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***Short Communication***

# Atypical Phenylketonuria with Mild Mental Retardation Caused by Tetrahydrobiopterin Deficiency in a Chinese Family

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Tetrahydrobiopterin ($BH_4$) is the cofactor for aromatic amino acid hydroxylases, including phenylalanine hydroxylase (EC 1.14.16.1) which is deficient in classical phenylketonuria (PKU, McKusick 26160). Most atypical PKU due to defects in biopterin metabolism have been reported to be very severe (Smith *et al.*, 1975) and have been described as 'malignant hyperphenylalaninaemia' (Danks *et al.*, 1979). The $BH_4$ deficiencies may be caused by deficient activity of dihydropteridine reductase (DHPR; EC 1.6.99.7; McKusick 26163), GTP cyclohydrolase I (EC 3.5.4.16), or 'dihydrobiopterin synthetase' (DHBS; McKusick 26164 and 26169) (Niederwieser *et al.*, 1982). Autosomal recessive inheritance is proved in DHPR deficiency, but is only suspected in DHBS deficiency (Dhondt, 1984). The incidence of $BH_4$ deficiency among hyperphenylalaninaemic babies was estimated to be 1.5–2% in the Caucasian population (Niederwieser *et al.*, 1982; Dhondt, 1984). Very few cases of PKU of Chinese origins have been reported (Hsiao *et al.*, 1984) and no case of $BH_4$ deficiency has been published.

We recently found two hyperphenylalaninaemic brothers, Y.S. (4.7 years old) and Y.C. (6.7 years old), from a Chinese family presenting with mild mental retardation (I.Q.: 53 and 65, respectively). They were both full-term normal spontaneously delivered well babies at birth, but delayed milestones were found gradually. They could not walk until 4 years old. Seizures began at about 1 year old. Although anticonvulsant drugs have been given since then, seizure activity persisted. They were referred to our special clinic for evaluation of their growth and psychomotor retardation. Neurological examination revealed decreased muscle tone, deep tendon reflex, and slurred speech. EEG revealed diffuse cerebral dysfunction. The parents have no consanguinity and their third boy is normal. We report here the clinical observations and biochemical evidence that these two patients have atypical PKU caused by defective synthesis of biopterin.

## MATERIALS AND METHODS

The dry blood spot phenylalanine (Phe) was determined by the Guthrie test. The same specimen was used to assay the activity of DHPR by measuring the pterin-



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