An overview of drug-resistant epilepsies based on advances in genetics: a cohort study

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ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7, 2022

OBJECTIVES

Drug-resistant epilepsy (DRE) is approximately one-third of all epilepsy patients and poses the greatest challenge in clinical epilepsy practice. DRE is defined as the failure of at least two anti-seizure drugs given in sufficient doses, alone or in combination, to produce seizure-freeness. The etiology is multifactorial, and usually has both acquired and genetic factors (1). However, only a small percentage of affected patients are genetically diagnosed. Nowadays, with the developments in genetics, specific gene panels and whole exome sequencing (WES) have increased the opportunities for specific diagnosis and treatment. In this cohort study, we tried to determine the specific diagnostic value of gene panels and WES analysis in our cases followed up with the diagnosis of DRE.

Mutation	Numbers of Cases	Inheritance	Mutation	Numbers of Cases	Inheritance
SCN1A	13	AD	UBE3A	2	AD
CDKL5	7	XLD	WWOX	2	AR
STXBP1	5	AD	CLN6	2	AR
MECP2	3	AD	CLN8	2	AR
TREX1	3	AD	GRIN2A	2	AD
CACNA1H	3	AD	SLC2A1	2	AD, AR
PRUNE1	3	AR	FLNA	2	XL
CLP1	3	AR	SCN8A	2	AD
PNKP	3	AR	SCN9A	2	AR
TPP1	3	AR	KCNQ2	2	AD
KCTD7	3	AR	PRICKLE2	2	AR

Table 1. Significant pathogenic changes detected in our study

METHODS

The records of 2897 cases followed up in the pediatric neurology outpatient clinic of Istanbul Medipol University between November 2017 and August 2021 were reviewed. Clinical characteristics, neuroimaging, biochemical, metabolic and genetic results of cases followed by DRE that have been tested by True Sight One panel (130 cases) and WES examination (303 cases), were evaluated.

RESULTS

Significant pathogenic changes were detected in 105 (34.6%) of 303 patients who underwent WES. The spesific diagnosis was made in 25 (19.2%) of 130 cases in which the True Sight One panel was studied. Totally significant mutations (30%) were detected in 130 of 433 patients. Pathogenic changes were detected most frequently in SCN1A (n= 13), CDKL5 (n=7) and STXBP1(n= 5) genes. Afterwards, significant pathogenic changes also were detected in many different genes (Table 1).

CONCULSIONS

A large percentage of patients with epilepsy were classified as idiopathic in the past. As molecular genetic tests are increasingly used in clinical practice, epidemiological studies revealed that genetic factors have a major role in epilepsies, especially for those with DRE. The clinical features of these disorders often overlap, making a systematic diagnosis difficult (1). This study has enabled us to identify common genetic changes unique to our region, as well as determining that especially WES analysis studies significantly increase the rate of specific diagnosis in DRE cases. Providing a spesific genetic diagnosis is very important in terms of avoiding unnecessary tests, choosing specific treatment and genetic counseling. Therefore, WES analysis can be preferred primarily because of the chance of early diagnosis, reanalysis opportunity and cost-effectiveness.

REFERENCES

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