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Genotype, Phenotype and Follow-up in Taiwanese Patients with Congenital Nephrogenic Diabetes Insipidus

Min-Hua Tseng[1], SHih-Hua Lin[2]
[1]Department of Pediatric Nephrology, Chang Gung Memorial Hospital, Chang Gung University, Taiwan
[2]Department of Medicine, Tri-Service General Hospital, Taiwan

Objectives: Genotype, phenotype, and follow-up outcome in Taiwanese patients with congenital nephrogenic diabetes insipidus (CNDI) due to arginine vasopressin V2 receptor (AVPR2) and the aquaporin 2 (AQP2) genetic mutations are not well evaluated. The aims of this stiudy is to investigate the phenotypic, genetic characteristics, and outcomes in the Taiwanese families with CNDI.

Methods: Twenty-two patients (M:F=18:4, age 22 ± 17) with CNDI belonging to fourteen unrelated Taiwanese families were enrolled. Genomic DNA from blood leukocytes was analyzed for *AVPR2* and *AQP2* genes mutations. dDAVP stimulation was administered to separate these two gene mutations. Clinical symptoms and biochemical studies at the first presentation as well as follow-up were examined.

Results: Of the 22 patients with CNDI, 15 have *AVPR2* mutations and 7 have *AQP2* mutations. Ten mutations, including 5 missnese, 2 novel small deletion, 2 large deletion, and 1 nonsense mutation, and three mutations, including Q57P, G100V, and 592InsC were identified in *AVPR2* and *AQP2* gene, respectively. Q57P and G100V were recurrent mutations of *AQP2*. All patients developed phenotypic polyuria and polydipsia. One symptomatic female patient with heterozygous V115X mutation in *AVPR2* gene had inactivated X chromosome in another allele. Three patients who carried same mutation (F178Q) from one family have different phenotypic severity. All patients with *AVPR2* mutation have blunted extrarenal response to dDAVP. Nine patients have non-obstructive hydroureteronephrosis. Seven patients, 4 *AVPR2*, 3 *AQP2*, reached chronic kidney disease (CKD, stage III-V) at the follow-up. Patients with large deletion of *AVPR2* have more severe phenotype than those without.

Conclusions: Large deletions of *AVPR2* are not uncommon, and intrafamilial phenotypic variability existed among members with *AVPR2* gene mutation. Patients with CNDI may be at increased risk for the development of CKD during long-term follow-up.