Thus, dietary management has significantly improved clinical outcomes for these patients.[1,3,4]

Studies have shown that subdural hematoma (SDH) is more common in GA1 (around 15% - 30%), either spontaneously or following trauma.[5-9] The association of this sign with this disease is so strong that some studies have suggested diagnostic testing for GA1 in the presence of SDH in combination with other changes on imaging, such as bilateral enlargement of the Sylvian fissures and widened cerebrospinal fluid (CSF) spaces, particularly in the frontotemporal region.[2,5,6,8] This case describes the presentation of bilateral SDH in an infant previously diagnosed with GA1. It highlights the importance and need for a multidisciplinary approach to assess the risks and benefits of surgical *versus* conservative management. It also aims to provide evidence of the potential spontaneous regression of SDH in such cases.

CASE REPORT

We present the case of an infant diagnosed with glutaric aciduria type 1 on the 14th day of life through NBS. He was started on a low-lysine diet and lysine-free, tryptophan-reduced, and arginine-enriched amino acid mixtures

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and carnitine supplementation, with good compliance. Macrocephaly was present since birth and transfontanellar ultrasound at three weeks of age showed enlargement of the subdural space (~5 mm) and bilateral subependymal cysts. Head circumference consistently remained above the 97th percentile; however, between three and six months of age, there was a marked acceleration of head growth, which led to even further deviation from the growth curve, as illustrated in Fig. 1. A transfontanellar ultrasound was repeated at three months of age, revealing a large enlargement of the bifrontal subdural spaces and wide Sylvian fissures. The case was discussed with the neurosurgery team and the patient was evaluated at that time. Since during the follow-up there were no abnormalities in psychomotor development or symptoms of intracranial hypertension, no history of trauma or signs of abuse, and the transfontanellar ultrasound repeated at four months of age was similar, a cranial magnetic resonance imaging (MRI) was requested. An eight-month cranial MRI (Fig. 2) showed bilateral SDH with significant intracranial mass effect and wide CSF spaces anterior to the temporal horns and in the Sylvian fissures.

Surgical treatment was considered; however, due to the absence of symptoms of cranial hypertension, the risks associated with surgery (a potential precipitant of AEC), the metabolic diseases team recommended conservative management with close monitoring. One month later, cranial CT showed a significant reduction of the SDH, particularly on the right side (Fig. 3). Head circumference remained above the 97th percentile for age but followed a curve more parallel to the percentile and even approached it.

By the age of three, the child demonstrated normal acquisition of motor and language skills, with head circumference stabilizing around the 97th percentile for age and no abnormalities detected on neurological examination. No AEC occurred during the first six years of life. Subsequent imaging studies showed significant improvement (Figs. 4 and 5). In addition to SDH, the images revealed GA1-specific findings such as frontotemporal hypoplasia ('batwing' sign).

He continues to be followed and, at the age of 11, has no neurological signs or symptoms.

