Genetic analysis of PRRT2 for benign infantile epilepsy, infantile convulsions with choreoathetosis syndrome, and benign convulsions with mild gastroenteritis

Atsushi Ishii1,2, Sawa Yasumoto1, Yukiko Ihara1,2, Takahito Inoue1, Takako Fujita1, Noriko Nakamura1, Masaharu Ohfu1, Wang-Tso Lee3, Sunao Kaneko4 and Shinichi Hirose1,2

1) Department of Pediatrics, Fukuoka University, Fukuoka, Japan
2) Central Research Institute for the Molecular Pathomechanisms of Epilepsy, Fukuoka University, Fukuoka, Japan
3) Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
4) Department of Neuropsychiatry, Hirosaki University, Hirosaki, Japan
To identify PRRT2 mutations in infantile convulsions in Asian families with benign familial infantile epilepsy (BFIE).
Autosomal Dominant Inheritance
High Penetrance
Onset age at 3 to 24 months
Seizures in cluster
Spontaneously remission
Good response to carbamazepine
Good prognosis
26 Japanese families with individuals affected by infantile seizures

BFIE: 19 families

None family history: 4 individuals

Infantile Convulsions with Choleoathetosis syndrome (ICCA):

3 families

Department of Pediatrics, School of Medicine, Fukuoka University, Japan
Subjects

17 individuals with benign Convulsions with mild Gastroenteritis (CwG)

50 families with Benign Familial Neonatal Epilepsy (BFNE)
BFIE

E+  E-

E+  E+

E+  E+

E+

ICCA

E+  E-

E+

Paroxysmal kinesigenic choreoathetosis

Infantile seizure

Febrile seizure

Department of Pediatrics, School of Medicine, Fukuoka University, Japan
Mutations

c. 649dupC; p.Arg217ProfsX8

\[
\begin{align*}
  & CGAGTGCTGCAGCAGCTGGTTG \\
  & GCCGGGGGGGGGGGAGTGCTGCAGCAGCTGGTTGA
\end{align*}
\]

16 /26 probands 3/3 ICCA

No mutation in 17 CwG and 50 BFNE

Department of Pediatrics, School of Medicine, Fukuoka University, Japan
Results

- c.649dupC in 15 of 26 individuals with benign infantile epilepsy (52.1%)

- All ICCA families harbored the same mutation

- A novel mutation (c.1012+2dupT) was found in BFIE

- No mutation in CwG or BFNE

Department of Pediatrics, School of Medicine, Fukuoka University, Japan
Conclusions

- c.649dupC of PRRT2 is a hot spot mutation resulting in BFIE or ICCA
- Screening for PRRT2 mutation, might be useful in differentiating BFIE from CwG at an early stage
- There might be different pathomechanisms between BFIE and BFNE

Department of Pediatrics, School of Medicine, Fukuoka University, Japan