pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2016;12(3):376-377 / http://dx.doi.org/10.3988/jcn.2016.12.3.376

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

Taner Sezer[a]
Oya Balci[b]

[a]Department of Pediatric Neurology, Baskent University Faculty of Medicine, Ankara, Turkey
[b]Department of Pediatric Gastroenterology and Nutrition, Kecioren Research and Training Hospital, Ankara, Turkey

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 intemittent 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 m^2). 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 approciate fluid and bicarbonate treatment, and vigabatrine (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/m^2/day) was administered intramuscularly twice a week while he received vigabatrine. 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

Received December 2, 2015
Revised January 19, 2016
Accepted January 22, 2016

Correspondence
Taner Sezer, MD
Department of Pediatric Neurology, Baskent University Faculty of Medicine, Ankara 06490, Turkey
Tel +90 (312) 212 68 68
Fax +90 (312) 215 75 97
E-mail mdtanersezer@yahoo.com

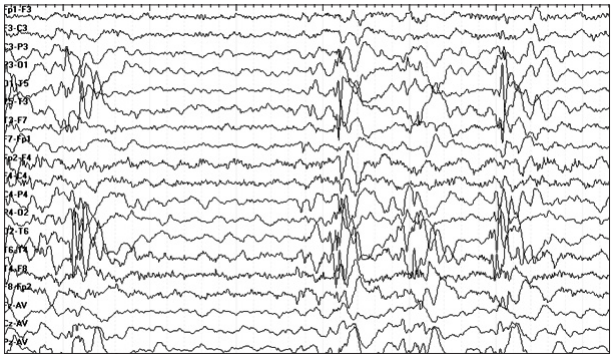

Fig. 1. Interictal sleep EEG. Hypsarrhythmia with some periodicity.

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 B_{12} 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 administereting ACTH, vitamin B_6, vigabatrine, or other antiepileptic drugs. Steroids and ACTH can affect protein catabolism so as to lead to catastrophic metabolic decompensation when an inborn errors of metabolizm 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.

REFERENCES

1. Ozgul RK, Karaca M, Kilic M, Kucuk O, Yucel-Yilmaz D, Unal O, et al. Phenotypic and genotypic spectrum of Turkish patients with isovaleric acidemia. *Eur J Med Genet* 2014;57:596-601.
2. Gkampeta A, Pavlou E. Infantile spasms (West syndrome) in children with inborn errors of metabolism: a review of the literature. *J Child Neurol* 2012;27:1295-1301.
3. Erol I, Alehan F, Gümü A. West syndrome in an infant with vitamin B12 deficiency in the absence of macrocytic anaemia. *Dev Med Child Neurol* 2007;49:774-776.
4. Campeau PM, Valayannopoulos V, Touati G, Bahi-Buisson N, Boddaert N, Plouin P, et al. Management of West syndrome in a patient with methylmalonic aciduria. *J Child Neurol* 2010;25:94-97.
5. Rutledge SL, Snead OC 3rd, Kelly DR, Kerr DS, Swann JW, Spink DL, et al. Pyruvate carboxylase deficiency: acute exacerbation after ACTH treatment of infantile spasms. *Pediatr Neurol* 1989;5:249-252.