Dihydropteridine Reductase Deficient Hyperphenylalaninemia in Chinese

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Dihydropteridine reductase (DHPR) regenerates the tetrahydrobiopterin (BH_4) from its oxidized form, namely quinonoid dihydrobiopterin, produced in the pathway of the hydroxylation of aromatic amino acids. Defect in DHPR will result in BH_4-deficient hyperphenylalaninemia (HPA) (MIM 261630) with characteristic clinical presentations of progressive neurological degeneration and mental retardation. DHPR-deficient HPA is the second common form of BH_4-deficiency and requires different treatment from classical HPA (MIM 261600). DHPR-deficient HPA could be detected in the neonate stage by newborn screening and differentially diagnosed by BH_4 oral loading test with a dosage of 20 mg /kg wt and/or measurement of blood DHPR activity. Three patients from two families were diagnosed as DHPR-deficient HPA in Taiwan so far. One of these patients was detected by newborn screening and showed partial response to BH_4 loading (7.5 mg/ kg wt) with residual DHPR activity in blood (10% of normal). The other two patients were born in a consanguineous family and were detected by high risk metabolic screening for mentally retarded school children. The blood DHPR activity of these two siblings were not detectable. These three DHPR-deficient patients were on dietary treatment plus BH_4 and neurotransmitter replacement and folinic acid supplementation. A single base transition c.508G>A (Gly170Ser) on the DHPR cDNA was identified in the consanguineous DHPR deficient siblings. With regard to the other patient, a heterozygous c.697A>C (T233P) mutation was identified with no other nucleotide alternation being detected in the coding sequence and exon/intron boundary of the DHPR gene. Prenatal diagnosis was successfully performed by measuring DHPR activity in amniocytes and RFLP linkage analysis for the DHPR-deficient family.