Clinical, biochemical data and molecular analyses of 3 cases affected of Hyperornithinemia, Hyperammonaemia and Homocitrulliuria

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Introduction

Hyperornithinemia-Hyperammononemia-homocitrullinuria syndrome is a rare autosomal recessive disorder of urea cycle caused by mutations in SLC25A15 gene which encodes mitochondrial (mt) ornithine carrier (ORC1) for ornithine transport across the inner part of mt membrane, resulting in low mitochondrial ornithine, required for OTC to prime UC. Carbamyl-phosphate (CP) level increases which binds Lysine, forming homocitrulline, leads to homocitrullinuria and stimulation of pyrimidine resulting in orotic aciduria.
Clinical features

**Neonatal onset (8%)** poor feeding, vomiting, tachypnea, letargy and hepatitis like attacks.

**Infancy, childhood, adulthood (92%)** either, with chronic neurological course with protein intolerance, neurocognitive error, seizures, ataxia and pyramidal dysfunction and/or chronic liver disease.

**Treatment**: Ammonia remover medication for hyperammonaeiam attacks, low protein diet, essential amino acids, arginine to treat low arginine, citrulline for better control and creatine to treat creatine deficiency resulted from low arginine and AGAT inhibition by high ornithine level in cytosol.
Methods; A retrospective study of 3 cases affected of 3H syndrome since 2000 up to now.

Case A; a male, referred at 17 year of life with motor delay, spastic paresis, ataxia, speech disorder.

Case B; a 2 years old female, with convulsion at 14 month, poor gain weight, walking delay.

Case C; a 22 years old male, referred at 27 months, with poor feeding, tachypnea and lethargy, on 2nd day of life and the similar attack at 15 months, with hypotonicity, hepatomegaly up to 7 years on follow up to now.
Biochemical data: high plasma glutamine; 893-955 (normal, 345-645 µmol/L), high ornithine; 145-257 µmol/L (26-110 µmol/L), and homocitrullinuria. Blood ammonia; (118-145 µmol), all had hepatic presentation. Molecular analyses; Homozygous c.706 A> G, (p.R236G) and Homozygote c.117G>À and p.Thr36Thr.

Conclusion

We reported one acute neonatal phenotype of 3H syndrome with neurologic & hepatic presentation, now he is 23 years old, an asymptomatic student of college with normal growth and two others with childhood phenotypes still symptomatic due to late treatment.