A Rare Case Of Urea Cycle Defect: Carbamoylphosphate Synthase 1 (Cps1) Deficiency

Pelin Teke Kisa¹, Zelin Icen², Buse Soysal³, Semra Gursoy⁴, Filiz Hazan⁴, Tulin Gokmen Yildirim³

¹Dr. Behçet Uz., Departments of Pediatric Metabolism and Nutrition, Izmir, Turkey
²Dr. Behçet Uz Children's Diseases Training and Research Hospital, Child Health and Diseases, Izmir, Turkey
³Dr. Behçet Uz Children's Diseases Training and Research Hospital, Departments of Neonatology, Izmir, Turkey
⁴Dr. Behçet Uz Children's Diseases Training and Research Hospital, Departments of Pediatric Genetics, Izmir, Turkey

Introduction and Purpose

Carbamoylphosphate synthetase I deficiency (CPS1 deficiency) is the most severe of the urea cycle disorders. Individuals with complete CPS1 deficiency rapidly develop hyperammonemia in the newborn period. The worldwide prevalence ranges between 1/526,000-1,300,000 live births. CPS1 deficiency is currently divided into two types of neonatal onset and late onset. Typically, the neonatal-onset patient with CPS1D appears to be healthy at birth, but deteriorates rapidly into severe hyperammonemia, presenting poor feeding, vomiting, hypotonia, irritability, seizures, hypothermia, lethargy, coma, apnea, and even death after first feeding. Here we report the case of a newborn with lethal hyperammonemia.
She was apparently healthy at birth with weight of 3425 grams. The second day, she was admitted to the hospital with poor feeding, vomiting, and sleepy and then developed presenting respiratory distress, hypotermia, and hypotension, she was immediately intubated and transported to NICU (Glasgow Coma Scale: 3). Midazolam infusion was started with levetiracetam and phenobarbital loading due to recurrent seizures. Laboratory investigations on admission revealed hyperammonemia (3417 µmol/l). Treatment for undiagnosed urea cycle disorder was initiated with continuous hemodiafiltration, and administration of carnitine 50 mg / kg / g, sodium phenyl acetate + sodium benzoate 250 mg / kg loading + maintenance, carglumic acid 100 mg / kg / d. Her ammonia levels decreased immediately after initiation of acute therapy. Unfortunately, the patient deteriorated continually into multiple-organ failure and even had cardiac arrest with no spontaneous breathing. Laboratory tests revealed decreased citrulline and arginine levels and increased glutamine and alanine levels. Additionally, to confirm the disease the genetic analysis revealed a homozygous variant in the CPS1 gene which was c.3048_3050delGGT (p. Val1019del).
Life-threatening findings are observed with severe hyperammoniemia in neonatal-onset CPS1 deficiency. Although, a newborn with hyperammoniemia is early detected and treatment is rapidly initiated in the NICU. These patients, who are exposed to many serious interventions such as catheter, hemodialysis, continue to have a mortal course due to bleeding, infection, and similar complications.