22q11.2 Deletion Syndrome

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Contributor: Catherine Yang

22q11.2 deletion syndrome (which is also known by several other names, listed below) is a disorder caused by the deletion of a small piece of chromosome 22. The deletion occurs near the middle of the chromosome at a location designated q11.2.

Keywords: genetic conditions

1. Introduction

22q11.2 deletion syndrome has many possible signs and symptoms that can affect almost any part of the body. The features of this syndrome vary widely, even among affected members of the same family. People with 22q11.2 deletion syndrome commonly have heart abnormalities that are often present from birth, recurrent infections caused by problems with the immune system, and distinctive facial features. In affected individuals, the muscles that form the roof of the mouth (palate) may not close completely, even though the tissue covering them does, resulting in a condition called submucosal cleft palate. The abnormal palate is often highly arched and there may be a split in the soft flap of tissue that hangs from the back of the mouth (bifid uvula). Submucosal cleft palate can also interfere with normal speech by causing air to come out of the nose during speech, leading to nasal-sounding speech. Affected individuals may also have breathing problems, kidney abnormalities, low levels of calcium in the blood (which can result in seizures), a decrease in blood platelets (thrombocytopenia), significant feeding difficulties, gastrointestinal problems, and hearing loss. Skeletal differences are possible, including mild short stature and, less frequently, abnormalities of the spinal bones.

Many children with 22q11.2 deletion syndrome have developmental delays, including delayed growth and speech development, and some have mild intellectual disability or learning disabilities. Older affected individuals have difficulty reading, performing tasks involving math, and problem solving. Children with this condition often need help changing and adapting their behaviors when responding to situations. Additionally, affected children are more likely than children without 22q11.2 deletion syndrome to have attention-deficit/hyperactivity disorder (ADHD) and developmental conditions such as autism spectrum disorder that affect communication and social interaction.

Because the signs and symptoms of 22q11.2 deletion syndrome are so varied, different groupings of features were once described as separate conditions. Doctors named these conditions DiGeorge syndrome, velocardiofacial syndrome (also called Shprintzen syndrome), and conotruncal anomaly face syndrome. In addition, some children with the 22q11.2 deletion were diagnosed with the autosomal dominant form of Opitz G/BBB syndrome and Cayler cardiofacial syndrome. Once the genetic basis for these disorders was identified, doctors determined that they were all part of a single syndrome with many possible signs and symptoms. To avoid confusion, this condition is usually called 22q11.2 deletion syndrome, a description based on its underlying genetic cause.

2. Frequency

22q11.2 deletion syndrome affects an estimated 1 in 4,000 people. However, the condition may actually be more common than this estimate because doctors and researchers suspect it is underdiagnosed due to its variable features. The condition may not be identified in people with mild signs and symptoms, or it may be mistaken for other disorders with overlapping features.

3. Causes

Most people with 22q11.2 deletion syndrome are missing a sequence of about 3 million DNA building blocks (base pairs) on one copy of chromosome 22 in each cell. This region contains 30 to 40 genes, many of which have not been well characterized. A small percentage of affected individuals have shorter deletions in the same region. This condition is described as a contiguous gene deletion syndrome because it results from the loss of many genes that are close together.

Researchers are working to identify all of the genes that contribute to the features of 22q11.2 deletion syndrome. They have determined that the loss of a particular gene on chromosome 22, *TBX1*, is probably responsible for many of the syndrome's characteristic signs (such as heart defects, a cleft palate, distinctive facial features, hearing loss, and low calcium levels). Some studies suggest that a deletion of this gene may contribute to behavioral problems as well. The loss of another gene, *COMT*, in the same region of chromosome 22 may also help explain the increased risk of behavioral problems and mental illness. The loss of additional genes in the deleted region likely contributes to the varied features of 22q11.2 deletion syndrome.

3.1. the genes and chromosome associated with 22q11.2 deletion syndrome

- COMT
- TBX1
- chromosome 22

4. Inheritance

The inheritance of 22q11.2 deletion syndrome is considered autosomal dominant because a deletion in one copy of chromosome 22 in each cell is sufficient to cause the condition. Most cases of 22q11.2 deletion syndrome are not inherited, however. The deletion occurs most often as a random event during the formation of reproductive cells (eggs or sperm) or in early fetal development. Affected people typically have no history of the disorder in their family, though they can pass the condition to their children. In about 10 percent of cases, a person with this condition inherits the deletion in chromosome 22 from a parent. In inherited cases, other family members may be affected as well.

