Clinical and biochemical study for the diagnosis, treatment and prenatal diagnosis of tetrahydrobiopterin deficiency due to 6-pyruvoyl tetrahydropterin synthase deficiency

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Objectives To study the diagnosis, treatment and prenatal diagnosis of tetrahydrobiopterin (BH_4) deficiency due to 6-pyruvoyl tetrohydropterin synthase (PTPS) deficiency.

Methods 10 patients (2 boys and 8 girls) with PTPS deficiency were reviewed. Urine pteridines and blood dihydropterindine reductase were analyzed for the diagnosis. Combined loading tests with phenylalanine (Phe) and BH4 were further investigated in 2 patients. PTPS gene in 7 patients and their parents was studied. Amniocytes DNA of the fetuses from 2 families were analyzed for the prenatal diagnosis. Three patients were treated by supplementation of BH_4, L-dopa and 5-hydroxytryptophan.

Results Varied heperphenylalaninemia (HPA) and extremely decrease of urine biopterin were confirmed in 10 patients. 7 cases were detected by clinical investigation. They began to develop progressive neurological abnormality from the early infant period. Severe psychomotor retardation was found in the 7 patients. Among them, 6 had epilepsy and malnutrition, 5 had hypotonia and 2 had dystonia. 6 died in pneumonia or convulsion status at the age of 2.5 ? 6 years. 3 patients were detected by neonatal screening. 2 were treated by Phe-restricted diet and hospitalized at their age of 5 and 12 months because of much delayed development. After supplementation of BH_4, L-dopa and 5-hydroxytryptophan, clinical improvement was observed. A girl who was treated from the age of 1 month showed normal development. Nine mutations (155A>G, 226C>T, 256C>T, 259C>T, 272A>G, 286G>A, 317C>T, IVS3+1 G>A, IVS1-291A>G) in PTPS gene were identified from 7 families. The third fetuses from two families were not affected by PTPS deficiency. One healthy boy and one girl were born from each family. Normal phenotype

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had been confirmed by clinical follow and restudy of PTPS gene after birth.

Conclusions PTPS deficiency is the most common form of BH_4 deficiency. Early diagnosis and BH_4 supplement are the key points to improve the prognosis of the patients. The differential diagnosis for BH4 deficiency should be carried out in all patients with HPA from classical PKU. Amniocytes PTPS gene study is a reliable method for the prenatal diagnosis of PTPS deficiency.

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