

CONTRIBUTION OF THE DIFFUSION-WEIGHTED MRI IN THE DIAGNOSIS AND FOLLOW-UP OF ENCEPHALOPATHY CAUSED BY MAPLE SYRUP URINE DISEASE IN A FULL-TERM NEWBORN

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Maple syrup urine disease (MSUD) or leucinosi is caused by a deficiency of the catalytic components of the α -ketoacid-dehydrogenase complex, which is responsible for the catabolism of branched-chain amino acids (leucine, isoleucine, and valine)^{1,2}. It is an inherited genetic disease with an autosomal recessive pattern affecting approximately 1 out of 120,000–500,000 infants worldwide^{3,4}. Diagnosis is made clinically based on the peculiar maple syrup odor or sugar burnt of the urine, encephalopathy, increased levels of branched-chain amino acids in the plasma and urine, and the presence of α -hydroxyacid and branched-chain α -ketoacids in urine. The presence of plasma L-alloisoleucine and urinary α -hydroxyisovalerate are pathognomonic for MSUD². According to the literature, five forms of MSUD have been described: classic, intermediate, intermittent, thiamine-responsive, and dihydrolipoyl dehydrogenase-deficient. The commonest and severest form of the disease is the classic type, which is characterized by a neonatal onset of encephalopathy². Magnetic resonance imaging (MRI) studies in the acute phase of classic MSUD are characterized by diffuse edema corresponding to both myelinated and unmyelinated areas of the brain³⁻⁶.

The purpose of this case report is to show conventional MRI and diffusion-weighted imaging (DWI) findings of the different evolutionary phases in MSUD of a newborn that evolved with brain white matter lesions.

CASE

A full-term male infant born from an uneventful pregnancy and delivery, with a birth weight of 3.245g and Apgar scores

of 9/10 (at 1 and 5 min, respectively), was hospitalized because of sucking difficulties, weak cry, and lethargy. At 10 days of life, the baby had episodes of seizures, bradycardia, and apnea, leading to coma. Biochemical examinations showed hypoglycemia and metabolic ketoacidosis. Brain MRI at 10 days of life showed hypersignal lesions on DWI and corresponding hyposignals on ADC maps throughout the white matter of the brainstem, cerebella and internal capsules (Fig 1).

At 20 days of life the clinical condition of the baby became critical and maple syrup odor or sugar burnt was noted in the urine. A repeat MRI at this time showed increasing myelinating white matter lesions and new hypersignal lesions on T2-weighted sequences and hyposignal on the diffusion-weighted images located in the unmyelinated white matter of the frontal, parietal and temporal lobes (Fig 2).

At 25 days of age, chromatography showed an increase of the branched-chain amino acids in the plasma with elevated levels of leucine = 2,982 $\mu\text{mol/L}$ (normal values: 48–160 $\mu\text{mol/L}$); isoleucine = 648 $\mu\text{mol/L}$ (normal values: 26–91 $\mu\text{mol/L}$) and valine = 677 $\mu\text{mol/L}$ (normal values: 86–190 $\mu\text{mol/L}$). The baby was treated with a specific aprotic diet and 48-hours of dialysis, which dramatically improved the clinical status. Treatment was continued only with a special nasogastric diet.

Repeat chromatography at 5 months of age showed persistently elevated plasma branched-chain amino acids levels with leucine = 764 $\mu\text{mol/L}$ (normal values: 47–155 $\mu\text{mol/L}$), isoleucine = 91 $\mu\text{mol/L}$ (normal values: 31–86 $\mu\text{mol/L}$) and valine = 65 $\mu\text{mol/L}$ (normal values: 64–294 $\mu\text{mol/L}$).

At 8 months of age, a follow-up MRI was performed that showed persisting white matter lesions in the frontal, parietal and temporal lobes with associated hypersignal on DWI and hy-

CONTRIBUIÇÃO DA SEQUÊNCIA DIFUSÃO DA MR NO DIAGNÓSTICO E ACOMPANHAMENTO DA ENCEFALOPATIA POR DOENÇA DA URINA EM XAROPE DE BORDO EM NEONATO A TERMO

