9th ASIAN-EUROPEAN WORKSHOP OF INBORN ERRORS OF METABOLISM

Unexplained familial methylmalonic aciduria: a benign situation or an unidentified inborn error?

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Elevated urine methylmalonic acid concentrations in children could be seen due to various etiologies such as vitamin B12 deficiency, bacterial overgrowth in the intestines but also some inborn errors. A total of five patients aged 9 months–11 years (two siblings) have been being followed-up in the Department of Metabolism because of unexplained methylmalonic aciduria ranging from 68 to 1194 mmol/mol creatine (Normal: 0). All the children have mild mental retardation. There were no specific findings in tandem mass examinations, normal B12, folic acid and homocysteine levels. No specific findings were seen with valine and isoleucine loading tests and neither with a short therapy of metranidasole. No specific excretion of any metabolite other than methylalonic acid was noticed with gas chromatography. Investigations of the cobalamine defects and methylmalonyl CoA mutase activities in three of them revealed normal results. The similarity of the clinical as well as the laboratory findings in all children suggest an unidentified genetic background. Further investigations are planned.

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Developments of neonatal screening in Taiwan

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Some of the congenital metabolic disorders have no specific clinical symptoms during neonatal period, if not treated early irreversible damages such as mental retardation will occur. The permanent damages can be avoided if these are able to be detected biochemically by neonatal screening in the early stage of life, and treated immediately with appropriate therapy and intervention. Method development pilot programs (including dried blood sample collecting, screening tests, confirmatory diagnostic procedures and treatments) were carried out in mental retarded children between 1982 and 1983 in Taiwan. Based on the methods developed, the nationwide project to set up neonatal screening for congenital hypothyroidism (CHT), phenylketonuria (PKU), maple syrup urine disease (MSUD), homocystinuria (HCU), and galactosemia (GAL) was started in January 1984. After the nationwide neonatal screening system was established in July 1985, the method for screening of glucose-6-phosphate dehydrogenase (G6PD) deficiency was developed. The incidence of G6PD deficiency was estimated to be about 2 % (male 3 %, female 0.9 %) in Taiwan based on the screening program. Since no MSUD was found from 200,000 newborns screened, after a two year (1985.7–1987.6) pilot study on G6PD screening, MSUD was replaced by G6PD in the routine nationwide neonatal screening program. The screening coverage rate in Taiwan has reached 80 % in 1990 and 99 % since 1996. From 1984.1 to 2002.12, 4,462,600 newborns have been screened. The incidences of CHT, PKU, HCU, and GAL were reported to be about 1/1,800, 1/31,400, 1/263,000, and 1/744,000, respectively. Most of the affected cases were detected and treated accordingly within one month of birth and are developing normally at the present time.

Each of the three neonatal screening centers in Taiwan has started individual voluntary program paid by the parents for selective screening of congenital adrenal hyperplasia (CAH) and defects in other amino acids and acylcarnitines metabolisms, which were detected by tandem mass spectrometry (MS/MS), since 2000.3 and 2001.8, respectively. The incidence of CAH was estimated around 1/15,000 from 600,000 newborns screened between 2000.3 and 2003.10. Six cases of 3-methylcrotonyl-CoA carboxylase deficiency (3MCC), 4 cases of citrullinemia (CIT), 3 cases of MSUD, 2 cases of glutaric aciduria type I (GAI), 1 case of methylmalonic aciduria (MMA), and 1 case of nonketotic hyperglycinemia were detected from 216,000 newborns by the MS/MS screening between 2001.8 and 2003.10.

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