Many testing roads can lead to KCNQ2 diagnosis.

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Objective:
To evaluate different genetic testing approaches for *KCNQ2* related disorders.
Background:
Mutations in the *KCNQ2* gene are associated with a broad phenotypic spectrum, from Benign Familial Neonatal Epilepsy to Neonatal Epileptic Encephalopathy. A diagnosis of *KCNQ2*-related epilepsy can be a confusing process. Genetic testing is key to confirm clinical diagnosis and guide prompt therapeutic treatment.
Design/Methods:
We reviewed clinical indications for individuals with pathogenic mutations in *KCNQ2* detected by NGS multi-gene panel testing (MGPT) and diagnostic exome sequencing (DES).
Results:
KCNQ2 mutations were identified in a total of 13 patients, age range from 3 months to 23 years old. Six (3.75%) patients were tested by MGPT and seven (0.63%) by DES. Of the detected alterations, 5 were truncation and 7 were missense mutations. There was 1 whole gene deletion detected by MGPT. Interestingly, *KCNQ2* alterations in all 7 patients tested by DES were confirmed to be *de novo*. All patients have history of seizures. Only 3/6 patients who had MGPT presented other phenotypic features: cardiac or cutaneous disorders and migraine. None of these cases demonstrated developmental delay (DD). 57.1% of EEG and MRI results were normal. Patients tested by DES displayed a wider variety of additional symptoms such as vision disorder, hearing impairment, dysmorphic features, gastrointestinal disorder, and spasticity. 6/7 patients had DD. 86% of the patients had at least one metabolic screening and 40% of EEG and MRI results were abnormal.
Conclusions:
KCNQ2 positive patients tested by DES had a more complex medical history than those tested by MGPT. Patients with a more complex phenotype may benefit DES testing to avoid a long diagnostic journey, while others may benefit from direct MGPT testing. Although ~10% of pathogenic *KCNQ2* variants have been reported to be *de novo*, our findings suggest the *de novo* rate is higher than previously reported.