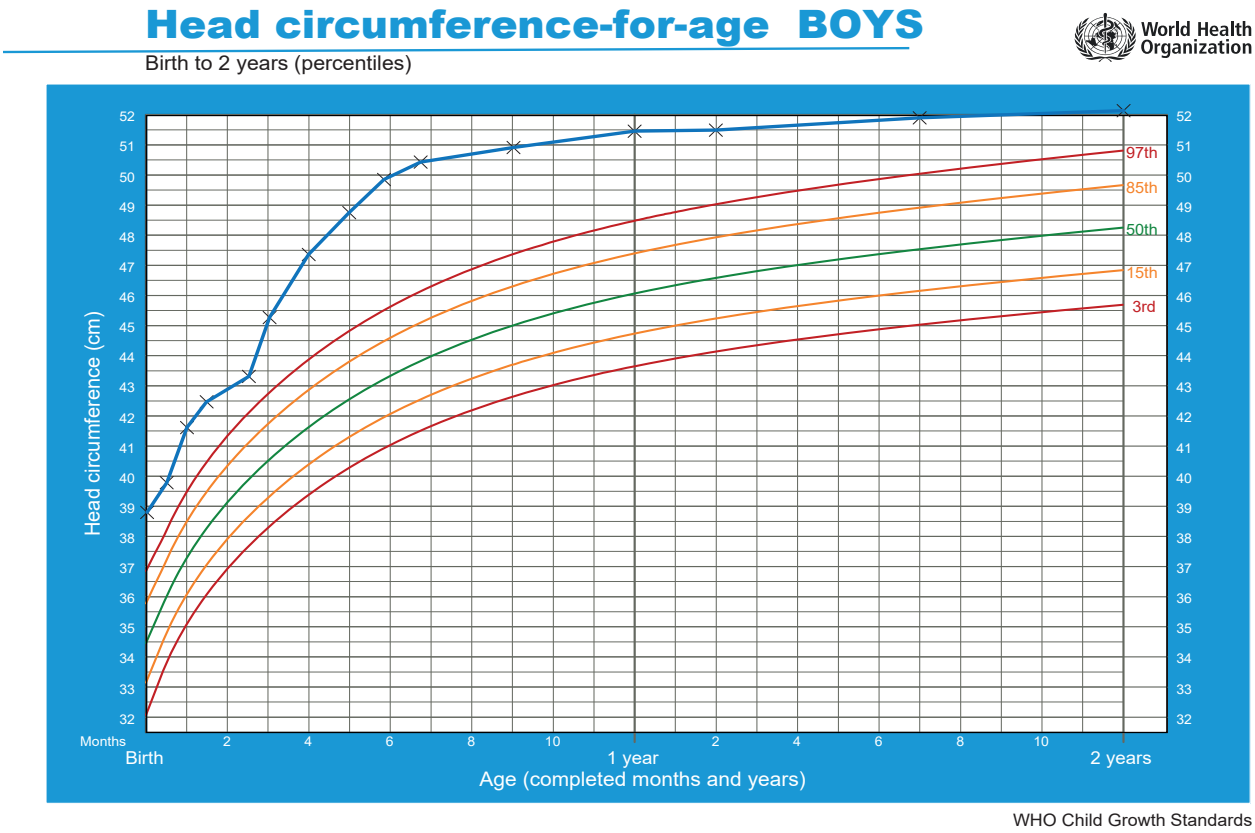

Figure 1 – Head circumference progression during the first two years of life, above 97th percentile for age

Source: Head circumference-for-age BOYS - Birth to 2 years (percentiles) © World Health Organization - This material was published for non-commercial purposes under the CC BY-NC-SA 3.0 IGO licence and is available at https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/head-circumference-for-age/cht_hcfa_boys_p_0_2.pdf?sfvrsn=3829cc5_9.

No modifications were made to the image, aside from marking the evaluation of this child's growth (blue line with crosshairs).

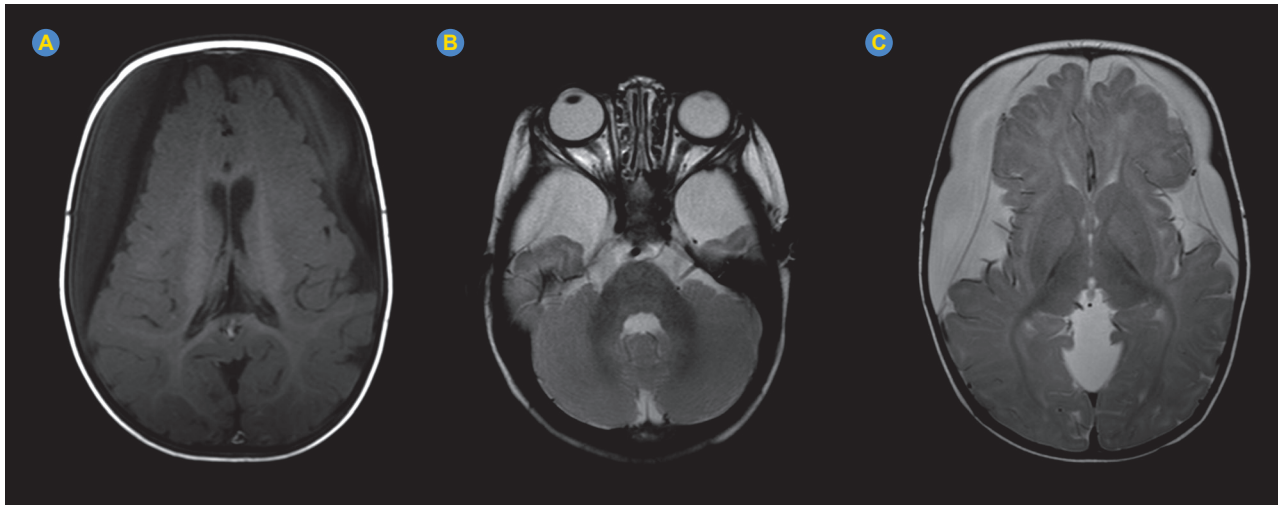

Figure 2 – Cranial MRI at 8 months of age. (A) T1-weighted spin echo axial image showing bilateral subdural hematomas, measuring 22 mm and 21 mm of width on the right and left convexities, respectively, causing significant mass effect over the adjacent cerebral parenchyma. (B) and (C) T2-weighted spin echo axial images showing wide cerebrospinal fluid (CSF) spaces anterior to the temporal horns (B) and in the Sylvian fissures (C). No significant signal or morphodimentional abnormalities can be noted in the basal ganglia (C), *dentate nuclei* or *substantia nigra* (not seen).

