Mental Retardation, Autosomal Recessive 36

Alternative Names
MRT36
Intellectual Disability-Strabismus Syndrome

Record Category
Disease phenotype

WHO-ICD
Congenital malformations, deformations and chromosomal abnormalities > Other congenital malformations

Incidence per 100,000 Live Births
0-1

OMIM Number
615286

Mode of Inheritance
Autosomal recessive

Gene Map Locus
19p13.3

Description
MRT36 is a disorder characterized by severe cognitive impairment and strabismus. Patients may also suffer from microcephaly, failure to thrive, short stature, hypotonia, and spasticity. Neurological features include epilepsy and mild brain abnormalities such as dilated ventricles, delayed myelination, arachnoid cysts, and white matter changes. Affected individuals may also present with dysmorphic facial features, including hypertelorism, epicanthus, telecanthus, a prominent or high forehead, up-slanted palpebral fissures, a depressed nasal bridge, and a short nose. In a few cases, behavioral issues such as aggressiveness and hyperactivity have also been noted.

The disorder affects both men and women equally. Symptoms become apparent during infancy and early childhood. While the causal mutation has been predicted to be a major source of intellectual disability in the Arab world, currently less than 50 cases of MRT36 have been discovered. Diagnosis of the disorder is based on genetic analysis of the ADAT3 gene. While intellectual disabilities do not have a cure, patients may benefit from speech therapy, physical therapy, and educational aids.

Molecular Genetics
MRT36 follows an autosomal recessive pattern of inheritance. The disease is caused by mutations in the ADAT3 gene. ADAT3 encodes an adenosine deaminase that is responsible for the conversion of adenosine to inosine at the wobble position of the t-RNA anticodon. Only one homozygous missense mutation, c.382G>A (p.V128M), has been reported to date.

Epidemiology in the Arab World

Saudi Arabia

Alazami et al. (2013) studied eight consanguineous Saudi families with individuals affected by severe intellectual disability and esotropia. The affected patients also showed a variable presentation of microcephaly, hypotonia and a failure to thrive. Mild brain abnormalities, such as arachnoid cysts, delayed myelination and dilated ventricles, were noted in some subjects. Linkage analysis, homozygosity mapping and exome sequencing helped uncover a novel homozygous missense mutation c.382G>A (p.V128M) in the ADAT3 gene of all affected individuals.

El-Hattab et al. (2016) reported on 15 individuals with MRT36. Of these patients, 14 belonged to ten unrelated Saudi families, while one boy was from an Emirati family of Yemeni origin. All patients suffered cognitive impairment in the moderate to severe range. Other symptoms included strabismus in ten patients, failure to thrive in 11, microcephaly in 11, short stature in 11, hypotonia in six, spasticity in six, and epilepsy in three patients. MRI scans revealed brain anomalies such as white matter changes, brain atrophy, and corpus callosum agenesis in nine patients. Other less common features included aggressiveness in four patients, hyperactivity in two, recurrent otitis media in two and low IGF-1 levels in three patients. Patients also showed a variable presentation of facial

dysmorphia which included a prominent or high forehead, up-slanted palpebral fissures, epicanthus, hypertelorism, telecanthus, depressed nasal bridge and a short nose. The Emirati child also suffered from growth hormone deficiency, hypothyroidism and microphallus. Genetic analysis found that all 15 individuals carried the homozygous missense mutation c.382G>A (p.V128M) in the ADAT3 gene.

UAE
See [Saudi Arabia > El-Hattab et al., 2016]

Yemen
See [Saudi Arabia > El-Hattab et al., 2016]

References

Alazami AM, Hijazi H, Al-Dosari MS, Shaheen R, Hashem A, Aldahmesh MA, Mohamed JY, Kentab A, Salih MA, Awaji A, Masoodi TA, Alkuraya FS. Mutation in ADAT3, encoding adenosine deaminase acting on transfer RNA, causes intellectual disability and strabismus. J Med Genet. 2013; 50(7):425-30. PMID: 23620220.

El-Hattab AW, Saleh MA, Hashem A, Al-Owain M, Asmari AA, Rabei H, Abdelraouf H, Hashem M, Alazami AM, Patel N, Shaheen R, Faqeih EA, Alkuraya FS. ADAT3-related intellectual disability: Further delineation of the phenotype. Am J Med Genet A. 2016; 170A(5):1142-7. PMID: 26842963.

Related CTGA Records

Adenosine Deaminase, tRNA-Specific, 3

External Links

https://aaidd.org/intellectual-disability/definition/faqs-on-intellectual-disability#.WA4igZN96Aw

Contributors

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