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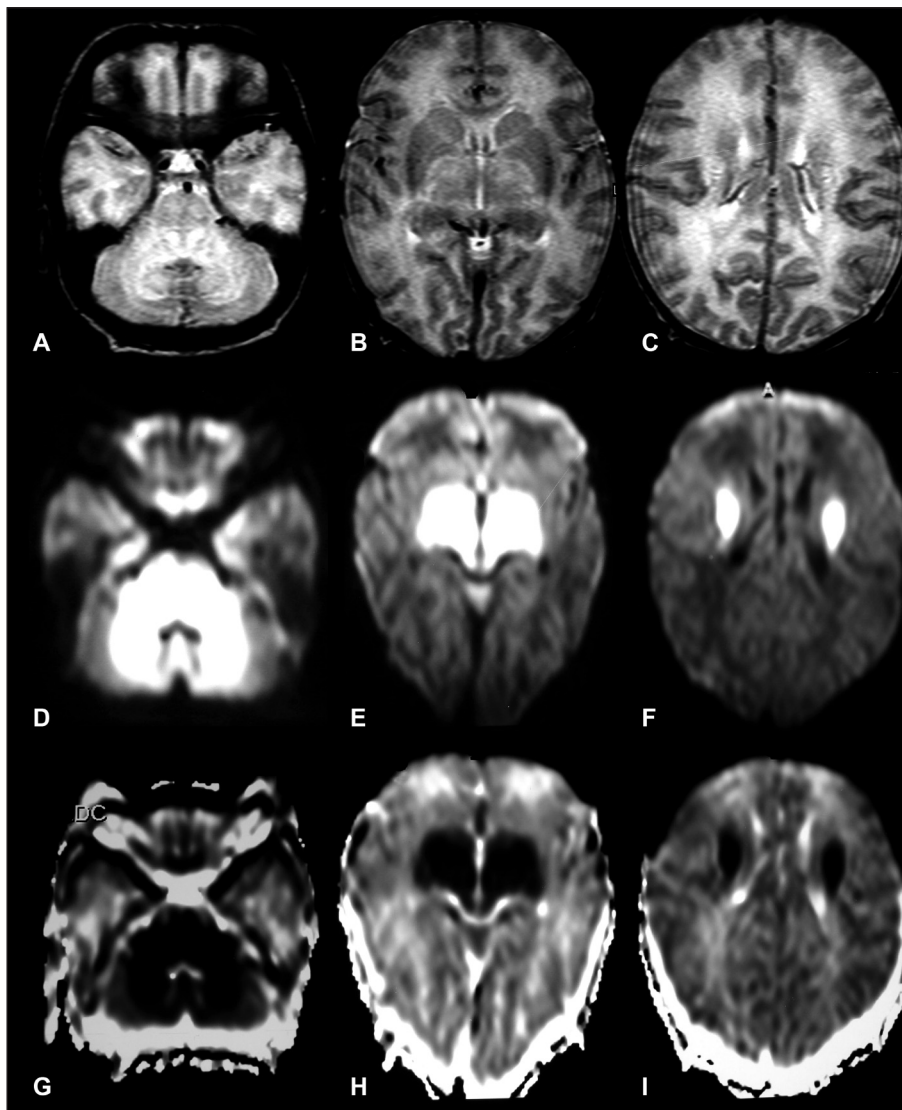


Fig 1. Axial - T2-weighted [A–C], diffusion-weighted [D–F], ADC maps [G–I]: in the acute metabolic decompensation shows hyperintense lesions on the diffusion-weighted images and hypointense on ADC maps in the brainstem, basal ganglia, thalami and white matter, which demonstrate a cytotoxic pattern of edema.

posignal on ADC maps (Fig 3). Chromatography of the amino acids at this time continued to show increased levels of isoleucine = 767 $\mu\text{mol/L}$ (normal values: 31–86 $\mu\text{mol/L}$) and valine = 1,128 $\mu\text{mol/L}$ (normal values: 64–294 $\mu\text{mol/L}$) but a decrease in the leucine level = 25 $\mu\text{mol/L}$ (normal values: 47–155 $\mu\text{mol/L}$) for the age.

This study was approved by the Ethics Research Committee of the Institution.

DISCUSSION

The present case report shows the findings of brain MRI DWI findings in different phases of classic MSUD in a full-term newborn with an unfavorable clinical outcome.

Conventional MRI during the acute metabolic decompensation phase of the disease is characterized by hyper-

signals on T2-weighted sequences and the contrary pattern in the signal on DWI and ADC maps, which occur both in myelinated and unmyelinated white matter, suggestive of different underlying pathogenetic mechanisms^{1,3,6}.

Myelinated white matter changes during the acute phase of MSUD are characterized by a decreased value of ADC that may be a result of neurotransmitter disorders, such as an increase in glutamate, an impaired energy metabolism associated with increases in brain lactate and decreased synthesis of lipid and proteolipid proteins⁷⁻⁹. On the other hand, an increase in ADC intensity in unmyelinated white matter may be due to blood-brain barrier alterations (vasogenic-edema)¹⁰.