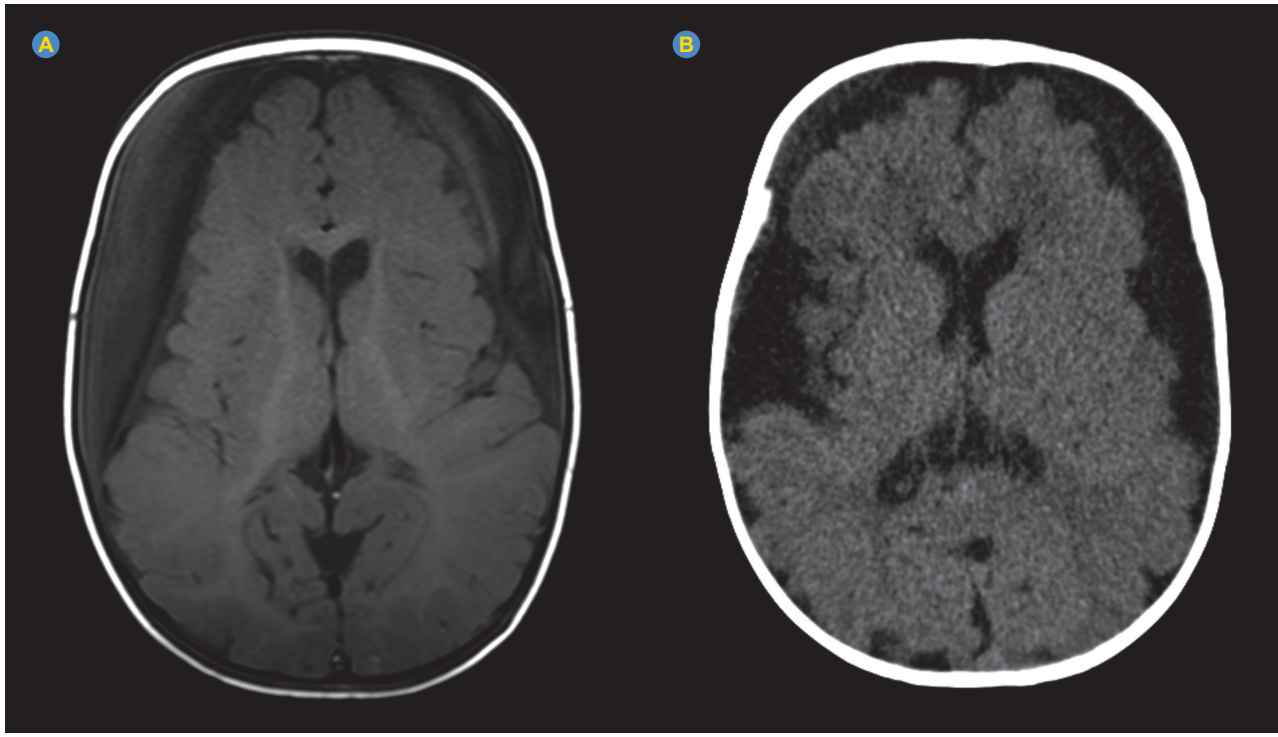

Figure 3 – T1-weighted sequence from the MRI examination performed at 8 months of age (A) side-by-side with a cranial CT-scan at 9 months of age (B), reformatted to be in the same plane. Image (B) shows a marked reduction in size of the bilateral subdural hematomas and of their mass effect compared to image (A), now measuring 10 mm on the right convexity and 20 mm on the left.

