Pelizaeus-Merzbacher- Disease (PMD) and Pelizaeus-Merzbacher-like disease (PMLD)

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Pelizaeus-Merzbacher- Disease (PMD) is a neurodegenerative disease that causes neurodevelopmental delay and hypotonicity in infancy. It is an X-linked myelin synthesis disorder. Symptoms initially begin before 3 months of age and gradually neurological manifestation such as seizure and optic atrophy appear. There is diffuse white matter involvement (dysmyelination) in the brain MRI.

PelizaeusMerzbacher disease (PMD) is a progressive disorder in myelin formation which is transmitted with an X-linked pattern of inheritance. This disease was first described in 1885 by Pelizaeus and in 1910 by Merzbacher. In 1964, Zeman and colleagues explained the role of proteolipid protein (PLP1) in the disease. The gene of PMD is located on the long arm of the X chromosome (Xq21.2q-22). Dysmyelination is the major pathologic defect in this disease. The brain MRI pattern is highly remarkable.

It shows arrest of myelination in the stage that the brain should be myelinated. The clinical severity is related to the pattern of myelinated white matter. The T1 weighted images show low intensity of all unmyelinated white matter structures; whereas, these structures show high signal intensity in T2 weighted. Mutation in PLP1 that encodes the essential intrinsic membrane protein of CNS myelin is the main cause of PMD.

Severe form of the disease is presented with severe hypotonia at birth. These patients have stridor and feeding difficulties and their symptoms are very similar to spinal muscular atrophy (SMA) without any involvement in anterior horn cells.

Spastic paraplegia type 2 (X-linked type of spastic paraplegia) is an allelic variant of PMD with PLP gene defect that presents with spasticity in the lower extremities and they have slow progression in their disease.

Pelizaeus-Merzbacher-like disease (PMLD) is a hypomyelinating leukoencephalopathy disorder with a genetically heterogeneous pattern. Mutations in the GJA12/GJC2 gene can cause one form of autosomal recessive pattern of Pelizaeus-Merzbacher-like disease.

Pelizaeus-Merzbacher-like disease (PMLD) is clinically similar to PMD and includesny stagmus, ataxia and hypotonicity followed by spasticity but mutation of the PLP1 gene is not detected. In most patients, no gene has been identified, but in a small group of them (less than 10%) mutation in GJC2 (so called GJA12) codon for Connexin 46.6 (Cx47) has been detected.

This gene is called GJA12 and encodes the gap junction protein 12. Mutation of the gap junction of protein alpha 12 causes one of the autosomal recessive types of PMLD.

Diagnosis is performed by sequencing the entire coding region of GJC2. This assay will detect point mutation, small deletion and small insertion. In this type of PMLD,

MRI shows diffuse white matter involvement and basal ganglia calcification.

On the other hand, some of PMLD cases are transmittedby an X-linked pattern. Gene locus is located on the outerpart of the PLP gene location on the X chromosome.

Orthmann and his colleagues reported a form of PMLD in a Turkish family (in 2004) that was transmitted by anautosomal recessive pattern .These patients had nystagmus, developmental delay, ataxia, dystonia, dysarthria and progressive spasticity. Their clinical manifestations were presented in early infancy. TEMG-NCV also showed mild peripheral sensory and motor neuropathy. Five different mutations in GJA12 gene were detected in these patients. Bugiani reported eight members of a Saudi Arabia family with PMLD. Brain MRI of these patients showed diffuse white matter involvement.

Were ported a new mutation of Pelizaeus-Merzbacher-Like Disease, first report from Iran, (a homozygote deletion as c902-918Del)in a 10-month-old girl from healthy second cousin parents that had not beenreported in previous studies. Her clinical manifestations were nystagmus, psychomotor delay, hypotonicity, head nodding and dysmyelination.

(New Mutation of Pelizaeus - Merzbacher - Like Disease; A Report from Iran, ParvanehKarimzadeh, FarzadAhmadabadi, OmidAryani, MassoudHoushmand, Alireza Khatami, Iran J Radiol. 2014 May; 11(2): e6913).

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