GATOR1 complex gene variation

To summarize the clinical and genetic characteristics of focal epilepsy in children caused by GATOR1 complex gene variation. Methods: The clinical data, gene variation and treatment outcome of 12 children with focal epilepsy caused by GATOR1 complex gene variation admitted to Beijing Children's Hospital Affiliated to Capital Medical University from June 2016 to October 2018 were retrospectively analyzed. Results: There were 7 males and 5 females in 12 cases. The epilepsy onset age was 5.5 (3.0, 12.0) months, and from 11 days to 16 months of age. The epileptic seizure types were all focal motor seizures, and one case combined with epileptic spasms. The frequency of seizures in all patients was more than one time per day. Seven cases had frontal lobe epilepsy and two cases had lateral temporal lobe epilepsy. One case had a family history of febrile seizures and two had a family history of suspicious epilepsy. Epileptic form discharges were observed in 9 patients during the interictal phase by electroencephalograms (EEG), and all of them were focal discharges. Eight cases had clinical seizures detected by EEG, in 4 of whom the seizures were originated in frontal region. There were no abnormalities in brain magnetic resonance imaging in 11 cases whereas 1 case had malformation of cortical development of left frontal lobe. Eight patients had DEPDC5 gene variation, one had NPRL2 gene variation, three had NPRL3 gene variation. One case had de novo variation and the other 11 had hereditary variation. There were 11 types of gene variation, including 5 nonsense variations, 3 missense variations, 2 frame shift variations and 1 in frame deletion variation. There was no clear relationship between the clinical phenotype and the genotype. During the follow-up period from 6 months to 2 years and 6 months, 6 cases had seizure control, 3 of them were controlled by oxcarbazepine. The other 6 cases had drug-refractory epilepsy, 2 of them failed with vagus nerve stimulation and ketogenic dietary therapy as well, meanwhile combined with mental retardation. Conclusions: GATOR1 complex gene variation can lead to genetic focal epilepsy, which usually has early onset with frequent seizures. Most of the patients have focal epileptic form discharges on EEG, and there is usually no structural lesion in brain imaging. Most of the patients have hereditary loss-of-function variations. Approximately half of cases are drug-resistant epilepsy [1)].

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Deng J, Fang F, Wang XH, Dai LF, Tian XJ, Chen CH. [Clinical and genetic characteristics of focal epilepsy in children caused by GATOR1 complex gene variation]. Zhonghua Er Ke Za Zhi. 2019 Oct 2;57(10):780-785. doi: 10.3760/cma.j.issn.0578-1310.2019.10.010. Chinese. PubMed PMID: 31594065.