EXPANDING THE CLINICAL, GENETIC, AND PATHOGENIC SPECTRUM OF NEONATAL EPILEPSIES ASSOCIATED WITH KCNQ2 MUTATIONS

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Background: Mutations in KCNQ2 and KCNQ3 genes encoding for potassium channel subunits underlie the M-current and cause benign familial neonatal seizures (BNFS). This is an autosomal dominant disorder, occurring in the first days of life. Although BFNS is considered a benign epileptic disorder, recently, several families have been described in whom some individuals show benign neonatal convulsions and favorable prognosis, while others present with epileptic encephalopathy.
Methods: We describe a 4-generation family with BFNS with 7 affected members in different generations. Six of them had a benign course while one 2-year-old girl had epileptic encephalopathy with difficult-to-control seizures and developmental delay, despite carrying the exact same mutation as the other family members.
Results: All affected members in this family carried a novel KCNQ2 mutation c.63-66delGGTG (p.K21fsX40), causing a framework shift and early chain termination.
Conclusions: This family supports the recent observation that KCNQ2 mutation should not be considered always as benign and genetic counseling in these families cannot guarantee a definite benign course. In summary, our family shows phenotypic variability in the same KCNQ2 mutation and this has implications for diagnosis, prognosis and genetic counseling. It is suggested that other modifier genes and environmental factors are involved in this heterogeneity.