MEF2C haploinsufficiency syndrome

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Aim:

MEF2C haploinsufficiency syndrome (MCHS) is a severe neurodevelopmental disorder. We describe the clinical phenotypes and genotypes of seven patients with MCHS to enhance the understanding of clinical manifestations and genetic alterations associated with MCHS.

Method:

Seven patients (6 females and 1 male, aged between 2 years 5 months and 6 years) who had MEF2C mutations, and their parents underwent trio-based whole-exome sequencing; subsequently, their clinical features were assessed. A literature review of patients with MCHS was performed by searching the PubMed and Online Mendelian Inheritance in Man databases.

Results:

Seven mutations were identified, of which six were unreported in the past; of the reported cases, five patients had

de novo

mutations but two had an undefined inheritance pattern. All patients presented delays in developmental milestones, severe intellectual disabilities and lack of speech. Six patients exhibited infantile hypotonia, five patients experienced stereotypic movements and were unable to walk, four patients exhibited poor eye contact indicative of autism and two showed poor performance. While six patients experienced seizure, five among them became seizure free after receiving anti-seizure medicine. Three patients showed a regression in their development, whereas the mothers of two patients exhibited mosaicism but were healthy without any abovementioned symptoms.

Interpretation:

Regression was not a common phenomenon but occurred in MCHS. The prognosis of MCHS patients with epilepsy was good, but most patients can achieve a seizure-free status. Healthy people may have low-level mosaicism and carry a pathogenic MEF2C mutation.