Newborn Screening, Inborn Errors of Metabolism

AB059. Clinical, biochemical, and molecular features of Thai patients with multiple acyl-CoA dehydrogenase deficiency

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Background: Multiple acyl-CoA dehydrogenase deficiency (MADD) is caused by mutations in the alpha (*ETFA*) and beta (*ETFB*) subunits of electron transfer flavoprotein, and electron transfer flavoprotein dehydrogenase (*ETFDH*) which involves in the mitochondrial electron transport from acyl CoAs to ubiquinone. Thus the mitochondrial oxidations of glutaryl CoA and branched-chain organic acids, and beta-oxidation of fatty acids are impaired. The phenotype is classified into neonatal-onset (severe), infantile-onset (intermediate), and late-onset (myopathic) forms.

Methods: We retrospectively reviewed the clinical features of patients with MADD who were diagnosed by urine organic acids or blood acylcarnitine analysis at Department of Pediatrics, Faculty of Medicine Siriraj Hospital. Molecular analysis was performed in biochemically confirmed cases.

Results: Among 11 Thai patients with MADD, the most common form is the late-onset (8 cases), 2 cases with the neonatal-onset form, and 1 case with the infantile-onset form. All cases with the late-onset form presented with muscle symptoms characterized by neck weakness. Muscle biopsy showed lipid myopathy. Some of them had hypoglycemia and cardiomyopathy. Interestingly, three cases had excessive weight loss. All late-onset cases were responsive to riboflavin treatment. Two patients with neonatal onset presented with hypoglycemia, acidosis, hyperammonemia, and sweaty feet odor since 1 day of age. Hypospadias was noted in one case, and mild dysmorphic face in another. The 2 cases were fatal, and died in infancy. One case with probably intermediate form was identified by newborn screening, and only mild acidosis was noted at 7 days of age. Not all patients with the late-onset form showed the characteristic profiles in blood acylcarnitines and urine organic acids. The c.250G>A (p.A84T) mutation in the *ETFDH* gene is commonly found in our late-onset, riboflavin-responsive patients.

Conclusions: We report a phenotypic spectrum of MADD in Thai population. The *ETFDH* mutations could predict the clinical phenotype and riboflavin responsiveness.

Keywords: Multiple acyl-CoA dehydrogenase deficiency (MADD); *ETFDH* mutations; riboflavin response

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