Newborn Screening, Inborn Errors of Metabolism

AB054. Experiences during newborn screening for glutaric aciduria type 1: diagnosis, treatment, genotype, phenotype and outcomes

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Background: Glutaric aciduria type 1 (GA-1) is an organic acidemia with potentially severe neurological sequelae. In Taiwan, newborn screening (NBS) for GA-1 began in 2001, but large-scale reporting is lacking. This study describes Taiwan's largest NBS population to date.

Methods: Between 2001 and 2015, a total of 1,490,636 newborns were screened for GA-1. Confirmatory examinations included the carnitine loading test. Confirmed patients were treated with a low lysine diet, carnitine, and high-energy intake during illness. Clinical, laboratory, and neuroimaging data were analyzed.

Results: Fourteen newborns were diagnosed with GA-1 (incidence: 1/106,474). C5DC concentration was clearly increased after carnitine loading in the affected newborns, but not in false-positive newborns (P=0.004), indicating that this test is useful as an adjuvant diagnostic method. Eleven patients followed in our hospital were enrolled, namely nine patients detected through NBS and two patients diagnosed clinically. A variant of *GCDH* gene, IVS10-2A > C, was the most common mutation identified in the study population. Two novel mutations (T36fs and N291K) were identified. Pendular nystagmus was found in two pediatric GA-1 patients. The corresponding pathology was optic atrophy in one patient, but remained undetermined in the other patient. The frequency of encephalopathic crisis decreased substantially following establishment of the NBS program. Among patients diagnosed by NBS, cognitive functioning was better among patients with good compliance than those of patients with poor compliance (P=0.03). Abnormalities were detected by brain MRI; these affected various brain regions at different stages of the disease. Basal ganglion injuries occurred after an encephalopathic crisis. White matter disease was prevalent among older patients, either with or without a history of encephalopathic crisis.

Conclusions: Early diagnosis by NBS followed by full compliance with treatment guidelines is important to yield a good outcome.

Keywords: Taiwan; glutaric aciduria type 1 (GA-1); newborn screening (NBS); nystagmus; optic atrophy

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