Proc 7th International Congress of Human Genetics, Berlin, p.336, 1986.

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ANALYSIS OF PTERINS IN AMNIOTIC FLUID FOR PRENATAL DIAGNOSIS OF ATYPICAL PHENYLKETONURIA CAUSED BY TETRAHYDROBIOPTERIN SYNTHESIS DEFICIENCY

Atypical phenylketonuria (PKU) due to tetrahydrobiopterin (BH_4) deficiencies may be caused by deficient activity of dihydropteridine reducatase, GTP cyclohydrolase I, or "dihydrobiopterin synthetase" (DHBS). Urinary pterin analysis by high performance liquid chromatography (HPLC) is a good diagnostic aid for differential variant forms of PKU and for detection of heterozygotes of atypical PKU caused by DHBS deficiency. Most atypical PKU found in Chinese is caused by DHBS deficiency. The determination of pterins in amniotic fluid by HPLC was studied for prenatal diagnosis of atypical PKU caused by BH_4 synthesis deficiency.

Pterins in amniotic fluid, collected from the 16th to 20th weeks of gestational age, were oxidized by maganese dioxide or iodine in acidic condition. After ultrafilterion, the analysis of total biopterin (B) and neopterin (N) was achieved by reverse phase (C-18) HPLC with fluorescent detection. 6-methylpterin was used as internal standard. The reference ranges (n=13) of B (pmol/ml), N (pmol/ml) and total biopterin ratio (B%=B/(B+N)) in amniotic fluid were 9.8-24.3, 26.1-48.0 and 16.7-36.9, respectively.

Fetal blood and amniotic fluid were taken by fetoscope at 19th week from a pregnancy at risk, which was found because a previous child had had malignant PKU caused by DHBS deficiency and was confirmed by demonstration that the parents had a heterozygous urinary pterin profile. Definitively conclusive result was not obtained from the determination of DHBS activity in fetal blood (Drs. Niederwieser & Shintaku, Children's Hospital, Zurich). The analysis of pterins (N=130.3, B=13.4 & B%=9.3) in amniotic fluid showed that the male fetus may be a heterozygote. A healthy child was born prematurely (36th week, 2450g). No hyperphenylalaninemia could be detected by blood spot screening at age of 5 days and of 2 months. The results indicate that analysis of pterins in amniotic fluid by HPLC will prove to be a successful method for prenatal diagnosis of atypical PKU caused by DHBS deficiency and may be extented for prenatal diagnosis of other variant forms of BH_4 deficiencies.

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