X-linked Myotubular Myopathy

Subjects: Genetics & Heredity
Contributor: Bruce Ren

X-linked myotubular myopathy is a condition that primarily affects muscles used for movement (skeletal muscles) and occurs almost exclusively in males. People with this condition have muscle weakness (myopathy) and decreased muscle tone (hypotonia) that are usually evident at birth.

Keywords: genetic conditions

1. Introduction

The muscle problems in X-linked myotubular myopathy impair the development of motor skills such as sitting, standing, and walking. Affected infants may also have difficulties with feeding due to muscle weakness. Individuals with this condition often do not have the muscle strength to breathe on their own and must be supported with a machine to help them breathe (mechanical ventilation). Some affected individuals need breathing assistance only periodically, typically during sleep, while others require it continuously. People with X-linked myotubular myopathy may also have weakness in the muscles that control eye movement (ophthalmoplegia), weakness in other muscles of the face, and absent reflexes (areflexia).

In X-linked myotubular myopathy, muscle weakness often disrupts normal bone development and can lead to fragile bones, an abnormal curvature of the spine (scoliosis), and joint deformities (contractures) of the hips and knees. People with X-linked myotubular myopathy may have a large head with a narrow and elongated face and a high, arched roof of the mouth (palate). They may also have liver disease, recurrent ear and respiratory infections, or seizures.

Because of their severe breathing problems, individuals with X-linked myotubular myopathy usually survive only into early childhood; however, some people with this condition have lived into adulthood.

X-linked myotubular myopathy is a member of a group of disorders called centronuclear myopathy. In centronuclear myopathy, the nucleus is found at the center of many rod-shaped muscle cells instead of at either end, where it is normally located.

2. Frequency

The incidence of X-linked myotubular myopathy is estimated to be 1 in 50,000 newborn males worldwide.

3. Causes

Mutations in the *MTM1* gene cause X-linked myotubular myopathy. The *MTM1* gene provides instructions for producing an enzyme called myotubularin. Myotubularin is thought to be involved in the development and maintenance of muscle cells.

MTM1 gene mutations probably disrupt myotubularin's role in muscle cell development and maintenance, causing muscle weakness and other signs and symptoms of X-linked myotubular myopathy.

3.1 The gene associated with X-linked myotubular myopathy

- MTM1

4. Inheritance

X-linked myotubular myopathy is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation must be present in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked myotubular myopathy, the affected male inherits one altered copy from his mother in 80 to 90 percent of cases. In the remaining 10 to 20 percent of cases, the disorder results from a new mutation in the gene that occurs during the formation of a parent's reproductive cells (eggs or sperm) or in early embryonic development. Females with one altered copy of the *MTM1* gene generally do not experience signs and symptoms of the disorder. In rare cases, however, females who have one altered copy of the *MTM1* gene experience some mild muscle weakness.

5. Other Names for This Condition

- CNM
- MTMX
- X-linked centronuclear myopathy
- XLMTM
- XMTM

References

1. Biancalana V, Caron O, Gallati S, Baas F, Kress W, Novelli G, D'Apice MR,Lagier-Tourenne C, Buj-Bello A, Romero N B, Mandel JL. Characterisation ofmutations in 77 patients with X-linked myotubular myopathy, including a familywith a v ery mild phenotype. Hum Genet. 2003 Feb;112(2):135-42.
2. Bijarnia S, Puri RD, Jain M, Kler N, Roy S, Urtizberea JA, Biancalana V, VermaIC. Mutation studies in X-linked myotub ular myopathy in three Indian families.Indian J Pediatr. 2010 Apr;77(4):431-3. doi: 10.1007/s12098-010-0057-6.
3. Cahill PJ, Rinella AS, Bielski RJ. Orthopaedic complications of myotubularmyopathy. J Pediatr Orthop. 2007 Jan-Feb;2 7(1):98-103.
4. Dowling JJ, Lawlor MW, Das S. X-Linked Myotubular Myopathy. 2002 Feb 25[updated 2018 Aug 23]. In: Adam MP, Ardi nger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): Universityof Washington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1432/
5. Echaniz-Laguna A, Biancalana V, Böhm J, Tranchant C, Mandel JL, Laporte J.Adult centronuclear myopathies: A hospit al-based study. Rev Neurol (Paris). 2013 Aug-Sep;169(8-9):625-31. doi: 10.1016/j.neurol.2012.12.006.
6. Hoffjan S, Thiels C, Vorgerd M, Neuen-Jacob E, Epplen JT, Kress W. Extremephenotypic variability in a German family with X-linked myotubular myopathyassociated with E404K mutation in MTM1. Neuromuscul Disord. 2006Nov;16(11):74 9-53.
7. Lawlor MW, Alexander MS, Viola MG, Meng H, Joubert R, Gupta V, Motohashi N,Manfready RA, Hsu CP, Huang P, Buj -Bello A, Kunkel LM, Beggs AH, Gussoni E.Myotubularin-deficient myoblasts display increased apoptosis, delayedprolif eration, and poor cell engraftment. Am J Pathol. 2012 Sep;181(3):961-8.doi: 10.1016/j.ajpath.2012.05.016.
8. McEntagart M, Parsons G, Buj-Bello A, Biancalana V, Fenton I, Little M,Krawczak M, Thomas N, Herman G, Clarke A, Wallgren-Pettersson C.Genotype-phenotype correlations in X-linked myotubular myopathy. NeuromusculDisord. 2002 Dec;12(10):939-46.
9. Pierson CR, Tomczak K, Agrawal P, Moghadaszadeh B, Beggs AH. X-linkedmyotubular and centronuclear myopathies. J Neuropathol Exp Neurol. 2005Jul;64(7):555-64. Review.