Long-term follow-up of Taiwan Chinese patients who received early treatment for 6-pyruvoyl-tetrahydropterin synthase deficiency

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In Taiwan, 6-Pyruvoyl- tetrahydropterin synthase (PTPS) deficiency is the cause of approximately one-third of all cases of hyperphenylalaninemia (HPA). The prevalence of PTPS deficiency in this country (1/132,000) is considerably higher than in Caucasian populations (1/1,000,000). This provides us with more opportunities to observe and treat this form of illness within a single medical center. The treatment of PTPS deficiency consists of replacement with BH4 and the neurotransmitters L-DOPA and 5-HTP. Descriptions of the outcomes of patients with BH4 deficiency, particularly over long periods of observations, remain scarce. The proper amount of neurotransmitter replacement should be based on the levels of cerebrospinal fluid (CSF) neurotransmitter metabolites. However, these measurements are not available here. Therefore, the administration of each agent was based only on the clinical response and development of adverse effects at our clinics. We have been concerned that replacement of neurotransmitters guided by clinical observations may not be the most appropriate for these patients, and that long-term inappropriate treatment may be the source of subtle brain damage and gradual neurological dysfunction. In this study, we reviewed the characteristics of 13 PTPS-deficiency patients who were found by newborn screening and accepted early treatment. All of these patients were followed at our clinics for more than 5 years (range 5-20 years). The relationships among treatment, clinical manifestations, biochemical findings, genotypes, and outcomes were analyzed. The average intelligence quotient (IQ) scores of these patients was 97. The genotype, birth body weight and the age at commencement of BH4 and neurotransmitters replacement had a significant relationship with the IQ scores. Our results revealed that the outcome of the early-treated PTPS deficiency patients is as good as that of classical phenyketonuria patients under diet restriction therapy, even when the adiministration of neurotransmitters was based on clinical response and adverse effects.