Published on *My46* (https://www.my46.org) 01/20/2022

My46 Trait Profile

Epilepsy limited to females with mental retardation

Other Names: Juberg-Hellman syndrome, Early Infantile Epileptic Encephalopathy-9

Epilepsy restricted to Females with Mental Retardation is a genetic condition affecting only females and is characterized by early-onset epilepsy. It is caused by mutations in the PCDH19 gene which makes the protein called protocadherin 19.

Characteristics of Epilepsy limited to females with mental retardation

Epilepsy restricted to Females with Mental Retardation (EFMR) is an X-linked genetic condition with features limited entirely to females. This condition is characterized by early-onset epilepsy, varying degrees of intellectual disability, and autistic behaviors. The average age of seizure onset is fourteen months, but ranges widely from four to thirty-six months. Febrile seizures (i.e., seizures that occur due to high fevers) and seizures occurring in clusters are often seen in females with EFMR. The types of seizures seen in EFMR include generalized tonic clonic, myoclonic, and complex partial seizures. Although a common feature, not all females with EFMR have intellectual disability. Autistic features, obsessive and aggressive behaviors are often seen in this condition.

Diagnosis/Testing

EFMR is caused by a mutation or change in the PCDH19 gene which encodes the protocadherin 19 protein. This protein, along with other protocadherins, help cells adhere to each other and to their surroundings. Mutations in the PCDH19 gene is thought to somehow affect the adhesiveness of the protein. Additionally, the protochadherin 19 protein is known to be primarily expressed in the brain, thus explaining the neurological features seen in EFMR.

Management/Surveillance

Management of EFMR often includes medication for seizure control, as well as developmental evaluations and educational interventions for individuals with developmental delay/intellectual disability and/or autistic behaviors.

Mode of inheritance

EFMR is inherited in an X-linked female-limited expression pattern. This means females that inherit one PCDH19 mutation show signs of EFMR, while males that inherit one PCDH19 mutation typically do not show any signs of EFMR. The mutation can be inherited from an affected mother, unaffected father or it can occur brand new (de novo) in an affected daughter.

Risk to family members

The risk to family members depends on whether or not the individual with EFMR has a parent with a PCDH19 mutation. If a father has a PCDH19 mutation, 100% of his daughters will have EFMR. If a mother has a PCDH19 mutation, 50% of her daughters will have EFMR, and 50% of her sons will be unaffected carriers. If neither parent has a PCDH19 mutation, the risk of future pregnancies being affected is very low.

Special considerations

The clinical features of EFMR may resemble another genetic condition called Dravet syndrome, also known as

severe myoclonic epilepsy of infancy. Compared to EFMR, Dravet syndrome tends to have earlier onset of seizures, and affects females and males equally. However, since it can be difficult to distinguish these two conditions based solely on clinical features, results from genetic testing are often used to aid in making a diagnosis.

Resources

About Kids Health: Epilepsy Resource Centre
http://www.aboutkidshealth.ca/En/ResourceCentres/Epilepsy/Pages/default.aspx
Epilepsy Therapy Project
http://www.epilepsy.com
Special Kids Special Help: Epilepsy and Seizures
http://www.specialkidsspecialhelp.org/LearnAboutYourChildsIllness/EpilepsyandSeizures.aspx

References

Dibbens, LM. et al. (2008)."X-linked protocadherin 19 mutations cause female-limited epilepsy and cognitive impairment." Nature Genetics 40: 776-781.
Depienne, C. et al. (2009)."Sporadic Infantile Epileptic Encephalopathy Caused by Mutations in PCDH19 Resembles Dravet Syndrome but Mainly Affects Females." PLoS Genetics 5(2): e1000381.
Jamal, SM. et al. (2010)."Novel de novo PCDH19 mutations in three unrelated females with epilepsy female restricted mental retardation syndrome." American Journal of Medical Genetics 152A(10): 2475-2481.
Scheffer, IE. et al. (2008)."Epilepsy and mental retardation limited to females: an under-recognized disorder." Brain 131: 918-927.
Specchio, N. et al. (2011)."Spectrum of phenotypes in female patients with epilepsy due to protocadherin 19 mutations." Epilepsia 52(7): 1251-1257.

Created: 02/2013 **Created by:** Seema Jamal, MSc, LCGC
Updated: mm/yyyy