In our case, during the acute phase of MSUD the brainstem myelinated areas and the internal capsules were

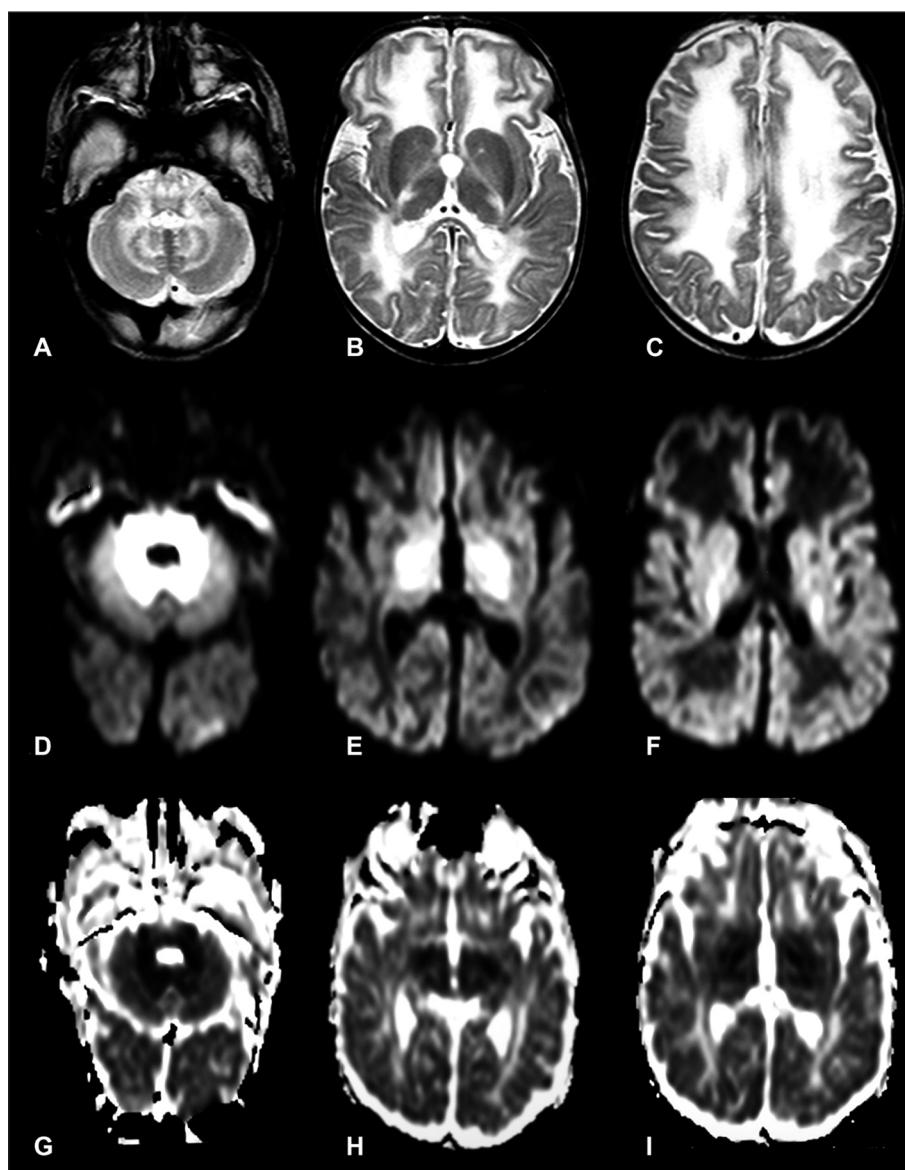


Fig 2. Follow-up after twenty days show new hyperintense lesions on the T2-weighted images and hyperintense on ADC maps in the unmyelinated white matter of the frontal, parietal and temporal lobes, which demonstrate a vasogenic pattern of edema.

characterized by hypersignal on DWI and hyposignal on ADC maps, which suggests the presence of intramyelinic cytotoxic edema. At this time, an increase in branched-chain aromatic amino acids in plasma (leucine, isoleucine, and valine) was observed coinciding with the appearance of cerebral edema and the consequent clinical aggravation characterized by seizures, bradycardia and apnea leading to coma.

Subsequently, the lesions in brain regions that are myelinated early improved but new lesions appeared in the periventricular and subcortical white matter after the first year of life. The new lesions had hyposignals on ADC maps compatible with cytotoxic edema. These new lesions showed a rapid and progressive disease course fol-

lowing the normal brain myelination, which was concurrent with clinical deterioration associated with anemia, urinary tract infection and a persistent increase in isoleucine and valine amino acids.

The unfavorable outcome in the present report may be justified because the diagnosis and specific treatment were delayed; there was no improvement in the imaging pattern and amino acid plasma levels in follow-up study.