DISCUSSION

Although macrocephaly is a common feature in GA1, presented in 75% of the cases,[2] one study found an association between both macrocephaly and SDH in GA1,[6] while others suggested an association of SDH with wide external CSF spaces,[5,7] which can predispose to stretching of the bridging cortical veins. Both macrocephaly and wide CSF spaces were present in our case. Subdural hematoma can occur in the absence of trauma and can be bilateral,[6,8] as demonstrated in this case. Regarding age, SDH is more

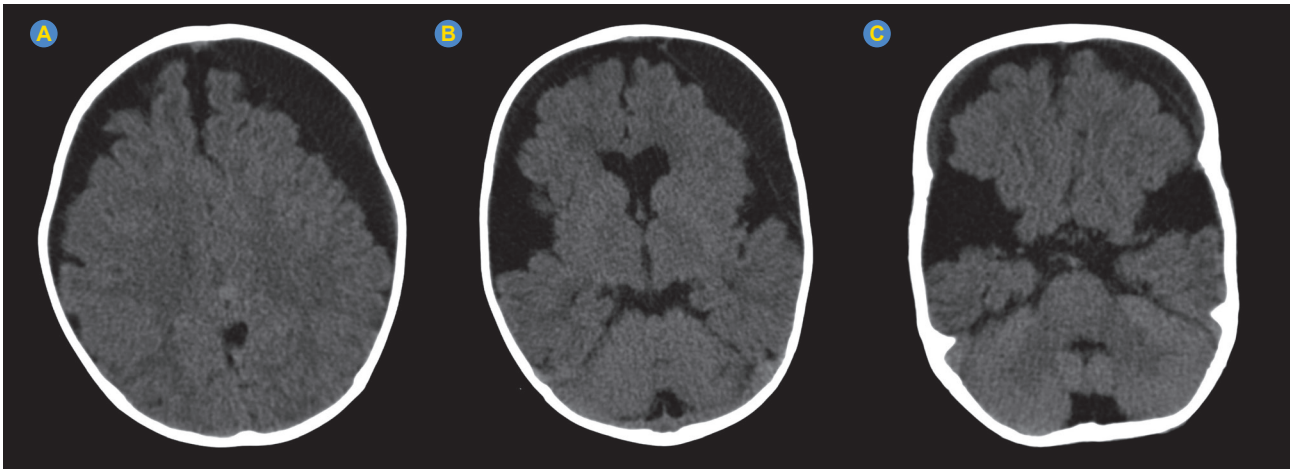

Figure 4 – Cranial CT-scan at 11 months of age (A - C) showing further reduction in size of the subdural hematoma on the right frontotemporal convexity, without any signs of re-bleeding.

common between the vulnerable period of three months and two to three years,[6] which aligns with the age of our patient. Despite the association between GA1 and SDH, it is important to look for signs of abuse that can mimic these lesions, as abuse can occur at the same time as any illness and children with chronic illnesses may be more vulnerable.[8] Cranial MRI also showed GA1-specific findings, consistent with other cases of GA1.[6,8]

In GA1, in addition to ongoing treatment, emergency management (high-energy intake, transient cessation of natural protein and support of endogenous detoxification by increased carnitine supplementation) should be done in catabolic episodes such as febrile illness or perioperative fasting, being vital to prevent AEC and subsequent irreversible damage.[1,2] Surgical intervention in children with undiagnosed GA1 presenting with SDH could lead to dangerous outcomes.[5] Even in cases of established diagnosis, surgery is a known precipitator of AEC, despite measures to avoid a catabolic state,[2] and carries inherent risks like any surgical procedure. Therefore, if there is a higher incidence of SDH in GA1 patients and reports of spontaneous resolution, as some studies suggest,[6-8] and this case as well, conservative treatment should be considered after a multidisciplinary discussion weighing the risks and benefits of both approaches.

This case report highlights the potential for spontaneous regression of SDH in GA1 and supports a conservative approach when there are no signs of intracranial hypertension and the neurological examination is normal, even with large dimensions and associated intracranial mass effect. However, being a single case report, it has limitations. Also, due to the rarity of GA1 and the possibility of asymptomatic cases of SDH, there is insufficient data to provide definitive guidance on treatment approaches.

To the best of our knowledge, this is the first report in Portugal of the complete evolution of an infant with SDH in the context of GA1, showing regression even with large dimensions and a significant intracranial mass effect.

PATIENT PERSPECTIVE

As parents, we were anxious about the possibility of surgery, knowing the risks involved given our son's condition. However, we felt much more reassured by the medical team, who carefully studied the literature and case descriptions to guide their approach. Their decision to follow a conservative treatment plan proved to be the right one, bringing us great relief. We hope that our experience can support other doctors in helping families facing GA1 with greater confidence and peace of mind.

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AUTHOR CONTRIBUTIONS

LM: Data acquisition, literature search, writing of the manuscript.

PLP: Data acquisition, writing of the manuscript.

HLC: Writing of the manuscript.

