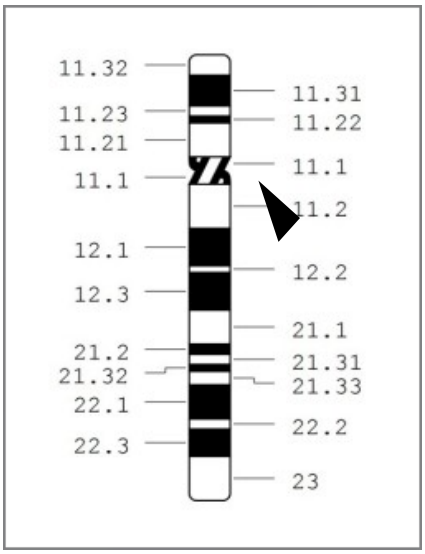
YOU ARE NOT ALONE

CHROMOSOME DISORDER OUTREACH

DISTAL 18Q DELETION INFORMATION

DISTAL 18Q DELETION

Distal 18q deletion is a deletion that occurs on the long arm of chromosome 18. This deletion is characterized by only one break point within the chromosome, and not two. Two break points would result in interstitial 18q deletion.



These distal deletions are most often de novo and vary in the exact breakage point per individual. No two unrelated individuals will have the same breakpoints.

This variation in break points results in a wide range of phenotypic variance among patients with the deletion. The exact prevalence of this deletion is unknown but is estimated to be 1:55,000 births[1].

Distal 18q deletion is a well known condition. The first publication about this disorder appeared in 1960s, and sometimes patients with this deletion may be presented as “De Grouchy syndrome” by the author of the first well recognized publication about 18q deletion.

Key manifestations of distal 18q deletions include a wide spectrum of neurodevelopmental problems, hearing impairment, complex of structural abnormalities and autoimmune disorders.

The most common problem in patients with distal deletion 18q is developmental delay. The severity of developmental delays varies widely

among patients depending on their specific deletion breakpoint. Those with deletions distal to position 18q21.33 usually have mild developmental delays, while those with deletions proximal to 18q21.31 have more severe delays[2], but the level of delay may significantly vary even between patients with similar level of chromosomal loss. The ZNF407 and NETO1 genes are considered to play roles in mental functions, although the involvement of other genes is more than likely.

On average patients have been found to be delayed across all motor and language milestones. This includes rolling over, sitting alone, crawling, standing alone, walking alone, first words, speaking in sentences, and toilet training during the day and at night[3]. Many patients have delayed myelination of the nerves, but there is no strong correlation between delay in myelination and other neurodevelopmental problems.

Many patients with distal 18q deletions are also affected by mood disorders. Of those affected, many will have anxiety (75%) and externalizing behavior disorders (44%). More specifically, this includes induced anxiety disorders, generalized anxiety disorders, social phobias, separation anxiety, posttraumatic stress disorders, obsessive compulsive disorders, panic disorders, and specific phobias. Specific externalizing behavior disorders include conductive disorder, oppositional defiant disorders, and disruptive behavior disorders which are often characterized by outbursts[4].

Short stature caused by growth hormone deficiency[2] is very common feature. The 1.7 Mb area between 73.5 Mb and 75.2 Mb is considered a critical segment for short stature.

Facial dysmorphism in these patients include a hypoplastic middle third of the face, deeply set eyes and characteristic “carp-shaped” mouth. Although head circumference is usually less than in healthy peers, severe microcephaly is not common. Abnormalities of the palate are very common (57%). Most patients have high palate, submucosal cleft palate or bifid uvula. However cleft lip is very rare.

A very characteristic finding in distal 18q deletion is hearing impairment. Many patients have abnormalities of external ear including aural atresia or

stenosis of external ear canals[5]. Even the patients without defects of external ear may reveal sensorineural hearing loss.

Many patients have feet defects as pes planum or pes cavus, abnormal toe placement and metatarsus adductus.

Heart defects may be found in a third of patients. Most of them have atrial septal defects (ASD), ventricular septal defects (VSD) or stenosis of the pulmonary artery. These defects are usually mild and do not require surgical intervention.

Most boys have cryptorchidism, some of them may have hypospadias. Defects of the kidneys are usually mild.

Patients with distal 18q deletions often present with autoimmune disorders, IgA deficiencies, and allergies. Autoimmune disorders (31%) include myalgia, arthritis, and hypothyroidism[3]. This phenotype also increases an individual's susceptibility to various infections. This includes repeated ear infections. Allergies and associated symptoms are present among patients. This includes allergic rhinitis, chronic sinusitis, eczema, and asthma[3]. Patients have also been seen to lack or are completely deficient in factors responsible for controlling the body's reactivity to self-antigens and preventing autoimmunity[6].

There are no current cures for patients with distal 18q deletions. The most common mode of treatment is treating symptoms as they arise. It is recommended that various screenings take place throughout the patient's life. As a newborn, it is recommended that they be evaluated for hypospadias, kidney, ureter, and bladder abnormalities, umbilical hernias, foot anomalies, and congenital heart disease. Seeing an ophthalmologist, audiologist, endocrinologist, physical therapist, occupational therapist, or speech therapist is also recommended[3].

Most patients with this condition have sporadic deletions. Direct transmission of the deleted chromosome from mildly affected mothers has been reported in extremely rare cases. The situation when one of the parents is a carrier of a balanced translocation is much more common – at least 10-15% of all patients with distal 18q deletions received the deleted

chromosome from the parent with a balanced translocation. Cytogenetic examination of the parents of every patient with distal 18q deletion is a necessary condition for prognosis of further offspring in a family.

REFERENCES

[1] Bohîlţea, R.E., Cîrstoiu M.M., Nedelea, F.M., et al. Case report of a novel phenotype in 18q deletion syndrome. Rom J Morphol Embryol. 2020, v 61, 905-910.

[2] Feenstra I., Vissers L.E, Orsel M., et al. Genotype-phenotype mapping of chromosome 18q deletions by high-resolution array CGH: an update of the phenotypic map. Am J Med Genet A 2007, v. 143A, 1858-1867.

[3] Cody J.D., Hasi M., Soileau B., et al. Establishing a reference group for distal 18q-: clinical description and molecular basis. Hum Genet 2014, v. 133, 199-209.

[4] Daviss W.B., O'Donnell L., Soileau B.T., et al. Mood disorders in individuals with distal 18q deletions. Am J Med Genet B 2013, v 162B, 879-888.

[5] Dostal A., Nemeckova J., Gaillyova R., et al. Identification of 2.3-Mb gene locus for congenital aural atresia in 18q22.3 deletion: A case report analyzed by comparative genomic hybridization. Otol Neurotol. 2006, v. 27, 427-432.

[6] Hogendorf A., Zieliński M., Constantinou M., et al. Immune dysregulation in patients with chromosome 18q deletions - searching for putative loci for autoimmunity and immunodeficiency. Front Immunol. 2021, v. 12:742834.

Chromosome Disorder Outreach

You Are Not Alone.

CHROMOSOME DISORDER OUTREACH

support for chromosome and gene mutation disorders

P.O. Box 724

Boca Raton, FL 33429-0724

Family Helpline

(561) 395-4252

info@chromodisorder.org

Copyright 2022 Chromosome Disorder Outreach, Inc. All Rights Reserved