中文題目：水通道蛋白突變所致之腎因性尿崩症及慢性腎衰竭

英文題目：A Novel AQP-2 Insertion Mutation in a Chinese Family with Autosomal Dominant Nephrogenic Diabetes Insipidus and Chronic Renal Failure

作　　者：蔡炳煌[1], 鄭智仁[1], 王翠華[2], 林石化[1]

服務單位：[1]三軍總醫院內科部腎臟內科, [2]三軍總醫院外科部移植外科

Background:

The autosomal inheritance of nephrogenic diabetes insipidus (NDI) caused by AQP2 mutation is recessive in most cases featuring severe hypotonic polyuria soon after birth. In rare cases, the pathogenic AQP2 mutations can be inherited as autosomal dominant and often resulting in milder symptoms compared to autosomal recessive AQP2 mutations. The previously reported autosomal dominant AQP2 mutations are located at the cytoplasmic carboxyl-terminal domain and disrupt the membranous trafficking of aquaporin-2. We described a family of autosomal dominant NDI carried a novel AQP2 mutation but presented a severe phenotype, which led to early-onset renal failure.

Methods:

A 26-year-old Chinese female manifested polyuria, polydipsia, and nocturia after birth. Her family history was non-revealing. She did not have non-obstructive hydronephrosis and never received NSAID or thiazide to treat her polyuria. Pertinent laboratory investigations showed abnormal renal function with serum creatinine 3.4 mg/dL, and hyperchloremic metabolic acidosis (chloride 115, HCO_3^- 19 mmol/L), persistently low urine osmolality (around 50-100 mOsm/kg.H_2O) and markedly increased serum von Willebrand factor and coagulation factor VIII in response to desamino-8-D-arginine AVP (DDAVP) test. Direct sequencing of *AVPR2* and *AQP2* gene showed two nucleotide GC insertion at c.755 of AQP2, resulting in a frameshift mutation (p.R253Dfs*82, +52 AA) and altering the amino acid sequence between R254 to A271. Of note, her one-year-old son also exhibited severe polyuria two days after birth and was found carrying the same mutation.

Conclusions:

We presented the first autosomal dominant NDI family with a severe phenotype, including early-onset polyuria in the neonatal period and renal failure in early adulthood. The genotype-phenotype association highlights the critical function of the C-terminal tail of AQP2. The functional experiment focusing on autosomal dominant AQP2 mutations in the C-terminal end is warranted.