Clinical features of KCNQ2 mutation in a Romanian family

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INTRODUCTION

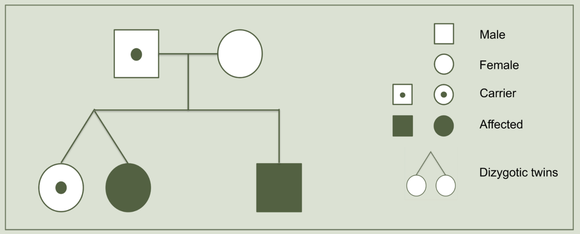
- KCNQ2 gene encodes a potassium channel subunit (Kv7.2)
- KCNQ2 mutations are known to be inherited in an autosomal dominant pattern.
- KCNQ2 mutations are associated either with self-limited (benign) familial neonatal epilepsy or with development and epileptic encephalopathy.

OBJECTIVE

- To assess the phenotypic variability of KCNQ2 mutation.

METHODS

- We present the case of a family with heterozygous twin girls aged 4 and an 8 month old boy in which we studied the clinical evolution, neuroimaging and electroencephalographic findings.
- Multiplex ligation-dependent probe amplification (MLPA) and sequence analysis were used to test all the members of the family and revealed the same KCNQ2 mutation in 4 members of the family.



RESULTS

	TWIN I	TWIN II	BOY	FATHER
Age at onset	-	3 weeks old	3 days old	-
Seziures	-	Focal motor seizures -unilateral tonic-clonic seizures	Focal motor seizures that alternate sides from seizure to seizure and epileptic spasms.	-
Course of illness	-	Remission at 11 months old	Remission at 8 days old	-
Treatment	-	Topiramate*	Phenobarbital	-
Developmental milestones	Normal	Normal	Normal	Normal
Neurological exam	Normal	Normal	Normal	Normal
EEG	Normal	Left to right asymmetry (Figure 1)	Burst-supression pattern (Figure 2)	-
Genetic test	**Heterozygous mutation of KCNQ2 -deletion of exons 2-4** (pathogenic variant)			
Brain MRI	-	No abnormal signs	No abnormal signs	-

* The seizures were initially managed using Phenobarbital and the patient was seizure free until 11 months old, when withdrawal of the medication was attempted. At that point seizures started to reappear. Although courses of treatment with Levetiracetam and Clobazam were followed, the seizures responded to Topiramate.

Current status: **all members of the family are seizure free and without medication.**

CONCLUSIONS

- The fact that all the children are currently seizure and treatment free, while having developed normally stands as ground for the diagnosis of self-limited neonatal epilepsy.
- The particularity of this case is that although the father and children have the same genotype(deletion of exons 2-4 of gene KCNQ2) the phenotype differs from one member of the family to the other.
- The father and one of the twins are completely asymptomatic which raises questions on the pathogenicity of the mutation.
- We suggest taking into consideration genetic testing when a familial epilepsy diagnosis is suspected.

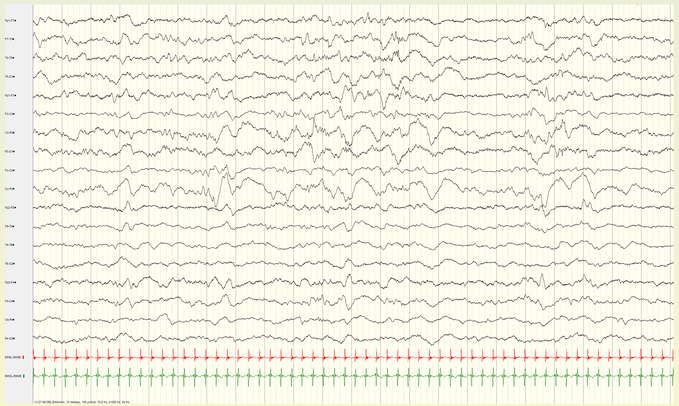


Figure 1- Sleep EEG shows left to right asymmetry. Paper scrolling speed 15mm/s

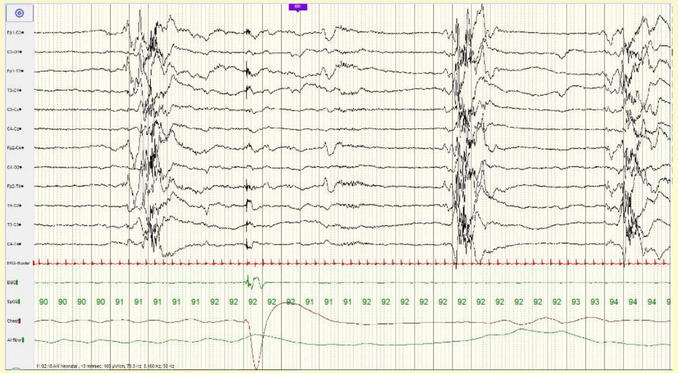


Figure 2-Sleep EEG showing burst-supression. Paper scrolling speed 15mm/s

REFERENCES

- Kato M, Yamagata T, Kubota M, Arai H, Yamashita S, Nakagawa T, et al. Clinical spectrum of early onset epileptic encephalopathies caused by KCNQ2 mutation. Epilepsia. 2013;54(7):1282–7.
- Goto A, Ishii A, Shibata M, Ihara Y, Cooper EC, Hirose S. Characteristics of KCNQ2 variants causing either benign neonatal epilepsy or developmental and epileptic encephalopathy. Epilepsia. 2019;60(9):1870–80.

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