Newborn Screening, Inborn Errors of Metabolism

AB014. Beta-ketothiolase deficiency: phenotype, genotype and outcome of 48 Vietnamese patients

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Background: Beta-ketothiolase deficiency (BKT) is an inherited metabolic disease of isoleucine and ketone body caused by mutations in the *T2* gene. It is a rare disease with over 100 patients reported worldwide. We aimed to describe phenotypes and genotypes and to evaluate outcomes of Vietnamese patients with BKT.

Methods: Patients who were diagnosed with BKT, and followed up at National Children Hospital from January 2015 to June 2017 were enrolled.

Results: Forty-eight patients from 40 different and unrelated families were diagnosed through high risk screening in Vietnam. Forty-six patients (96%) presented with acute episodes of intermittent ketotic acidosis (pH <7.1, increased anion gap), and were asymptomatic between episodes. Ages of onset were between 6 and 18 months. Characteristics of metabolic chemistry revealed elevated urinary 2-methylacetoacetate, 2-methyl-3-hydroxybutyrate, tiglylglycine, and plasma C5:1 and C5:OH carnitines. We identified 8 different mutations with 9 kinds of genotypes. The common mutations of *T2* gene were p.R208X and IVS10-1g>c (85%). Five novel mutations were identified (IVS10-1g>c, c.1032_1033insA, p.S284N, exon 6 -11del, and c.163_167delinsAA). Eight out of nine genotypes were null mutations. There was no correlation between genotypes and phenotypes. The outcome was good in most patients with 83% had complete recovery, 7% mental consequences, and 12% death. All patients had normal growth rate according to growth chart by World Health Organization (WHO) 2007.

Conclusions: BKT is a common inborn error of metabolism in Vietnam with good outcome in most patients. A newborn screening program for BKT may have a high detection rate in Vietnam.

Keywords: Beta-ketothiolase deficiency (BKT); T2 deficiency; mitochondrial acetoacetyl-CoA thiolase deficiency; Vietnam

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