PCDH19-related epilepsy

https://pubmed.ncbi.nlm.nih.gov/32057594/

PCDH19-related epilepsy is a distinct childhood-onset epilepsy syndrome characterized by brief clusters of febrile and afebrile seizures with onset primarily before the age of three years, cognitive impairment, autistic traits, and behavioral abnormalities. PCDH19 gene is located in Xq22 and produces nonclustered delta protocadherin. This disorder primarily manifests in heterozygote females due to random X chromosome inactivation leading to somatic mosaicism and abnormal cellular interference between cells with and without delta-protocadherin. This article reviews the clinical features based on a comprehensive literature review (MEDLINE using PubMed and OvidSP vendors with appropriate keywords to incorporate recent evidence), personal practice, and experience. Significant progress has been made in the past 10 years, including identification of the gene responsible for the condition, characterization of clinical phenotypes, and development of animal models. More rigorous studies involving quality-of-life measures as well as standardized neuropsychiatric testing are necessary to understand the full spectrum of the disease. The recent discovery of allopregnanolone deficiency in patients with PCDH19-related epilepsy leads to opportunities in precision therapy. A phase 3 clinical study is currently active to evaluate the efficacy, safety, and tolerability of adjunctive ganaxolone (an allopregnanolone analog) therapy.