Clinical Evaluation of Childhood Rare Genetic Epilepsies; Multicentric collaboration study

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INTRODUCTİON

As new generation sequencing methods develop, rare epilepsy is increasing in number and is a burden on national health systems. Community building among rare epilepsies fuels collaboration, research, and resource development (1). The estimated annual incidence of single-gene epilepsies in the well-defined population is 1 in 2120 live births (2). Recent advances in molecular genetics have led to the identification of many genes related to epilepsy. The prevalence of multiple comorbidities in children with rare epilepsy, especially those diagnosed with epilepsy in the first year of life, is high and medically complex. Comorbidities should be carefully considered in the diagnosis and treatment of children with rare epilepsy (3).This multicentric study evaluated the clinical features of children diagnosed with genetic epilepsies.

METHODS

Seizures and epilepsy syndromes were classified based on the ILAE terminology. We surveyed demographics, clinical findings, imaging studies, Electroencephalographies, medications. The neuromotor developmental stage was examined. The concomitant comorbid diseases were noted.

Table 1. Clinical feaures of the patients.

Physical examination	
Neuromotor developmental delay	116 (74.4%)
Microcephaly	80 (51.3%)
Hypotonia	53 (34%)
Normal	37 (23.7%)
Brain MRI findings	
Corpus callosum involvement	11(7.1%)
Cerebral atrophy	10 (6.4%)
Cerebral ve cerebellar atrophy	15 (9.6%)
Lissencephaly	2 (1.3%)
Periventricular leukomalacia	4 (2.6%)
Other	18 (11.5%)
Normal	96 (61.5%)
The presence of two or more types of seizure	87 (55.8%)
Main types of seizures	
Tonic-clonic	78 (50%)
Tonic	22 (14.1%)
Epileptic spasm	15 (9.6%)
Myoclonic	14 (9%)
Atonic	6 (3.8%)
Clonic	4 (2.6%)
Other	17 (10.9%)
EEG	
Normal	19 (12.2%)
Focal	59 (37.8%)
Generalized	78 (50%)
Seizure frequency	
Daily	30 (19.3%)
More than once a week	16(10.3%)
Less than one a week	13 (8.3%)
More than one in a month	23 (14.7%)
Less than one in a month	74 (47.4%)
The number of drugs used	
Without medication	3 (1.9%)
1 drug	30 (19.2%)
2 drugs	42 (26.9%)
3 drugs or more	81(52%)
The most efficient drug	
Sodium valproate	31 (19.9%)
Clobazam	15 (9.6%)
Levetirecetam	9 (5.8%)
Topiramate	9 (5.8%)
Carbamazepine	6 (3.8%)
Ketogenic diet therapy	5 (3.2%)
Stiripentol	4 (2.6%)
Comorbidities	128 (82%)
Intellectual disability	110 (70.5%)
Developmental delay	50 (32.1%)
Movement disorders	20 (12.8%)
Autism	11 (7.1%)
Attention deficit hyperactivity disorder	7 (4.5%)
Others	6 (3.9%)

RESULTS

We included 156 patients from the nine tertiory health centers in our study. The median age was forty months old. Eighty (51.3%) patients were female and 76 (48.7%) were male. The onset of the seizure was six months (median). Fifty-nine (37.8%) patients had a family history of epilepsy. Sixty (%36,5) patients had consanguinity among parents.

The genetic mutations were distributed to 36 patients (23,1%) SCN1A, 14 (9%) with KCNQ2, 10 (6,4%) PCDH19, 6 (3,8%) with SCN8A, 5 (3,2%) with SLC2A1, 5 (3,2%) with WWOX, respectively. The remaining 80 patients (%51,3) were with other mutations. The clinical characteristics and other findings were tabled below (Table 1). It was observed that the neuromotor development of the patients regressed in the follow-up (p=0.001).

CONCULSION

Rare genetic epilepsies may not remain rare in the future with the rapid advances in genetic diagnostic methods. Despite using multiple antiseizure medications, most of our patients had drug-resistant epilepsy, and concomitant developmental delay. We observed that the degree of developmental delay varied according to the mutation type. Since a complete cure cannot be achieved in the vast majority of these patients further studies with centers' collaboration might help improve therapeutic decisions and personalized treatment methods.

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