Newborn Screening, Inborn Errors of Metabolism

AB017. Gene panel study for target metabolic diseases of newborn screening in Japan

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Background: Newborn screening (NBS) using tandem mass spectrometry has been performed since 2014 in all over Japan and the target metabolic diseases (TMDs) increased from 4 to at least 17 diseases. Molecular diagnosis for TMDs is not commercially available in Japan and until recently such molecular analyses were mainly performed by pediatricians with "volunteer spirits". To change the situation, we designed and conducted molecular diagnosis for TMDs using a gene panel.

Methods: We designed a gene panel, which consists of more than 60 genes covering the TMDs and the related diseases. This research was financially supported by Japan Agency for Medical Research and Development. DNA was purified from patients' blood at Gifu University and the gene panel analysis was performed at Kazusa DNA Research Institute using the MiSeq or NextSeq (Illumina®). Sanger sequencing was performed to confirm the detected mutations. Pediatric coauthors in this study are experts responsible to make mutation reports.

Results: We analyzed 138 patients who were positively screened during three years (January 2014 to March 2017) and 44 patients who were diagnosed before that period. The number of patients with TMDs detected by NBS was as follows: propionic acidemia [35], hyperphenylalaninemia [19], methylmalonic acidemia [17], VLCAD deficiency [15], Maple syrup urine disease [13], methylcrotonylglycinuria [13], galactosemia [10], primary systemic carnitine deficiency [9], MCAD deficiency [8], and others [43]. In most cases, we could find the gene mutations in their corresponding genes and found some common mutations for some TMDs in a Japanese population.

Conclusions: Clinical course and severity may differ among patients in some TMDs. One major factor to determine clinical phenotype is of course genotype. Hence, it is important to follow up mutation-defined patients to evaluate efficacy of treatment and management. We will individualize clinical guidelines by genotypes in some TMDs soon.

Keywords: Newborn screening (NBS); target metabolic diseases (TMDs); gene panel

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