



Infantile Spasms during Acute Metabolic Decompensation in an Infant with Isovaleric Acidemia

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Dear Editor,

Isovaleric acidemia (IVA) is a rare branched-chain organic acidemia caused by deficiency of isovaleryl-CoA dehydrogenase (IVD). Acute and chronic intermittent forms of IVA have been described. The acute form typically present during the neonatal period with acute encephalopathy, vomiting, dehydration, and severe metabolic acidosis. The chronic intermittent form is characterized by periodic vomiting, lethargy, coma, ketoacidosis, and a 'sweaty feet' odor. Epileptic seizures have rarely been reported during the metabolic decompensation period.¹

Infantile spasms (IS) occur occasionally in patients with inborn errors of metabolism, including organic acidurias.² Here we report the occurrence of IS in a male infant diagnosed with IVA during an episode of metabolic decompensation, whose spasms were controlled with adrenocorticotropic hormone (ACTH) treatment.

A 5-month-old boy was referred to our emergency room with symptoms of lethargy, vomiting, and flexor spasms marked by a series of sudden flexions of the head, trunk, arms, and legs over a 24-hour period. There was first-degree consanguinity between the parents, and the pregnancy was unremarkable except for intrauterine growth retardation. There was no history of psychomotor retardation or acute encephalopathy attacks. A laboratory investigation revealed metabolic acidosis with a high anion gap (pH: 7.31), lactic acidosis (7.8 mmol/L), and hyperammonemia (182 mol/L). The patient had mild renal failure (54 mg/dL blood urea nitrogen, 0.9 mg/dL serum creatinine, 7.2 mg/dL uric acid, and estimated glomerular filtration rate: 52.6 mL/min/1.73 m²). EEG revealed hypsarrhythmia, and so he was diagnosed with IS (Fig. 1). The findings of magnetic resonance imaging of the patient's brain at diagnosis were normal. His acidosis and renal failure were treated with appropriate fluid and bicarbonate treatment, and vigabatrin (100 mg/kg/day) was initiated for spasms. Despite an improvement of metabolic acidosis and renal failure on the 6th day of hospitalization, the spasms were not controlled. Therefore, high dose synthetic ACTH (150 IU/m²/day) was administered intramuscularly twice a week while he received vigabatrin. His spasms improved on day 5 of treatment, and the hypsarrhythmia resolved by day 30. IVA was diagnosed on the 8th day of hospitalization, based on urine organic acid analysis showing an elevated concentration of isovalerylglycine and tandem mass spectrometry of acylcarnitines in dried blood spots showing elevated C5-carnitine (isovalerylcarnitine). Enzyme analysis of cultured fibroblasts showed decreased IVD levels. A protein-restricted diet, L-carnitine (100 mg/kg i.v. per day), and hydroxycobalamin were initiated for IVA. The side effects of ACTH therapy were noted, including irritability and weight gain. After 1 month, ACTH was ended and the patient remained seizure-free at 18 months after the treatment.

IVA is an uncommon branched-chain organic acidemia characterized by acute episodes of metabolic acidosis with a high anion gap, which may lead to coma and death. Developmental delay is the most common neurologic finding of IVA. Epileptic seizures have rarely

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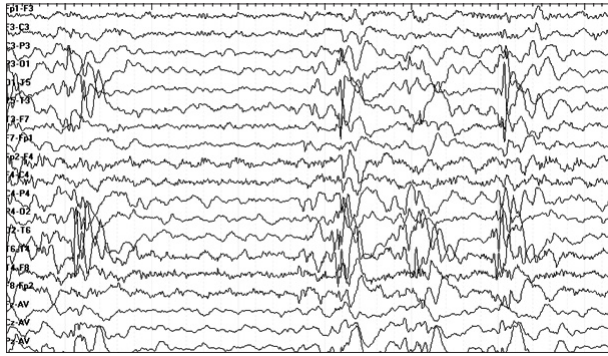


Fig. 1. Interictal sleep EEG. Hypsarrhythmia with some periodicity.

been reported during the metabolic decompensation period or follow-ups. Ozgul et al.¹ reported epileptic seizures in only 3 out of 26 patients with IVA.

IS are uncommonly reported in inborn metabolic disorders, but their prevalence is probably underestimated. More than 25 types of inborn errors of metabolism have been considered etiologic or predisposing factors for IS.³ Many studies have shown an association between branched-chain metabolic disorders and IS, including vitamin B₁₂ deficiency, methylmalonic aciduria and propionic acidemia.^{3,4} To the best of our knowledge, our case is the first to show an association between IVA and IS.

IS is treated by administering ACTH, vitamin B₆, vigabatrin, or other antiepileptic drugs. Steroids and ACTH can affect protein catabolism so as to lead to catastrophic metabolic decompensation when an inborn errors of metabolism is present. Rutledge et al.⁵ reported an IS patient controlled with

ACTH who subsequently developed severe lactic acidosis, which led to a diagnosis of pyruvate carboxylase deficiency. On contrast, Campeau et al.⁴ described an infant with methylmalonic aciduria whose spasms were fully controlled by hydrocortisone therapy and without severe side effects. In the present case, we initiated ACTH after correcting metabolic acidosis, and we did not observe any metabolic decompensation episode during follow-up.

This present case illustrates that organic acidemias including IVA should be kept in mind in the differential diagnosis of IS. Also, shortly after correcting metabolic decompensation, ACTH can be used safely and effectively to control IS in patients with IVA.

Conflicts of Interest

The authors have no financial conflicts of interest.

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