Alpha-Thalassemia/Mental Retardation Syndrome, X-Linked

Alternative Names
ATRX
Alpha-Thalassemia/Mental Retardation Syndrome, Nondeletion Type
ATR-X Syndrome
ATR, Nondeletion Type

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
301040

Mode of Inheritance
X-linked recessive

Gene Map Locus
Xq21.1

Description
Alpha-Thalassemia/Mental Retardation Syndrome, X-Linked (ATRX) is a condition characterized by severe to profound mental retardation, distinctive craniofacial features, hypotonia, genital abnormalities, and hematological features of alpha thalassemia, in the absence of mutations in the alpha-globin gene complex. The distinctive craniofacial features include microcephaly, telecanthus, a short triangular nose with flat nasal bridge and anteverted nostrils, mid face hypoplasia, tented vermilion of the upper lip, and thick or everted vermilion of the lower lip. Genital abnormalities include hypospadias, micropenis, or ambiguous female external genitalia. Most patients have mild to moderate anemia, secondary to alpha-thalassemia. Interestingly, the alpha-thalassemia component is not present in all affected patients.

Diagnosis is based on the clinical features. Most patients tend to show the presence of HbH inclusion bodies in their erythrocytes. However, this is not always the case. Molecular genetic testing for mutations in the ATRX gene is the only confirmatory diagnostic test. Management of the condition involves treating the symptoms. Infants need to be put on calorie dense formula. Excessive drooling can be managed by administration of anticholinergics or botulinum toxin type A injection of the salivary glands, or by surgery. The anemia is mild and does not usually require treatment.

Molecular Genetics
ATRX is transmitted in an X-linked recessive manner, through mutations in The ATRX gene. Affected male patients either have a de novo mutation or have mothers who are asymptomatic carriers of the mutation. The ATRX gene codes for a chromatin remodeler protein that functions as a histone chaperone complex, thus playing a major role in normal development.

Epidemiology in the Arab World

United Arab Emirates
See Yemen > Hamzeh et al, 2016

Yemen
Hamzeh et al (2016) reported two Yemeni siblings with ATRX. The younger of the two brothers was noticed at infancy to be floppy and have delayed motor and speech development. Upon examination, he was found to have mild facial dysmorphism, including borderline microcephaly, broad forehead, brachycephaly, mild hypertelorism, epicanthic folds, borderline low-set angulated ears, depressed nasal bridge with anteverted nostrils, carp-like mouth, protruded tongue, and a high arched palate. He had bilateral clinodactyly of the fifth fingers and bilateral equino-valgus, along with mild scoliosis. Lower limbs were hypotonic, and he was found to have hypospadias. MRI Brain showed mild cortical atrophy. Hematological indicators were generally normal, and HbH inclusions could not be detected. His older brother had a similar history of developmental and speech delay, facial dysmorphic

features, and abnormal brain MRI. Both brothers were found to carry a novel hemizygous mutation in the ATRX gene.

References

Hamzeh AR, Nair P, Mohamed M, Saif F, Tawfiq N, Al-Ali MT, Bastaki F. A novel missense mutation in ATRX uncovered in a Yemeni family leads to alpha-thalassemia/mental retardation syndrome without alpha-thalassemia. Ir J Med Sci. 2016 Feb 9. PMID: 26860117

Related CTGA Records

ATR-X Gene

External Links

http://www.orpha.net/consor4.01/www/cgi-bin/OC_Exp.php?lng=EN&Expert=847
https://ghr.nlm.nih.gov/condition/alpha-thalassemia-x-linked-intellectual-disability-syndrome#diagnosis
https://www.ncbi.nlm.nih.gov/books/NBK1449/

Contributors

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