5. Other Names for This Condition

- 22q11.2DS
- autosomal dominant Opitz G/BBB syndrome
- CATCH22
- Cayler cardiofacial syndrome
- conotruncal anomaly face syndrome (CTAF)
- deletion 22q11.2 syndrome
- DiGeorge syndrome
- Sedlackova syndrome
- Shprintzen syndrome
- VCFS
- velo-cardio-facial syndrome
- velocardiofacial syndrome

References

1. Antshel KM, Kates WR, Roizen N, Fremont W, Shprintzen RJ. 22q11.2 deletionsyndrome: genetics, neuroanatomy and cognitive/behavioral features keywords.Child Neuropsychol. 2005 Feb;11(1):5-19. Review.

2. Bassett AS, McDonald-McGinn DM, Devriendt K, Digilio MC, Goldenberg P, HabelA, Marino B, Oskarsdottir S, Philip N, Sullivan K, Swillen A, Vorstman J;International 22q11.2 Deletion Syndrome Consortium. Practical guidelines formanaging patients with 22q11.2 deletion syndrome. J Pediatr. 2011Aug;159(2):332-9.e1. doi: 10.1016/j.jpeds.2011.02.039.
3. Fine SE, Weissman A, Gerdes M, Pinto-Martin J, Zackai EH, McDonald-McGinn DM, Emanuel BS. Autism spectrum disorders and symptoms in children with molecularlyconfirmed 22q11.2 deletion syndrome. J Autism Dev Disord. 2005 Aug;35(4):461-70.
4. McDonald-McGinn DM, Gripp KW, Kirschner RE, Maisenbacher MK, Hustead V,Schauer GM, Keppler-Noreuil KM, Ciprero KL, Pasquariello P Jr, LaRossa D,Bartlett SP, Whitaker LA, Zackai EH. Craniosynostosis: another feature of the22q11.2 deletion syndrome. Am J Med Genet A. 2005 Aug 1;136A(4):358-62.
5. McDonald-McGinn DM, Hain HS, Emanuel BS, Zackai EH. 22q11.2 Deletion Syndrome.1999 Sep 23 [updated 2020 Feb 27]. In: Adam MP, Ardinger HH, Pagon RA, WallaceSE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle(WA): University of Washington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1523/
6. McDonald-McGinn DM, Sullivan KE. Chromosome 22q11.2 deletion syndrome(DiGeorge syndrome/velocardiofacial syndrome). Medicine (Baltimore). 2011Jan;90(1):1-18. doi: 10.1097/MD.0b013e3182060469. Review.
7. Paylor R, Glaser B, Mupo A, Ataliotis P, Spencer C, Sobotka A, Sparks C, Choi CH, Oghalai J, Curran S, Murphy KC, Monks S, Williams N, O'Donovan MC, Owen MJ,Scambler PJ, Lindsay E. Tbx1 haploinsufficiency is linked to behavioral disordersin mice and humans: implications for 22q11 deletion syndrome. Proc Natl Acad Sci U S A. 2006 May 16;103(20):7729-34.
8. Robin NH, Shprintzen RJ. Defining the clinical spectrum of deletion 22q11.2. JPediatr. 2005 Jul;147(1):90-6.
9. Shprintzen RJ. Velo-cardio-facial syndrome: 30 Years of study. Dev Disabil ResRev. 2008;14(1):3-10. doi: 10.1002/ddrr.2. Review.
10. Solot CB, Sell D, Mayne A, Baylis AL, Persson C, Jackson O, McDonald-McGinnDM. Speech-Language Disorders in 22q11.2 Deletion Syndrome: Best Practices forDiagnosis and Management. Am J Speech Lang Pathol. 2019 Aug 9;28(3):984-999. doi:10.1044/2019_AJSLP-16-0147.
11. Sullivan KE. The clinical, immunological, and molecular spectrum of chromosome22q11.2 deletion syndrome and DiGeorge syndrome. Curr Opin Allergy Clin Immunol. 2004 Dec;4(6):505-12. Review.
12. Vorstman JAS, Morcus MEJ, Duijff SN, Klaassen PWJ, Heineman-de Boer JA, BeemerFA, Swaab H, Kahn RS, van Engeland H. The 22q11.2 deletion in children: high rateof autistic disorders and early onset of psychotic symptoms. J Am Acad ChildAdolesc Psychiatry. 2006 Sep;45(9):1104-1113. doi:10.1097/01.chi.0000228131.56956.c1.
13. Yagi H, Furutani Y, Hamada H, Sasaki T, Asakawa S, Minoshima S, Ichida F, Joo K, Kimura M, Imamura S, Kamatani N, Momma K, Takao A, Nakazawa M, Shimizu N,Matsuoka R. Role of TBX1 in human del22q11.2 syndrome. Lancet. 2003 Oct25;362(9393):1366-73.