Meier-Gorlin Syndrome 1

Alternative Names
MGORS1
Ear, Patella, Short Stature Syndrome
EPS
Microtia, Absent Patellae, Micrognathia Syndrome
Meier-Gorlin Syndrome

Record Category
Disease phenotype

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

Incidence per 100,000 Live Births
N/A

OMIM Number
224690

Mode of Inheritance
Autosomal recessive

Gene Map Locus
1p32.3

Description
Meier-Gorlin syndrome (MGORS) is a condition characterized by short stature. It is considered a form of primordial dwarfism because of the intrauterine growth retardation. After birth, affected individuals continue to grow at a slow rate. Other characteristic features of this condition are underdeveloped or missing patellae, small ears, and often, microcephaly. Most people with Meier-Gorlin syndrome have normal intellect. Some patients may have other skeletal abnormalities, such as unusually narrow long bones in the arms and legs, genu recurvatum, and delayed bone age. Most people with Meier-Gorlin syndrome have distinctive facial features. In addition to being abnormally small, the ears may be low-set or rotated backward. Additional features can include microstomia, micrognathia, full lips, and a narrow nose with a high nasal bridge. Abnormalities in sexual development may also occur in this condition. Some males with this condition have cryptorchidism. Affected females may have hypoplasia of the labia majora and small breasts. Both males and females with this condition can have sparse or absent axillary hair.

The prevalence of Meier-Gorlin syndrome is unknown. Management of the condition is focused on taking care of the symptoms, including the feeding problems, hearing loss, luxating patellae, knee pain, gonarthrosis, and pulmonary complications associated with the condition. Growth hormone therapy might be beneficial for the small subset of patients in whom growth retardation does not normalize even after the first year of life.

Molecular Genetics
Meier-Gorlin is an autosomal recessive inherited metabolic disorder. MGORS can be caused by mutations in one of several genes that provide instructions for making one of a group of proteins known as the pre-replication complex. These genes include ORC1, ORC4, ORC6, CDT1, and CDC6. Mutations in any of these genes can impair formation of the pre-replication complex and disrupt replication licensing, thereby leading to Meier-Gorlin syndrome.

Epidemiology in the Arab World

Saudi Arabia
Bicknell et al. (2011) studied a cohort of nine members of a consanguineous Saudi-Arabian family with two children who had microcephalic primordial dwarfism. Both affected individuals in this family had very marked growth retardation (−6.5 SD) from the age-related normal population mean. The first patient was a male, who had a

small chin, mildly small ears, and full lips, with a normal intellect. They also had mild, nonspecific icythyosis. Growth hormone stimulation test was suboptimal, IGF1 levels were normal, and there was no response to growth hormone therapy. The second patient in this family was a female who had small anterior fontanelle and relatively small ears. She suffered from gastro-oesophageal reflux, and had a normal brain MRI. Genome wide homozygosity mapping in this family enabled the identification of a homozygous A>G transition (c.314A>G) in exon 4 generating a non-conservative amino acid substitution (p.Glu127Gly).

Syria

Bicknell et al. (2011) studied a Syrian family with one member affected with microcephalic primordial dwarfism. This female child had marked growth retardation (-7.6 SD). Dysmorphic facial features included mild micrognathia, small ears, mild synophrys, and full lips. Intellect was normal. She also had bronchomalacia, gastro-oesophageal reflux and craniosynostosis that required surgery. Skeletal analysis at birth showed hyper-extended dislocated knees. Tibia was posteriorly dislocated and surgically corrected, while patella was present. Bicknell et al. (2011) identified a homozygous mutation in the ORC1 gene in the patient.

References

Bicknell LS, Walker S, Klingseisen A, Stiff T, Leitch A, Kerzendorfer C, Martin CA, Yeyati P, Al Sanna N, Bober M, Johnson D, Wise C, Jackson AP, O'Driscoll M, Jeggo PA. Mutations in ORC1, encoding the largest subunit of the origin recognition complex, cause microcephalic primordial dwarfism resembling Meier-Gorlin syndrome. Nat Genet. 2011; 43(4):350-5. PMID: 21358633

Related CTGA Records

Origin Recognition Complex, Subunit 1, S. cerevisiae, Homolog of

External Links

http://rarediseases.org/rare-diseases/ear-patella-short-stature-syndrome/
https://ghr.nlm.nih.gov/condition/meier-gorlin-syndrome
https://ojrd.biomedcentral.com/articles/10.1186/s13023-015-0322-x
https://www.magicfoundation.org/
http://www.kumc.edu/gec/support/skeldysp.html

Contributors

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