Ha et al.¹ described a case of MSUD in which cytotoxic edema regressed parallel to the increasing ADC value, however vasogenic-interstitial edema evolved to brain atrophy with worsening of the ADC value. The patient also had increased leucine plasma levels at follow-up.

On the other hand, normalization of signal chang-

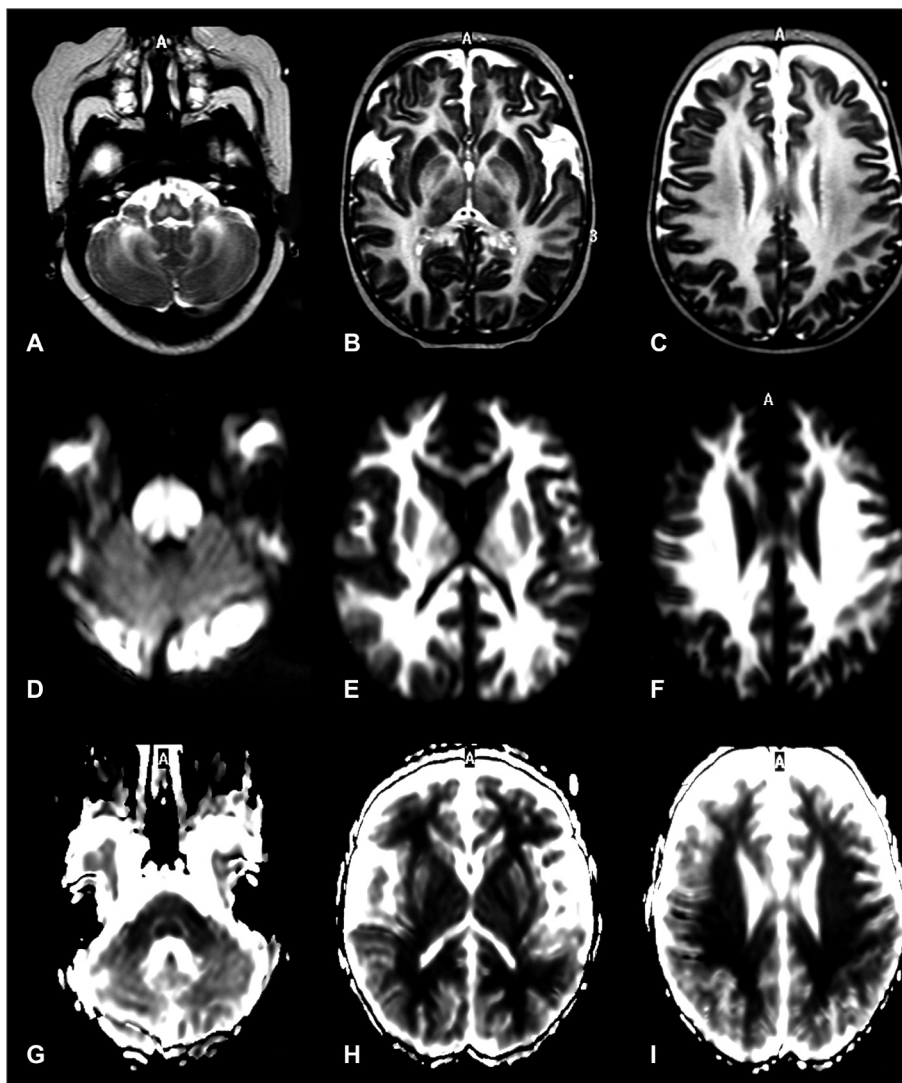


Fig 3. After eight months, there are persistence of hyperintense lesions on the T2-weighted images in the white matter frontal, temporal and parietal lobes with hyperintense in diffusion-weighted images and hypointenses on ADC maps, which demonstrate a cytotoxic pattern of edema.

es of DWI and ADC maps on MRI follow-up have been shown in patients with decreases of amino acid plasma levels and corresponding clinical improvement, which is attributable to both the duration of encephalopathy in the acute phase of MSUD and the success of early specific treatment^{3,5,6,11}.

The unfavorable outcome in children with MSUD is consistently bad when the disease is diagnosed after 14 days^{1,12}. According to Morton et al.¹² the prolonged deficiencies of one or more of the amino acids caused by excessive dietary restriction causes anemia and immunodeficiency, as well as dysmyelination, poor head growth and overall developmental delays. These authors also mentioned that the brain edema and hyponatremia were associated with hypersignals on T2-weighted MRI throughout the deep gray matter, different to what was observed

in our case in which the serum sodium levels remained normal.

Diffusion-weighted MRI can demonstrate the involvement of myelinated white matter in newborns in the acute phase of MSUD. Follow-up DWI associated with amino acid plasma level measurements may be of predictive value for the clinical outcome and the efficacy of treatment.

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