Epilepsy in CblC Type Methylmalonic Acidemia

Yixiao Li[1, 2], Junxia Luo[3], Chuan Wang[4], Dong Wang[1], Caiyun Yu[1], Guangshun Hou[3], Yujie Guo[3], Qingwei Guo[5], Haozheng Zhang[1], Xiaojing Zhao[6], Meili Fan[7], Zaifen Gao[3], Kaihui Zhang[1, *]

[1]Pediatric Research Institute, Children's Hospital Affiliated to Shandong University, Jinan, China

[2]Department of Ophthalmology, Shandong Provincial Hospital, Cheeloo College of Medicine, Shandong University, Jinan, China

[3]Epilepsy Center, Children's Hospital Affiliated to Shandong University, Jinan, China

[4]Science and Education Section, Children's Hospital Affiliated to Shandong University, Jinan, China

[5]Emergency Department, Children's Hospital Affiliated to Shandong University, Jinan, China

[6]Cardiology Department, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, China

[7]Enuresis Clinic of Tuina Department, Children's Hospital Affiliated to Shandong University, Jinan, China

Email address:

khz83@163.com (Kaihui Zhang)

[*]Corresponding author

Abstract

Methylmalonic acidemia (MMA) is a common organic acidemia brought about by mutations in methylmalonyl-CoA mutase or disruption of adenosyl-cobalamin synthesis. The inborn error causing the cblC subtype most commonly affects vitamin B12 (cobalamin) metabolism in MMA patients. Epilepsy often occurs in patients with the cblC subtype of MMA. In this study, 86 cblC MMA patients (43 males and 43 females) were precisely diagnosed by next-generation sequencing from May 2016 to May 2023. Nineteen probands were diagnosed with MMA with epilepsy, and eight probands have abnormal electroencephalography (EEG). The abnormal EEG for most of the cblC subtype of MMA had shown diffuse slow-wave background during the wakefulness period, and EEG abnormalities almost precede seizures. EEG with only posterior brain region slow wave showed a favorable prognosis, and EEG presented multifocal or diffuse discharge had a poor prognosis. A significant statistical difference by unpaired t-test was observed in the age distribution of our cohort between those that had epilepsy or abnormal EEG and those that did not develop it, in which the late-onset patients with epilepsy or abnormal EEG are very high prevalence than those without the symptoms. In addition, the blood ammonia of 23 cases in the cohort was all within normal range. In conclusion, metabolic toxins in patients with MMA often damage the central nervous system, and abnormal EEGs can be detected at an early stage of the disease.

Keywords

Methylmalonic Academia, Epilepsy, MMACHC, Electroencephalography