AG, PJ: Writing and critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

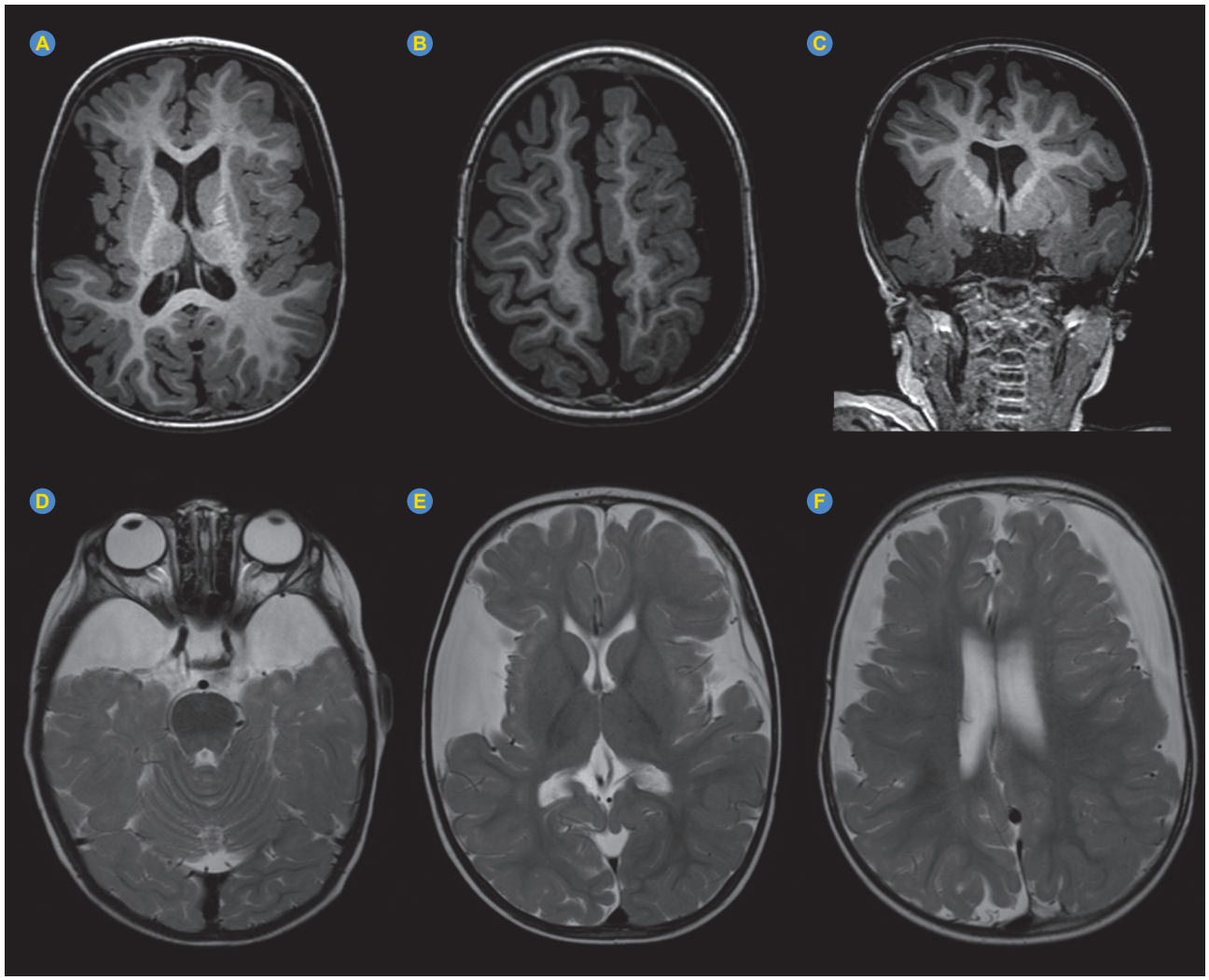

Figure 5 – Cranial MRI at 13 months of age. (A - C) T1-weighted spin echo images in the axial (A, B) and coronal (C) planes, showing complete reabsorption of the subdural hematoma (SDH) on the right, and a reduction in size of the SDH on the left to 12 mm, associated with a reduction of their mass effect. (D - F) T2-weighted spin echo images in the axial plane showing stability of widened CSF spaces, particularly in the frontotemporal region and Sylvian fissures ('batwing' appearance, best depicted on image (E). No myelination changes can be noted, nor signal abnormalities in the basal ganglia, thalami or *dentate nuclei*.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PARENTAL CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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